# ABSTRACTS BOOK EORS 2008

# EUROPEAN ORTHOPAEDIC RESEARCH SOCIETY



# 17th ANNUAL MEETING MADRID April, 24 - 26

Editor: E. Gómez-Barrena Co-editor: N. Bonsfills

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# Index

COMMITTEE	S	07
ACKNOWLEDGMENT AND REVIEWERS		08
ACKNOWLE	DGMENT AND MODERATORS	09
WELCOME A	ADDRESS	10
WORKSHOP	S	12
ORAL SESSIC	DNS INVESCOT-EORS	13
ORAL SESSIC	DNS EORS	
(	DRAL SESSION 1 - HIP IMPLANTS 1	26
(	DRAL SESSION 2 - HIP IMPLANTS 2	29
(	DRAL SESSION 3 - STEM CELLS	35
(	DRAL SESSION 4 - TISSUE ENGINEERING	43
(	DRAL SESSION 5 - HIP CLINICAL 1	48
(	DRAL SESSION 6 - HIP CLINICAL 2	54
(	DRAL SESSION 7 - BONE	60
(	DRAL SESSION 8 - LIGAMENT AND TENDON	67
(	DRAL SESSION 9 - HIP (OTHER)	71
(	DRAL SESSION 10 - IMAGING	74
(	DRAL SESSION 11 - SPINE	82
(	DRAL SESSION 12 - GROWTH	88
(	DRAL SESSION 13 - GAIT AND KINEMATICS	140
(	DRAL SESSION 14 - BIOMATERIALS	147
(	DRAL SESSION 15- AWARD SESSION	153
(	DRAL SESSION 16 - KNEE IMPLANTS	158
(	DRAL SESSION 17 - KNEE SOFT TISSUES	165
(	DRAL SESSION 18 - SHOULDER 1	170
(	DRAL SESSION 19 - SHOULDER 2	176
(	DRAL SESSION 20 - CARTILAGE AND MENISCUS	179
(	DRAL SESSION 21 - HAND, WRIST, ELBOW, FRACTURES, OTHER	187
POSTER SES	SIONS	
F	POSTER SESSION 1- SPINE	94
F	POSTER SESSION 2- SHOULDER	102
F	OSTER SESSION 3- TISSUE ENGINEERING AND BIOMATERIALS	107
F	POSTER SESSION 4- CLINICAL, GAIT, GROWTH	112
F	POSTER SESSION 5- KNEE	115
F	POSTER SESSION 6- BONE AND CARTILAGE	125
F	POSTER SESSION 7- LIGAMENT AND TENDON	134
F	POSTER SESSION 8- INFECTION	136
F	POSTER SESSION 9- HAND, FOOT, FRACTURES, TUMOR	196
F	POSTER SESSION 10- HIP	209



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# WELCOME ADDRESS



Dear Colleagues,

The 17th meeting of European Orthopaedic Research Society is taking place in Madrid in April 24-26, 2008. The local organizers chaired by Enrique Gómez Barrena have succeeded to find an excellent location and are preparing a very attractive social program. As you may know, this meeting is the first one that is organized in a bi-annual fashion. Hence, from now on EORS meetings are every two years and are organized independent from the EFORT.

The EORS meetings provide a platform for clinicians, researchers and industry to discuss orthopaedic research, issues and innovations. We therefore invite all individuals that are working in this field to submit their abstract to the upcoming Madrid meeting. The deadline for abstract submission is December 1st, 2007.

We plan to have an excellent program with invited keynote speakers, instructural courses, podium and poster presentations. From the submitted abstracts two papers are awarded. The first one is the EORS-2008 award, which is pre-selected from the 5 highest-ranked abstracts. In a special award-session these 5 papers are presented and the best paper/presentation is awarded with the EORS-2008 award. The other award is the Göran Selvik Award which is selected from the five best ranked abstracts concerning radiographic methods and measurements. In addition, there are 3 poster awards that will be selected during the conference.

Obviously Madrid needs no further introduction. It is very easy to reach from anywhere in Europe and offers an excellent transportation system. In addition, Madrid is a city with a living soul, with a unique history and many cultural high lights. Hence, a perfect city to organize a scientific meeting and combine it with a social visit.

We very much like to welcome you in April 2008 at the 17th meeting of the EORS. Bienvenidos,

#### **Nico Verdonschot PhD**

President of the European Orthopaedic Research Society



# WELCOME ADDRESS



Dear Colleagues and Friends,

On behalf of all the organization of this 17th Meeting of the European Orthopaedic Research Society, I would like to welcome you to Madrid. We have been working hard to prepare a very exciting meeting, both scientifically and socially, and this represents an important challenge after the success of Bolonia in 2006.

An EORS Meeting is always an opportunity to interact from different backgrounds and different countries. Networking strengthens Europe, and the rich spectrum of research related to Orthopaedics offers both clinicians and basic researchers, from different origins but a shared interest in Orthopaedics, a complementary view in our field. The scientific progress needed to better understand, prevent, and treat the Orthopaedic injuries and diseases, together with new opportunities for innovation and evolution in our skills and resources to offer the best for our patients, are guiding the efforts of our Society all over Europe.

With this in mind, we focused on the balance of a spread scientific program based on short presentations and fruitful discussions, but also learning opportunities for younger colleagues and interaction among groups. The participation of you, the researchers in Orthopaedics, both clinicians and non-clinicians, and the impressive progression of Orthopaedic Science based on the quality of your research, will set the interest and significance of the Meeting.

For the unique Meeting that we are expecting, we look for providing an Academic scenario at the Campus of the Medical School of the "Universidad Autónoma de Madrid", which offers outdoor and indoor facilities to enjoy the Spring in Madrid. Madrid's impressive social opportunities will hopefully allow for a pleasant stay with us, from the visits to Museums and historic sites, to the peculiar gastronomy and spectacles.

I am sure that your expectations will be met and you will find a rewarding Meeting in the scientific and social aspects. Welcome to Madrid.

Enrique Gómez-Barrena, MD PhD Chair, EORS 2008 Meeting



# **Invited lectures, Workshops**

# **INVITED LECTURES**

## THURSDAY, April 24th

18:30 h- 19:00 h Room: Aula Magna

Bone marrow stromal cells: in vitro expansion and interaction with biofunctionalised substrates for bone tissue engineering N. Baldini

# FRIDAY, April 25th

13:30 h – 14:00 h

h Room: Aula Magna

European FP7 research funding and networking C. Hernández E. Fernández

# **SATURDAY, April 26th** 09:00 h - 09:30 h Room: Aula Magna

Biologic Strategies to Repair Lost bone Due to Periprosthetic Osteolysis: Bench to Bedside S.B. Goodman

# WORKSHOPS

FRIDAY, April 25th08:00 h- 09:00 hRoom: Aula Magna

Implant-related infection Chair: J. Esteban

Introduction J. Esteban

Genetics of biofilm development in the genus Staphylococcus. I. Spiliopoulou

Immunohistopathological differences and similarities between septic and aseptic loosening Y. Konttinen

# FRIDAY, April 25th

08:00 h- 09:00 h Room: Seminario 1

Bone structure: the role of microCT Chair. P. Esbrit

Introduction P. Esbrit

Structure-function assessment in bone using microcomputed tomography H. van Lenthe

Variations in Trabecular Microstructural Parameters and its Relationship with Biomechanical Properties S. Dapía Robleda

### SATURDAY, April 26th

08:00 h- 09:00 h Room: Aula Magna

Gait Analysis Chair: Estrella Rausell

Methods in clinical motion anñaysis. Do we need to change our approach? B. Muller

Gait Analysis based on internal sensors J. Favre

# SATURDAY, April 26th

08:00 h- 09:00 h Room: Seminario 1

Regenerative Medicine The European Science Foundation "Regenerative Medicine" Research Network program Y. Konttinen

Development of an artificial bone using fetal cell therapy. D. Pioletti

Growth factors released by platelets in bone regeneration E. Cenni

Production of TGF-beta3 and its use in cartilage tissue engineering Y. Konttinen

# ORAL SESSIONS INVESCOT - EORS

Thursday, April 24th

ORAL SESSION INVESCOT Thursday, April 24th

# **INVESCOT 001**

ESTRATEGIAS PARA LA ESTABILIZACIÓN DINÁMICA ARTIFICIAL DE LA RODILLA CON LESIÓN DE LIGAMENTO CRUZADO ANTERIOR. ESTUDIO EXPERIMENTAL EN GATOS SOBRE ESTIMULACIÓN MUSCULAR

N. Bonsfills García, Á. Núñez Molina, E- Gómez Barrena Hospital Universitario La Paz. Madrid

#### INTRODUCCIÓN

En el control de la estabilidad articular, tanto la resistencia del músculo como la contracción muscular derivada del control neuromuscular son piezas fundamentales. En la rodilla con lesión del ligamento cruzado anterior (LCA), este control neuromuscular está alterado, por lo que puede ser necesaria su compensación mediante estimulación muscular. En este sentido, las bases de la Estimulación Funcional Eléctrica (FES) proponen dos estrategias de control articular: una primera que potencie la contracción agonista-antagonista, aumentando la resistencia del músculo, y una segunda que transmita el estímulo en el momento apropiado de manera eficaz, de forma similar a la actuación del sistema propioceptivo. Nuestra hipótesis es que la excesiva traslación tibial anterior (TTA) de la rodilla inestable por lesión del LCA puede ser controlada mediante estimulación eléctrica de cuádriceps e isquiotibiales, bien por aumento de la resistencia muscular, bien a través de una !

contracción ajustada en el tiempo. Nuestros objetivos son medir la reacción muscular (longitud de fibra) y la laxitud anterior de la rodilla (TTA), antes y después de la aplicación de un estímulo eléctrico a cuádriceps e isquiotibiales, observando además el efecto de la estimulación repetida sobre la laxitud articular.

#### MATERIAL Y MÉTODO

Se estudiaron 17 rodillas de gato común (Felis catus) bajo anestesia general para evitar la contracción muscular voluntaria. La longitud de fibra muscular se estudió mediante ultrasonomicrometría de los principales músculos periarticulares. La laxitud articular se midió a partir de registros de vídeo sobre el plano sagital de la rodilla. Se sometió a las extremidades a tracción tibial anterior con una fuerza de hasta 24,5 N antes y después de la sección experimental del LCA, tanto a 90° como a 30° de flexión. En las rodillas inestables, se siguió un protocolo de estimulación con trenes de pulsos cuadrados de 0,2 ms al inicio (pre-tracción) y al final de la tracción máxima (post-tracción), y se aplicaron series de 500 ms, 100 ms, y 20 ms. Para cada músculo se calculó su deformación normalizada y la pendiente de la misma, y su actividad eléctrica pre-estimulo.

La TTA y la deformación del músculo se compararon entre los distintos grupos: rodillas normales, inestables,



# Sala Pagoda 15:45 - 17:10 h O 001-010

con estimulación pre-tracción, y con estimulación posttracción, tanto en valores máximos como a lo largo del movimiento. El análisis estadístico se realizó mediante la prueba de ANOVA con prueba post-hoc de Tukey. Para ver el efecto de la estimulación repetida, se contabilizó el número de series de estimulación que recibía cada extremidad, y se comparó la TTA entre dos grupos con límite en 12 series de trenes mediante la prueba de Mann-Whitney.

#### RESULTADOS

En la rodilla inestable, se observó un aumento de la deformación relativa de cuádriceps e isquiotibiales, y, de forma más selectiva, de su pendiente de deformación, mostrando una resistencia menor a ser estirados. Con la estimulación a 500 ms, los valores de deformación muscular se aproximaron a los de las rodillas control, y los de su pendiente fueron incluso menores que éstos, sugiriendo un aumento de esa resistencia muscular.

En cuanto a la respuesta mecánica, la TTA se controlaba con la estimulación experimental. Cuando el estímulo eléctrico se aplicaba al inicio de la tracción, los valores máximos de TTA no fueron diferentes a los de las rodillas normales, mientras que si se aplicaba al final de la tracción, la laxitud sólo se controlaba a 30° de flexión. A lo largo del movimiento de tracción, se observó cómo las rodillas inestables alcanzaban rápidamente el nivel de inestabilidad, que se conseguía controlar con los trenes de diferente duración cuando se aplicaban al inicio de la fuerza de tracción. Estos mismos trenes aplicados al final de la tracción muscular capaz de reducir la laxitud articular de la misma forma.

Por último, cuando se estudió el efecto de la estimulación repetida, se observó una tendencia a una menor laxitud de la rodilla con más series de estimulación, a 30° de flexión.

#### CONCLUSIONES

El estímulo sincronizado con la tracción favorece el control de la TTA dentro de límites normales en el momento en que se precisa, lo cual concuerda con la recuperación o sustitución del sistema propioceptivo. Por otro lado, el estiramiento muscular más lento de las rodillas estimuladas sugiere una resistencia aumentada del músculo a ser deformado con la fuerza de tracción tibial anterior, lo cual va a favor de un sistema siempre preparado con aumento del tono muscular de agonistas-antagonistas. Este estudio propone las bases de ambas estrategias en la rodilla, que serían por tanto aplicables para el control de la inestabilidad por lesión del LCA. A la vista de los resultados, la estimulación eléctrica de la rodilla resultaría más eficiente si se aplica en el momento apropiado, al mismo tiempo que su reiteración colaboraría en mantener la TTA dentro de la estabilidad.





# CURRENT DENSITY AND FIELD DISTRIBUTIONS IN DC ELECTRICAL FIELD STIMULATION FOR HUMAN SPINAL CORD INJURY

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Parapléjicos (SESCAM) Finca La Peraleda . Toledo, Spain.

## INTRODUCTION

Applied DC electrical fields (EFs) stimulate and direct axonal growth in animal models of spinal cord injury (SCI), and clinical trials are underway to establish their efficacy in humans. The electrostimulation system proposed for human use utilizes low amplitude (~ 500 μV/mm) EFs applied via indwelling electrodes placed outside the vertebral channel. Although this strategy prevents additional neural damage, the electrical resistivity of interposing tissues could reduce field intensity within the spinal cord below therapeutic range.

#### MATERIAL AND METHOD

Here we present a finite element model of electrical magnitudes in the human cervical spinal cord during voltage application through electrodes of varied sizes and locations. Field intensity, distribution and direction, together with current and charge densities were analyzed in normal and injury conditions.

#### RESULTS

The electrode placement had a profound effect on EF intensity and direction within the spinal cord, with electrodes located outside the vertebral channel producing very low EFs that would compromise their therapeutic effects. Furthermore, field gradients were not homogeneous and their direction changed substantially in different regions of the spinal cord. The use of larger electrodes or higher potentials increased the fields to therapeutic values, whereas circular electrodes produced much more homogeneous field gradients. Electrodes placed inside the vertebral channel produced therapeutic field intensities with lower applied voltages. In addition, when a circular electrode was placed surrounding the lesion site inside the vertebral channel, therapeutic EF values were obtained with half the applied voltage.

#### CONCLUSIONS

Finite element models of the human spinal cord are a powerful method to study current distribution and electrical field intensities within the spinal cord and may guide the optimization of electrostimulation systems for neural repair.



# ANÁLISIS POR ELEMENTOS FINITOS DE LAS TENSIONES EN LA FISIS FEMORAL PROXIMAL EN ADOLESCENTES SANOS

C. Barrios, M. J. Gómez-Benito, D. C. Botero, J. M. García-Aznar, M. Doblaré

Unidad de Traumatología y Cirugía Ortopédica, Departamento de Cirugía, Facultad de Medicina, Universidad de Valencia Valencia

#### INTRODUCCIÓN

En este trabajo, el modelo paramétrico del fémur proximal de un niño, propuesto recientemente por los autores1, se adapta a las medidas geométricas de la cadera de un grupo de adolescentes sin patología previa de cadera. El objetivo de este trabajo es determinar computacionalmente las tensiones sobre el cartílago fisario proximal del fémur sano en distintas actividades (subir escaleras, caminar y sentarse) y analizar si dichas tensiones varían en consonancia con las variaciones anatómicas consideradas dentro de la normalidad.

#### MATERIAL Y MÉTODO

Un grupo de 23 adolescentes sanos con una edad media de 12.2 años (10-15) fueron sometidos a un estudio radiológico convencional de la pelvis y ambas caderas. De acuerdo con la sistemática de valoración radiográfica propuesta por Barrios y cols2, se cuantificaron distintos parámetros geométricos de una de las caderas entre los que incluían el ángulo de inclinación fisaria, el ángulo cuello-diáfisis, el ángulo de intersección, el ancho del cuello femoral y de la fisis, la altura del trocánter mayor y el ángulo de inclinación posterior de la fisis en las Rx axiales. Las mediciones de cada sujeto fueron introducidas en el modelo paramétrico obteniendo modelos de elementos finitos específicos para cada caso. En cada modelo se simularon tres situaciones diferentes de carga mecánica: caminar, subir escaleras y sedentación. Las cargas aplicadas fueron proporcionales al peso de cada sujeto. Se estudió la distribución de tensiones de Tresca, von Misses y Rankine sobre el cartílago fisario.

#### RESULTADOS

La distribución de tensiones en el cartílago fisario muestra un patrón similar en todos los sujetos. Las mayores tensiones se obtuvieron en la simulación de subir escaleras. En ese estadio, el 61% del volumen del cartílago fisario soportaba tensiones menores de 1MPa y sólo un 10% de la superficie fisaria soportaba tensiones de von Mises mayores de 1.5MPa. Si se analizaban las tensiones de Tresca, estas cifras pasaban a ser del 46% del volumen de la placa (<1MPa) y del 16% del volumen de la placa (>1.5MPa). La región solicitada por mayores tensiones es la zona más medial de la fisis tanto para tensiones de von Mises como de Tresca. Las tensiones en la placa fisaria estaban directamente correlacionadas con el ángulo de inclinación fisaria en Rx AP y el ángulo de inclinación posterior de la fisis en Rx axiales. Los sujetos con ángulo de intercesión <10° presentaban unas tensiones medias menores que aquellos sujetos con ángulos

superiores a 10°. Variaciones en el án!

gulo cuello-diáfisis, en la anchura del cuello femoral o de la placa fisaria y en la altura del troncánter no modificaban sensiblemente las tensiones medias, ni su distribución.

#### CONCLUSIONES

Teniendo en cuenta las simplificaciones que introduce el modelo paramétrico adaptable a los parámetros geométricos de cada sujeto, su utilización ha permitido analizar el comportamiento mecánico de la fisis proximal del fémur en adolescentes sanos. Este modelo ha mostrado la influencia de factores anatómicos en la distribución e intensidad de las tensiones soportada por la placa fisaria en distintas actividades de la vida diaria. En casos particulares puede ser útil para predecir la aparición de epifisiolisis de cadera, es decir fallo mecánico de la fisis proximal.



# ANÁLISIS BIOMECÁNICO DE DOS SISTEMAS DE OSEOSÍNTESIS DE LA CABEZA FEMORAL EN NIÑOS CON EPIFISIOLISIS

C. Barrios Pitarque<sup>1</sup>, M. J. Gómez-Benito<sup>2</sup>, J. Sanz-García<sup>2</sup>, J. M. García-Aznar<sup>2</sup>, M. Doblaré<sup>2</sup>

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#### INTRODUCCIÓN

El tratamiento habitual de la Epifisiolisis de la cabeza femoral (ECF) en fases trepanas y la osteosíntesis preventiva de la cadera contralateral consiste habitualmente en la inserción de uno o dos tornillos, a través del cuello femoral, que bloqueen el desplazamiento de la cabeza femoral. El principal objetivo de este trabajo es estudiar la estabilidad de la placa de crecimiento en diversas situaciones de carga y la influencia de la osteosíntesis de la cabeza femoral mediante uno o dos tornillos por medio de simulación por elementos finitos del fémur proximal de un niño afecto de Epifisiolisis.

#### MATERIAL Y MÉTODO

Se realizaron los modelos de elementos finitos de ambos fémures de un niño de 14 años y 95 kg de peso afecto de ECF en su fémur izquierdo. En ambos modelos, sano y enfermo, se simuló la fijación interna de la cabeza femoral por medio de la inserción de uno y dos tornillos canulados (7mm Ø, Lafitt, España). Se desarrollaron, por lo tanto, seis modelos de elementos finitos, un modelo de cada fémur (sano y enfermo) sin tornillos, con uno y dos tornillos respectivamente. Se simularon los ciclos de caminar y subir escaleras por medio de la aplicación de las cargas correspondientes a estos ciclos. Se estudió la estabilidad lograda en cada uno de los casos, analizando la distribución de deformaciones y tensiones en la placa de crecimiento.

#### RESULTADOS

Las máximas tensiones sobre la placa de crecimiento se observan en el ciclo de subir escaleras para todos los casos. Se observa una disminución importante de las tensiones con la inserción de los tornillos. En el momento más desfavorable del ciclo de caminar, el 5% de la placa fisaria del fémur con EFC está solicitada por tensiones superiores a 0.9MPa; sin embargo, en el caso sano este límite máximo se reduce a 0.65MPa. Tras la inserción de un tornillo se consigue una disminución de estas tensiones, encontrándose tan solo un 5% del volumen de la placa de crecimiento en unas tensiones superiores a 0.35 y 0.25MPa en los casos enfermo y sano respectivamente. Tras la inserción de dos tornillos, las tensiones máximas se reducen a 0.18MPa y 0.17MPa en los casos sano y enfermo.

#### CONCLUSIONES

Tras el estudio de la influencia de uno y dos tornillos en un fémur afectado por ECF y su contralateral sano se observa una reducción importante de las tensiones en la placa de crecimiento lo que evitaría el deslizamiento de la cabeza femoral. Sin embargo, la reducción en las tensiones máximas cuando se insertan dos tornillos respecto al caso con un solo tornillo no es tan significativa. Esta observación corrobora los resultados obtenidos en estudios experimentales in-vitro de tipo mecánico realizados sobre el sistema de fijación mediante tornillos en el cuello femoral. Los datos obtenidos tras la simulación mediante elementos finitos de un caso de ECF apoyan la recomendación de la osteosíntesis mediante un solo tornillo. La estabilidad alcanzada mediante el uso de dos tornillos es ligeramente superior, pero quizá no justifique el mayor riesgo de complicaciones quirúrgicas que conlleva la inserción de dos tornillos en la cabeza femoral.



ESTUDIO DE BUSQUEDA DE LA DOSIS OPTIMIZADA DE RADIACIÓN RECIBIDA POR PACIENTES ADOLESCENTES SOMETIDOS A ESTUDIO DE TOMOGRAFIA COMPUTERIZADA DE COLUMNA VERTEBRAL PARA EXPLORACIÓN DE INSTRUMENTACIONES E. Hevia Sierra, N. Blazquez Salvador, J. Burgos Flores, A. Bach Mona, C. Barrias Pitargua, L. A. Alvaraz García Do Quasada

Moya, C. Barrios Pitarque, L.A Alvarez García De Quesada, O. Riquelme García, I. Sanpera Trigueros, G. Pizá Vallespir. Hospital Central La Fraternidad-Muprespa .Madrid

#### INTRODUCCIÓN

Valorar las dosis que reciben los pacientes adolescentes sometidos a exploraciones diagnósticas de TAC de control de columna vertebral con amplias instrumentaciones tras intervenciones por escoliosis, y

mostrar la posible reducción que se consigue optimizando los protocolos de rutina.

#### **MATERIAL Y MÉTODO**

El cálculo de dosis efectiva de un TAC de un paciente para control de una instrumentación de escoliosis se llevó a cabo utilizando la hoja de cálculo desarrollada por ImPACT. Para ello se necesita conocer el valor del índice de dosis de tomografía computerizada normalizado medido en aire (CTDI n), y el resto de los parámetros con los que se ha llevado a cabo la exploración (kV, mAs, t rot, pitch, y colimación).

Para la medida del CTDI en aire, se han utilizado un detector de estado sólido de la marca RTI modelo CT-SD 16. También se calcularon los valores del CTDI vol y del producto dosis-longitud (DLP).

#### RESULTADOS

El valor del CTDI vol que hemos obtenido para el protocolo de rutina de columna vertebral que utiliza el escáner en el que se ha realizado el estudio es de 22,9 mGy, valor que supera lo recomendado en la guía de Europea sobre Criterios de Calidad para TCMD del año 2004. Optimizando este protocolo se ha conseguido reducir el CTDI vol a menos de un 40 % a costa de una degradación en la calidad de la imagen, pero de calidad suficiente para el objetivo clínico que perseguimos. Es decir, partiendo de una dosis efectiva equivalente a unas 1000 radiografías de tórax se puede llegar hasta una dosis efectiva equivalente a realizarse del orden de 325 radiografías de tórax.

#### CONCLUSIONES

Un TC de control de grandes instrumentaciones de adolescentes sobrepasa las dosis recomendadas, por lo que debe valorarse siempre la correcta indicación para cada caso concreto. Además, atendiendo a la Comisión Internacional de Protección Radiológica (ICRP), la legislación europea y española vigentes, si la exploración está justificada, deben optimizarse los protocolos para procurar que la dosis de radiación recibida sea siempre tan baja como sea razonablemente posible, sin menoscabo del valor diagnóstico de la misma.



# ESTUDIO DE LA PROTEÍNA OLIGOMÉRICA DE LA MATRIZ DEL CARTÍLAGO EN MENISCOS HUMANOS ARTRÓSICOS

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#### INTRODUCCIÓN

Los meniscos sufren cambios a nivel celular y molecular con la artrosis. La Proteína Oligomérica de la Matriz del Cartílago (COMP), desempeña un papel fundamental en el mantenimiento de la estructura tridimensional de la matriz meniscal.

Realizamos un estudio de los cambios en las células y en la matriz de meniscos artrósicos, en especial de la distribución de la COMP.

#### **MATERIAL Y MÉTODO**

Valoramos los tejidos meniscales de 31 pacientes diagnosticados de gonartrosis que se sometieron a cirugía de artroplastia total de rodilla y los de 5 pacientes jóvenes con rotura meniscal reciente.

Los tejidos meniscales fueron procesados para histología, inmunohistoquímica e hibridación in situ. Se estudió la proliferación celular mediante inmunotinción con Ki67, apoptosis mediante la técnica de TUNEL y la distribución de proteoglicanos mediante tinción de las muestras con azul alcian. El anticuerpo frente a COMP se obtuvo a partir de Aquiles bovino usando una modificación de la técnica de Hauser. Se diseñaron cebadores específicos según la secuencia génica de la COMP humana, teniendo especial cuidado en que no hibridasen con otras trombospondinas, para el diseño de la ribosonda.

#### RESULTADOS

En meniscos artrósicos el número de células, el porcentaje de células y la matriz extracelular inmunoteñidas frente a COMP, así como el número de núcleos que hibridaban frente a COMP fueron menores que en meniscos procedentes de meniscectomía. Se observaron células proliferando en meniscos procedentes de mensicetomías y sólo en uno de los artrósicos. El 70% de los meniscos artrósicos presentaban células apoptóticas y sólo uno de los meniscos procedentes de mensicectomía.

#### CONCLUSIONES

En los meniscos artrósicos se observa una disminución de la población celular y menor actividad anabólica de las células, expresada como menor síntesis celular de COMP. La alteración en la síntesis de COMP o la alteración en su distribución en la matriz extracelular, podría provocar la desorganización de la red tridimensional de colágeno y cambiar las propiedades del fibrocartílago y por tanto de sus funciones.



# SIMULACIÓN DEL PROCESO DE OSTEOINTEGRACIÓN DE UN VÁSTAGO NO CEMENTADO TIPO ZWEYMULLER

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### INTRODUCCIÓN

El aflojamiento del vástago es uno de los mayores problemas de las prótesis no cementadas. La principal causa del aflojamiento anterior viene por la falta de estabilidad en los primeros instantes posteriores a la cirugía. Esta estabilidad es fundamental para el posterior proceso de osteintegración hueso-implante y por lo tanto para el éxito de la fijación. Existen diversos trabajos computacionales que han simulado el crecimiento óseo alrededor del implante, pero ninguno de dichos estudios

ha tenido en cuenta el proceso evolutivo (deterioro y osteointegración) de interfases vivas. En este trabajo se pretende aplicar un modelo numérico desarrollado con anterioridad a la predicción del proceso de osteointegración/daño de una prótesis de cadera no cementada deZweymuller. Además se analizará el efecto de diversos factores sobre dicho proceso de osteointegración en la interfaz hueso-implante.

#### MATERIAL Y MÉTODO

Se ha desarrollado un modelo numérico basado en la teoría de la Mecánica del Daño Continuo. La formulación del modelo se establece en términos de las componentes normales y tangenciales de las tensiones y de los desplazamientos relativos. El comportamiento mecánico de la interfaz

viene dado por 4 propiedades que se pueden obtener experimentalmente. Se define una variable que es la que describe el grado de osteointegración del implante y que viene dada por el cociente entre la rigidez actual de la interfaz y la de la interfaz completamente osteointegrada. También se define la evolución de este parámetro en función de los desplazamientos relativos hueso-implante que se producen. El modelo se ha aplicado a la simulación del proceso de osteointegración en la interfaz hueso-implante de la prótesis no cementada Zweymuller. Se ha desarrollado un modelo de elementos finitos tridimensional de la prótesis. Inicialmente la interfaz se considera completamente suelta, y tras un periodo de una semana de reposo, se simulan 300 días de actividad que combina: caminar, subir escaleras, estar de pie y descansar. Se han realizado diversos análisis estudiando el efecto de varios aspectos: la rigidez del vástago, la actividad del paciente, el acabado superficial del vástago y las propiedades mecánicas de la interfaz hueso-implante.

#### RESULTADOS

De los efectos analizados se observa cómo la utilización de un vástago más flexible hace que el grado de osteointegración se vea reducido sobretodo en la zona proximal. Los resultados numéricos coinciden con lo observado clínicamente en este aspecto. Se ha analizado también el efecto que produce sobre el grado de osteointegración la actividad que realiza el paciente, obteniéndose que un aumento del tiempo de reposo mejora el proceso de osteointegración. Finalmente, se obtiene también de la simulación que un vástago pulido aumenta el grado de unión de la interfaz hueso-prótesis, resultado que también coincide con lo observado in vitro.

### CONCLUSIONES

El modelo presentado es capaz de simular el progresivo deterioro y crecimiento óseo al mismo tiempo. A pesar de que el modelo presenta algunas limitaciones principalmente debido a la falta de ensayos experimentales, esta metodología permite determinar la influencia de varios factores mecánicos en el grado de osteointegración en la interfaz hueso-cemento y en el comportamiento de un implante no cementado.



# SUSCEPTIBILIDAD ANTIBIÓTICA DE BIOFILM DE STAPHYLOCOCCUS AUREUS FRENTE A VANCOMICINA Y RIFAMPICINA. DIFERENCIAS CON LOS ESTUDIOS CONVENCIONALES DE SENSIBILIDAD

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### INTRODUCCIÓN

La formación de biofilm por parte de las bacterias causantes de infección ortopédica es uno de los principales factores de patogenicidad de las mismas en las infecciones relacionadas con diversos biomateriales. Es conocido que las bacterias que forman el biofilm presentan mayor grado de resistencia fenotípica a los antibióticos que las bacterias en estado libre, por lo que, a la hora de plantear un tratamiento debería tenerse en cuenta este hecho, y no sólo los resultados de los estudios de sensibilidad tradicionales. Sin embargo, no todos los antimicrobianos se comportan de igual manera frente a las bacterias dentro del biofilm, por lo que el estudio in vitro sería de gran utilidad, sobre todo cuando en la actualidad el número de bacterias multirresistentes está creciendo, y las opciones terapéuticas disminuyen. Nuestro objetivo es desarrollar una técnica que permita el estudio de la actividad antimicrobiana sobre biofilms desarrollados.

#### **MATERIAL Y MÉTODO**

Se estudió la sensibilidad de la cepa de S. aureus 15981 (proporcionada por el Dr. Lasa (Valle J et al. Mol Microbiol. 2003; 48: 1075-1087)), cepa de colección productora de biofilm, frente a rifampicina y vancomicina, tanto en estado libre como en biofilm desarrollado. Para el estudio de sensibilidad in vitro convencional se emplearon tiras de E-test (AB Biodisk) en agar Müller-Hinton de acuerdo con las recomendaciones del CLSI. Para el estudio de sensibilidad de biofilm se empleó la técnica de Gualtieri et al. (J Antimicrob Chemother 2006; 58: 778-783) modificada: Se utilizaron placas de 6 x 4 pocillos en las que se depositó en el fondo un disco de thermanox® para cultivo celular (Nunc). Se inocularon con una suspensión equivalente a 0,5 McFarland. Se desarrolló el biofilm tras 24 hors de incubación. A continuación, se retiró el medio y se sustituyó por idéntico medio con concentraciones dobles de antibiótico, comenzando por la concentración inferior a l!

a Concentración Mínima Inhibitoria (CMI). Tras 24 horas de incubación, se retiraron los discos y, tras lavarlos, se sonicaron durante 5 minutos. El número de bacterias viables se calculó mediante diluciones seriadas del sonicado inoculadas en TSA-5 % sangre de carnero. Se empleó como control un pocillo en el que el medio se cambió por uno idéntico al resto, pero sin antibiótico. Todos los experimentos fueron realizados por triplicado.

#### RESULTADOS

El estudio de sensibilidad convencional permitió obtener una CMI de 1 mg/L para vancomicina y de 0,03 mg/L para rifampicina.

El número medio de Unidades Formadoras de Colonias (UFC) detectado en el control fue de 1,61 x 109. Tras calcular el % de UFC viables en las concentraciones de antibiótico en relación con el control, se objetivó un descenso progresivo concentración-dependiente en la vancomicina, desde 2,44 % (0,5 mg/L) hasta 1,37 % (64 mg/L). Por contra, la rifampicina presentó una actividad más uniforme en las diversas concentraciones estudiadas (desde 1,16 % en 0,03 mg/L hasta 0,18 en 64 mg/L). No se consiguió erradicar el 99 % del inóculo control (Concentración bactericida del biofilm) con vancomicina, mientras que en el caso de rifampicina dicho objetivo se consiguió a partir de 0,06 mg/l.

#### CONCLUSIONES

A pesar de los resultados de sensibilidad in vitro convencionales, vancomicina no es eficaz frente a un biofilm desarrollado de S. aureus. Por contra, rifampicina resulta eficaz frente a dicho biofilm a una concentración muy próxima a la obtenida por métodos convencionales. El modelo desarrollado es útil para el estudio de sensibilidad de biofilms frente a diversos antimicrobianos.



# ROTURA DE UN VASTAGO DE LORD DE 22 AÑOS DE EVOLUCION. ESTUDIO CON MICRO-TC Y MICROSCOPIO ELECTRONICO.

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#### INTRODUCCIÓN

Las fracturas del vástago femoral ha sido una complicación frecuente en las prótesis de primera generación, con prevalencias que varian desde un 0,23% en la prótesis de Charnley hasta un 11% en otros diseños. Se ha atribuido a factores como defecto de material, de fabricación y de diseños. Con las mejoras de las caracteristicas de superficie y los materiales desde los años 80, esta complicación casi ha desaparecido.

#### MATERIAL Y MÉTODO-CASO CLINICO

Se trata de una paciente de 72 años, con múltiples alergias. El indice de masa corporal es de 33. Es portadora de una prótesis de rodilla izquierda modelo Natural tipo II desde hace 2 años implantada mediante navegación con buena evolución clinico-radiológica. La paciente fue operada por una coxartrosis derecha hace 22 años implantándole un vástago no cementado de LORD con un cotilo cementado de polietileno.

#### **RESULTADOS**

Sin antecedente traumático refiere que tras un mal giro empieza con clínica dolorosa con impotencia funcional, observándose una rotura del vástago con una fractura periprotésica subtrocantérea asociada tipo B1 de Vancouver. Durante la cirugía se observa que el fragmento proximal y distal del vastago estaban muy osteointegrados siendo muy difícil la extracción. Tras un abordaje lateral ampliado se extrae el vastago roto, siendo necesario la realización de ventanas óseas y la reconstrucción mediante una placa de Zimmer y aloinjerto. Se realiza un estudio de las piezas mediante microscopio electrónico y micro-TC.

### CONCLUSIONES

Las tradicionales prótesis de Exeter y Charnley se fueron modificando para mejorar las caracteristicas a fatiga. Así pues las superficies de titanio o Cr-Co-Mo rara vez se fracturan. Se citan una serie de factores responsables del fracaso por fatiga del implante como son: las características del paciente, material y diseño, técnica de cementado, orientación del implante, perdida osea femoral proximal. La fractura de los vástagos se suelen iniciar en la zona anterolateral del tercio medio del vastago, zona sometida a una alta concentración de tensiones. El vastago de Lord presenta una superficie madrepórica que facilita la osteointegración. En 2004 Grant y cols. presentan una serie de 116 casos con una supervivencia de un 98% a 17,5 años. Tan solo aportan un caso de fractura del vástago femoral. El tiempo desde la cirugía varia ampliamente lo que indica que existen otros factores además de la calidad del material. En condiciones normales de carga, las tensiones en el vástago pueden alcanzar niveles suficientes para producir una fractura por fatiga sin existir signos de aflojamiento. Puesto que el aflojamiento y la fractura del vástago son dependientes del tiempo, se recomienda un seguimiento clínico y radiológico para analizar los posibles factores de riesgo.

#### **INVESCOT - EORS O-010**

# A QUANTITATIVE EVALUATION OF ARTICULAR CARTILAGE AFTER MENISCUS REPLACEMENT IN RABBITS

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#### INTRODUCTION

Experimental and clinical studies have documented that meniscal allografts show capsular in growth in meniscectomized knees. However it remains to be established whether meniscal allograft transplantation can prevent degenerative changes after total meniscectomy. In this study, functional changes in articular cartilage after meniscus transplantation in rabbits were evaluated quantitatively.

#### **METHODS**

Thirty rabbits were divided into five groups. Group A and Group C were subjected to meniscectomy. Group B and Group D underwent meniscal transplantation immediately after meniscectomy. Group E had delayed transplantation 6 weeks after meniscectomy. Six nonoperated knees served as controls. Using image analysis with QwinPro software functional changes of articular cartilage were examined 6 weeks (Groups A, B) and 1 year (Groups C, D, E, controls) after surgery by measuring the lactate dehydrogenase (LDH) activity in chondrocytes as a measure of their vitality and the proteoglycan content of the extracellular matrix as a measure of its quality.

#### RESULTS

All experimental groups demonstrated a significant decrease in proteoglycan content of the cartilage as compared with the control group. At 6 weeks and 1 year follow-up, no significant differences were found between the postmeniscectomy group and immediate transplant group. The delayed transplant group showed a significantly decreased proteoglycan content as compared with the postmeniscectomy group. Compared to the control group, no significant differences in cellular LDH activity were found in the postmeniscectomy group and immediate transplant group at 6 weeks and 1 year. However, delayed transplantation caused diminished vitality of chondrocytes. No significant differences were found between the postmeniscectomy group and immediate transplant group at 6 weeks and 1 year. The delayed transplant group showed a significant decrease in LDH activity as compared with the postmeniscectomy group.

#### CONCLUSIONS

It can be concluded that immediate meniscal transplantation in rabbits did not significantly reduce degenerative changes of articular cartilage whereas delayed transplantation leads to even more degenerative changes than meniscectomy.



# ORAL SESSIONS EORS

Friday, April 25th



# ORAL SESSION 1 Hip Implants 1

#### O-001

# CASE SPECIFIC FINITE ELEMENT MODELS PREDICT FEMORAL FAILURE RISK BETTER THAN EXPERIENCED PHYSICIANS

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#### Introduction

Bone metastases occur in about 15% of all cancer cases. Pathological fractures that result from these tumours most frequently occur in the femur. Unfortunately, it is extremely difficult to determine the fracture risk with the current X-ray methods, even for experienced physicians. As a result, many patients are surgically over-treated, whereas some patients, who are defined to be at low risk, may fracture their bones [1]. The purpose of this study was to develop a femur (patient) specific finite element model to improve the prediction of failure risk under stance loading. In addition, we tested if our model was better in predicting failure risk under stance loading than experienced physicians.

#### Methods

Eight human cadaver femora, with and without simulated metastases, were CT-scanned (Philips, ACQsim, 120kV, 220mAs, 3mm slices). A solid calibration phantom (Image Analysis, 0, 50, 100 and 200 mg/ml calcium hydroxyapatite) was included in each scan. From the scans, eight finite element (FE) models were generated using brick elements with sizes of about 1x1x3 mm. The ash density of each element was computed from the calibrated CT scan data. Using ash densities, non-linear isotropic mechanical properties were implemented [2].

After scanning, laboratory experiments were performed. The femora were loaded under compression until failure. During the experiments the failure forces and the course of failure were registered. These experiments were simulated in the FE-models, in which plastic deformation simulated failure of the bones. The relationship between the experimental failure force and predicted failure force was determined using Pearson's correlation.

Five experienced physicians, three orthopaedic surgeons, one musculoskeletal radiologist and one radiation oncologist, were asked to rank the femora on strength using X-rays (AP and ML) and additional information on gender and age.

The Spearman's rank correlation coefficients was calculated between prediction and experiment for both the FE-model and the expert rankings to compare the performance of the physicians.

#### Results

A strong correlation (r2 = 0.93) was found between the experimental failure force and predicted failure force (Fig 1). The course of failure, visible by the plastic deformation, showed similarities with the failure locations found in the experiments (Fig 2).

# Aula Magna 10:00 - 10:50 h O 001-005



Fig1: Pearson's correlation between experiment and FEsimulation was r2= 0.93.



Fig2: Failure location in FE-model and experiment



Fig3: The FE-model shows the best Spearman's rank correlation between the experiment and prediction

The Spearman's rank correlations between experiment and predictions ranged between r2=0.23 and r2=0.54for the physicians, whereas it was significantly higher, r2=0.86, for the FE-model (Fig 3).

#### Discussion

In daily practice, the prediction of fracture risk has been mainly based on X-rays. We showed that femur specific FE models better predicted femoral failure risk under axial loading than experienced physicians. When the model is further improved by adding, for example, other loading conditions, it can be clinically implemented to predict in vivo fracture risk for patients suffering, for example, bone metastases or osteoporosis.

#### References

- 1. Van der Linden et al, JBJS, 86B:566-573, 2004.
- 2. Keyak et al, Clin Orthop Rel Res, 437:219-28, 2005.



# BONE REMODELLING MODELS. APPLICATION TO A RESURFACED PROSTHESIS

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#### Introduction

Resurfacing prostheses (SRA, Surface Replacement Arthroplasty) are nowadays widely used as an alternative to total hip replacement (THA), especially for the young and active patients. Because of the more physiological distribution of the load in the femur, this technique is particularly known to reduce bone loss due to the stress shielding behaviour, a major problem encountered with THA. However, high peaks stress have been shown in some sites of the femoral head as well as in the proximal neck, leading to bone remodelling which is undesired. Indeed, this process involves that the old bone has to be resorbed while new bone tissue is formed, creating instability at the bone-cement and bone-implant interfaces and consequently making the implant subject to aseptic loosening. Here, a bone remodelling analysis is performed with the aims of investigate: (1) the validity of using bone remodelling models in order to predict the intact femur bone density distribution and (2) its application to evaluate the bone structure changes postoperatively.

#### Materials and methods

Using the software Mimics, the medical images have been segmentated as a mean to get the personalized geometry of a 48 years old male femur with no known bone disorder. Then, after a CAD reconstruction in Catia V5, two finite element models were developed using ANSYS WorkBench; a first intact and the second with an implant. For both analyses, three load cases are applied based on the normal walking activity. In the healthy and implanted femur, bone is assumed as anisotropic and heterogenerous with its mechanical properties estimated pointwise from the application of a bone remodelling model [1,2]. The stem and cement of the resurfaced femoral implant are considered linear and elastic with Young modulus of 200GPa and 2.2 GPa, respectively and Poisson's ratio of 0.28 and 0.3, respectively. The finite element analyses are performed using the commercial software Abagus.

The results of the bone remodelling analysis over the intact femur are compared with the bone density distribution computed from the CT-scan images by means of Mimics and a linear relationship that relates the bone density distribution with the Hounsfield Units (HU) [3]. This comparison enables a validation of the numerical

method in order to perform an adequate computation of the effect of the resurfaced implant in the bone structure.

#### Results

For the bone remodelling analysis over the intact femur, the initial bone density distribution is 0.5 gr/cm3. After 100 increments of analysis the bone density distribution predicted is in good agreement with the one obtained from the CT-scan images. The relative error between the predicted bone density distribution and the bone density from the CT-scan images was computed, and over 50% of bone volume shows a difference below 25%.

Once the bone remodelling model has been qualitatively and quantitatively validated it is used to predict the effect of a resurfaced femoral implant on the bone structure (Fig. 1). As it was expected an increased of the bone density was observed in the femoral head and in the proximal neck (Fig. 1).



Fig. 1: Bone density distribution in a resurfaced femoral implant.

#### Discussion

The methodology proposed in this study combines both image and computational models in order to predict the bone density distribution of the femur with a resurfaced prosthesis. From the results obtained, it may be concluded that the numerical simulation used in this study is a useful tool in predicting bone remodeling inside a cemented resurfaced femoral head.

#### **References:**

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[2] Doblaré M., García J. M. J Biomech, 35 :1-17, 2002.
[3] Peng L., Bai J., Zeng X., Zhou Y. Med Eng Phys, 28 :227-233, 2006.

#### O-005 A COMBINED FINITE ELEMENT AND RADIOLOGICAL ANALYSIS OF THE PROXIMAL FEMUR POST HIP RESURFACING ARTHROPLASTY

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# Introduction

Sectioned femoral components retrieved from failed hip resurfacing athroplasties show resorption of the proximal femoral bone or formation of a fibrous membrane at the bone cement interface, in a proportion of cases1 (Fig. 1). We hypothesize that both scenarios create a functional discontinuity zone (FDZ), which exacerbates off-loading the proximal bone thereby promoting resorption. We have used finite element modeling to examine the effects of the presence of an FDZ on bone remodeling following hip resurfacing arthroplasty. A radiographic analysis of the proximal femur following hip resurfacing was also conducted in order to draw a comparison to clinical findings.

#### **Materials and Methods**

Previously developed 3-D FE models of a natural femur and BHR were implemented with modifications for FDZ simulation2. Non-homogeneous, isotropic, linear elastic material properties were assigned to the trabecular bone based on the donor QCT data and reported density-modulus relationships3. The hip resurfacing FE models were oriented in 3 distinct stem-shaft angles: 136° ("neutral"), 120° ("varus") and 150° ("valgus"). A low-modulus (2 MPa) FDZ (approx. 2mm thick) was simulated proximal to the device. Clinically relevant femoral joint (2.4×BW) and muscle loads were applied to simulate peak joint loading during gait4. Interface stress was compared for the normal and simulated FDZ resurfaced femurs. Bone remodelling stimuli was determined using changes in strain energy. A retrospective radiological analysis was simultaneously undertaken to study changes in the proximal femur following hip resurfacing arthroplasty. Radiographs of 98 hips with a minimum of 5 years follow up were examined. Measurements of the prosthesis-shaft angle, pre- and post-operative femoral head offset and femoral neck diameter at 2 and 5 years were undertaken. The results of the FE analysis were compared to the radiological findings.

#### Results

The presence of the simulated FDZ in the FE analysis resulted in increased proximal medial bone resorption and slightly greater bone formation surrounding the stem (Fig. 2A). Correspondingly, device-bone interface stresses were found to decrease proximally under the loading platform and increase at the stem, particularly adjacent to the stem-head junction (Fig. 2B). The valgus BHR femur led to increased resorption, especially around the periphery of the neck and on the medial side (Fig. 3), consistent with trends from previous studies2. The radiological analysis identified 2 groups; 22 hips (Group 1) had a mean 5.61mm (sd±2.07) reduction in neck diameter over 5 years and 76 hips (Group 2) demonstrated slow reduction in neck diameter, mean 1.13mm (sd±0.97). Neck thinning at 2 and 5 years was significantly greater for Group 1 (p<0.0001). Group 1 hips had significantly



greater reduction in femoral offset (p=0.041), with greater valgus angle oriented components (p=0.09). Reduction in femoral offset was significantly associated with greater valgus orientations (p<0.0001). The Group 1 revision rate was 36.4% compared to 2.6% in Group 2 (p<0.0001).

#### Discussion

The FE results support the hypothesis that the presence of a FDZ decreases load transfer to the proximal bone, resulting in increased medial stress shielding and resorption. These results are consistent with the Group 1 clinical findings in which accelerated neck thinning and increased revision rates were exhibited. In order to better understand the cause of implant failures in hip resurfacing arthroplasty, additional retrieval studies are necessary.







Fig. 2: Effect of a FDZ on (A) initial bone remodeling and (B) pressure at the device-bone interface.



Fig. 3: Effect of orientation on initial bone remodeling in normal bone and bone with a FDZ.

#### References

[1] Campbell et al., Clin Ortho Rel Res, 453, 35-46, 2006[2] Ong et al., JBJS (Br) 88-B, 1110-1115, 2006 [3] Morgan et al., J Biomech., 36, 897,

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# ORAL SESSION 2 Hip Implants 2

#### **O-006**

# STABILITY OF FEMORAL STEMS IN A CEMENT-IN-CEMENT REVISION MODEL DURING FATIGUE TESTING

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#### Introduction

The number of revision hip arthroplasties being undertaken is increasing. Several aspects of this surgery could be further improved. One method of reducing intraoperative complications is the cement-in-cement technique. Some concern exists regarding the retention of the existing fatigued cement mantle. The primary cement mantle that is found in the femoral canal at the time of a cement in cement revision has been subject to a "fatigue cycle" from patient usage. It has also been subject to the biological environment for an extended period of time. It was hypothesised that leaving the existing fatigued and conditioned cement mantle does not degrade the mechanical properties of the cement in cement revision construct. The aim of this research was to test this hypothesis using in vitro fatigue testing of analogue cement in cement constructs.

#### **Materials and Methods**

Primary cement mantles were formed by cementing a large polished stem into sections of tubular stainless steel using polymethylmethacrylate with chlorophyll and Gentamicin. The stem was implanted into the cement using a specifically designed insertion rig. This allowed accurate placement of the primary and revision stems. At this stage, the specimen was chosen to be in the test group or the control group. If in the test group, it underwent a fatigue cycle of 1 million cycles at a maximum load of 2kN at 10 Hz according to ISO 7206-4 [1]. This was carried out in a specifically designed rig and a fatigue testing machine (Instron Hydraulic 8874). The fatique was undertaken with the specimens in Phosphate buffered saline (PBS) at 50oC. This was in an attempt to degrade the cement to some degree. Into these fatigued and unfatigued primary mantles, the cement within cement procedure was carried out using methods which replicated the in vivo procedure. Simplex P cement with antibiotic was prepared and inserted using modified third generation cementing techniques. Both groups were fatigue tested with the same settings as described above. Subsidence of the stems and their inducible displacement was recorded. Sectioning of the specimens at the end of testing allowed measurements to be taken of the orientation of the revision stems. The number of 6 to 15 samples per group was calculated as an adequate sample size based on standardised test guidelines and on a power analysis calculation [2].

#### Results

Figure 1 shows the subsidence of the specimens in the unfatigued primary mantles (blue lines) versus the specimens in the pre-fatigued primary mantles (red lines). Completion of a Mann Whitney test (non-parametric

# Aula Magna 11:10 - 12:00 h O 006-011

test) on the endpoints of the subsidence curves revealed that there is no statistical difference between the data sets (medians 0.49, 0.48 means 0.51, 0.46, n=10 + 10, p = 0.496). This data was also



Figure 1.

calculated for the inducible displacement. Again, there was no statistical difference in the separate groups for this parameter (means 0.38, 0.36, p = 0.96). The 48 hours that the pre-fatigued mantles were stored in the PBS at 50oC equates to being contained in the in vivo environment for approximately 2 months. This is based on findings of Hughes et al. [6]. The mean displacement of the primary stems is 0.24 (median 0.26, n = 13).

#### Discussion

From the results one can see that the pre-fatigued and conditioned primary mantle did not significantly affect the subsidence or the inducible displacement of the revision stem. A limitation of the experiment was that the pre-fatigue cycle and the storage in PBS at 50oC only approximately represented 1 year and 2 months in vivo respectively [3]. However testing in a fluid medium replicates the in vivo situation more accurately than testing in air. Fatigue testing at 50oC generates an accelerated creep test for the cement. This allowed us to replicate rates of subsidence for the primary stems similar to those that have been observed in vivo [4]. This validates our experimental construct to some degree. This methodology produces a complex 3 dimensional reconstruction of the cement in cement revision which replicates the in vivo structure. This reconstruction has undergone fatigue testing. Neither of these two aspects has been produced for the study of cement in cement revision before.

#### Conclusion

A fatigued and conditioned primary cement mantle does not appear to degrade the mechanical properties of the cement in cement revision construct.

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# EORS 2008 · MADRID

# O-007 CERA

# CERAMIC-ON-METAL: HARD-ON-HARD BEARING REDUCES WEAR IN HIP IMPLANTS?

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### Introduction

Ceramic and metal hip implants born (as solution) to solve the problems due to the wear of polyehtylene. Alumina ceramic and metal articulations are harder, biocompatible, and result in reduced wear and particles to the surrounding tissue. Alumina ceramic hip implants produce lower wear rates than other combinations (i.e. metal-on-metal and metal/ceramic-on-polyehtylene) [1,2]. However, ceramic present some limitations: a higher fracture rate in the case of alumina components [3] and hydrothermal degradation for zirconia [4]. Otherwise, metal-on-metal articulations have shown in vivo a high metal ions release and a higher lymphocytic immune response [5,6]. A combination of new materials that can reduce the concerns of the aforementioned materials is clearly of considerable interest to the orthopaedic community. Using a differential hardness hard-on-hard (like ceramic-on-metal) bearing it would reduce wear and ion release compared to a typical metal-on-metal bearing and it would lower the risk of ceramic fracture.

Aim of this study was to investigate the wear properties of a novel hip bearing using ceramic-on-metal and compare it to currently used ceramic-on-ceramic articulations.

# **Materials and Methods**

Six commercial components (CeramTec, Germany) have been tested in a 12-station (Shore Western, USA) hip joint simulator. In particular, three Biolox Delta femoral heads (36-mm) tested in conjuction with three CoCr alloy acetabular cups (COM) were compared with three femoral heads Biolox Forte (36-mm) coupled with homologous acetabular cups (COC). Wear tests were carried out applying a sinusoidal load with a peak of 2.2 KN with a frequency of 1.1 Hz for five million cycles. Specimens were removed from the simulator for gravimetric measurements firstly (0-3 Mc) at 0.5 Mc and then (4-5 Mc) every 1 Mc. Bovine calf serum (25v/v balanced with deionized water) was used as lubricant.

#### Results

All the tested specimens completed the planned five million cycles. Fig. 1 shows the gravimetric evolution of the wear behaviour.

Significant statistical differences were observed between COM vs. COC (non- parametric two-sample Kolmogoronov-Smirnov test).



Fig. 1 - Weight loss of acetabular components

#### **Discussion & Conclusions**

The wear rate of COM acetabular cups was found to be higher than for COC configuration. In particular, COC pairings showed approximately 40 times less wear than COM pairings. These results appear not in agreement with those found by Firkins and coworkers [7]. However, it was stressed that different conditions occourred between these studies: different metal alloy and ceramic, different diameter of the prosthesis (36-mm vs. 28-mm). Nevertheless, in a clinical report on a metal (head) on ceramic (liner) coupling it was found a high rate of metal wear ended in an implant failure [8].

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30



# FOLLOW-UP OF IMPLANT PERFORMANCE USING RSA

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### Introduction

The success of a total hip replacement (THR) is mainly judged by the patient on immediate pain reduction and improved functionality. The long-term implant performance however, depends on the degree of periprosthetic bone loss and micromotion of the prosthesis. Radiostereometric analysis (RSA) is a technique that can be used to measure in-vivo micro-motion of the components of hip arthroplasty. Follow-up using RSA is not routinely used in orthopaedic surgery. To evaluate the potential added value of this assessment method we studied 86 patients who received THR. In this study the migration has always been measured in relation to the femoral bone.

#### **Materials and Methods**

Patients eligible for THR who agreed with the study requirements were included in the study after having given their informed consent. 86 patients received a titanium custom-made prosthesis (1). The average age was 64 years (20y -84y). During the study 30 patients out of 86 received a cementless femoral stem. The choice of stem fixation is determined by the quality of the bone. In all cases a 36 mm cobalt chromium head is used.

Spherical tantalum markers, chosen because of the proven biocompatibility were inserted into stable locations in the femoral bone during surgery using a specialized insertion tool, according to the protocol of Lawrie et al (2). Evaluation was done 1, 6, 12, 24, 52 weeks after surgery.

# Results

Overall subsidence follows a parallel pattern for the cemented and uncemented prosthesis that is slightly stronger for the uncemented prosthesis. In this study group the pattern of subsidence is different in the female group compared to the male group. In the latter we observe a slower onset up till 6 weeks with a faster decline afterwards.

Over the 6 months evaluation period the prosthesis migrates towards the lateral side with 0.25 mm in both groups. An anteroversion of 0.5° to 1° is noted at 6 months follow-up. The varus valgus movement of the prosthesis is similar for both groups at 6 months. At 6 weeks a slight valgus flexion is noted, this is reversed at 3 months. At this point in time the effect is more pronounced in the group with a cemented prosthesis.

# Discussion

Micro motion is difficult to assess on plain radiography. In this study more subsidence is noted in the uncemented prosthesis compared to the cemented. The degree of rotation of the stem measured in our study is comparable with those reported by others (3).

In revision surgery as reported by Ornstein et al (4) most stem migrations were observed between day 1 - 14after the intervention. In our primary THR we observe a bi-modal movement pattern except that for the subsidence the initial movement up till 6 weeks is reversed at 3 months follow-up and at 6 months the prosthesis seems stabilized, though longer follow-up is required to confirm stabilization.

Both cemented and cementless implanted titanium hip stems showed a sufficient primary and short-term stability with excellent clinical results.

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#### O-009 IMPINGEMENT WEAR OF LARGE X3 BEARINGS

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### Introduction

Acetabular rim damage due to femoral neck to acetabular rim impingement is found in up to 56% of retrieved acetabular inserts and has been associated with increased wear and contact stresses, instability and implant loosening in total hip replacement devices [1-8]. Increasing the femoral head to femoral neck diameter ratio will increase range of motion until impingement, reduce the chance of rim damage and increase joint stability [9]. The increased femoral head diameter requires thinner acetabular liners for a given size cup which may be a concern for high rim stress conditions if impingement occurs.

Highly crosslinked UHMWPE have proven to have superior wear performance compared to conventional UHMWPE [10-12], but may have reduced mechanical strength if remelted [13]. X3 UHMWPE (Stryker Orthopaedics, Mahwah NJ) is a sequentially crosslinked and annealed highly crosslinked polyethylene that has superior wear resistance, oxidation resistance and maintained mechanical properties [10]. Although thinner components may not have been possible with mechanically weaker materials, X3 is available in a thickness of 3.8mm. These components have proven survivorship in a severe rim loading fatigue test [14] but resistance to rim impingement wear is unknown. An aggressive rim impingement wear model previously described was used to assess these larger diameter hip implants [15].

# **Materials and Methods**

Acetabular liners of two different sizes were tested under impingement and standard walking gait conditions (n=3) (Trident, Stryker Orthopaedics, Mahwah, NJ). 36mm ID 3.9mm thick and 40mm ID 3.8mm thick liners were compared to previously reported [15] 28mm ID 7.9mm thick liners. Matching CoCr femoral heads were used for articulation. All standard product liners were machined from X3 UHMWPE material stock. Two million cycles of hip simulation (MTS, Eden Prairie MN) were run using physiological component orientation (50° cup inclination) and a 23° biaxial rocking motion to simulate the walking gait. Paul type loading with a maximum of 2450N was applied at 1Hz. Alpha Calf Fraction serum (Hyclone Labs, Logan UT) diluted to 50% with DI water and EDTA was used as a lubricant.

Six stations were outfitted with a torque controlled impingement system that applies aggressive rolling sliding contact of the femoral neck analogue to the posterior rim of the PE acetabular inserts during the toe off phase of gait. Details for this impingement system have been previously published [15].

Gravimetric wear measurements were assessed at every 0.25 million cycles (mc).

# Results

The 36 and 44mm results were statistically equivalent under ideal alignment (p=0.43) as well as impingement (p=0.72) conditions, allowing the two sizes to be combined. Both sizes show increased wear rates under impingement conditions (p=0.0008). The average wear rate for these large inserts is 0.62mm3/million cycles (mc) under standard conditions and 2.96mm3/mc under impingement conditions. The wear rates of these larger bearings under impingement conditions is not statistically different from the wear rate of the 7.9mm thick 28mm size X3 components previously tested (4.7mm3/ mc) under the same impingement condition (p=0.33)[15]. This represents an average 94% reduction in wear rate as compared to conventional UHMWPE 28mm acetabular inserts evaluated under the same impingement condition.

A significant deformation area was observed at the posterior rim on both impinged liner sizes. Visual observations yielded no cracks at or around the impingement deformation zone of any acetabular liner.

# Discussion

Rim deformation was apparent on all cups tested under the impingement condition. Rim failure or cracking was not found at or around the impingement deformation point of any component, regardless of size or thickness. Although wear rates were increased in both large X3 liners under impingement conditions, the large X3 insert wear rate under the impingement condition remained superior to the conventional PE wear rate and equal to the conservative size 28mm X3 insert. The X3 wear rate ( 2.96mm3/mc) under impingement was superior to conventional PE wear (19.51mm3/mc) under standard ideal conditions.

Increased bearing diameter decreases the chance of implant impingement and increases joint stability. The current impingement wear testing shows that these new larger X3 bearings exhibit superior wear resistance as compared to conventional PE bearings and similar wear rates as smaller sized X3 bearings. These new larger X3 bearings offer decreased chance of impingement as well as reduced overall wear even if impingement occurs.

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# FIXED OR LOOSE? DICHOTOMY IN RSA DATA FOR CEMENTED CUPS

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### Background

Migration by Roentgen Stereometric Analysis (RSA) is said to predict late loosening. This is based on studies on mixed patient groups from the 1980-ies, with a very high loosening risk and large early migration. With modern operating techniques, the early migration is much less. It is not known if a small increase in early RSA migration infers an increased risk of loosening with modern operating techniques. RSA cannot discern whether a single prosthesis is fixed or migrating below the detection level. Samples of patients usually show migration values that appear to be continuously distributed. Is there such continuity, or is there a dichotomy between stable and migrating prostheses? In the latter case, also small migration makes a difference.

The hypothesis of a dichotomy has, to our knowledge, not been tested. This paper presents an exploratory evaluation of such a dichotomy using a mixture distribution algorithm, which is not generally available in commercial statistical packages.

#### Methods

We analysed the migration of 147 cemented acetabular cups of 7 different designs, by use of a new set of algoritms for frequency distribution analysis called Rmix (Reference). The migration vector lengths were assumed to be a compound of log-normal distributions. The algoritm then calculated if the observed frequency distribution is best explained by on or more log-normal distributions. Components of the distribution of migrated distances along each axis were considered to be normal, and analysed similarly. The component corresponding to the stable group was expected to exhibit a zero mean value and a low standard deviation for each axis analyzed.

#### Results

We first analysed a migration vector, regardless of direction. After 2 years there was a significant dichotomy (p=0.006) between 2 lognormal subgroups within the sample (Figure 1). Although some types of cups were over-represented in one of the subgroups, neither cup design, sex or operating department could explain the dichotomy into two groups, which appears to reflect the existence of two basically different types of behaviour of the cups. We next analyzed the migration along the 3 axes in space, and found a similar dichotomy. During the second year, around 80 % of the patients belonged to a distinct, normally distributed subgroup with a mean not different from 0 mm and a small variation, corresponding to the measuring error (Figure 2). The remainder differed significantly from this subgroup and showed migration.

### Interpretation

There is a dichotomy in the migration pattern. During the second postoperative year, the majority of the cups belonged to a subpopulation that appeared completely stable. The unstable remainder is probably at risk of loosening. For a single type of prosthesis, the relative size of the stable subgroup might be a good index of the expected performance. The possibility to detect subgroups within a seemingly continuous sample might become useful in many medical fields.



Figure 1. Frequency distribution of the length of the migration vector (mm) from postop to 2 years. histogram indicates observations. Curves indicate the estimated distributions under the assumption that the material consists of one or more groups with lognormal distribution. Triangles indicate the mean of the 2 subgroups. Dichotomy significant, p=0.006.



Figure 2. Frequency distribution along the y-axis from 1 to 2 years. Histogram indicates observations. Curves

indicate the estimated distributions under the assumption that the material consists of one or more

groups with normal distribution. Triangles indicate the mean of the subgroups.

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www.math.mcmaster.ca/peter/mix/mix.html

# MIGRATION PATTERN IN TOTAL HIP ARTHROPLASTY (THA) AND THE EFFECTS OF A SINGLE-DOSE OF ZOLEDRONIC ACID IN PATIENTS WITH OSTEONECROSIS OF THE FEMORAL HEAD

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Introduction

Aseptic loosening is the most frequent cause of implant failure in total hip arthroplasty (THA). Although cementless implants may be beneficial, failure rate was still found by some authors to be increased in patients with osteonecrosis of the femoral head (ON-FH). Since implant loosening is commonly associated with periprosthetic bone loss in cementless THA, bisphosphonates have been proved to be beneficial by several authors, although a direct link between periprosthetic bone loss and aseptic loosening has not been shown so far. On the other hand, it is well evidenced that low initial fixation and early migration precedes and predicts long-term failure rate of both, the acetabular and femoral component in THA. Moreover, we previously found that revision surgery because of aseptic loosening was linked to an increased early subsidence in patients with ON-FH. For this, implant failure due to aseptic loosening still remains a major concern in THA, while very few is known about the efficacy of bisphosphonates to prevent early implant migration, however.

# Methods

This double-blind, randomized, controlled study was primarily designed to evaluate whether a single infusion of 4 mg of zoledronic acid is sufficient to prevent implant migration determined by the EBRA-digital method. Secondary objectives included assessments of biochemical parameters reflecting bone turnover inter alia. The protocol was developed by the investigators as accepted by the local ethic committee, and the study was performed independently from any industrial sponsorship. Fifty patients were consecutively enrolled between July 2002 and March 2005 to receive either 4 mg zoledronic acid (ZOL) or saline solution (CTR) one day after THA (Zweymüller system, cementless). The main inclusion criterion was the diagnosis of end-stage osteonecrosis of the head based on clinical and radiographic findings, which was confirmed by MRI and/or microscopic examination. The patients had to be willing to complete a minimum follow-up period of 2 years. Plain radiographs were performed postoperatively and all parameters were evaluated at each follow-up meeting interval at 7 weeks, 6 months, 1 year, and yearly thereafter during a median follow-up period of 2.8 years.

# Results

An acute rise in bone resorption markers was found with a peak at 7 weeks after surgery (ICTP, P=0.0001; and



CrossLaps, NS; Wilcoxon Signed Rank test), thereafter continuously decreasing below baseline levels (P<0.05 at 1 and 2 years for CrossLaps and ICTP, Wilcoxon Signed Rank test). The bone formation marker osteocalcin (OC) also significantly increased after THA, but peaked at 6 months (P<0.05, Wilcoxon Signed Rank test) and remained significantly increased during the whole followup period compared to preoperative values. This was accompanied by an increasing subsidence of up to -1.2 mm ± 0.6 SD at 2 years in CTR (P<0.001). Less but a similar, near curve-linear shaped migration pattern was also found for the acetabular component, with an averaged medialization of 0.6 mm  $\pm$  1.0 SD and a cranialization of 0.6 mm  $\pm$  0.8 SD at 2 years (P<0.05, Friedman ANOVA) at 2 years. Treatment with ZOL significantly suppressed the values of CrossLaps within 7 weeks post surgery, which remained significantly decreased during follow-up (P<0.0001, Wilcoxon Signed Rank test) as well when compared to CTR at each follow-up interval (P<0.0001, Mann-Whitney U test). Similarly, the values of OC were also significantly decreased in ZOL compared with CTR during the follow-up (P<0.05, ANOVA), but changes compared to baseline values failed statistical significance (Wilcoxon Signed Rank test). The significant reduction in bone turnover markers was accompanied by a complete prevention of cup migration in both, the transverse and vertical direction (P<0.05, ANOVA), while there was only a trend to a decreased subsidence in stems (-0.91 mm ± 0.51 SD versus -1.18 mm ± 0.64 SD at 2 years after THA).

# Discussion

The study provides useful data which demonstrate that a single infusion of zoledronic acid is a save and sufficient method to reduce and prevent implant migration of THA. Importantly, the migration of the acetabular components was completely prevented by ZOL, suggesting that the migration of cups may be determined primarily by biological factors (i.e., bone remodeling), while the migration of stems may be superimposed by others, non-biological factors, which cannot be substituted by a pharmacological decrease of bone turnover (i.e., mechanical factors). However, these findings are promising and support the suggestions, that bisphosphonates may offer significant opportunities for improving long-term durability of THA and will expediently join the huge family of implant designs for further improvements in the long-term outcome of THA.

# ORAL SESSION 3 Stem Cells

#### **O-012**

# INFLUENCE OF FGF-2 AND PTHRP ON CHONDROGENIC DIFFERENTIATION OF HUMAN MESENCHYMAL STEM CELLS

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#### Introduction

Common in vitro protocols for TGF-] driven chondrogenic differentiation of mesenchymal stem cells (MSCs) lead to hypertrophic differentiation of cells. This might cause major problems for articular cartilage repair strategies based on tissue engineered cartilage constructs derived from these cells. BMPs have been described as alternate inductors of chondrogenesis while PTHrP and FGF-2 seem promising for modulation of chondrogenic hypertrophy. The aim of the resent study was to identify chondrogenic culture conditions avoiding cellular hypertrophy. We analyzed the effect of a broad panel of growth factors alone or in combination with TGF-]3 on MSC pellets cultured in vitro and after transplantation in SCID mice in vivo.

#### **Materials and Methods**

Chondrogenic induction of human bone marrow derived MSC spheroid cultures was modified by addition of factors suspected to stimulate or inhibit chondrogenic hypertrophy. Existence or absence of hypertrophic differentiation was assessed by immunohistochemical analysis (collagen type I, - II, -X, alcianblue), quantitative real-time RT-PCR (Col1A1, Col2A1, Col10A1, MMP-13) and quantification of ALP activity for up to 6 weeks of differentiation. After 6 weeks under chondrogenic conditions in vitro micromasses were transplanted subcutaneously in SCID mice and were investigated immunohistologically after 4 weeks in vivo.

#### **Results and Discussion**

Chondrogenic differentiation was successful after supplementation of the chondrogenic medium by TGF-]3 (10 ng/ml) as confirmed by positive type II collagen and alcian blue staining. None of the other single growth factors (BMP-2, -4, -6, -7, FGF-1, IGF I, 10ng/ml each) led to sufficient chondrogenesis as indicated by negative type II collagen and alcian blue staining. Each of these factors, however, allowed chondrogenesis in combination with TGF-without suppressing collagen type X expression. Combination of TGF-]3 with PTHrP or FGF-2 suppressed COL2A1 and COL10A1 expression and ALP activity, induced MMP13, and prevented differentiation to chondrocyte-like cells when added from day 0. Delayed

# Seminario 10:00 - 11:10 h O 012-019

addition of PTHrP or FGF-2 stopped chondrogenesis at the reached level and repressed ALP activity along with COL2A1 and COL10A1 expression. The treatment of MSC constructs with bFGF or PTHrP in the last 3 weeks before transplantation did not prevented hypertrophy and calcification in vivo.





# CHONDROGENIC DIFFERENTIATION AND STRETCH-ACTIVATED ION CHANNELS

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#### Introduction

Mechanoregulation theories have been proposed to explain how mechanical stimuli may regulate the differentiation of mesenchymal stem cells (MSCs)1. Prendergast et al1 proposed that it is a combination of strain and fluid flow, however few studies have investigated the effects of mechanical stimuli on MSC differentiation in a 3D scaffold. In this study, we hypothesis that cyclic tensile strain will regulate the chondrogenic differentiation of MSCs in a collagen-GAG scaffold2, and that stretchactivated (SA) ion channels are involved in the mechanotransduction process. A poroelastic computational model is also developed to predict the biophysical stimuli generated within the scaffold during cyclic loading.

#### **Materials and Methods**

Bone-marrow derived MSCs were isolated from the tibia and femur of adult male Wistar rats, following CO2 asphyxiation. MSCs were isolated using a plastic adherence technique and expanded for 3 weeks. MSCs were characterized using immunocytochemistry to probe for CD90 and CD105, known markers of MSCs. Flow cytometry was used to quantify the expression of CD90 and CD45, a haematopoietic stem cell marker.

A custom designed 5-station stretching bioreactor was designed and fabricated in-house. Collagen-GAG scaffolds2 were clamped uniaxially, seeded in situ and cultured statically for 7 days to allow for migration. After 2 days, constructs were treated with 10 ng/ml TGF-]1, 50 µM ascorbic acid and 100 nM dexamethasone. A continuous loading regime of 10% strain at 1Hz for 7 days was applied, and a clamped (constrained) group was kept as a control. The rate of sulphated-GAG synthesis per cell was determined. 5 µCi/ml [35S] sulphate radiolabel was added to cultures for the final 24 hours and the counts per minute were normalized to the total cell number, determined using the Hoechst 33258 assay. The involvement of SA-ion channels was assessed by adding 10 µM gadolinium chloride (GdCl3) to the cultures for the duration of the loading.

A poroelastic finite element model of the scaffold was developed in Abaqus 6-6.1 to simulate the experimental conditions and to quantify the biophysical stimuli (strain, fluid flow and pressure) developed.

# **Results and Discussion**

CD90 and CD105 epitopes were present on the MSCs as assessed using immunocytochemistry (data not shown). Flow cytometry demonstrated that 96.9 $\pm$ 0.4% (n=7) of MSCs expressed CD90 and 2.65 $\pm$ 0.8% (n=7) expressed CD45 thereby demonstrating that we obtained a reasonably homogenous population of MSCs.

Application of 10% cyclic strain significantly increased the rate of GAG synthesis compared to the constrained controls (p < 0.001, Fig. 1). The addition of GlCl3 to the stretched group significantly reduced GAG synthesis thereby demonstrating involvement of SA-ion channels in mechanotransduction (p < 0.05, Fig. 1). A significant difference remained between the constrained and stretched groups cultured in the presence of GlCl3 (p < 0.05, Fig. 1) which demonstrates that other mechanotransduction mechanisms must also be active in our model.



Figure 1: 10% cyclic tensile strain increased the rate of GAG synthesis, and 10  $\mu$ M GdCl3 reduced this effect demonstrating involvement of SA-ion channels in mechanotransduction. Two-way ANOVA, \* p < 0.05, \*\*\* p < 0.001, n=5.

A heterogeneous distribution of fluid flows, pressures and strains were developed within the scaffold under 10% cyclic strain. Pressure reached a maximum value of 150 Pa and it is expected that this did not influence cell synthesis as physiological pressures in cartilage during walking are ~7 MPa3. Fluid velocities of 0 - 19  $\mu$ m/s and maximum principal strains up to 23% were developed4 and are comparable to stimuli found to regulate the chondrogenic differentiation of MSCs in an agarose gel5. Additionally, strain6 and fluid flow7 have previously been demonstrated to induce activation of SA-ion channels in chondrocytes.

#### Conclusions

In the presence of TGF-]1, 10% cyclic strain was found to modulate the differentiation of MSCs along the chondrogenic lineage, and involved activation of SA-ion channels. Computational modelling results suggested that strain and fluid flow were the main biophysical stimuli in mediating these responses.

#### Acknowledgements

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36



# POLY-L-LACTIC ACID/HYDROXYAPATITE ELECTROSPUN NANOCOMPOSITES INDUCE CHONDROGENIC DIFFERENTIATION OF MESENCHYMAL STEM CELL

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#### Introduction

The use of mesenchymal stem cells (MSCs) for cartilage and bone tissue engineering has been widely investigated [1-2]. Scaffolds represent the structure of the engineered tissue and establish an environment for the synthesis of neo-extracellular matrix. Moreover, they can release stimuli for modulate cell activity. Advances in stem cell biology have shown that differentiation of MSCs depends primarily on the environment in which they are placed [3].

In this study, we focused on the questions of whether MSC can differentiate when cultured upon a membrane of electrospun fibers of poly-L-lactic acic (PLLA) loaded with nanoparticles of hydroxyapatite (HAp) developed by the authors.

#### Material and method

The PLLA/HAp nanocomposite was prepared by electrospinning technique, starting from a dispersion of Hap nanopowder in a PLLA solution. Briefly, 1 g PLLA was dissolved in 6.5 mL dichloromethane, and 0.1 g Hap were dispersed in the polymer solution.

The obtained suspension were electrospun (DC voltage 15kV, distance 15 cm) forming a non-woven cloth. Microstructure of the membranes was evaluated by Field Emission Scanning Electron Microscopy (FE-SEM). Prior to cell culture test, PLLA/HAp membranes were sterilized, punched out to disk 8 mm in diameter and placed into a 96-well plate. Then a standard static seeding was performed using human bone marrow MSC (passage 2) at the density of 500 103 cell/cm2 [4]. Cells were then cultured either in basal medium (Dulbecco's minimum essential medium (DMEM) supplemented with 10% fetal bovine serum (FBS), 100 units/ml penicillin, 100 µg/ml streptomycin) or Chondrogenic Differentiation Medium (Lonza Biologics). Media were changed every 2 days. 3 days after seeding cell attachment and engraftment was assessed by means of confocal microscopy staining cells on the scaffolds for F-Actin with Rhodamine Phalloidin and nuclei using TOTO as nuclear counterstain. 14 days after seeding the membranes were embedded in OCT, snap frozen, and cut. 7µm slides where immunostained with Antibodies against CD29, SOX-9 and Aggrecan. Nuclei were stained using TOTO. Slides were imaged under the confocal microscope. Slides were also stained

with Toluidine blue and Saflanine O and imaged under a light microscope.

## Results

FE-SEM analysis reveled that the PLLA/HAp membrane obtained was composed of nanofiber of 7  $\mu$ m ±1 of diameter (Fig). The Hap nanopowder was visible on the fiber surface.

3 days after seeding, MSCs were well adhered on the PLLA/HAp fibers with a spindled shape (fig 2). After 14 days of culture all MSCs were positive for the chondrogenic transcription factor SOX-9 in both basal and chondrogenic media groups. Aggrecan was present around the cells. MSCs were either CD29 positive or negative. Toluidine blue and Safranin O staining shown the presences of neo-extracellular-matrix produced around the cells. Cells were mainly localized on the seeding surface of the membrane with few cells localized inside.

#### Discussion

By using a combination of cells biomaterials, tissue engineering offers a technology that will both regenerate the matrix and fully restore normal function to either the bone or the articulating joint. The scaffold must therefore allow maintenance of the cells' phenotype and if possible induces differentiation of progenitor cells. In this study we demonstrated that PLLA/HAp nanocomposites are able to induce differentiation of MSCs in a chondrocyte like cells that produces proteoglycan based matrix as shown by both matrix and immono-staining.

Since HAp is known to have osteoinductive properties [5], the chondrogenic phenotype acquired by the MSCs induced by the PLLA/HAp may be either stable over time or an intermediate stage toward the enchondral bone formation process. The presence of CD29 and SOX-9 double positive cells indicate intermediate differentiation phases.

This nanocomposite could be a susceptible scaffold for bone or cartilage tissue engineering using undifferentiated bone marrow MSCs. Advanced seeding techniques and multiphasic biomaterials should be used for de-novo formation of complex tissue structures by inducing lineage-specific differentiation of pluripotent precursor cells.

#### Conclusion

In conclusion, the PLLA/HAp electrospun nanocomposite membrane induces MSC defferentiation in chondrocyte like cells, therefore is expected to

be good osteochondral tissue scaffold.

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# VITALISATION OF PERACETIC ACID-TREATED BONE ALLOGRAFT WITH HUMAN MESENCHYMAL STEM CELLS

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#### Introduction

Bone grafting is one of the most common orthopaedic procedures1 being indicated for spinal fusion procedures and for the treatment of osseous defects due to trauma, tumor, degenerative or congenital deformities, as well as to infection.

Major drawbacks associated with autologous bone graft are the risk of donor site morbidity and its limited availability.2 Sterilized bone allograft, however, lacking osteoinductive properties, carries the risk of graft failure resulting from insufficient osseointegration of the graft.3

Mesenchymal stem cells (MSCs) can be easily isolated and culture expanded from bone marrow aspirates and provide an excellent source of osteoprogenitor cells due to their ex vivo differentiation and proliferation capacity.4

The aim of this study was therefore to vitalize bone allograft with human osteoprogenitor cells under GMPconform conditions. For this purpose we investigated proliferation, osteogenic differentiation and large-scale gene expression of human MSCs cultured three-dimensionally on peracetic acid (PAA)-treated5 spongious bone chips.

#### **Materials and Methods**

MSCs were isolated from bone marrow aspirates from healthy donors (N=5) by gradient centrifugation and tissue culture polystyrene adhesion, maintained in basic cell culture medium consisting of DMEM supplemented with 10% FCS, and seeded onto PAA-treated spongious bone samples (dimensions ~ 5x5x5 mm, DIZG, Germany) and 6-well plates, respectively, under GMP-conform conditions. Proliferation (total protein assay), osteogenic differentiation (cell-specific alkaline phosphatase (ALP) activity assay, quantitative gene expression analysis of selected osteogenic marker genes), and morphologic evaluation (histology, scanning electron and confocal laser scanning microscopy) were assessed after 1, 7, 21, and 42 days of cultivation. RNA was isolated after 3, 6, and 14 days of observation and microarray analysis was performed using the PIQORTM Stem Cell Microarray system (Miltenyi Biotec) including 942 target sequences.

#### Results

Increasing cellularity was observed during the 42 d observation period of MSC/bone allograft-constructs while cell-specific ALP activity peaked at day 21 (Fig. 1). Figure 2 depicts representative scanning electron micrographs demonstrating effective proliferation and adhesion of human MSCs on PAA-treated spongious bone. This finding was confirmed by histological and confocal laser scanning microscopic evaluation.



Figure 1 Proliferation (left graph) and cell-specific ALP activity assay (right graph) of MSCs cultured on PAA-treated bone allograft



Figure 2 Scanning electron micrographs of human MSCs cultivated on PAA-treated bone allograft for 42 d

Gene expression of early (Runx-2), intermediate (ALP), and late (osteocalcin) osteogenic marker genes was present during 42 days of cultivation period.

Microarray analysis of MSCs cultivated on bone allograft versus two-dimensional tissue culture demonstrated temporal upregulation of genes involved in extracellular matrix synthesis (e.g., matrix metalloproteases, collagens), osteogenesis (e.g., BMP receptor 1b, Runx-2) and angiogenesis (angiopoietin, VEGF). Most of the genes investigated were differentially expressed at day 6 of cultivation.

#### Conclusion

PAA-treated spongious bone allograft is a biocompatible carrier matrix for long-term ex vivo cultivation of MSCs as observed by favorable proliferation, cell distribution, gene expression profile, and persisting osteogenic differentiation in the presence of non-osteogenic cell culture medium. GMP-grade vitalisation of bone allograft by cultivation with autologous MSCs represents a promising clinical application for the treatment of osseous defects.

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### RESISTANCE OF UNDIFFERENTIATED MESENCHYMAL STEM CELLS (HMSCS) TO THE OSTEOGENIC MECHANORESPONSE IN OBESE PATIENTS

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### Introduction

The ability of hMSCs to differentiate into several mesenchymal cell lineages including the osteoblast lineage plays a key role in skeletogenesis and bone regeneration, and a number of studies have convincingly shown the feasibility of MSC grafts for tissue engineering purposes. The induction of differentiation is a highly programmed lineage-specific process and several studies have provided great insight into the microenvironment affecting differentiation of multipotential hMSCs, including hormones, cytokines and growth factors. In this regard, the importance of physical factors in the development and maintenance of bone tissue has been recognized for many years, but only little is known about its effects on undifferentiated hMSCs. The high intrinsic heterogeneity of hMSCs constitutes one of the key characteristics of hMSCs and is thought to represent the high developmental flexibility apparent in undifferentiated stem cells. However, several authors suggested that the functional habits of hMSCs may be profoundly affected by donorspecific biological parameters, e.g., in osteoarthritis, osteoporosis, or even under the conditions of skeletal unloading. The study aimed to determine the early osteogenic differentiation response of undifferentiated hMSCs to physiologically-based mechanical tensile strain with possible contributions to donor-specific physiological conditions.

### Methods

Bone marrow derived hMSCs were isolated from ten donors (5 female and 5 male) undergoing elective orthopaedic surgery. To provide cells in an undifferentiated state, hMSCs were expanded under standard culture conditions for cell growth. Additionally, cells were seeded at low (subconfluent) cell density to prohibit contact inhibition and spontaneous differentiation. In an effort to eliminate possible cofounders influencing cell differentiation not related to mechanical load, the individual response of undifferentiated hMSCs to cyclic tensile strain (CTS) was determined in a two-armed study design (strained versus unstrained (CTR)). Mechanical stimulation was applied with a computer-assisted 4-point bending device, for which uniaxial elongation has been shown to be transferred properly to cell monolayers. The magnitude of tensile strain was restricted to a maximum of 3,000 µstrain in order to avoid a pathological response previously found in monolayer culture systems due to the application of supra-physiological strains.

Phenotypic effects were characterized by analyzing cell numbers, cell viability and ALP activity. The mRNA levels of marker genes for early osteogenic differentiation (RUNX2, ALPL, SPARC, SPP1), protein synthesis (COL1A1), and cell cycle (MKI67) were determined by real-time RT-PCR. To elucidate donor-related variability in the response to CTS, linear correlation analysis was performed between the mechanoresponse of hMSCs and anthropomorphometric variables as well as posthoc measurements of triglycerides, cholesterin, glucose, leptin, adiponectin, resistin, and estradiol within fasting bone marrow plasma, which constitutes part of the biochemical microenvironment of the stem cells in vivo.

### Results

We found a significant up-regulation of the osteogenic marker genes due to CTS, including RUNX2 (1.9 fold), ALPL (2.4 fold), SPP1 (2.8 fold), and SPARC (4.1 fold), which was accompanied by an increase in cell-based ALP activity from 6.1  $\pm$  1.2  $\mu$ M/min/106 in CTR to 8.5  $\pm$  1.7 µM/min/106 in CTS (plus 39.6 ± 9.8% SEM, P<0.05). Cell density was significantly lower following CTS (minus  $20.0 \pm 4.7\%$ , P<0.05), which was accompanied by a reduction in cell viability as tested by XTT (minus 17.8  $\pm$ 5.6%, P<0.05). As a consequence, the ALP activity w/o normalization ranged widely from minus 30.8% to plus 60.1% between individual donors. Linear correlation analyses showed that the phenotypic CTS response reflected in ALP activity and cell numbers was a function of donor's BMI (r=-0.91, P<0.0001), weight (r=-0.73, P=0.016), and age (r=-0.65, P=0.041). Additionally, leptin and estradiol levels determined within bone marrow plasma were significantly correlated to the mechanoresponse (r=-0.71, P=0.028, and r=0.67; P=0.039; respectively). No differences in the osteogenic response were found between male (m) and female (f) donors.

### **Summary and Conclusion**

The findings demonstrate that (i) the application of CTS provides an inherent osteogenic differentiation stimulus for undifferentiated hMSCs in vitro, and (ii) the functional response of hMSCs to CTS was found to be highly related to donor's BMI / fat mass, suggesting an imprinting process of the hMSCs within bone marrow tightly linked to donor-related fat metabolism. This novel findings might be of relevance to some of obesity-linked problems apparent in orthopaedic surgery (e.g., aseptic TEP-loosening, bone healing disturbances, etc.), where it may be speculated that resistance to mechanical stimuli might be involved in the pathogenesis, particularly.

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### O-017

### LARGE-SCALE GENE EXPRESSION PROFILING OF MESENCHYMAL STEM CELLS EXPOSED TO SMOOTH TANTALUM VS. TITANIUM SURFACES

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### Introduction

Metallic implants are widely used in orthopedic, oral and maxillofacial surgery. Advantages of metallic prostheses include their durability in mechanically demanding weight-bearing situations. Durable osseous fixation of an implant requires that osteoprogenitor cells attach and adhere to the implant, proliferate, differentiate into osteoblasts, and produce mineralized matrix. In a previous study, we observed that human mesenchymal stem cells (MSCs) adherent on smooth tantalum (Ta) surfaces demonstrated superior biocompatibility compared with titanium (Ti) coatings.1 In the present study, we investigated the interactions between MSCs and smooth surfaces of Ta and Ti by means of whole-genome microarray technology.

### **Materials and Methods**

Plain float-glass discs of 35 mm in diameter were sputter-coated with Ti and Ta as described previously.1

Immortalized human mesenchymal stem cells2 were cultivated on the surface samples at a density of 50.000 cells/cm2 and cultured in 1% fetal bovine serum at 5% CO2 and 37°C. Total RNA was extracted after culturing for 1, 2, 4, and 8 days using Trizol method. Total RNA samples (n=2/observation period for each type of coating) were hybridized to the Affymetrix Gene Chip Human Genome U133 Plus 2.0.

Replicate arrays were averaged and the ratios of gene expression by MSCs cultivated on Ta versus Ti coating (Ta/Ti ratio) were calculated. Absolute fold differences were also calculated and lists of upregulated genes (threshold 1.5-fold change) were generated for each of the 8 conditions arising from the 2 types of coating and 4 time points investigated. Gene Ontology (GO) annotation analysis of differentially regulated genes was performed using DAVID.3

For cluster analysis, Ta/Ti ratios were filtered based on variance using the arbitrary threshold of standard deviation=0.2 and exclusion of 'absent' probe sets.

### Results

For both Ta and Ti coatings, the vast majority of genes were upregulated after 4 d of cultivation (Fig. 1).

Genes upregulated by MSCs cultivated on Ta coating for 4 d were annotated to the relevant GO terms "cell signaling" and "membrane proteins", "chondroitin sulfate proteoglycan", and "response to wounding". Ti-regulated GO annotation clusters were predominantly transcription-related.



*Fig.1* Number of genes upregulated by MSCs cultivated on tantalum and titanium coating

By using the K-means clustering algorithm, 10 clusters containing more than 5 genes were identified out of a total of 1516 filtered genes. Figure 2 depicts a cluster consisting of 137 genes upregulated by MSCs cultivated on Ta coating which is of special interest in this context. Moreover, various genes related to osteogenesis and cell adhesion were upregulated by MSCs exposed to tantalum surface.



*Fig. 2* Cluster of interest consisting of 137 genes upregulated by MSCs cultivated on tantalum coating for 4 d

### Conclusion

Microarray analysis of MSCs exposed to smooth metallic surfaces of both Ta and Ti generally showed a huge increase in transcriptional activity after 4 d of cultivation. According to GO annotation analysis Ta coating may induce increased adhesion and earlier differentiation of MSCs compared to Ti surface. These findings makes Ta a promising biocompatible material for bone implants and correlates well to previous studies addressing metabolic response and morphological evaluation of MSCs exposed to these types of smooth metallic coatings1.

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### LOW ALKALINE PHOSPHATASE ACTIVITY AND IN VIVO CALCIFICATION AFTER IN VITRO CHONDROGENESIS OF SYNOVIUM-DERIVED MESENCHYMAL STEM CELLS

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### Introduction

Mesenchymal stem cells (MSC) are suitable candidates for the cell-based reconstruction of different tissues including cartilage and have been isolated from different sources such as bone marrow (BMSC), adipose tissue (ATSC) and synovium (SMSC). In ATSC and BMSC hypertrophic markers like collagen type X and alkaline phosphatase (ALP) are known to be up-regulated during in vitro chondrogenesis indicating that MSC do not develop into stable cartilage but rather undergo a differentiation program related to endochondral ossification. As a consequence the MSC-derived cartilage tissue may not fulfil the functional requirements for repair of articular cartilage defects. The aim of this study was to analyze the tendency of BMSC, ATSC and SMSC to undergo hypertrophy during chondrogenic induction in vitro and to evaluate their in vivo development after ectopic transplantation into SCID mice in order to determine which cell source is most suitable for cartilage regeneration.

### **Materials and Methods**

Human BMSC, ATSC and SMSC were cultured under chondrogenic conditions for five weeks. Differentiation was evaluated based on histology, gene expression, and analysis of alkaline phosphatase activity (ALP) in culture supernatants and kryosections of pellets. Expression levels of the cell surface markers CD29, CD34, CD44, CD45, CD73, CD90, CD105, CD146 and CD166 were analyzed by flow cytometry. To evaluate in vivo development, pellets were transplanted subcutaneously into SCID mice after chondrogenic induction for 5 weeks and analyzed 4 weeks later by histology.

### Results

Irrespective of the tissue source, Col2A1 and Col10A1 mRNA was up-regulated during in vitro chondrogenesis in all cultures and Col2A1:Col10A1 ratios were similar. SMSC displayed a low and heterogenic ALP activity in vitro which correlated with calcification of spheroids in vivo. SMSC from only one of five donors calcified, while the other transplants specifically lost their collagen type II, but not collagen type I and proteoglycans in vivo, or were fully degraded. In vitro controls of SMSC transplants which were degraded in vivo displayed similar levels of Col2A1 mRNA expression, but higher levels of MMP-2, MMP-3, MMP-13 mRNA expression.

BMSC and ATSC pellets always underwent vascular in-

vasion, calcification and microossicle formation within 4 weeks in vivo. Compared to ATSC and SMSC, the BMSC populations contained higher fractions of CD146+ cells and displayed high ALP activity after in vitro chondrogenesis. Single BMSC samples had the capacity to undergo a development related to endochondral bone formation resulting in woven bone or fully developed ossicles with hematopoietic tissue surrounded by a bone capsule.

### Conclusion

We conclude that BMSC, ATSC and SMSC have similar tendencies to express collagen type X in vitro, but different tendencies to upregulate ALP enzyme activity which correlated with in vivo calcification. In contrast to articular chondrocytes, neither BMSC nor ATSC or SMSC were able to form stable ectopic cartilage. Possibly due to higher ALP activities and CD146 expression, BMSC rather underwent developmental processes related to endochondral ossification instead of forming stable ectopic cartilage. SMSC in contrast displayed lower ALP activities and ectopic transplants rather tended to undergo fibrous dedifferentiation resulting in degradation.

This study demonstrates that ectopic transplantation of MSC spheroids after chondrogenic in vitro differentiation has the potential to study distinct aspects of ectopic endochondral bone formation as opposed to direct bone formation from MSC in the presence of an osteoconductive carrier. This approach will allow a more detailed understanding of molecular and cellular aspects of chondrogenic differentiation of MSC from different sources and help with their guidance to stable in contrast to transient cartilage. Beside appropriate induction, locking of cells in the desired differentiation state is, thus, a further challenge for adult stem cell-based cartilage repair which could be further dissected for distinct cell populations in this model of ectopic tissue formation.

41



### THE EFFECT OF ALLOGENIC VERSUS AUTOLOGUE MESENCHYMAL STEM CELLS IN BONE RECONSTRUCTION

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### Introduction

In the orthopaedic surgery, whether it is trauma, reconstructive surgery or alloplastic surgery, the need for fast and strong bone regeneration is often essential. In order to obtain these effects, autologue or allogenic bone graft is widely used. This procedure, however, has a number of limitations. For example, a potential infection risk of allogenic bone graft from the donor, and the limitated amount of autologue bone graft. As an alternative, or as a combination, the interest in using mesenchymal stem cells (MSC) in reconstruction of a bone defect has increased drastically during the later years. Several studies have shown that these multipotential cells are capable of inducing an efficient bone reconstruction1, since they have the capability to differentiate into osteblasts, as well as other cell lines. MSC can easily be grown in vitro from a bone marrow aspirate and cryopreserving have no effect on either their growth or osteogenic differentation2 These properties make them easy to handle in the laboratory. Nevertheless, in the clinical practices, this is inconvenience that limits its applications. e.g. bone marrow needs to be harvested from the patient ahead of the surgery that might involve the risk of infection. The aim of the current investigation was to compare the potential effects of allogenic MSC with autologue MSC on bone defect healing using an implant sheep model. Materials and Methods:

Eight adult female sheep were used in this study. Bone marrow was harvested and the MSC was isolated and cultured in a medium consisting of MEM+10%Fetal Bovine Serum (FBS)+1%pen/strep. Each sheep had four implants inserted in 10mm (diameter=depth) drilled bone defects, i.e. bilateral implants were inserted in both medial and lateral distal femur condyles. The implants were cylindrical with a diameter and height of 10 mm. Between the two end caps, there was a tantalum core with a structure that resembles trabecular bone. The diameter of the core was 8 mm, which made a 1mm concentric gap from the surrounding bone to the trabecular metal. The implants were randomly divided into four groups (Table 1), and each sheep had one from each group inserted, hence each sheep was its own control. The sheep were paired two by two, donating the allogene MSC to the other.

Eight weeks after surgery the sheep were euthanized and the implants including the surrounding bone were removed. A destructive push-out test was performed to measure the Shear Failure Energy (SFE), which is the energy needed to detach the actual implant from the surrounding bone, and thereby measuring the degree of bone in growth (bone fixation) into the actual implant. The results were analyzed statistically using one-way ANOVA, and a p-value <0.05 was chosen as significant.

Implant#1	Implant#2	Implant#3	Implant#4
0.5x10 <sup>6</sup> MSC	5x10 <sup>6</sup> MSC	5x10 <sup>6</sup> MSC	Medium*
(autologue)+	(autologue) +	(allogenic) +	
medium	medium	medium	

### Results

The destructive push-out test showed that all four groups had certain degree of bone fixation across the critical gap. Compared to the control with medium alone, only the group with allogenic MSC (group#3) revealed to have a significantly higher mean SFE (Fisher's LSD-test). The other groups (#1 and #2) had a slightly higher mean SFE, but not statistically significant (Figure 1).



Fig 1: Mean Shear Force Energy values for each group with 95% confidence interval.

### **Discussion and Conclusion**

This investigation has demonstrated that MSC has a positive influence on bone regeneration in a critical sized bone defect. The use of allogenic MSC can efficiently be used. Although this study has shown that allogenic MSC is at least as good as the autologue MSC, but due to the limited number of sheep used, further studies are needed, especially in the use of allogenic versus autologue MSC to provide further insight into an alternative bone graft in orthopaedic bone defect healing. This information is essential regarding using allogenic MSC in clinical practices.

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### ORAL SESSION 4 Tissue engineering

### **O-020**

### IN VIVO EVALUATION OF HUMAN FETAL BONE CELLS FOR BONE TISSUE ENGINEERING APPLICATIONS

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### Introduction

Recently, human fetal bone cells were characterized in vitro to investigate their potential use for tissue engineering (1). They were shown to be able to proliferate and differentiate into mature osteoblasts in vitro when seeded on poly(L-lactic acid)/5 %wt]-tricalcium phosphate (PLA/ TCP) scaffolds (2). In the present study, we describe the combination of fetal bone cells with PLA/TCP implants for cortical and trabecular bone repair. Fetal bone cells were used in their proliferating phase without induction of differentiation to evaluate their osteogenic potential in vivo. Cortical and trabecular bone regeneration were assessed in rat cranial defect, respectively in metaphyseal trabecular network of rat femoral condyle with PLA/TCP implants with and without human fetal bone cells.

### **Materials and Methods**

Human fetal bone cells were obtained from our cell bank comprising eight donors at the end of April 2007 (1). Biocomposite scafold made of PLA reinforced by ceramic particles were used in this study (2). Scaffolds were placed in 24-well plates and cells were seeded by direct pipetting at a density of 2x106 cells/scaffold. Wistar rats (females, 84-92 days old, 275-300 g) were used for the femoral condyle models. At sacrificied (2 months; n = 6in each group) femoral sections were obtained. Sections were stained with toluidine blue enabling the distinction between the non-mineralized osteoid and the mineralized bone matrix.

### Results

Histology of femoral samples. 1. PLA/TCP: implants were surrounded by new bone, formed either by prolongations of the cortical shell or by expansions of the metaphysiseal trabecular lattice, confirming the osteoconductivity of these structures. Infiltrations of newly synthesized bone were strong at the periphery of the

### Seminario 11:30 - 12:10 h O 020-024

scaffolds and remained reduced in the center (Fig 1A). 2. PLA/TCP seeded with fetal bone cells: implants were also well anchored into the neighboring bone. Notable stronger infiltrations of new bone were assessed in the volume of the scaffolds when compared with PLA/TCP alone (Fig. 1B).

PLA/TCP PLA/TCP + fetal cells

Fig. 1 Representative photomicrographs of histological femoral sections 2 months after implantation. A) PLA 5% üTCP alone and B) PLA 5% ü-TCP seeded with fetal bone cells.

### Discussion

The aim of this study was to test the association of fetal bone cells with ceramic reinforced PLA scaffolds for tissue engineering. As animal models, the craniotomy and the femoral condyle approaches in rats were chosen to follow cortical and trabecular bone repair processes. Key findings were the observation of complete bone bridging 12 months after implantation in skulls of PLA porous structures seeded with human fetal bone cells, and a strong induction of trabecular bone ingrowth in femoral condyles 2 months after surgery. The osteogenic properties observed in xenogeneic implants might have been reduced due to adverse response of the hosts, as reported with MSCs from rats used in mice, although immunoprivilege of fetal and adult MSCs is described (4). Further studies must be undertaken to evaluate the respective actions of host and donor cells in the healing process observed. A preliminary study showed that human cells were still detectable in cranial implants 4 weeks after surgery. In conclusion, we demonstrate here, the high potential of human fetal bone cells associated with PLA/ceramic composite structures processed by supercritical gas foaming for their use in cortical and trabecular bone repair.

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### Acknowledgements

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ORAL SESSIONS - FRIDAY



### HEPARIN CROSS-LINKED COLLAGEN COATED TCP/HA GRANULES AS A CARRIER FOR BMP-7

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### Introduction

The clinical application of bone morphogenetic proteins (BMPs) offers solutions to many challenging problems in orthopaedics. However, a practical clinical problem is to obtain a controlled release of the BMPs. The collagenous extracellular matrix of bone is considered to be an optimal delivery system for BMPs. The collagen carriers that have been used in clinical studies effect an initial bulk release, followed by a more gradual release thereafter. The attachment of heparin to biomaterials may result in an appropriate matrix for the binding, modulation, and sustained release of biologically active BMPs. Heparin binds to (and modulates) a variety of bioactive components. Binding of growth factors to heparin stabilizes these growth factors, protects them from proteolytic degradation, and prolongs the half-life of BMPs in culture media 20-fold [1]. In addition, heparin has been shown to enhance the osteoblast differentiation induced by BMPs, and recently, it has been shown that heparin stimulates bone formation in-vivo. In the present study, we created a carrier based delivery system with a localized sustained release by loading a heparin cross-linked collagen coated tricalciumphosphate/hydroxyapatite (TCP/HA) bone substitute with BMP-7.

### Methods

### **Preparation of granules**

The TCP/HA granules were composed of 20% HA [Ca10(PO4)6(OH)2] and 80% TCP [Ca3(PO4)2] (BoneSave<sup>™</sup>, Stryker Osteosynthesis, Freiburg, Germany). We used granules with a diameter of 2 to 4 mm. We compared TCP/HA granules, TCP/HA granules coated with crosslinked collagen (TCP/HA-Col) and TCP/HA coated with crosslinked collagen and heparin (TCP/HA-Col-Hep). Insoluble type I collagen was isolated and purified from bovine achilles tendon as described previously [2]. A homogenous 0.5% (w/v) collagen suspension was made and swollen o/n at 4°C. The TCP/HA granules were put in the collagen suspension and frozen individually in liquid nitrogen. Crosslinking of collagen in the presence and absence of 1.2% (w/v) heparin was performed using 1-ethyl-3-(3-dimethyl aminopropyl)carbodiimide (Fluca Chemica, Buchs, Switzerland) and N-hydroxysuccinimide (Fluca Chemica, Buchs, Switzerland) [2]. Subsequently, Chinese hamster ovary-derived recombinant human BMP-7 (25µg/ml; R&D Systems, Minneapolis, MN, USA) was loaded onto the TCP/HA granules by mixing in 150µl 0.9% (w/v) saline solution for 2 hours.



### Characterization of the granules

The granules were characterized using Scanning Electron Microscopy (SEM) to analyze the morphology of the coated collagen with and without heparin. Immunofluorescent assay (IFA) was done to indicate the amount of attached collagen, heparin and BMP-7. The free amino group content of the non-cross-linked and cross-linked TCP/HA-COL-HEP granules were measured spectrophotometrically after a reaction with 2,4,6trinitrobenzene sulfonic acid [2]. The heparin content was determined by hexosamine analysis using p-dimethylaminobenzaldehyde [2]. The amounts of BMP-7 on and the release kinetics of BMP-7 from TCP/HA, TCP/HA-Col and TCP/HA-Col/HEP granules were determined by immerging the granules (50mg) in 1 ml microcentrifuge tubes containing 150 µl phosphate-buffered saline (PBS, pH 7.4) and 0.02% (w/v) sodium azide. The tubes were incubated at 37 °C with continuous agitation. At various time points (0 hours, 2 hours, 1 day, 3 days, 7 days and 14 days), the supernatant and granules were withdrawn. The amounts of BMP-7 in the supernatants were determined with an ELISA kit (Human BMP-7 Duoset, R&D Systems, Minneapolis, MN, USA). In addition, the degraded products (both granules and supernatant) were visualised by staining with 0.2% AgNO3 (Drijfhout, Amsterdam, The Netherlands), 0.2% NH4NO3 (Sigma), 5% Na2CO3 (Fluka Chemica, AG, Buchs, Switzerland) and 1% tungsten acid (Fluka Chemica) [3]. The experiments were performed in triplo.

### Results

SEM analysis showed a highly porous collagen network on both TCP/HA-Col and TCP/HA-Col-Hep granules [Fig.1]. IFA showed heparin and BMP-7 on the granules [Fig.2&3]. Cross-linking in the presence of heparin resulted in a two-fold reduction of free amine groups compared with cross-linking in the absence of heparin. The retention profiles of the TCP/HA, TCP/HA-Col and TCP/HA-Col-Hep are shown in Fig. 4.

### Discussion

The system developed in the present study has several advantages for BMP-7 delivery. The TCP/HA-Col-Hep granules exhibited a sustained release of BMP-7, while BMP-7 was released more rapidly from the TCP/HA and TCP/HA-Col granules. The sustained delivery system is based on the inherent capacity of heparin to bind to various growth factors. This delivery system could probably also be applied to deliver dual or multiple growth factors that have affinities for heparin such as VEGF, BMPs and PDGF, which could synergistically enhance osteogenesis by increasing vascularity. The local and sustained delivery system for BMP-7 developed in this study may provide a powerful modality for bone regeneration. However, it should be further optimized and evaluated in-vivo first.

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### NOVEL NANO-COMPOSITE BIOMATERIAL FOR OSTEOCHONDRAL TISSUE ENGINEERING: PILOT CLINICAL STUDY

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### Introduction

Osteochondral articular defects represent a key concern in orthopedic surgery. Current surgical techniques to repair osteochondral defects lead to poor subchondral bone regeneration and fibrocartilage formation, often associated with joint pain and stiffness. The objective of this pilot clinical study was to test safety and performance of a newly developed type-I collagen-hydroxyapatite (HA) nanostructural bio-mimetic osteochondral (O.C.) scaffold which reproduces cartilage-subchondral bone morphology.

### Methods

A gradient composite O.C. scaffold, based on type-I collagen-HA, was obtained by nucleating collagen fibrils with hydroxyapatite nanoparticles at physiological conditions.

30 cases (9F, 21M, mean age 29,3 years) with knee osteochondral lesions (8 medial femoral condyle, 5 lateral condyle, 12 patella, 8 femoral troclea) were treated with scaffold implantation from January 2007 to July 2007. The lesions size went from 2 cm2 to 6 cm2. All patients achieved minimum 1 year follow up and were clinically evaluated using the International Repair Cartilage Society score. MRI evaluation was performed in all patients and evaluated with MOCART score. In 4 cases second look arthroscopy was performed at 6 months.

### Results

IKDC objective score improved after 1 year showing a normal or nearly normal knee in 80% of patients at 1 year of follow up. Similar results were obtained with the IKDC subjective score and with Tegner score. Cases with previous surgery had the worst results, while associated surgery doesn't influenced significantly the clinical outcome. 1 case failed and were reoperated.

MRI evaluation demonstrated good bone and cartilage formation and only in the failed case no integration of the graft was found. Second look showed good coverage and integration of the graft in patients with good clinical outcome, while deterioration of cartilage with delamination from the subchondral bone was observed in the failed case.

### Conclusions

This open one-step surgery was used for treatment of big osteochondral defects. The results of this technique at short follow-up are encouraging. Better results can be obtained in young patients with no previous surgery. A clinical study with a longer follow up and randomized studies are due to confirm the high potential of this novel O.C. scaffold.



### NOVEL SCAFFOLDS FOR TISSUE ENGINEERING DEVELOPED BY FLOCK TECHNOLOGY SUPPORT CHONDROGENESIS IN VITRO

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### Introduction

Flock technology is a method well known from textile industry. Short fibres are applied almost vertically on a substrate, coated with a flocking adhesive. Until now this technology has not been used in the field of biomaterials although this method offers the possibility to create matrices with anisotropic properties that have a high compressive strength despite of high porosity. Matrices presently used in matrix assisted autologous chontrocyte implantation (MACI) do not show any orientation of the embedded chondrocytes. However column orientation and anisotropic direction of embedded cells and collagen fibers are thought to be necessary for proper cartilage matrix biomechanics. Chondrogenically differentiated mesenchymal stem cells (MSC) derived from bone marrow or adipose tissue appear to be attractive sources for cell therapeutic applications like the treatment of cartilage lesions. Combination of both anisotropic matrices as a guiding structure and MSC could offer new possibilities in the treatment of focal cartilage defects including articular chondrocyte like column orientation of embedded cells and synthesized cartilageous matrix.

### Objective

Our aim was to evaluate whether anisotropic scaffolds produced by electrostatic flocking are capable to support and maintain a cellular cartilaginous phenotype in vitro.

### Methods

Matrices with anisotropic properties were produced by electrostatic flocking. Experiments were performed using a membrane made of mineralised collagen as substrate, gelatine as adhesive and polyamide flock fibres. Chondrogenic cells including bovine chondrocytes, nucleus pulposus cells, bone marrow and adipose tissue derived mesenchymal stem cells were embeded in the scaffolds using a collagen gel as a carrier. Adherence, vitality and proliferation of bone marrow derived mesenchymal stem cells inside the matrices was assessed using confocal laser-scan microscopy. Chondrogenic induction was performed in the presence of TGF-beta 3 over 42 days. Accumulation of proteoglycans was determined by alcian blue quantification and collagen type II synthesis by ELISA after extraction of the newly synthesized cartilaginous matrix.

### Results

46

DAY ORAL SESSION - SATURD

Confocal laser-scan microscopy showed active proliferation of embedded MSC over 42 days as evidenced by DAPI/Phalloidin stain. Vitality of embedded cells remained above 90% over the selected time period. Native cells of cartilagineous tissues as articular chondrocytes and nucleus pulposus cells synthesized proteoglycans and collagen type II, which accumulated in the scaffolds over time. Additionally bone marrow and adipose tissue derived mesenchymal stem cells, embedded in the flock scaffolds differentiated and increased their chondrogenic phenotype over the selected time period as evidenced by the accumulation of proteoglycans extracted after 42 days of in vitro culture.

### Summary

Using laser-scan microscopy and biochemical

analyses we could demonstrate that cells adhered and proliferated well in this new type of scaffold. Furthermore our study showed that the new scaffolds are capable to support induction and maintenance of the chondrogenic phenotype. Therefore we can summarise that flocking is a technology, suitable for fabrication of scaffolds for cell cultivation and cartilage tissue engineering.



# TENDON REGENERATION USING CELL SEEDED SCAFFOLDS IN A RAT MODEL

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### Introduction

Irreparable tendon ruptures constitute a grave clinical problem. Especially in the realm of rotator cuffs, there often is no primary causal therapy available for dehiscent irreparable tendon ruptures. As a sad result, the development of a rotator cuff tear arthropathy of the shoulder is more often than not inevitable. Our study investigates the effects of scaffold based tendon regeneration with special focus on mesenchymal stem cells in a rat model. As scaffolds we used a polyglycol acid (PGA) and a collagen Typ I scaffold. Both have already been tested in various clinical trials for their suitability as cartilage substitute scaffolds.

### Material&Methods:

We used 'native' bone marrow cells and cultivated mesenchymal stem cells that were donated from male rats and were then implanted into female rats which allowed us to verify, after the completion of the experiment, the presence of the cells in the female animals. A fullthickness-defect of 2-3 mm in the middle third of the rats' achilles tendon was created, which was then filled, according to group, with either cell-seeded or not cellseeded scaffolds and, due to the low primary stability of the scaffolds, fixed with a 4-0 suture. After completion of the experiment (12 weeks), a DNA PCR was conducted to verify the existence of male Y-chromosomes in the female regenerated tissue. We determined the maximum tensile load of the regenerated tissue and also had it histological characterized.

### Results

Macroscopically the regenerated tendons were much bigger in diameter, much firmer and also much less elastic than a normal tendon. In the 'mesenchymal stem cells' group the implanted cells could be clearly identified after 12 weeks by DNA PCR. In the biomechanical examination we could show that there was approximately comparable tensile load in both the 'collagen scaffold' group and the 'healthy tendons' control group. The 'PGA scaffold' group achieved a significantly worse result compared to the control group. We could not prove any positive influence of the cells on the mechanical stability of the regenerated tissue. Histological examination showed that there was bone formation in all study groups in a varying intensity.

### Conclusions

Our findings indicate that both collagen and mesenchymal stem cells have stimulating effects on bone formation while the influence of PGA and the absence of mesenchymal stem cells seems to rather reduce ossification. Nevertheless both scaffolds seem to be, in the examined form, unsuitable for tendon replacement in vivo. Further testing needs to be done to improve the scaffolds regarding their primary stability as well as the porosity of their structure, in order to optimize cell seeding. Furthermore we are testing the effect of differentiated tenocytes on the forming of regenerated tissue as well as the influence of various scaffolds on differentiation, regarding the varying ossification tendency of the individual cell types in vitro.

### ORAL SESSION 5 Hip Clinical 1

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### HIP RESURFACINGS IN PATIENTS OVER 65 YEARS OF AGE? A SINGLE SURGEON CASES SERIES OF 111 BIRMINGHAM HIP RESURFACINGS IN 105 PATIENTS.

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Hip Resurfacings in the younger, more active and independent patients are gaining popularity for end stage arthrosis of the hip enabling them to return to almost full activities post surgery. This bone preserving procedure is less well described in the much older population over 65 years of age. Despite good bone quality, independence and active lifestyle, older age seems to be a deterrent for hip resurfacings among most orthopaedic surgeons and the performance of hip resurfacings in patients over 65 years is not well described in the literature.

### AIMS

We analysed the results of Birmingham Hip Resurfacings of a total of 114 patients over the age of 65 to determine radiological and clinical out come.

### Methodology

We did a retrospective analysis of 105 consecutive patients (111 hips) who underwent a Birmingham Hip resurfacing from 2000 to 2006 performed by a single surgeon to determine the radiological and clinical outcome.

Patients who were 65 years and above, with active, independent lifestyle with no severe medical co-morbidities and an acceptable (surgeon defined) T-score on bone density study were included in the study after informed consent. These patients were warned of the increased likelihood of post operative femoral neck fractures before surgery.

A single anaesthetist performed all anaesthesia, and a posterior approach used for the resurfacings. All patients were mobilised between 4-12 hours after surgery using our early mobilization and pain managament technique (Developed by our authors in Sydney, 1999)

Patients follow-up radiographs, preoperative and post operative functions were analysed until the most recent follow-up.

### Results

There were a total of 105 patients (27 females and 78 males) who underwent a Birmingham hip resurfacing between Jan 1999 and Jan 2007. There were 50 left sided and 61 right sided resurfacings (Total 111 resurfacings) with 8 patients having bilateral resurfacings. Mean age of surgery was 69 yrs (65 to 87 yrs) with a mean



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follow up of 3.8 yrs (2 mths to 7.1 yrs).

62 were performed in the age group 65-79 yrs, 33 performed in the 70 to 74 age group, 12 hip resurfacings done in the 75 to 89 age group and 4 done in the 80-89 age group.

4 (3.6%) fracture neck of femora were identified post surgery, all of them after sustaining trauma (falls), all of them were within the first 6 months after surgery. All 4 patients subsequently had reoperation and conversion to a hybrid total hip arthroplasty.

71.3% of the patients were discharged within 24hours (using the multi modal pain management technique described by our our authors in Sydney, Australia, since 1999).

No wound infections, PE or DVT were noted until the most recent follow-up. No dislocations or gross loosening were noted on X-rays until the most recent followup. Clinical outcomes until the most recent follow-up using SF -36 and WOMAC scores showed excellent post operative outcome.

### **Clinical Relevance**

Hip resurfacing is a challenge in patients who are over the age of 65 years of age. Using our selection criteria, hip resurfacings in older patients can be successful and functional outcome may be comparable



### BONE REMODELLING IN THE PROXIMAL FEMUR POST HIP RESURFACING ARTHROPLASTY

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### Introduction

The potential for bone remodeling in the proximal femur may be detrimental to the long term survival of resurfacing prosthesis. Although preservation of bone mineral density in the femoral neck has been reported following resurfacing arthroplasty1, bone resorption underneath the femoral shell and thinning of the femoral neck has been demonstrated2,3, Figures 1 and 2. We present a radiological analysis of the incidence, rate, site of neck thinning and changes observed within the femoral neck, in 100 cases, post resurfacing arthroplasty.

### **Materials and Methods**

Following hip resurfacing arthroplasty, a retrospective analysis of radiological changes in the femoral neck was undertaken for 96 patients (100 hips, 76 males and 24 females), with a minimum of 5 years follow up. The mean age at surgery was 53.8 years. Femoral neck diameter was measured post-operatively at the head neck junction (HNJ) and 5 mm below (J+5), at two years and at 5 years, Figure 3. Pre and post-operative head to neck ratios, femoral head-shaft offset, femoral neck to shaft and implant stem to femoral shaft angles were also measured.

### Results

Two groups of patients were identified with differing rates of reduction in their femoral neck diameter. Over the first two years, Group A (24%) mean reduction was 2.02mm/year while Group B (76%) mean reduction was 0.33 mm/year. At 5 years, the Group A mean reduction was 5.64mm (sd $\pm$ 2.03mm) while Group B reduction was 1.16mm, (sd $\pm$ 0.97mm). The difference was significant at both time points (p<0.01). Larger head-neck ratios were observed in the former group, both pre and post operatively (p<0.01).

### Discussion

We have observed a variable amount of thinning in the femoral neck post resurfacing arthroplasty. The area most affected by this change is at the head-neck junction. The rate of reduction in the femoral neck diameter was found to be greatest in the first two years. The viability of bone underneath the femoral head may be compromised as a consequence of a nonphysiological bone loading mechanism. Finite element analysis has predicted significant stress shielding underneath the femoral head and loading of the mini stem4. Compromised blood supply of the retained epiphyseal remnant may also play a part in femoral head resorption. The head-neck ratios in group A was significantly larger than B. With an increasing femoral head diameter, the epiphyseal portion retained will be larger. A further mechanism that could be influential in the development of femoral neck thinning and bone resorption may be due to fluid pumping mechanism causing osteolytic erosion at the bone cement interface5.

### Conclusion

In conclusion, femoral neck thinning is a phenomenon of unproven aetiology which is affecting almost one quarter of our resurfacing cases. Clinical experience beyond five years suggests that neck thinning is not an innocent process and we advocate further investigations do determine its aetiology and remedy.



Figure 1. AP radiographs (left) post-op, (right) 5 years following hip resurfacing, showing neck thinning.



Figure 2 Retrieved resurfacing, showing resorption underneath femoral head and neck thinning.



Figure 3. Mean neck diameter measured at 2 and 5 years at head-neck junction and 5mm below.

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### HIP RESURFACING ARTHROPLASTY AND FEMORAL NECK FRACTURE: AN ANATOMICAL STUDY

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### Introduction

Femoral neck fracture is a serious complication in hip resurfacing arthroplasty and reducing its risk is a major challenge given the large number of publications on the topic. From a biomechanical point of view geometrical characteristics of the proximal femur have a large impact on the forces and moments acting in the hip joint. These characteristics can easily be changed during surgery, influencing the risk for neck fracture. In order to gain better understanding of the geometrical factors influencing the forces and stresses in the femoral neck and of the risks of influencing them during surgery we have performed an anatomical study.

### **Patients and Methods**

The radiographs of 140 adult patients have been analyzed using ROMAN (Institute of orthopaedics, Oswestry, UK). 85 patients with different characteristics for age, gender, bodyweight, height, and leg-dominancy, have been included in this study.

Certain characteristics of the proximal femur of 49 women aged 36-88 (mean 59.7), height 1.46-1.83 (mean 1.63), weight 50-118 (mean 76.1) and 36 men aged 33-82 (mean 53.8), height 1.52-1.92 (mean 1.74), weight 62-140 (mean 90.1) have been measured bi-laterally and are illustrated in Figure 1: Neck Shaft Angle (NSA), Femoral Head Diameter (FHD), Femoral Neck Diameter (FND), Lateral Neck Height (LNH), Hip Axis Length (HAL), Body Moment Arm (BMA), and Abductor Moment Arm (AMA).



Figure 1: Schematical representation of the proximal femur and the human body centre of gravity. F\_body and F\_Abductor represent the forces acting on the hip joint. Results have been analyzed using the two-sided t-test, whereby p-values less than 0.05 have been considered significant.

### Results

The dimensions in men were significantly larger as in women for the FHD, FND, and HAL, except for the NSA, which was the same. Statistical indication could not be found for influence of leg-dominancy on geometrical

dimensions. A linear relation between the FHD, FND, and LNH shows an increasing FND and LNH by an increasing FHD. The average head-neck ratio for both left and right was about 1.4 and remained constant in age.

Another linear relation was found between the AMA and the LNH and FND showing an increasing LNH and FND by increasing AMA. The ratio between the body and abductor force can be described by the ratio of the BMA and AMA which is about 2.1 for both left and right. This ratio also remains constant in age, but slightly decreases by increasing bodyweight.

### Discussion

The differences in men and women have been analyzed after stratifying the FHD, FND, HAL, and NSA for height and/or weight, and show a significant anatomical difference between men and women.

The relation between FHD and FND indicates that in hip resurfacing arthroplasty the femoral component should be chosen according to the natural FHD.

The ratio between the BMA and AMA in combination with the bodyweight determines the static forces and stresses in the femoral neck. The ratio decreases by increasing bodyweight which relatively decreases the abductor force. The FND and LNH increase by increasing AMA which enabling the femoral neck to handle much greater forces. Interesting to see is that the ratio doesn't change with age, which indicates that the ratio is not affected by loading as older people are considered to be less active. Changing the geometrical properties in surgery would therefore have a considerable influence on the risk for femoral neck fracture.

### Conclusion

As we have seen in this study the influence of the geometrical characteristics on the forces and stresses inside the femoral neck can be enormous and can easily be affected in surgery. Whether and how these characteristics could be changed during surgery in order to minimize the risk for neck fracture is still to be researched.

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### CHANGES OF BONE REMODELLING AND FIXATION OF THE EPOCH STEM DESIGN. 7 YEARS FOLLOW UP IN A RANDOMISED STUDY WITH USE OF RADIOSTEREOMETRY AND DXA

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### Introduction

In a previous report from a randomised study we reported excellent fixation and less proximal periprosthetic bone mineral loss around the Epoch design at 2 years follow up when compared with a solid stem of similar design. We now present the 7 year follow-up.

Patients and Methods. 38 consecutive patients (20 men, 10 women, mean age 57, 41-74, 40 hips) with noninflammatory osteoarthritis were randomised to receive either a cementless porous-coated composite stem with reduced stiffness (Epoch) or a cementless stiff stem with a porous coating (Anatomic). Patients were followed for 7 years with repeated evaluations using radiostereometry, DXA, conventional radiography and Harris Hip Score.

### **Results and Discussion**

At 7 years 1 stem had been revised (Anatomic) due to late infection. There were no other reoperations. Subsidence and stem rotations were close to zero without any difference between the two groups

(p> 0,12). Median wear rates were lower than expected (0.7mm up to 7 years) for both stem designs. At 2 years the loss of bone mineral density was less in Gruen regions 1, 2, 6 and 7 for the Epoch stems (p<0.04), but this difference tended to disappear with time.

At 7 years only the calcar region (Gruen region 7) had significantly denser bone in the Epoch group (p<0.001). The Harris Hip Scores did not differ (median 98, 51-100). No stem was radiographically loose.

Conlusion. The Epoch stem achieved excellent fixation. Wear rates were low despite use of conventionally gamma sterilised polyethylene. This low modulus stem had positive effects on early proximal bone remodelling, but this effect decreased with time.





### EARLY PERIPROSTHETIC BONE REMODE-LLING AROUND CEMENTED AND UNCE-MENTED CUSTOM-MADE FEMORAL COM-PONENTS AND THEIR UNCEMENTED ACETA-BULAR CUPS.

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### Introduction

Peri-prosthetic bone loss is a documented cause of aseptic loosening of the femoral component, mostly leading to re-operation.

We present the results of a prospective longitudinal follow-up study of DXA measurements of the evolution of BMD in patients where the surfaces of the stem and cup are hydroxyapatite coated, the custom made stem can be cemented or uncemented but the cup has always a cementless fixation.

### Materials and methods

86 patients received a total hip arthroplasty (THA) with a standard uncemented cup and an intra operatively manufactured stem prosthesis. Fixation of the stem was cementless (n=30) or partially cemented (n=56). The choice of the stem fixation is determined by the bone quality, the latter is predominantly dependent on the patient's age. Post-operative DXA scans are obtained in peri-prosthetic bone at 10 days, 6 weeks, 3, 6 and 12 months after THA. Peri-prosthetic BMD values in the proximal femur were obtained in the 7 Gruen zones as well as a net average value(1).

A 4 region of interest model (ROI), together with a net value as proposed by Wilkinson et al,(2) is also calculated after the acquisition of the acetabular region with the same software. The analysis of the repeated measurements (% changes in BMD), correcting for the stem fixation, is statistically done using the Proc mixed procedure of the Statistical Analysis Software.

### Results

Bimodal significant femoral BMD changes are found in all Gruen zones except for zone 1 of the cemented group where an immediate recovery is observed. The recovery mostly starts after 6 months of follow-up and the highest remodelling is found in the calcar region reaching even values of -16% at 6 months but no statistical significance was observed between the two groups.

Significant linear losses (p<0.0001) are observed in the pelvis region independent of type of fixation except the opposite change (p<0.01) in the inferior region obser-

ving an immediate recovery in the uncemented group. **Discussion** 

The changes observed in acetabular BMD are in line with earlier findings attributing this phenomenon to the differences in stiffness between the acetabulum and the cup created at the interface between prosthetic implant and the host bone(3). We compared the impact of a cemented stem with a non cemented stem on the bone remodelling of the cup and found that there was a correlation between the type of fixation and the mode of remodelling at the acetabular level. This suggests that a parameter such as the flexibility my have an influence on the bone remodelling at the acetabulum level. The pattern of bone remodelling observed on the different Gruen zones reflects the local load transfer to periprosthetic bone.

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### Acknowledgement

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## RISK STRATIFICATION FOR FAILURE OF A MODULAR HIP IMPLANT

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### Introduction

A modular Hip implant using a new design of a neck module which was attached to the stem of the implant by means of a conical coupling was introduced in 2003 (Falcon®, Varicon®, Mödling Austria). All mechanical examinations for certification purposes were shown eventless in regard to mechanical strength and resistance to failure. However, there occurred fractures at the conical coupling in vivo due to a corrosion phenomenon. This study has been designed to estimate an individual risk stratification for patients who carry this type of implants.

### **Materials and Methods**

For statistical analysis all patients of the author's institution who received the Varicon modular hip stem were evaluated. From March 2003 to December 2004, 170 Varicon® stems were implanted in 167 patients, 103 females and 67 males. At the time of operation their mean body weight was 76,6 kg (51-124) and mean body size was 166,1 cm (145-192). For the neck module there were 4 types available: N: normal length and angle (77 patients), L: long length, normal angle (52 patients), NL: increased offset with long length, reduced angle (37 patients), and SL: short length, reduced angle (4 patients). Between Feb. 2005 and March 2007 there occurred 10 fractures at the conical coupling, 9 males and 1 female, in average 21,6 months (8-33) after the operation. The variety of neck modules used at the fractured stems was: N: 1 L: 3, NL: 6, SL: 0. The average body weight at the operation for patients who had a fractured stem was 96,5 kg (72-124) and the average body size was 174,8 cm (170-180). All fractured stems had been revised with a non-modular implant of similar geometry but manufactured of one single Titanium block (Falcon®, Monocon®). For statistical analysis we estimated univariate logistic Regression models in order to clarify the meaning of the potentially prognostic factors (body weight, age at the operation, body size, gender, type of neck module) for the probability of an implant fracture. The Firth-Correction was used to avoid a distortion of the estimation of parameters due to the small number of events (implant fractures). Based on the results of the univariate analyses we calculated a multiple logistic Regression Model with the prognostic factors of body weight, body size, gender and type of neck module, in order to estimate the probability for an implant fracture for each event1. With these estimated probabilities it is possible to rank the patients according to their degree of risk. To each possible cutoff of the estimated probability, sensitivity and specificity were calculated.

### Results

The overall failure rate in this patient group was 5,9%. The statistical analysis showed a significant correlation between genders and implant fracture (p=0,0028) and type of neck module and implant fracture (p=0,016). Patients who encountered an implant fracture had a statistically significantly higher body weight (p=0,0009) and body size (p<0,0001) if compared with patients without implant fractures. There was no significant difference regarding age at the operation (p=88). Thus, statistically the risk factors were identified: Men have a far higher risk for implant fracture than women, and neck modules of the type L and NL had a significantly higher risk than N and SL. Body weight and body size were also strong risk factors for implant fractures. When patients are ranked according to the individual risk score, the first event of implant fracture occurred at a score of 6.60 (=6.6% probability for implant fracture). If this value is seen as a possible Cutoff, a risk group can be defined of 46 stems out of 170. Sensitivity for this Cutoff is 100% - and the Specificity is 76,9%.

### Discussion

It was possible to statistically define a group of patients, who have an increased risk for implant failure. The specificity of 76,9% however, is weak as it means that only 23,1% of the patients in the risk group actually encountered an implant failure. It has to be taken into account that there must exist parameters, others than these individual factors, that influence the event of failure. Possible factors lie in implantation techniques, which could create an uneven attachment of the neck module. thus enabling local corrosion processes. The risk stratification in this case of implant failure is clinically used to inform the patients at risk and perform a closer followup in 6 months intervals with registration of changes in body weight. We furthermore use hard beam x-rays to investigate the conical coupling for signs of corrosion. The specificity of 76,9% is too low to clinically justify any prophylactic revisions of implant stems at risk.

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1. Heinze, G., and Schemper, M. A solution to the problem of separation in logistic regression. Statistics in Medicine, 21, 16, 2409-2419, 2002.

53

**ORAL SESSION 6** 

**BIOMECANICAL TESTING** 

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**Hip Clinical 2** 

O-031

Ireland

### **Introduction** The number of revision hip arthroplasties being undertaken is increasing. This is in line with our aging population. The cement-in-cement femoral revision technique is a possible method of reducing complications in these complex procedures [1]. It involves simply disimpacting the old stem and cementing a smaller femoral prosthesis into the existing stable femoral cement mantle. During recent in vitro research on the subsidence and

During recent in vitro research on the subsidence and inducible displacement of 125mm cement-in-cement revision stems some interesting findings were observed. A number of the inner cement mantles contained macropores. Microdamage in the cement was also noted, often in proximity to these pores. It was hypothesized that porosity of the cement mantle influenced the subsidence and inducible displacement of the revision stems. The aim of this research was to study this hypothesis by calculating the porosity of the specimens and assessing its relationship to subsidence and inducible displacement.

**RELATIONSHIP BETWEEN CEMENT POROSITY** 

AND PERFORMANCE OF A CEMENT-IN-

CEMENT REVISION HIP CONSTRUCT IN

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### **Materials and Methods**

Primary cement mantles were formed by cementing a large polished stem into sections of tubular stainless steel using PMMA. The primary (and subsequently the revision stems) were inserted into the constructs using a specifically designed insertion rig, which was later At this stage, the specimen was chosen to validated. be in the test group or the control group. If in the test group, it underwent a fatigue of 1 million cycles at a maximum load of 2kN at 10 Hz according to ISO 7206-4 [2]. This was carried out in a specifically designed rig and a fatigue testing machine (Instron Hydraulic 8874). If in the control group, no such fatigue was carried out. Into these fatigued and unfatigued primary mantles, the cement-in-cement procedure was carried out using methods which replicated the in vivo procedure. Both groups were fatigue tested with the same settings as described above. Subsidence of the stems and their inducible displacement was recorded by the actual displacement sensor on the fatigue machine.

On completion of this fatigue, the composites were sectioned in the axial plane in the centre of each of the Gruen zones (Thomas 315, Italy). The surfaces were polished and red dye penetrant (Johnson and Allen Ltd., UK) was applied. They were examined under a microscope (Leica S6D, Germany) and digitally photographed. A composite image of the surface was prepared using



### Aula Magna 15:10 - 16:00 h O 031-036

GIMP software (Free software Foundation, U.S.). These images underwent image analysis (ImageJ software, NIH, U.S.) The total area of porosity (in millimeters squared) was calculated for the inner and outer mantles of each individual section of each specimen. The location of any microdamage in the cement was also noted.

### Results

The mean of the subsidence in the test and the control groups was 0.48mm and 0.49mm (S.D. 0.11, 0.09, n = 10 + 10) respectively. The mean of the inducible displacements was 0.36mm and 0.38mm (S.D. 0.01, 0.01).

Multiple regression and a general linear model selected that subsidence was inversely correlated to the porosity of the inner "fresh cement" in Gruen zones 3 and 5 (p = 0.021, R2 = 0.36)(SPSS, U.S.). These tests also discovered that inducible displacement was inversely correlated to porosity of the inner "fresh cement", again in Gruen zones 3 and 5 (p = 0.001, R2 = 0.61).

23 areas of microdamage were identified in total in all the specimens (13 in the test group and 10 in the control group). No damage was identified at the cementcement interface. 15 areas of microdamage originated from pores.

### Discussion

Decreased inducible displacement was seen with increased porosity in Gruen zone 3 and 5. A possible explanation is that the stem was able to subside more due to the higher porosity. It can then find a more stable position due to an increased wedging effect. The loading and stabilizing forces on the stem are in equilibrium and the stem is more stable.

The most important result in relation to the microdamage analysis is that there was no evidence of significant damage at the cement – cement interface. 65% of the microdamage originated from pores, emphasizing that pores can be initiation sites for damage.

The relationship of subsidence to porosity is not one that would be expected intuitively. The reason for this could be related to the fact that this experiment did not utilize a system of monitoring the migration of the revision stems in purely distal, anterior, or medial directions.

### Conclusion

The subsidence and inducible displacement of these stems is influenced by porosity, specifically by the porosity of the distal inner cement. Microcracks occurred at sites of porosity leading us to advise that the minimisation of porosity is of great importance in this revision technique.

### References

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# **DRAL SESSION - SATURDAY**

### O-032

### INCREASED SUBSIDENCE OF POLISHED AND ANTEVERTED STEMS RANDOMISED COMPARISON BETWEEN 3 SURFACE TREATMENTS OF THE LUBINUS DESIGN: 5 YEAR FOLLOW-UP OF 84 HIPS.

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### Introduction

The Lubinus SP 2 design (Waldemar Link) is the most commonly used cemented hip arthroplasty in Sweden. In 2006 more than 5500 implants were inserted. According to the Annual Report 2006 from the Swedish Hip arthroplasty Register, the 15-year survival is about 95% in a population with an average age of 70 years. The success of the Lubinus implant in Sweden might be related to a number of factors such as implant design, surgical technique and patient selection. Earlier reports1,2 have shown that surface treatment influences the survivorship of tapered hip implants. To assess the role of surface finish for other stem shapes we evaluated three modifications of the Lubinus SP2 stem

### Methods

80 patients (31 male, 49 female, 68 (46-78 years), 84 hips) with non-inflammatory osteoarthritis randomly received either stem type: cemented matte with collar (M, standard design), polymethylmetacrylate-coated with collar (PC) or polished without collar (P, collarless). Component fixation and wear were studied with radiostereometric analysis (RSA) and the bone mineral density was measured with DXA around the stem in 40 patients at 6 months, 1, 2 and 5 years. Non-parametric tests were used for statistical evaluation.

### **Results and Discussion**

The polished design showed increased distal migration at 6 months (Mean and range) P: -0.21mm -0.52 to 0.09, M: -0.07mm -0.34 to 0.26, PC: -0.03 -0.18 to 0.18 and at 5 years P:-0.49mm -1.46 to 0.16, M: -0.18mm -0.80to 0.33, PC: -0.12mm -1.40 to 0.12 (p< 0.0001). This increased subsidence occurred inside the cement mantle. The rotations of the stem did not differ (p>0.4). Neither did the migration of the cemented cup and the wear differ between the 3 groups (p>0.1).

After 1 and 2 years the polished stems had lost significantly less bone mineral in Gruen zones 1, 2, 6 and 7 (p 0.004 to 0.03). After 5 years this difference had disappeared. The Harris Hip Scores at 5 years did not differ. There were no reoperations during the 5-year follow-up and no patients were revised.

### Conclusion

A polished surface without collar on an anteverted stem design resulted in increased subsidence of the stem in-

side the cement mantle up to 2 years. Between 3 and 5 years the subsidence equalized. The period of improved bone remodelling around the polished version coincided with the early period of increased subsidence suggesting that stem motions inside the mantle resulted in a favourable loading of the proximal femur.

### References

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### METALOSIS IN METAL-ON-METAL PPF TO-TAL HIP ARTHROPLASTIES

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### Introduction

The development of metalosis, (osteolytic bone reactions, fluid production, soft tissue necrosis) is a not commonly reported complication after THR. Cases of metalosis have been found following the use of second generation metal-on-metal hip replacements (Beaule et al. 2001). The exact reasons are unknown (Willert et al. 2000), but hypersenstivity reaction is favoured ahead of toxic effects, immun defects and exogen causes (Thomas 2007). The purpose of our study was to analyze metalosis cases in the first consecutive year of metal-on-metal implantation. The phenomenon of metalosis occured at an unpredictable time in situ and was often misinterpreted as a low grade infection.

### **Materials and Methods**

In a retrospective study, we analysed all 173 (102 women and 71 men) primary and single cementless PPF total hip replacements (STRATEC®) with metal-on-metal (low carbide 0.00-0.08% carbon content) articulation of 1995. 1 patient was lost to follow-up, 18 patients were deceased. The average age at the time of surgery was 63.3 years (range: 31 to 76 years). The mean duration of follow-up was 115 months (range: 64 to 149 months). Blood parameters, periarticular histology, bacteriology and in 3 cases i.a. metal analysis were performed. Results: 40 (23.1%) metalosis cases were observed. Revision was done in 29 (16.8%) patients: 3 femur fractures (1 with metalosis), 5 cases of infection and 21 cases of metalosis. The median HHS at follow-up was 95. 18 cases (10.4%) had clinical or radiological metalosis signs as follows: 6 patients (3.2%) had periprosthetic osteolysis and pain, 16 patients (9.2%) had osteolysis without pain and 9 patients (5.2%) had pain without osteolysis in the radiographs. Pain caused by metalosis typically occurred inguinal and at an average time of thirty months postoperatively (range: 5-58 months). Pain in the area of the trochanter major and at initial walking was concomitant. Dislocation was observed in 13 cases at an average time of 44 months with an average cup inclination of 48°. Out of 40 metalosis cases, 10 (25%,  $\emptyset$  47°) dislocations were recorded. At revision surgery in the case of macroscopic metalosis, a smooth, slightly red to orange coloured synovial membrane was found in

the newly formed hip capsule. Extensive necrosis within this synovial membrane was observed and diffuse lymphoplasmacytic infiltrates were noted. In most cases the bursa ileopectinea was highly filled and in this synovia extremely elevated intra-articular metal levels from Cr 32 - 46095 µg/l and Co 30 - 67410 µg/l were detected.

### Conclusions

The results of our analysis provide, that the PPF total hip replacements with low carbide metal-on-metal articulation were not as satisfactory as those of the conventional polyethylene-on-ceramic articulation with a revision rate below 5% at 10 years follow-up (Legenstein et al. 2006). Since 2003 we do not implant or recommend metal-onmetal for total hip arthroplasty anymore. Close radiographic and computertomographic monitoring with high mark on typical osteolysis and exact clinical evaluation is recommended for all patients after total hip arthroplasty with metal-on-metal bearings. Symptoms are minimal and occur late. Low grade infections have to be identified and differentiated. Symtomless patients with severe osteolysis must be detected and head and inlay changes performed.



### ANTERIOR SUPINE INTERMUSCULAR APPROACH FOR TOTAL HIP ARTHROPLASTY: A 90 DEGREE TURN-AROUND

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### Introduction

Due to increasing interest for minimal invasive surgery new techniques are being developed. Besides new methods, old or lesser-practised techniques are reintroduced, as is the case with the anterior supine intermuscular approach for total hip arthroplasty. With the short Smith-Peterson approach and specially designed inserters, placement of a hip prosthesis is possible without dissecting muscles as occurs with lateral approaches or with risk of muscle atrophy as can occur after posterior approach.

To investigate whether this development is favourable, data was gathered prospectively on the first 25 patients receiving uncemented hip arthroplasty through ASI approach in the Reinier de Graaf Groep hospital, Delft, The Netherlands. With this the short term results of the ASI approach and also the depiction the learning curve for this approach and it's potential pitfalls are presented.

### **Materials and Methods**

2 surgeons performed uncemented hip arthroplasty using the ASI approach on 25 consecutive patients (15 and 10 respectively). Both surgeons followed hands-on training with an expert and anatomic specimen course before putting the ASI-approach in practice. Both surgeons were once visited, and assisted at surgery, by the previously mentioned expert, during their series (respectively on patient-number 10 and 5). Surgery was fluoroscopy assisted and performed on a normal radiolucent table, not a extension-table.

The Taperloc stem in combination with the Magnum head and Recap uncemented cup were used (Biomet, Warsaw, USA).

Data was gathered pre- and per-operatively, during hospital stay and on 6 weeks and 3 months follow-up. Patient characteristics, hip function, functional score lists (HHS, Oxford hip, HOOS, SF-12), incision length, per-operative findings and treatment, mobilisation and complications were assessed.

### **Results and Discussion**

At time of submission dataset was not completed nor fully analysed. Further gathering and analysing of data is necessary and depicted results should be interpreted carefully. Final follow up of the patients is achieved for the EORS2008 meeting. Dataset at time of submission exists of 16 patients.

Preliminary results show a steep learning curve for the ASI approach for surgeons experienced in total hip arthroplasty. This is seen by a rapid decline of session duration in consecutive patients: 132 compared to 88 minutes for the first 6 compared to the last 6 patients in our current dataset (spreading: 61-163 minutes).

12 of 16 patients had non-complicated surgery. Two patients after first receiving spinal anaesthesia had to be fully anaesthetised to enable femoral preparation and stem implant. One patient received cemented cup placement due lo lack of grip for the uncemented cup. One patient had a large osteophyte in the rectus femoris, which caused impingement and luxation after hip placement during testing in the theater. After removal of the osteophyte, which was accommodated by the anterior approach, stability was obtained. All patients proved stable on testing during surgery.



Postoperative hospital-stay on average was 5 days. One patient received blood-transfusion due to an haemoglobin level below 5 mmol/l. No further complications were documented during admittance. All patients were able to walk with the aid of two elbow crutches.

On follow-up, patients show good short term results with rapid recovery and mobilisation. All patients show full weight bearing on 6 week follow-up, several without the use of aids. 1 superficial wound infection was seen which was treated with oral antibiotics. 1 patient complained of not being able to raise the operated leg in supine position. This was due to a near complete lesion of the sartorius muscle as was confirmed by ultrasonography.

We realise that our data is non-randomised and noncontrolled. We believe though that critical assessment of every new technique is important and therefore believe that this study brings forth relevant information, especially since articles on this approach are scarce.

Further studies on this topic in the form of prospective randomised clinical trials are in preparation for our clinic. One of the critical steps in the ASI-approach is the mobilisation of the femur. Based on our experience we recommend adequate capsulotomy, especially of the posterior capsule to enable femoral exposition.

### **Conclusions / Summary**

Preliminary results show total hip arthroplasty through anterior supine intermuscular approach without the use of a extension table as a promising development with regard to duration of surgery, in hospital stay, patient mobilisation and satisfaction and short term results. The learning curve for this approach is steep. The trajectory course of wet-lab surgery, hands on visit and expert onsite visit is an excellent method to get acquainted with this new technique. Further analysing of our data will have to confirm our assumptions.



# THE EFFECT OF A KNEE BRACE ON HIP FLEXION AND ADDUCTION.

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### Introduction

Posterior dislocation of replacement hips may occur during hip flexion and adduction. To restrict movement, a hip brace can be used. However, these braces are cumbersome and have a low patient compliance. Knee braces are more comfortable to wear, and also restrict hip movement by tightening the hamstrings. This study investigated the effect of a knee brace on hip flexion and adduction.

### Methods

The movement of 20 normal hips in 20 healthy volunteers aged 25-62, were assessed using a magnetic tracking system (Polhemus Fastrak). Tracking sensors were attached over the iliac crest and lateral thigh. Subjects were then asked to lie on a couch and flex and adduct their hip three times with their knee bent as shown in figures 1 & 2. A knee brace was then applied and the subjects were asked to flex and adduct their hip with the knee extended, as shown in figures 3 & 4. During each movement the tracker recorded hip flexion and adduction angles, with an accuracy of 0.15 degrees.





Fig 1: Neutral

Fig 2 Hip & Knee Flex



Fig 3: Neutral Brace

Fig 4 Brace Flex

### **Results and Discussion**

When the knee was flexed, the mean hip flexion angle was 66.00 (CI95 = 61.1, 70.8). When the knee was braced, the mean hip flexion angle was 35.30 (CI95 = 28.5, 42.1). Hence the knee brace reduced hip flexion by 46

% (30.70). A paired t-test found this highly significant (P << 0.001).

When the knee was flexed, the mean hip adduction angle was 23.70 (Cl95 = 20.6, 26.9). When the knee was braced, the mean hip adduction angle was 21.60 (Cl95 = 19.2, 24.1). Hence the knee brace reduced hip adduction by 9 % (2.10). A paired t-test found this was not significant (P = 0.3).

These results are shown graphically in figure 3.



Figure 3:- Results

### Conclusion

These results indicate that a knee brace can restrict hip flexion by almost 50%. This information may be useful for patients in whom restriction of hip flexion provides hip stability. As the knee brace is more comfortable than the hip brace, a better patient compliance is expected.

### MANAGEMENT OF HIP FRACTURES IN PATIENTS TAKING CLOPIDOGREL (PLAVIX) U Butt, S Reehana, A Malik,

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### Introuction

Plavix is an anti-platelet drug recommended as lifelong treatment by NICE (national institute of clinical governance) for all patients following stoke, MI, and peripheral vascular disease. It stops platelet aggregation and prevents clots formation. Current recommendations are to stop clopidogrel 7 days before elective surgery. Currently there is no such evidence to support delay in the management of hip fracture in patients taking clopidogrel.

### Objective

To determine current practice and literature with regards to management of hip fracture in patients talking clopidogrel admitted to trauma unit and to review outcome with respect to its withdrawal and subsequent timing of surgery

### Method

Retrospective audit was carried out from January 2006 to May 2007. Patients with hip fractures taking clopidogrel were included in our study. We measured mortality and cerebrovascular complications following the surgery in relation to delay in the surgery.

### Results

The mortality following the hip fracture was 25% (3 of 12) at thirty day. Average delay in surgery among these patients was 10 days (7 to 13). Eight patients developed cerebrovascular complications post-operatively in the form of CVA, MI, and PE.

### Conclusion

Delay in operation is associated with increase risk of death and cerebrovascular complication in patients taking clopidogrel. A well designed prospective randomised trial is required to compare outcome following early versus delay surgery in this increasing cohort of patients to provide evidence-based guidelines to optimise patient management.

### **References:**

1: C Morgan, Russel T. Early Mortality After Hip Fractures. Journal of Bone and Joint Surgery 483-489, 2005. 2: Dominic S. Inman. Perioperative Management Of Trauma Patients Admitted On Clopidogrel. Injury Journal. 38, 625-630,

2007



Seminario

O 037-043

### ORAL SESSION 7 Bone

### O-037

### MESOPOROUS BIOCERAMICS COATED WITH PTHRP (107-111) STIMULATES OSTEOBLAS-TIC FUNCTION IN VITRO

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### Introduction

Mesoporous ordered materials with a pore size distribution in the mesoporous range (2-10 nm) have been proposed as matrixes for coating biological agents [1]. SBA-15 is a siliceous material with hexagonal arrangement of tubular pores of 9 nm connected by micropores, a high pore volume and abundant Si–OH groups [2]. These hydrophilic groups interact with specific chemical species to yield hydrophobic Si–O–R structures which can adsorb biological peptides. In this study, nonfunctionalized and functionalized (with C8- or C3-alkyl groups) SBA-15 materials were coated with the C-terminal peptide of parathyroid hormone–related protein (PTHrP) (107-111) to assess their effects in osteoblastic cells in vitro.

### **Materials and Methods**

SBA-15 was prepared following a previously described procedure [3]. Functionalized SBA-15 materials were obtained by dissolving either octyl or propyl trimethoxy-silane (C8 or C3 precursor, respectively) in acetonitrile for 24 h under reflux. These materials were coated with PTHrP (107-111) (or not, controls) by dipping in a solution of this peptide (10 nM) for 24 h at 4 °C. After air drying at room temperature, they were transferred to culture dishes [4].

Mouse osteoblastic MC3T3-E1 cells were cultured in differentiation medium (]-MEM with 10% fetal bovine serum, 50  $\mu$ g/ml ascorbic acid, 10 mM ß-glicerol-2-phosphate) for 2, 4, 6, 8 and 10 days with SBA-15, C8 -SBA-15 and C-3-SBA-15, loaded or not with PTHrP (107-111). Medium was replaced every other day.

Cell viability and proliferation were evaluated by trypan blue exclusion and Celltiter 96 Proliferation Kit (Promega), respectively. Alkaline phosphatase (ALP) activity was determined by colorimetric method based on p-nitrophenyl phosphate hydrolysis. Collagen secretion was evaluated using SircoITM collagen assay (Biocolor). Gene expression of osteoblastic markers [ALP, osteocalcin (OC), osteoprotegerin (OPG), PTHrP, and vascular endothelial growth factor (VEGF)] was analyzed by real-time PCR using an ABI PRISM 7500 system (Applied Biosystems). MC3T3-E1 mineralization was assessed by Alizarin red staining in confluent cells (at day 10).

### Results and Discussion

In MC3T3-E1 cells, PTHrP (107-111)-coated SBA-15 increased cell proliferation (50%), cell viability (20%), and ALP activity (15%) over control within 4 days. At day 2, gene expression of VEGF, PTHrP, and ALP

14:00 - 15:00 h

significantly increased in these cells. At day 8, these changes decreased to control levels. Collagen secretion was elevated (20%) at this time period. PTHrP (107-111)-coated C3 or C8-SBA-15 materials failed to affect either cell proliferation and viability, ALP activity, collagen secretion, or gene expression of the aforementioned markers at day 2 of culture. However, PTHrP (107-111)coated C3-SBA-15 increased cell proliferation, ALP activity and ALP, PTHrP and VEGF gene expression (by 30-40%) at day 4. In contrast, .PTHrP (107-111)-coated C8-SBA-15 did not change either cell proliferation or cell viability for one week of culture. Both the former and collagen secretion slightly increased (10-15%) at day 10. At day 8, this functionalized material affected the gene expression of the osteoblastic products described above in a similar manner to nonfunctionalized SBA-15 at day 2. At day 10, mineralization similarly increased (30-40%) with any of the tested materials coated with the PTHrP peptide in MC3T3-E1 cells.

### Conclusions

SBA-15 mesoporous bioceramics coated with PTHrP (107-111) induced osteoblastic function in vitro. C3- or 8-functionalization of this material postponed but did not abolish this effect of the PTHrP peptide. Our data might have a clinical impact for the putative use of this type of material as functionalized implants in vivo.

### Acknowledgements

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60



THE EFFECTS OF HIGH FREQUENCY, LOW MAGNITUDE MECHANICAL VIBRATIONS USING THE JUVENT DYNAMIC MOTION THERAPY DEVICE ON FRACTURE HEALING IN OESTROGEN DEFICIENT RODENT MODELS.

(Nizam I, Oliver R, Walsh WR)

### BACKGROUND

Osteoporosis is a disease characterized by the progressive loss of bone tissue, a common complication of aging. Peak bone mass is reached at approximately 30 yrs of age and there after bone mass is lost at a rate of 1-2% per year. In females after menopause it can reach 3-5% per year, 3-8 years after menopause.

Osteoporosis is one of the commonest causes of fractures in the older population. In these individuals, prevention of such fractures or enhancing the process of fracture healing is vital to return them to functional capacity as early as possible.

There are several methods used in the enhancement of fracture healing including low-intensity ultrasound, electromagnetic fields, osteoconductive and osteoinductive biomaterials/growth factors and mechanical stimulation. The effects of mechanical stimulation with high frequency, low magnitude vibrations on bone mass in premenopausal women have shown to increase bone mineral density (Beck et al, J Bone Miner Res 2006), and other studies in children by Clint Rubin et al (2004, J bone Min Res) showed mechanical vibrations were anabolic to trabecular bone and increased BMD in postmenopausal

women (Rubin et al, Endoc soc trans 2002). There are no published data on the effects of low mag-

nitude vibrations on the influence of healing fractures especially in an osteoporotic environment.

### AIMS

This study is designed to evaluate the effects of high frequency, low magnitude

vibrations using the Juvent Dynamic Motion therapy (DMT) device on fracture healing in oestrogen deficient rodent models.

### Methodology

20 Sham (non ovarectomised) and 20 ovarectomised Srpague Dawley rats were recruited in the pilot study. At 22 weeks of age, all the rats underwent surgery whereby a k-wire was introduced into the right femur (IM) from the knee to the right hip, then a controlled fracture performed midshaft with 3-point bending pliers.

The animals were divided into subgroups of 3 week Sham and Ovx treated and non-treated and 6 week Sham and Ovx treated and non-treated groups.

The treated animals were vibrated for 20mins daily on a DMT( dynamic motion therapy) platform which has a frequency of 30hz, 8micron vertical displacement and 3g force. The rats were euthanased appropriately at the end of the study protocol, femora harvested and Xrays, Dexa studies, Micro CTs, Histological analysis and Mechanical studies performed.

### Results

Those animals treated with DMT had more bridging callus on radiographical and micro CT analysis than the non-treated groups especially the OVX groups at 3 weeks compared to controls or Shams (assessed using Image J software). DEXA studies showed increased bone mineral density and bone mineral content in the treated animals compared to the controls. Histological analysis showed increased callus and woven bone being laid down in the treated OVX groups.

In the 6-week groups, the treated OVX groups had healed, remodelled fractures compared to the non treated groups or Sham controls where the fracture gaps were still visible. Although significance was not achieved on mechanical analysis due to small sample size, in the OVX non-operated femora group that were treated with DMT there were indications that they may be stronger than the control counterparts.

### Conclusion

As the population increases, so will the number of older individuals with osteoporotic fractures.

Hence preventative measures improving the quality of bone (BMD) and improvements on enhanced healing of such fractures is important. In this pilot study, low magnitude vibrations with the Juvent DMT device seems to enhance fracture healing on oestrogen deficient models. The study is being repeated with larger sample size to obtain reasonable mechanical data and also look at the role of DMT in bone defects.

### EORS 2008 · MADRID



### O-039 EXTRACORPOREAL SHOCK WAVES INDUCE BONE REPAIR ACTION IN MURINE CALVARIA OSTEOBLASTS.

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### Introduction

The osteoclastogenesis is regulated by a complex signaling system between the pro-apoptotic factors (Bax-Cyclin E2-Cdk2) and the tumor necrosis factor family (RANKL-RANK-OPG) (1). Extracorporeal Shock Waves Therapy (ESWT) have recently been used in orthopaedic treatments to induce bone repair (2), but their mechanisms of action are not sufficiently investigated (3). So we studied the effect of shockwaves on murine osteoblastic cells.

### **Materials and Methods**

Osteoblast cultures were subjected to a single shockwave with combinations of low energy intensities (0.05mJ/mm2) and 500 number of shocks (impulses), whereas control cells received no treatment. We valued the cell viability quantifying the expressions of Bax and Opg by PCR.

### **Results and Discussion**

We found an immediate negative effect on cell viability, that occurs with an increase of Bax protein expression after 3 hours of treatment (4). After a longer time lapse a stimulatory effect on cell proliferation, as reflected by the increase of a G(1)-S phase marker, was observed. In fact, in the following 24, 48 and 72 hours after ESW treatment, we found a stronger association of Cyclin E2 and Cdk2, forming active cyclin E-Cdk2 kinase, compared to untreated cells at the same times. We further explored the molecular mechanism for the ESW induction of osteogenesis: by Real Time PCR an enhancement of Runx2 mRNA, evident 48 hours after the treatment, was found. A link between physical ESW and Runx2 activation has been already demonstrated. ESW-induced O2- production, followed by tyrosine kinase mediated ERK activation and Runx2 activation, resulted in osteogenic cell growth and maturation. Moreover, we analyzed the cytokines RANK-L and OPG osteoblast expression, involved in regulation of osteoclastogenesis. A decrease in RANK-L /OPG ratio was found, perhaps leading to a

### Conclusions

reduced osteoclastogenesis.

The Shock waves have a repair action on bone and it can been explained by the regulation on osteoclastogenesis by the apoptoic pathway of BAX and OPG.

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### OSTEOPENIA IN CANCELLOUS BONE OF SHEEP INDUCED BY GLUCOCORTICOID ALONE

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### Introduction

There is a great need for suitable large animal models that closely resemble osteoporosis in humans, and that they have adequate bone size for bone prosthesis and biomaterial research. Previous investigations have shown that osteoporotic sheep model requires glucocorticoid (GC) treatment for a long period of time after ovariectomy (OVX) to induce osteoporosis (1). However, no information in literature is available whether osteoporosis (OP) in sheep can be induced by application of GC alone. This study aimed to investigate effects of GC alone without OVX on three-dimensional (3-D) microarchitectural properties and mechanical properties of sheep cancellous bone after a 7 months steroid treatment; and thus to validate a large animal model for orthopaedic implant/ biomaterial research.

### **Materials and Methods**

Eighteen female sheep were randomly allocated into 3 groups: group 1 (GC-1) received GC (0.60mg/kg/day methylprednisolone) 5 days weekly for 7 months; group 2 (GC-2) received the same treatment regime for 7 months, and further observed for 3 months without GC; and group 3 served as the control group, and left untreated for 7 months. The sheep were housed outdoors, and received restricted diet, i.e. grass pellets (0.55% calcium and 0.35% phosphorus) and hay.

After sacrifice, cancellous bone specimens from 5th lumbar vertebra, distal femur and proximal tibia were micro-CT scanned (vivaCT 40, Scanco Medical AG., Switzerland) to quantify their 3-D microarchitecture(2), and then bone samples were tested compressively (MTS Systems Co., USA) to determine their mechanical properties. At sacrifice, serum samples were collected, and biomarkers for bone formation (Osteocalcin) and resorption (Crosslaps) were determined. The results were analyzed statistically. One-way ANOVA were performed, A p-value <0.05 was considered significant.

### Results

After 7 months of GC treatment. Cancellous bone volume fraction of the 5th lumbar vertebra in the GC-1 group was reduced by -35%, trabecular thickness by -28%, and changed from typical plate structure to a combination of plate and rod structure with increased connectivity by 202% (Fig 1 & Table 1). Bone strength was reduced by 52% (Table 1). Bone formation marker, serum osteocalcin of GC-1, was reduced by 71% at 7 months, but recovered with an increase of 45% at 10 month in the GC-2 group (Fig 1). Similar trends were also seen in the femur and tibia. At 10 months, the GC-2 group had microarchitectural and mechanical properties similar to the level of the control sheep.

### **Discussion and Conclusion**

For the first time we have demonstrated that 7 month high-dose GC on bone density and microarchitecture are comparable with those observed in human after longterm GC treatment. Moreover, we have shown that the bone quality with regard to strength and microarchitecture recovers after 3 months further observation without GC. This suggests that a prolonged administration of GC is needed for long-term observation to keep osteopenic bone. Interestingly, osteocalcin was significantly reduced after 7 months but a rebound phenomenon was observed 3 months after cessation of GC.

In conclusion, this study has validated an osteopenia sheep model. Bone quality was significantly reduced following a 7 months GC-treatment and recovered after further 3 month observation without treatment. The model will be useful in pre-clinical studies.



Fig 1: 3-D microarchitecture of sheep vertebral cancellous bone. Significant microarchitectural changes are observed in the GC-1 group (middle) compared with the control (left). Whereas the control and the GC-2 (right) had similar 3D microarchitecture.

Table 1. Properties of vertebral cancellous bone and biomarkers, compared with CNT, \*p<0.001 (ANOVA)

Microarchitecture	Control	GC-1	GC-2
Bone volume fraction (%)	33±4.3	21±1.3*	33±3.8
Trabecular thickness (µm)	159±1.8	114±5.7*	179±18
Structure model index (-)	-0.8±0.5	0.2±0.2*	-0.8±0.4
Connectivity density (mm <sup>-3</sup> )	4.4±2.1	8.9±2.7*	2.7±0.8
Mechanical	1		
Bone strength (MPa)	22.5±2.9	18±4.5*	23.6±2.8
Biomarker			
Osteocalcin (ng/ml)	25.7±7.7	7.4±0.5*	37.3±7.9
Crosslans (ng/ml)	0.80+0.5	0 74+0 2	0.68+0.2

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### Acknowledgement

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### MECHANOBIOLOGICAL MODELLING OF TIS-SUE DIFFERENTIATION INSIDE A MECHANI-CALLY-CONTROLLED BONE CHAMBER

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### Introduction

The influence of the mechanical environment on tissue differentiation has been widely investigated. However many questions remain about the actual process and the parameters that govern it. It has been proposed that tissue differentiation is driven by a biophysical stimulus which is a combination of fluid flow and octahedral shear strain [1]. In order to further investigate the influence of the mechanical environment on tissue differentiation we have tested this hypothesis within a mechanically controlled bone chamber [2].

The bone chamber consists of a titanium cylinder with two bone ingrowth openings at one end which allow tissue to grow in from the subcortical cancellous bone (Fig. 1a). The interior of the chamber has a 2 mm diameter and it is equipped with a 1.8 mm diameter piston protruding into the chamber for the application of a known pressure to the ingrowth tissue.



Fig. 1: a) Bone chamber [2]. Red arrows point at ingrowth openings b) Finite element model. ----: ux = uy = 0; -----: ux = uy = uz = 0; (iiii) p = 0 (free fluid flow) c) Lattice inside a finite element representing the space for cell proliferation, migration and differentiation.

### Methods

A 3D poroelastic finite element model of the inside of the bone chamber was developed. The model consists of 14200 brick elements  $(0.1 \times 0.1 \times 0.1 \text{ mm})$ . The connections of the tissue with the wall were created by imposing appropriate boundary conditions (Fig. 1b). To model the dispersal of the various cell populations inside the tissue a lattice was created within each finite element, representing a space for both the cell and extracellular matrix (Fig. 1c). Cells migrated and proliferated following a random walk process [3]. The differentiation process of mesenchymal stem cells into fibroblasts, chondrocytes

and osteoblasts was by fluid flow and shear stress [1]. From the FE model shear strain and relative fluid/solid NIvelocity were calculated in each element and depending on these stimuli a tissue phenotype was predicted. The change in tissue phenotype in an element was implemented through a change in mechanical properties in the element. The material properties of the different tissue phenotypes were taken from the literature [3]. At the beginning of the simulation the chamber was assumed to be filled with granulation tissue. A pressure of 2 MPa was applied on the top surface during 3 sec every 12 hours during 3 weeks. The loading conditions correspond to those applied during conducted experiments in rats [2].

### Results

High fluid flow and shear strain at the top and bottom of the chamber favoured tissue differentiation towards fibrous tissue (Fig. 2). In the middle region, bone formed. A cartilage layer between the bone and the fibrous tissue was predicted, which is qualitatively in agreement with the experiments [2].



Fig. 2: a) Predicted evolution of tissue phenotype inside the bone chamber b) Chamber tissue specimen (marrow cavity next to the bottom, followed by a zone of trabecular bone and a zone with chondrocytes [2]).

### Discussion

Although acceptable simulation/experiment comparison is achieved, in reality great variation is found in experiments, whereas our simulations are deterministic. It is clear that deterministic simulations can not capture the nature of tissue differentiation in this chamber. Nonetheless, tissue differentiation algorithms based on fluid/strain stimuli and using lattice models for biological activity are a promising tool in their ability to predict tissue differentiation inside a mechanically-controlled bone chamber.

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# STUDY OF GROWTH FACTORS IN THE CALLUS FRACTURE IN RATS

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### **Abstract Body**

Introduction: In the last years there is an increase in the interest in the study of growth factors that take part in the process of consolidation of the fracture to be used as treatment. The different types of fixations modify the natural process of the fracture healing and the production of growth factors could also be affected.

There is not evidence in the literature of the effect that the intramedullary reaming has on the osteogenesis. We did a study to analyse the effect of intramedullary reaming on the production of growth factors during the process of fracture healing in the femur of rats.

### **Materials and Methods**

We did a pospective study in San Carlos Clinical Hospital from Madrid in which was made a fracture on the femur of 64 adults rats type Sprague-Dawley. The rats were divided in two main groups; each group received one different treatment: 30 rats with intramedullary nailing and 34 rats did not receive any treatment. The rats of each group were sacrificed in 4 different moments: at the 24th hour, 4th, 7th and 15th days after the fracture was done, and we measured the amount of growth factors that appeared in the callus fracture, by anatomopathology study.

### Results

The group in which was done the intramedullar nailing recovered normal walk after surgery. In this group were found more production of BMP and PDGF compared to the control group but did not reveal any significant difference between the groups (p > 0,05). Differences about other growth factors as TGF were not found.

Conclusions: Recently, the use of growth factors has more relevance in clinical practice. The study with rats presents the advantage to be an homogeneous group and so it's very easy to handle, the support and reproduction. The anatomy differences with the human body are the main inconvenient. In the results we have taken, the increase on BMP and PDGF could be produced by the intramedullary reaming by the surgery technique but we would need more studies.

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### INVESTIGATION OF MECHANICAL AND VISCOELASTIC PROPERTIES OF BOVINE BONE USING RESONANT ULTRASOUND SPECTROSCOPY

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### Introduction

Resonant ultrasound spectroscopy (RUS) is a technique that involves scanning the resonance structure of a compact specimen such as cube, parallelepiped, or short cylinder [Maynard J, 1996]. For some low-damping materials, a single measurement yields sufficient resonant frequencies to determine all of the anisotropic elastic constants (up to 21 for a low symmetry crystal) [Migliori A, 1997]. While bone has a high viscoelastic damping at ultrasonic frequency as resonance peaks of a cubical specimen tend to overlap, the usual RUS method must be modified for application to bone. The purpose of this study is to evaluate the applicability of RUS to the determination of bone elastic and viscoelastic properties.

### Method

Bovine bone specimens were rough cut into a cubic shape (~1cm3), and then fine cut with a diamond saw while moist with Ringer's solution. Additional rectangular specimens with 20% ratio between the dimensions (1:0.8:0.64) were prepared to split the fundamental torsion peak.

Three shear moduli from prior ultrasonic tests were assumed initially to obtain effective shear moduli (forward calculation) that govern torsional rigidity of a bar. The calculated effective shear modulus was used to determine the frequency range over which RUS experiments were to be conducted upon a cube of wet bovine bone (backward calculation). The three natural frequencies observed via RUS for the split lowest mode correspond to three effective torsional rigidities.

Parallel tests to obtain the shear moduli were also performed by using ultrasonic shear transducers (1 MHz). These shear moduli from ultrasonic shear tests are compared with the shear moduli from RUS experiment.

### Results



Figure 1 The RUS spectrum of the effective shear moduli (Geff) versus sample position suggests an increased stiffness in the mid part of the bone (Fig.1A). Tensor modulus values Cij from the ultrasonic transmission tests are shown in Fig.1B.



Figure 2. The RUS spectrum of the rectangular bovine sample with a 20% ratio between the dimensions

### Discussion

The overall change in stiffness was suggestive of the hypothesis of increased stiffness in the mid-shaft of the bone. Unfortunately, three tensorial shear moduli could not be obtained due to the high damping of bone (overlapping peaks). However, the parallelepiped specimens provided three split peaks which representing three torsional resonances.

Tensor modulus values versus sample position from RUS were similar to those of ultrasonic transmission tests, but in different magnitude. This was due to the different frequency range of testing. But, classical theories of a viscoelastic continuum predict the stiffness to increase with frequency. A decrease is possible only in non-classical theories which incorporate microvibration of structural elements. Therefore, lower stiffness in transmission ultrasound tests compared with RUS tests needs to be explained by causes other then viscoelastic dispersion in a continuum view, i.e. the influence of the difference in strain gradient direction and magnitude to the apparent stiffness of bone.

For future work, experiments using more rectangular specimens rather than cubes are recommended. Such studies may explore differences from age-related mineralization, or differences in the effects of diet or disease.

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### Acknowledgement

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### ORAL SESSION 8 Ligament and Tendon

### **O-044**

### COMPARTMENTAL PRESSURE, PRE- AND POST- PERCUTANEOUS TENOTOMY OF THE ACHILLES TENDON IN SPASTIC CHILDREN

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### Introduction

Spastic muscles show permanent contraction but also paradoxical muscular weakness. Compartmental muscular pressure in normal subjects oscillates between 0 and 5 mmHg.

### Objective

To study compartmental pressure in the posterior superficial compartment of the leg in children with spastic paralysis, to identify its variations after a percutaneous tenotomy of the Achilles tendon, and to find any possible correlation with arterial pressure or weight.

Materials and Methods: We study 19 cases in 12 patients who had undergone a percutaneous tenotomy of the Achilles tendon. Seven of them were tetraplegic ( bilateral tenotomies) and five hemiplegic. The following variables were taken: age, weight, systolic and diastolic arterial pressure and compartmental pressure of the superficial compartment of the leg, both pre- and post- Achilles tenotomy. The measurement of the compartmental pressure was taken using an automatic calibration monitor (error  $\pm 1$  mmHg). Statistics: Descriptive, non-parametric tests (Wilcoxon, Kruskall- Willis).

### Results

The average age was 9.3 years old, 11 in men and 7.5 in women. 89.5% of the total population was male and 10.5 % female. The average weight was 27.2 Kg, 28.1 Kg in men and 20.5 Kg. in women. Mean systolic pressure was 94.1 mmHg and diastolic pressure 41.3 mmHg. Mean pre-tenotomy compartmental pressure was 12.1 mmHg and 7.9 mmHg post-tenotomy, decreasing 34.5 % (p= 0.08, N.S.). Systolic pressure had no correlation with pre-tenotomy (r = -0.16) or post-tenotomy (r = -0.13) compartmental pressure. Diastolic pressure had no relation (r = -0.36, p = 0.2).

### **Discussion/ Conclusion**

The pressure of the superficial compartment of the leg is higher than normal in spastic patients, decreasing, although not significantly, after a percutaneous tenotomy of the Achilles tendon is performed.

### 15:20 - 15:50 h O 044-047

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### BMP SIGNALLING DURING TENDON REPAIR IS SENSITIVE TO MECHANICAL LOADING. A ROLE FOR FOLLISTATIN?

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### Introduction

Mechanical loading and biochemical signalling both control tissue repair. How they interact is largely unknown. Exogenous GDFs can stimulate tendon repair.1,2 Healing of the rat Achilles tendon is sensitive to mechanical loading, and the strength of the tendon callus is reduced by  $\frac{3}{4}$  after 14 days after Botox injections. The response to exogenous GDFs is also influenced by loading: if loading is prevented, more cartilage and bone is formed.1 This made us believe that BMP signalling is crucial during tendon repair, and that it is influenced by mechanical loading. We therefore studied the role of mechanical loading for BMP signalling in tendons and during tendon healing.

### Materials and methods

Sprague-Dawley rats, female, 67-70 days old were used. The experiment was approved by the regional animals ethics committee. 25 rats received 3U Botox® into the right calf muscles for unloading, and 25 rats were loaded controls. After 5 days, 5 loaded and 5 unloaded tendons were harvested. The remainder underwent tendon transection.1,2 Unrestricted activity was allowed during healing. Tendon regenerates were harvested after 3, 8, 14 and 21 days post-operatively. RNA extraction was performed using a combination of the Trizol method and RNAeasy Total RNA Kit.3 0.1 µg total RNA was reversetranscribed. Primers for OP-1, GDF-5, -6, -7, Follistatin, Noggin, BMP-receptor 1b and BMP-receptor 2 were used for real-time PCR where standard curves were used and each sample was normalized to 18S rRNA. Intact tendons were analysed by t-test and healing tendons were analysed by 2-way Anova, using loading status and time as independent variables.

### Results

50 specimens were analysed for all genes. The genes were expressed at all time-points except noggin that was never detected and GDF-6 in one sample. Loading had no detectable effects on intact tendons. During repair, loading decreased follistatin by more than half (p=0.0001), and increased GDF-5 (p=0.02). All genes showed significant changes during the repair process (p=0.0001), but the time sequences differed (Figure 1). GDF-5 and GDF-7 were generally more expressed compared to OP-1 and GDF-6. GDF-5 and GDF-7 were more expressed in normal tendons than during repair. Follistatin decreased continuously during repair, especially in the loaded tendons.

### Discussion

There was clearly less expression of follistatin in loaded tendons during healing. This finding makes sense: Loading would increase BMP agonist effects, thus mimicking the known effects of exogenous GDFs. Follistatin is expressed around the forming tendon in chicken embryos, where exogenous follistatin inhibits tendon formation.4 With mechanical loading in our model, tendon regenerates double their transverse area. This suggests that delimitation is decreased in parallel with the decrease in follistatin. The mechanosensitivity is likely to be of most importance at day 14 and 21 since the difference in strength between loaded and unloaded tendons is huge. An Anova with only these time points reveals effects of loading on GDF-5 and follistatin (p=0.0001 for both) and significant differences between the days for most variables. Our result also suggests that GDF-5 is specific for the mature tendon, and not much involved in repair. This contrasts to GDF-7, which is involved in both. OP-1 and GDF-6 seem to be involved in early healing. We have not analysed all BMPs, antagonists and receptors, and other factors within the BMP signalling system might play important roles that would change our understanding.



Figure 1. Gene expressions. Vertical axis shows the ratio to a house-keeping gene (18S rRNA). Horizontal axis shows time (days) after tendon transection, where 0 means intact tendons. Unloaded intact tendons were analyzed 5 days after Botox injection. N = 5 for each box. Loaded tendons (L) are darker, and unloaded (U) are lighter.

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### LOW-INTENSITY PULSED ULTRASOUND FOR TENDON HEALING: AN OVERVIEW

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### Introduction

Ultrasound (US) provides mechanical stimulation to the tissues by means of high-frequency, small-amplitude pressure waves. Ultrasound has been shown to have positive biological effects, including increased angiogenic, chondrogenic, and osteogenic activities. An increase in prostaglandin E2 (PGE2) production, osteoblast and fibroblast proliferation, and increased collagen, interleukin, and vascular endothelial growth factor production have been reported to occur with the application of ultrasound.

The aim of our study was to evaluate the evidence available in the scientific literature for the ultrasound treatment for tendon healing.

### **Materials and Methods**

To identify "best evidence" published research a computerized literature search of Medline, Cochrane, PEDro, IME, IBECS and ENFISPO and search of reference lists to find additional studies were realized. Keywords used to identify the study population and interventions were: ultrasound, low intensity pulsed ultrasound (LIPUS), physiotherapy, physical therapy, clinical trial, meta-analysis, practice guideline, randomized controlled trial, review, repair tendon and tendon healing. First titles and abstracts of identified published articles were reviewed to determine the relevancy of the articles. The scientific evidence of the group of selected documents were measured using the scale described by the US Preventive Task Force that defines with level I; those studies with bigger design quality and scientific rigor and with level III those of less. The assignment of the evidence level to each study was evaluated independently by two reviewers without communication among them. To determine interrather reliability Kappa index it was used (K) with a value of CI of 95%. It was carried out an analysis statistical, establishing the absolute and relative proportions with SPSS 13.0 for windows.

### **Results and Discussion**

The study populations were 39 pertinent recovered documents. The analysis of the reliability obtained an index of acceptable Kappa (0.6-0.8).

The findings suggest that therapeutic ultrasound can increase in collagen synthesis and enhance the maturation of collagen fibrils of repairing tendons. Researchers have reported that therapeutic ultrasound could facilitate tissue recovery and US with dosages between 0.125 W/ cm2 and 3 W/cm2 have been used in the treatment of tendon ruptures reported an improvement in both strength and energy absorption capacity of repairing rabbit or rat tendons with 1-MHz continuous US. Also,

pulsed US treatment could lead to better organization of the collagen bundles in the repairing tissue. Best results were: continuous US at 1 MHz, 0.5w/cm2 starting from day 5 after injury (early onset), 20 treatment sessions, 4 mi each session.

However, timing and mode of treatment are important factors affecting the outcome. Most studies with positive results have used continuous US at 1 MHz, but the effect of dosage has not been well-documented. There is not a general consensus on the choice of parameters for US treatment and the evidence for efficacy of therapeutic.

Limits of studies: The time needed to develop such an interface in humans was reported to be much longer than that reported in animal models. In humans, an increased rate of tendon healing would provide a great advantage in reducing the time required to restore normal function.

### **Conclusions / Summary**

Continuous and low-intensity pulsed ultrasound was able to accelerate tendon healing and facilitating earlier physiotherapy.

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### O-047 ELEVATED SYSTEMIC MATRIX METALLOPROTEINASES IN PATIENTS WITH ACHILLES TENDON RUPTURE

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### Introduction

Local dysregulation of the proteolytic matrix metalloproteinases (MMPs) and their tissue inhibitors of metalloproteinases (TIMPs) is a feature of tendon degeneration and rupture.1,2 To assess the role of systemic MMPs and TIMPs in tendon rupture we compared serum MMPs and TIMPs between patients who have previously suffered Achilles tendon rupture and healthy controls. We also followed serum MMPs and TIMPs prospectively in patients with acute tendon rupture.

### Methods

More than three years after injury, we measured serum MMP-1, -2, -3, -7, -8, -9 and -13 and TIMP-1 and -2 in eight patients who had suffered Achilles tendon rupture. Serum was also obtained from 12 blood donors with similar age and sex distribution. In another eight patients, MMPs and TIMPs were followed over time, with samples taken at the time of injury, and after 4, 8 and 24 weeks. MMPs were determined using Fluorokine Multi Analyte Profiling kits (R&D systems) in a Luminex 100 Bioanalyzer. TIMPs were analysed using ELISA kits (R&D systems). The study was approved by the ethics committee and written informed consent was obtained from all patients.

### Results

Patients who had previously suffered tendon rupture had increased levels of MMP-2, -7 and -13 and TIMP-2, as compared to controls (Table). In patients with acute tendon rupture, MMP-2 was the only MMP or TIMP to change significantly over time (p = 0.009). MMP-7 and MMP-13 appeared to be higher than control values already at the time of rupture (Figure).

### Summary

Patients with a history of tendon rupture had elevated serum levels of MMP-2, -7 and -13 and TIMP-2. Changes in MMP-7 and -13 might be present already at the time of rupture. This suggests that disturbances in proteolytic control might render tendons prone to rupture

### Figure

Time course of serum MMPs and TIMPs in patients with acute Achilles tendon rupture (n=8). Data shown as medians (open circles) and interquartile range (bars). As a reference, dotted lines indicate median values of control subjects (n=12).

### References

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### Table

Serum levels of MMPs and TIMPs in patients who have suffered Achilles tendon rupture more than three years ago (n=8) and control blood donors (n=12). All values are given in ng/ml except MMP-13 which is in pg/ml. MMP assays measure pro-MMPs, active MMPs and TIMP-bound MMPs. Data analysed by two-tailed Mann Whitney tests. Confidence intervals are non-parametric.



	Control		Previous tendon rupture		Difference		p-value
	median	95% CI	median	95% CI	median	95 % CI	1
MMP-1/TIMP-1 ratio	12	4 to 25	10	7 to 22	-2	-7 to 9	0.85
MMP-1	2.6	1.1 to 4.1	2.3	1.6 to 3.4	-0.3	-1.4 to 1.3	0.97
MMP-2	155	150 to 160	170	160 to 220	16	5 to 48	0.01
MMP-3	17	12 to 23	17	9 to 32	-0.5	-8 to 14	0.97
MMP-7	1.2	1.0 to 1.3	1.4	1.3 to 1.6	0.2	0.0 to 0.4	0.02
MMP-8	17	10 to 20	21	12 to 28	4	-5 to 14	0.38
MMP-9	519	330 to 740	700	570 to 790	186	-43 to 320	0.15
MMP-13	79	6 to 105	220	170 to 290	143	64 to 223	0.002
TIMP-1	181	150 to 310	190	150 to 270	4	-99 to 72	0.56
TIMP-2	93	76 to 120	130	110 to 140	33.5	5 to 54	0.02

### ORAL SESSION 9 Hip (other)

### **O-048**

### ASSESSING THE INFLUENCE OF BONE REMODELLING ON REVISION RISK OF CEMENTED HIP PROSTHESES: A PATIENT-SPECIFIC RETROSPECTIVE STUDY

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### Introduction

Aseptic loosening can be considered as a combination of both mechanical and biological failure scenarios.1 Mechanical factors, in particular the influence of acrylic bone cement failure, have been widely studied. In particular, such models are well suited to computational modelling and have been shown to have potential in predicting revision risk on a patient-specific basis.2 Biological failure mechanisms are less established in computational failure predictions, in particular for cemented hip replacement. One such biological factor that is amenable to computational simulation is bone remodelling.

This study aims to investigate the influence of including bone remodelling in the simulation of aseptic loosening of cemented hip prostheses.

### Methods

Seventeen patient-specific femoral-side hip replacement models were used from a previous study.2 Early failures were defined to be patients revised due to aseptic loosening in less than 10 years, resulting in 6 early failures and 11 unrevised cases.

A combined strain and damage stimulated bone remodelling algorithm3 was adapted for use on apparent tissue level continuum finite elements. At low strains resorption was assumed to occur through osteoclast activity at a constant rate (Fig. 1). At intermediate strains a 'dead zone' was applied in which cells were assumed quiescent. At strains above an upper threshold bone deposition was assumed to occur due to osteoblast activity. The rate of deposition was assumed to be lower than that for resorption.



Figure 1: Strain and damage adaptive bone remodelling thresholds and tissue adaptation rates

Damage accumulation was also simulated using life fractions derived from S-N curves. Osteoclast resorption was reactivated when damage accumulated above a critical level (Fig. 1). Osteoclast activity was also assumed to remove damage from affected regions as a function of the tissue resorption rate. All cell activity was assumed to occur as a function of surface area for a given



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representative volume element, which was expressed as a function of apparent tissue modulus. Mechanical coupling between damage and strain-adaptive remodelling was also included by allowing the elastic modulus to reduce as a function of accumulated damage.

This model was applied in conjunction with a bone cement and cement-metal interfacial damage accumulation algorithm applied in a previous patient-specific study of the same patient cohort. One year of walking activity was simulated and resultant migration of the prostheses was used to indicate revision risk.

### Results

Preliminary data for 11 of the 17 patients have been simulated at time of writing. Predicted mean resultant migration for the early revisions ( $0.224\pm0.067$  mm; n = 5) was higher than that for unrevised patients ( $0.130\pm0.052$  mm; n = 6). This preliminary trend was significant at a 0.05 level (p=0.014) according to a non-parametric Mann-Whitney test. Ranking the patients by predicted migration placed 4 out of the 5 early revisions in the top 5 highest migrating cases.

Bone remodelling was predicted in the proximal regions (see Gruen zones 1 and 7 in Fig. 2). Greater bone mass changes were predicted for zone 1 compared with zone 7.



Figure 2: Predicted mean normalised increment in bone mass for each Gruen zone for revised and unrevised patient groups

### **Discussion and Conclusions**

Preliminary results thus indicate that addition of bone remodelling to the simulations retained the ability to differentiate between early revisions and unrevised patients as predicted in the previous study that included only mechanical failure mechanisms.2 However, unrealistic remodelling was predicted for Gruen zone 1. This may be due to oversimplification of the muscle loading in this region or deficiencies in the bone remodelling rule and will be a subject of future investigation.

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### EORS 2008 · MADRID



O-049

### ASSESSING THE INFLUENCE OF BONE PROPERTIES AND ANATOMICAL ACCURACY ON COMPUTATIONAL PREDICTION OF REVISION RISK OF CEMENTED HIP PROSTHESES

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### Introduction

Computational modelling has the potential of becoming a useful tool in assessing revision risk on a patient-specific basis.1 However, there are many difficulties encountered in generating patient-specific computational models that have unknown influences on such predictions, e.g. accuracy of the anatomical geometry and material properties of the patient.

This study compares the influence of these two patientspecific parameters on predictions of revision risk due to aseptic loosening.

### Methods

Antero-posterior pelvic/femoral X-rays of 17 patients with one or both hips replaced were used to generate a study set. Six of the patients had their hip replacement revised in less than 10 years (early revisions), while the other 11 cases remained unrevised at the same period of time.

Two sets of finite element meshes were used in the study. The first set was taken from a previous study1 in which the extra-cortical geometries were generated by rigid scaling of a generic femur to match selected dimensions from each patient's post-operative X-ray. A second set was created using a more automated technique that generates 3D extra-cortical geometries from planar X-rays using a combination of 2D contour extraction and 3D warping of a generic model to match the extracted contour.2 Femoral resection and prosthesis positioning were applied using the post-operative X-rays as a visual guide (Fig. 1).

Bone properties were also varied for each of the previous geometric sets. First, constant cortical and cancellous bone apparent Young's moduli were assumed. A second set was generated using age dependent Young's moduli for each bone type.

A cement and cement-metal interfacial damage accumulation algorithm developed for the patient-specific study1 was applied to all models. One year of walking and stair-climbing activity was simulated and resultant migration of the prostheses was used to indicate revision risk.

### Results

72

Preliminary results have been obtained for 3 sets of simulations at time of writing (Table 1). Including age-dependent properties increased mean predicted migration and the strength of the difference between revised and unrevised groups for the first group of meshes. However, incorporating more realistically matched geometries reversed this trend.



Fig. 1: Example patient-X-ray and corresponding mesh from second geometry set

Table 1: Mean predicted migrations (mm) for 3 sets of simulations. Mann-Whitney tests were used to assess strength of difference in each case

### Geometric Set 1 (Lennon et al, 2007)

<b>Bone Properties</b>	Revis	ed	Unr	evi	sed	p
Constant	0.183 ±	0.100	0,107	±	0.068	0,066
Age-dependent	0.218 ±	0.081	0.112	÷	0.069	0.008
State of the second						
Geometric Set 2	(Current S	study)				
Geometric Set 2 Bone Properties	(Current S Revis	study) ed	Unr	evi	sed	p

### **Discussion and Conclusions**

Preliminary results indicate that both material properties and geometric accuracy influence the strength of computational predictions of revision risk. Unexpectedly, the use of more realistic geometries weakened the strength of predictions. This is most likely to be due to ongoing mesh-induced contact problems arising from the more automated generation of these models. More sophisticated statistical analysis will be possible when the full complement of simulations has been obtained.

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### ACETABULOPLASY INCREASED QUALITY OF LIFE IN PATIENTS AFFECTED BY ACETABU-LAR METASTASIS OF CARCINOMA.

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### Aim

pain is the main symptom of acetabular osteolysis due to metastatic carcinoma and is frequently associated to pathologic fractures. Radiotherapy alone usually is not effective for obtaining pain control and allowing weight bearing. Surgical procedures requiring an aggressive approach and as a consequence high morbidity are rarely indicated in multiple metastatic patients. PMMA has been widely used in neoplastic and spinal surgery as a bone filler, for his mechanical and biologic behaviours. The aim of the study was to evaluate the functional results of percutaneous injection of PMMA for the treatment of acetabular osteolysis due to metastatic carcinoma.

### **Materials and Methods**

Under spinal anaesthesia, through a dual portal approach, bone cement was introduced in the acetabulum under fluoroscopic control. The technique was tested upon 25 patients affected by secondary lesions (total 30 cases). The patients were evaluated clinically (ECOG,

HHS, Womac, VAS, SF-36) and radiografically (X-Ray and TC) upon 18 months.

The results obtained by means of the evaluation forms were statistically validated by ] 2 Test, and verified with Foster's exact test P < 0.05 was considered significant

### Results

All the patients demonstrated a significant improvement in term of pain and restore of function within 3 months (p<0.001 for all the different tests). After this period pain begun to recur, but it was still inferior with respect to the preoperative one. A worsening of the general condition was observed 1 year after the surgery, due to the death of 10 patients

Complications related to procedure as temporary increase of pain and fever disappeared within 4 days postoperatively were observed in 4 patients, while intravenous injection of PMMA without clinical symptoms was observed in 2 cases.

### Discussion

The results obtained demonstrated the easy reliability and effectiveness of this procedure. Clinical results showed a significant reduction of pain and the capability of restore the function. The indications can be extended also to the acetabular lesion at distance from the weight bearing zone reducing pain and the risk of pathologic fractures. The technique demonstrated to be effective in improving the quality of life of these metastatic patients.

### THE EFFECT OF HIP ROTATION ON BONE MINERAL DENSITY (BMD) AFTER RESURFACING TOTAL HIP ARTHROPLASTY (RTHA)

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### Introduction

Stress shielding is thought to relate to postoperative bone loss in total hip arthroplasty (THA). RTHA is claimed to transfer stress naturally to the femur neck and proximal femur avoiding stress shielding and thereby maintaining the bone stock. Dual-Energy-X-ray-Absorptiometry (DEXA) is used to detect BMD changes adjacent to a standard femoral stem. Due to the anteversion of the femur neck, the optimal scan is with the hip in internal rotation. Pain can compromise the internal rotation, thus impair acquisition of comparable scans in longitudinal studies. None of the DEXA studies on RTHA (1,2) have investigated the effect of rotation. We aimed to investigate the reproducibility of BMD in the femoral neck surrounding a resurfacing prosthesis, and to establish whether rotation of the hip affects the precision.

### **Methods and Materials**

15 patients (11 men and 4 women, 7 right and 8 left hips) aged 38 to 73 years at the time of surgery were included. Median time from surgery to DEXA scan was 11 months. All patients were operated with an ASR (DePuy®, Warsaw) RTHA. A Hologic 4500A (Waltham, MA) DXA-scanner was used to measure BMD applying the metal removal software. With the patient in supine position, the foot, leg and femur was strapped in a hard shell designed to ensure hip rotation at either 0°, 15°internal or 15°external during scanning. Measurements were repeated after complete repositioning in order to calculate the precision of the method in each position. BMD was analysed in the total femoral neck as well as in 6 smaller identical size regions of interest (ROI) described by Kishida; 3 medial (M1-3) and 3 lateral (L1-3) to the small stem. Statistics: Data are presented as mean and range in brackets. The 95% level was chosen for statistical significance. Standard Deviations (SD) were calculated on the differences and Coefficient of variations (CV) were computed as CV = SD\*100/mean BMD. For a conservative estimate of rotation effect, the SD of rotation was compared to the higher of two possible SDs from the repeated study. The CV in the rotation study was likewise computed using the higher of two potential BMDs. STATA 9.2 (StataCorp, Texas) software was used.

### Results

We found the reproducibility, for the combined rotations of the 6 ROI model, good with a mean SD of 0.044 gr/ cm2 (range 0.027- 0.074), corresponding to a mean CV



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of 4.6% (range 2.2% - 8.6%). In some sub- regions, the reproducibility was significantly lower with the hip in 15° external rotation. Leaving out this rotation the mean CV fell to 4.0%. When we compared BMD of the same region but in different rotations, the mean SD more than doubled to 0.109 gr/cm2 (range 0.034 -0.313), corresponding to a mean CV of 11.8% (range 2.7% - 36.3%). The differences were significant for the distal collum (M3, L2 and L3). The reproducibility for the combined rotations of the total femoral neck was high with a mean CV of 3.1% (range 2.5% - 3.7%). Over a 30° rotation arch, the precision of the total femoral neck was significantly affected with CV increasing to 7.2%. The CV-increase to 3.5% for 15° internal to neutral or 5.5% for neutral to 15° external did not reach statistical significance.

### Discussion

To our knowledge, this is the first study to evaluate the effect of hip rotation on BMD in the femoral neck around a RTHA. DEXA-scanning is a well-known method in estimating BMD in the Gruen zones around a standard femoral hip stem. When detailed information about regional BMD changes in the total femoral neck is required, the region must be divided into several segments. Our study demonstrates that with the leg properly fixated, CVs in a 6 ROI model match those found in Gruen zones (3-7), and clinical relevant changes in BMD can be diagnosed. The external rotation seemed to produce less consistent results. Perhaps the patients were more uncomfortable in this position and fought the rotation a little? The controlled rotation in the present study was used to illustrate the robustness of the method in a longitudinal study where the hip might be scanned in different rotations during the follow-up period. In the Gruen zones around a traditional THA, rotation affects the CV to a somewhat smaller extent in most studies (4,5,8). The present study clearly demonstrates that rotation has a substantial effect in the femur neck area. Rotation compromises the precision and thereby the detectable BMD changes. Within the sub-regions, the effect is most pronounced in the distal part of the femoral neck. It is logical, as this part of the bone over a rotation arch has the largest change of area. In the situation where less topographical detail is called for, the total femoral neck BMD might be adequate. This region is more precise than 6 ROI model and our data suggests that smaller rotations can be allowed without compromising the precision. Conclusions / Summary: This study demonstrates that DEXA is a reliable method to measure changes in femoral neck BMD around a RTHA. Rotation and patient positioning, however, are essential. We recommend that future longitudinal DEXA studies including RTHA be performed in a standardised fashion, with the hip in the

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neutral or internal rotation.

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# LEG LENGTH MEASUREMENT IN THA BY DIGITAL FUSION RADIOGRAPHY DFR

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# Introduction

Leg length discrepancies LLD after Total Hip Arthroplasty are a frequent cause for patient discomfort1. The surgeon's goal is to achieve equal leg length in a standing position. Usually this means to compensate the loss of length due to the pathology of the joint. However, there are many causes for an unequal limb length apart from the hip joint like an oblique pelvis or length variations in the remaining leg. In standard radiographs inaccuracies are due to single focus images causing an inherent distortion and varying focal distances. The Digital Fusion Radiography (DFR) uses multifocal scanned images of the limb in a standing position, which can provide an accurate measurement of distances and angles of the skeleton. We compared preoperative and postoperative DFR measurements with clinical measurements to evaluate the reproducibility and clinical relevance of DFR.

### **Material and Methods**

11 patients (5 female, 6 male, ø age: 62,7, Diagnosis: Coxarthrosis 4, CDH 7, Posttraumatic 1) underwent THA (9 Falcon medical®, 2 Zimmer®). Pre- and postoperative Digital Fusion Radiographs were taken. DFR is performed in standing position of the patient by means of a Digital Image Intensifier Tomography (Philips® Omni Diagnost) lasting approx. 5 Minutes. The line images are fused electronically to a full-length radiograph thus providing a scanned composition of single focus images with standardized focal distance and width over the full length of the limb. Therefore distortions and parallax errors are avoided. Measurements are taken digitally on screen by interactively determining landmarks while distances are calculated automatically (Phillips® Digital Spot Imaging R.5.). We used as landmarks: Hip centre of rotation (centre of the head), Acetabular shelf, upper margin of the Foramen Obturatorium, a tangent to the lower margin of the Os Ischium, lower margin of the lesser Trochanter, lower margin of the Femoral Condyles, upper margin of the Tibial Condyles and upper margin of the Talus roll. The leg length difference to the contralateral leg was calculated from the difference in the distance between the Talus and the Os Ischium. The distance between the femoral Condyles and the lesser Trochanter served as control. The post-operative DFR's were taken minimum 4 weeks after operation to ensure free standing with evenly distributed load on both legs. Clinical measurements of the leg length were performed pre- and postoperatively in supine position by manually determining the position of the Pelvis through the anterior Spines, positioning of the legs in a 90 degree angle to the pelvic plane, and measuring the distance between

the distal margins of the medial Malleoli.



FIG. I
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# Results

Measurements are given in Table 1

Pat		Clin.			DFR			Cont	-
#	pre	post	Δ	pre	post	Δ	pre	post	Δ
1	-10	0	1 0	-5	4	9	355	355	0
2	-15	8	23	-18	-1	17	354	350	-4
3	10	15	5	-1	4	5	381	378	-3
4	0	0	0	1	3	2	329	325	-4
5	-20	0	20	-9	2	11	339	338	-1
6	-10	0	1 0	-6	-5	1	369	363	-7
7	-5	0	5	1	6	5	364	378	14
8	-10	0	1 0	7	3	-4	374	377	3
9	-10	0	1 0	-2	4	6	315	316	1
10	-30	3	3	-11	0	11	381	380	-1
11	-5	10	1 5	-9	5	14	347	347	0
ø	9,5	3,3	1 2, 8	4,7	2,3	7,0	355, 2	355, 2	0,2

Table 1. mm of leg length difference LLD to the contralateral leg

# **Discussion and Conclusion**

With DFR the source of length discrepancies can clearly be determined. Pre- and postoperative DFR measurements were highly comparable and reproducible. Yet, length differences occur (Tab.1, case 7) that can be due to different leg positions like a preoperative flexion contracture resulting in a projection error of up to 14mm. Clinical examination showed preop. 50% and postop. 33% higher values in average if compared to DFR. This might be due to the inaccuracy of manually defining anatomical landmarks in supine position. In 10 out of 11 cases the lengthening of the operated leg was recognised by both techniques with variations in the total amount.

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# EORS 2008 · MADRID



# O-053

# A COMPREHENSIVE VALIDATION OF A NEW METHOD FOR CORRECTION OF RADIOGRAPHIC HIP PARAMETERS FOR PELVIC MALPOSITIONING

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# Introduction

Reliable diagnosis of hip diseases is substantially based on the correct interpretation of anteroposterior (AP) pelvic radiographs. However, most radiographic hip parameters vary considerably with individual pelvic tilt and rotation. We questioned if recently developed software for correction of radiographic hip parameters is (1) accurate, (2) valid, and (3) reliable/reproducible.

# **Materials & Methods**

The 3D conical geometrical model of the software Hip2Norm [1] comprises the assumption that all points of the acetabular rim are lying on a sphere (Figure). The software then calculates based on linear radiographic indices the projected acetabular rim and 23 measured hip parameters as if obtained in a standardized neutral orientation.



(1) External validation comprised the comparison of the computed values of every single parameter from radiographs of 40 cadaver hips in an arbitrarily chosen, unknown orientation with the reference values detected on xrays or computed tomography [2] in a neutral orientation.

(2) Internal validity was achieved by comparing the agreement of normalized values of each radiographic parameter for 20 cadaver pelves when calculated back from seven non-standardized positions to the individual neutral orientation.

(3) The interobserver reliability/intraobserver reproducibility of all parameters with the developed software was investigated in a clinical series consisting of 51 consecutive patients (100 evaluable hips). Their AP pelvic radiographs were analysed twice by two independent examiners blinded to the clinical data and details of the radiological report. Bland-Altman plots were used to detect any systematical errors of the external validation. Agreement was judged with the Kappa value or the intraclass correlation coefficient (ICC).

# Results

(1) No systematical errors were detected for any of the parameters. All except two values showed a good to very good accuracy for the comparison with conventional radiographs. A moderate accuracy was found for the acetabular index and the ACE angle.

(2) In terms of internal validity, the calculations of each parameter back to the neutral orientation achieved a good to very good validity for all computed values.

(3) A good to very good intraobserver variability was found for all parameters except for the reproducibility of the anteromedial coverage in craniocaudal direction for one observer. The interobserver reliability was good to very good for all parameters except the posteromedial craniocaudal coverage, the acetabular index, the ACM angle, the retroversion index and the ACE angle where moderate ICCs were found.

# Discussion

This study proves that most of the radiographic hip parameters can be corrected accurately and reliably with the proposed software. Some restrictions to this method do apply. It can only be used in hips with a more or less spherical joint configuration. In addition, good quality xrays taken under appropriate conditions are necessary to be able to trace the anterior and posterior rim of the acetabulum. Hip2Norm is able to evaluate the clinical relevance of the effect of pelvic malpositioning on the appearance of the acetabular morphology. In addition, it can be applied to hips with impingement, dysplasia and normal acetabular morphology to establish normalized radiographical guidelines for under- and overcoverage.

# Summary

This validated computer-assisted method allows standardized evaluation of all relevant radiographic parameters for evaluation of anatomic morphologic hip differences, making their clinical relevance for development of early hip osteoarthritis more valuable.

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# DEVELOPMENT OF A RSA CALIBRATION SYSTEM WITH IMPROVED ACCURACY AND PRECISION

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### Introduction

Radiostereometric analysis (RSA) is the most accurate radiographic method1 in orthopaedic clinical studies Recently, many RSA applications have focused on the measurement of small movements to evaluate newly developed implant design, materials and surgical techniques. The clinical and industrial interest in these evaluations require an extremely high measurement accuracy and precision. In most cases, these requirements approximate the measurable limitation of the conventional RSA, thus bring uncertainty into the interpretation of the measurement results. We believe that the RSA technique is capable of higher accuracy than previous reports. By optimizing the parameters of the calibration system, RSA accuracy and precision can be improved.

### Methods

In order to develop a new cage, we first applied numerical simulation technique2,3 for cage design, and then we developed a synthetic imaging technique to verify our design under realistic circumstances. After the cage was fabricated, we performed an experimental validation using a knee joint phantom.

Precision was evaluated from all three techniques under zero-motion with 12 repeated exposures and calculated as the standard deviation of the repeated examinations. Accuracy was assessed from 16 experimental measurements on all three cages, using linear-regression analysis to compare the measured motion with the true increments, and presented as the 95% prediction interval4. In the end, one-way ANOVA was applied with P values of < 0.01 deemed significant.

# Results

The final cage was fabricated as two compartments, each one with dimensions of  $460 \times 380 \times 208$  mm. The imaging planes were symmetrically placed at  $\pm 45^{\circ}$  with respect to vertical. The 64 spherical tantalum control points ( $\emptyset = 1.0$  mm) were positioned in a 300  $\times 233.34$  mm rectangular pattern with marker spacing of 16.67 mm along both the long and short sides. Correspondingly, 64 fiducial marks were set in a 400  $\times 320$  mm rectangular pattern, with a marker spacing of 25 mm in the long side and 20 mm in the short side (Fig. 1).



Fig. 1: Schematic illustration of the new calibration cage

Both numerical simulation and synthetic imaging predicted improved precision for the new cage design prior to fabrication (Table 1). Also experimentally determined precision was generally in good agreement with simulation, confirming the validity of numerical simulation and synthetic imaging analyses.

Our hypothesis that the RSA technique is capable of higher accuracy and precision than previous reports was confirmed by the phantom study. The results (Table 2) indicate that the accuracy and precision of the new cage was improved about 40% with respect to the biplanar cage and 70% with respect to the uniplanar cage. The one-way ANOVA test indicated that the improvements of both accuracy and precision were significant (P < 0.01).

 Table 1:
 Comparison of the new cage with the two clinical cages, with respect to the precision in all three directions using numerical simulation, synthetic imaging, and phantom tests.

		Χ (μm)	Υ (μm)	Z (µm)
Numerical	New	5.0	3.6	5.2
Simulation	Biplanar	11.1	5.1	10.7
(N = 500)	Uniplanar	10.4	7.6	17.9
Synthetic	New	4.1	2.6	4.3
Imaging	Biplanar	12.7	5.9	3.5
(N = 6)	Uniplanar	13.6	6.7	15.7
Phantom	New	4.3	6.1	4.3
Test	Biplanar	10.4	9.4	12.0
(N = 6)	Uniplanar	13.9	6.1	18.0

Table 2:
 Experimental comparison of accuracy and precision between the new, biplanar, and uniplanar cages.

Cage	Accuracy <sup>a</sup> (µm)	Precision (µm)		
New	±11	8		
Biplanar	±20	14		
Uniplanar	±39	28		

$^{\rm a}_{\rm \sim}$ For each linear regression equation $R^2 > 0.99$ and $p < 0.01$	
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### Discussion

We report a new calibration cage design, which significantly improves the accuracy and precision of RSA, compared to existing clinical systems. Optimization of the number of beads, the bead placement, and the configuration of the imaging planes all contributed to the observed improvement, which was confirmed by two types of simulation and by experimental measurements with a phantom.

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# FEASIBILITY OF MODEL-BASED RSA IN TMC JOINT REPLACEMENT

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# Introduction

Advanced stages of osteoarthritis of the trapeziometacarpal (TMC) joint frequently require surgical treatment. One of the treatment modalities is total joint replacement. This procedure can establish a pain-free, stable, and mobile joint with preservation of the trapezium and normal thumb length. Although progress is made with these small total joint arthroplasties, we are still not able to match the successes of large total joint arthroplasties. Aseptic loosening of the total TMC joint occurs frequently and may depend on the design of the prosthesis. Numerous TMC prosthesis designs are available, and new designs are being developed and tested. One of the problems in the clinical studies of TMC prosthesis is identifying and predicting prosthetic loosing at an early stage.

A method used in the assessment of new large joint prosthesis is Roentgen Stereophotogrammetric Analysis (RSA). This method allows assessment of three-dimensional micromotion of orthopaedic implants with high accuracy. Early micromotion (in first two years) of most prostheses is strongly correlated with the development of aseptic loosening. As far as we know no RSA studies of the TMC joint exist. We studied if RSA assessment was possible after total TMC joint arthroplasty. One of the questions was if a sufficient number of markers with a sufficient distance could be implanted to obtain accuracy of possible micromotion.

# **Materials and Methods**

In five cadaveric hands the TMC joint was replaced by the SR-TMC prosthesis according to the standard implantation technique as described by the manufacturer. Tantalum beads of 0.8 mm were implanted in the trapezium and first metacarpal bone without extending the standard surgical exposure. In general, in the trapezium three beads were implanted via the drilled hole for the prosthetic peg and two more were inserted through the exposed radial cortex. In the first metacarpal two beads were placed in metaphyseal bone as distal as possible via the reamed intramedullary cavity. Additionally one more bead was inserted in the ulnar trabecular bone of the metacarpal base and one or two beads secured in the exposed radial cortex. The metacarpal prosthesis component was provided with three or four 0.5mm beads, two at the tip and one or two at the base of the component. A three-dimensional surface model of the trapezium component of the SR-TMC prosthesis was prepared to facilitate model-based RSA, since attachment of beads to this part of the prosthesis is not feasible. After the surgical procedure, RSA radiographs were made of all hands in two commonly used positions for imaging of the TMC joint. The number of visually detected markers for each bone/implant was recorded. Of one cadaver hand, RSA radiographs were made in ten different positions. These radiographs were used to calculate the precision of the performed technique.

# **Results and Discussion**

The number of visually detected beads compared to the actual number of inserted beads (../..) in each specimen for the two radiographed positions (A and B) are shown in table 1.

	() — — — — — — — — — — — — — — — — — — —	1A	-	-	1B		A+B		2A	254	1.00	2B		A+B
14	L	R	Bo	L	R	Bo	All	L	R	Bo	L	R	Bo	All
М	6/6	6/6	6/6	6/6	6/6	6/6	6/6	4/4	4/4	4/4	4/4	4/4	4/4	4/4
Р	2/3	2/3	2/3	3/3	3/3	3/3	2/3	3/3	3/3	3/3	3/3	3/3	3/3	3/3
T	4/5	4/5	4/5	3/5	3/5	3/5	3/5	5/6	5/6	5/6	4/6	4/6	4/6	4/6
		3A	-		31	3	A+B		4A	1		4B		A+B
	L	R	Bo	L	R	Bo	All	L	R	Bo	L	R	Bo	All
Μ	4/4	4/4	4/4	4/4	4/4	4/4	4/4	5/5	5/5	5/5	5/5	5/5	5/5	5/5
Р	3/3	3/3	3/3	3/3	3/3	3/3	3/3	4/4	4/4	4/4	4/4	4/4	4/4	4/4
Т	4/5	5/5	4/5	5/5	5/5	5/5	5/5	5/6	5/6	5/6	5/6	6/6	5/6	5/6
	1	5A		1	5B		A+B			-				
	L	R	Bo	L	R	Bo	All	1						
М	4/4	4/4	4/4	4/4	4/4	4/4	4/4	1						
Р	4/4	4/4	4/4	4/4	4/4	4/4	4/4							
Т	5/5	4/5	4/5	5/5	5/5	5/5	4/5							

Table 1. M=metacarpal bone, P= metacarpal prosthesis, T= trapezium. L=left X, R=right X, Bo=both X. All = the least number of beads visual in all X.

Our observations showed that for the metacarpal bone, all beads were visible in all positions and both (L+R) RSA radiographs. For beads in the polyethylene metacarpal prosthesis component 3 beads seem sufficient, however in exceptional cases the most proximal placed bead might be invisible due to overprojection by the metal trapezium prosthesis component. Therefore the X-rays should be carefully checked at the radiology department before the patient leaves the ward. Alternatively, an extra bead can be placed in the prosthesis, although this is a lesser option due to possible weakening of the component caused by the placement of the beads.

The use of different sizes of beads (0.5/0.8 mm) in metacarpal and metacarpal prosthesis made the interpretation for the analyser easier.

The accuracy analysis is currently carried out. First results of these measurements are promising.

# Conclusion

Placement of tantalum beads for RSA analysis during TMC-joint replacement is feasible.



# EFFECTS OF PARATHYROID HORMONE (PTH) (1-34) TREATMENT ON THREE-DIMENSIO-NAL MICROSTRUCTURAL PROPERTIES OF RE-GENERATEDED BONE AFTER DISTRACTION OSTEOGENESIS IN A RABBIT TIBIAL LENG-THENING MODEL. A MICRO-TOMOGRAPHIC IMAGING STUDY

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### Introduction

We have investigated the effects of intermittent parathyroid hormone PTH (1–34) treatment on the microstructure of regenerated bone after distraction osteogenesis in rabbits. . Our hypothesis was that intermittently administered human PTH(1-34) injected in a 25 g/ kg dose would improve the architectural features of new regenerated bone. We analysed the specimens of distracted and regenerated bone by using the nondestructive microcomputer tomography scanning, which provides an excellent and realistic visualization of bone architecture (27), unbiased 3 dimensional evaluation of bone structure (28, 29) and can be used equally well for the study of both trabecullar and cortical bone (23)

# Materials and methods

After tibial mid-diaphyseal osteotomy the callus was distracted 1 mm/day for 10 days. The rabbits were divided in 3 groups and received daily either a PTH injection for 30 days, a PTH injection for 20 days, or a saline injection. The new-trabecular structure of the regenerate callus was assessed by three-dimensional microcomputed tomography ( $\mu$ CT). 51 specimen obtained from the lengthened tibia were scanned and evaluated morphometrically within three different volume of interests in this study. The computed morphometric parameters were trabecular number Tb.N\*, trabecular thickness Tb.Th\*, trabecular separation Tb.Sp\*, bone volume density (BV/ TV), bone volume (BV), bone surface (BS), connectivity density (Conn.D), degree of anisotropy (DA)

### Results

Results showed that intermittent treatment with PTH during distraction osteogensis resulted in a significantly higher Tb.N., better geometrical parameters of trabecular orientation and higher connectivity density, and in augmentation of bone mass. The values for the direct methods for Tb.N, Tb.Th and TB.Sp as well as the tra-

becular connectivity density and degree of anisotropy, which is a geometrical parameter of microarchitecture are consistent within all three VOI. From this consistent data, we feel safe to conclude that obtained direct 3D measurement of trabecular microstructure are the most powerful in this study and best represent the microarchitecture of newly regenerated bone.

We also found preliminary evidence that suggests that the newly regenerated callus treated with PTH was shifted to more mature bone structure, that is formation of new cortical shell in a new-trabecular bone was more detectable than in non-treated samples.

### Conclusion

To the best of our knowledge, it is the first study that used a microtomographic technique to quantify the new bone formation treated intermittently with PTH during distraction osteogenesis These findings demonstrate that PTH have a marked anabolic effect on newly regenerate bone indicating that PTH could be considered as a possible stimulating agent in orthopaedic surgery.

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# CT-BASED VISUALIZATION AND SEGMENTATION OF SOFT-TISSUE FEATURES FOR USE IN UPPER LIMB MODELING

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### Introduction

Biomechanical models have been successfully applied to identify potential risk factors for injuries and to plan and evaluate the effects of orthopaedic surgical procedures. [1] These models have made apparent the feasibility and necessity for the generation of subject-specific models that are aimed at custom clinical applications, including computer-assisted preoperative planning and navigated surgery, robotic-guided surgery and use in the design and analysis of customized orthopaedic implants. In order to develop a model capable of both accurate biomechanical analysis and prediction of position and characteristics of soft tissues and more specifically nervous and vascular structures, a method needs to be devised that allows accurate geometrical visualization and reconstruction of these structures. [2] In this study we present a methodology for obtaining both bony as soft-tissue features necessary for upper limb modeling from computer tomography alone.

### Methods

In order to visualize and reconstruct the different muscle segments of the shoulder girdle, flexible 0.7 mm copper wires were sutured from origin to insertion according to the fiber directions in ten different cadaver specimens. The nervous structures were dissected using an anterior approach and injected with an iodine contrast medium (visipaque), glycerine and toluïdineblue to highlight the tissue on CT imaging. At the same time sixteen 1.2 mm-diameter leaded markers were implanted in the plexus and peripheral nerves at topographically crucial via points for later enhanced recognition on CT reconstructions.

The specimens were studied using a helical CT scan with a 0,5 mm slice increment (Siemens/ volume zoom). The Mimics ® (Materialise NV, Heverlee, Belgium) software package was used for visualization and segmentation of CT images and 3D rendering of bones, muscle segments, brachial plexus and peripheral nerves. Major vascular structures could be segmented based on the presence of air in their luminae. The same method was applied to a formalin-embalmed female cadaver specimen containing a surgically placed plastic replica of the Delta reversed shoulder prosthesis ® (DuPuy Orthopaedics, Inc., Warsaw, IN ).

### Results

Bones, muscle, nerve and blood vessel features were visualized and segmented as separate masks. [Figure 1]. Analysis of the representations showed that the morphologic parameters were within the normal anatomical ranges. After applying a cluster method algorithm, interruptions of the masks, scattering rustle and small irregularities due to the copper wires were filtered. After reconstruction, the vascular and nerve segment paths were accurately approximated using the draw spline function in the Mimics® software package. Each segment was exported in STL format and the respective positions and lengths were calculated.



Figure 1

### **Discussion and conclusion**

The need for the generation of subject-specific biomechanical models that are aimed at clinical ap-plications, particularly in the design and analysis of orthopaedic implants, preoperative planning and ac-curate interpretation of postoperative outcomes, is becoming increasingly apparent. Currently, muscu-loskeletal imaging techniques such as MRI and CT can potentially provide a source for completely individualized models. However, the constraints of clinical reality, e.g. cost, time and exposure to unacceptable levels of radiation still preclude the creation of full complex models of a region of interest. This gap can be bridged by creating an idealized generic musculoskeletal model that can be morphed into a patient-specific model using limited CT, morphometric data and a database created from cadaver studies in which bone geometry and soft -tissue features are measured in detail.

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# . SESSION - SATURDAY

### O-059

# IMAGING OF THE MUSCULOSKELETAL SYSTEM USING 3D ULTRASOUND

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# Introduction

X-ray is the standard method for monitoring fracture healing however it is not an ideal imaging modality; signs of healing are not normally visible on X-ray until around 6-8 weeks post fracture when there is enough callus of sufficient density present. Ultrasonography allows the detection of both the initial haematoma, usually formed immediately after fracture, and the small calcium deposits laid down between broken bone ends in the first stages of fracture healing It has been reported that these early indicators of the healing process are visible on ultrasound as early as 1-2 weeks after fracture[1]. Furthermore, the surrounding soft tissues can be imaged using ultrasound.

We propose the use of Freehand 3D ultrasound to monitor the early stages of fracture healing. During 3D scanning images are recoded from the ultrasound machine and transferred to the PC using RF capture. The position and orientation of the transducer is also recorded. Segmenting features of interest on a sequence of 2D images (figure 1) enables a 3D model to be constructed (figure 2). These models are rotatable and provide views of the scanned anatomy that are not otherwise achievable using conventional ultrasound or X-ray.



Figure 1: A 2D ultrasound image from a healthy volunteer scan, features of interest are labeled.



Figure 2: 3D model constructed from a healthy volunteer scan. Yellow-skin, blue-subcutaneous layer, purple-extensor digitorun longus, redtibialis anterior, cyantibia

### Method

The Freehand 3D ultrasound system consists of a standard ultrasound machine, a PC running STRADWIN (Medical Imaging Group, Cambridge University) 3D software, and an optical tracking devise (NDI Polaris) to record the position and orientation of the ultrasound probe during scanning. Calibrating the system matches up the correct image with the correct probe position to produce a 3D dataset.

The system has been evaluated on healthy volunteers and patients undergoing lower limb reconstruction. Each individual recruited undergoes four 3D ultrasound scans each time they attend fracture clinic for routine care. Two scans will be carried out using a 5-10MHz probe and two using an 8-16MHz probe. 3D models are constructed for each dataset (figure 3).

# Results

To conduct a 3D ultrasound scan takes the same amount of time as a conventional 2D scan. The production of the 3D model takes between 15-60 minutes depending on the number of images recorded and level of detail required. A phantom study was conducted to assess calibration accuracy and distance measurements. Distances can be measured to within  $\pm 0.4$ mm meaning fracture gaps of sub-millimeter width can be resolved.

# Discussion

With 3D ultrasound it is possible to image and model both the surface of the bone and the soft tissues simultaneously. The 3D scan data can be resliced to provide unique views of the anatomy not normally available with 2D ultrasound (figure 4).



Figure 3: 3D model of patient undergoing tibial distraction using a lengthening nail. White – bone, yellow - new bone growth, grey – nail surface, mauve - cyst.

Figure 4: 2D reslice image showing a cyst developing in a tibial lengthening patient.

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# ORAL SESSION 11 Spine

# Seminario 16:45 - 17:35 h<u>O 060-065</u>

# O-060

# VERTEBRAL STRENGTH UNDER COMPRES-SION COMBINED WITH ANTERIOR BENDING: AN IN VITRO STUDY.

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# Introduction

Mechanical approaches based on finite-elements models have been proposed to predict strength of osteoporotic vertebrae or effects of vertebral tumours ex vivo. Most of the mechanical tests that have been carried out to validate these models concern vertebral bodies without posterior elements in axial compression[1, 2]. But in standing position gravity loads can induce a flexion component, especially for the last thoracic and first lumbar vertebrae. The aim of the study was to evaluate the strength of vertebrae from T11 to L2, with posterior elements, under combined compression and flexion.

# Material and methods

Fifteen vertebrae (T11-L2) from 5 donors (4 females, 1 male,  $88 \pm 14$  years old) were tested to failure in the following conditions.

The load was homogeneously distributed on the whole vertebral upper endplate through a polymetylmetacrylate (PMMA) layer which completely fills its concavity[3]. The load was transmitted to the vertebra through a ball, constrained in a hole, and situated at the one third of the vertebral body depth. The PMMA layer was rigidly linked with the steel plate containing the hole for the ball, so that they composed a single solid called upper plate (Figure 1). The 3D orientation of the load transmitted to the vertebral body, and the one of the vertebra and the upper endplate were assessed by means of a motion capture system (Polaris®, NDI, Canada) with an accuracy of 0.6 mm and 0.6°, thanks to tripods. Before the mechanical test, the position and the orientation of the marker-frames relatively to the vertebral frame were assessed using 3D reconstructions (obtained by bi-planar X-rays [4]) to be able to express all the movements in the vertebral frame during the test.

The outcome data were the displacement and the orientation of the upper plate. The load transmitted to the vertebra was calculated from the measurement of the vertical load (using the testing machine sensor) and the orientation of the plate (using the Polaris® system).



Figure 1. Assembly for the mechanical test.a/ Vertebra and upper plate with tripods.b/ 2D representation of the boundary conditions.

# **Results and discussion**

The protocol proposed allowed to collect all the data necessary to define: 1/boundary conditions of a finiteelement model close to the real conditions and 2/to validate a model. The combined loading allowed us to apply conditions close to the in vivo ones.

The mean flexion of the upper-plate is equal to  $1^{\circ}$  (± 0.7°), before the vertebra collapses. The mean failure load is equal to 2086N (± 810N) and the mean vertical displacement until failure is equal to 1mm (± 0.2mm).

The rotation of the upper plate between the initial position and the failure is weak. Thus, a simplified protocol could be proposed without the optoelectronic system, if the two pieces composing the upper-plate are rigidly linked and the initial 3D orientation of the upper plate relatively to the vertebral frame is assessed before the mechanical test.

The values of the failure load of the 15 vertebrae tested are consistent with a study made on T9 and T10 vertebrae under anterior bending loading (between 630 and 2970N) [5]. They are much lower than those assessed previously under axial compression (between 3000 and 5000N)[1, 2], showing that boundary conditions are of paramount importance to predict the vertebral failure.

### Acknowledgements

The authors gratefully acknowledge S. Persohn and J. Magnier for their technical help.

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# . SESSION - SATURDAY

O-061

# INFLUENCE OF CEMENT AUGMENTATION ON PEDICULAR SCREW MIGRATION INSERTED IN OSTEOPOROTIC VERTEBRAE

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Posterior internal fixation systems (PIFS) undergo internal constraints resulting in high load bearing requirement for the pedicular screw/bone interface. The integrity of this interface is therefore fundamental to ensure the implant's success. Different studies have proven that the screw performance is dependent on the bone quality, meaning that osteoporotic patient may be predisposed to larger PIFS failure rate. To diminish this tendency, the vertebral bone stock can be augmented with cement (polymethylmethacrylate -PMMA- or calcium phosphate cements) to increase stiffness and strength of the cancellous bone. The augmentation can be executed using perforated pedicular screws.

Only few studies deal with the impact of the vertebral augmentation on the migration of pedicular screws, which is directly linked with the PIFS stability.

In this study, the impact of the pedicular screw augmentation has been investigated under physiological load for osteoporotic vertebras. The data have been proceeded to reduce the influence of vertebral geometry, which generally leads to results devoid of statistical meaning.

# **Materials and Methods**

Two osteoporotic lumbar spines (L2, L3, L4 and L5; females of 79 and 72 years: body mass index -BMD- of 0.286 and 0.264 [g/cm2] respectively) have been prepared for the implantation of Synthes Inc. Click'X perforated pedicular screws (outer diameter 6.5mm and 50mm length). In each of the eight obtained vertebrae, two screws have been inserted: a non-augmented on one side and an augmented (using 2 ml of PMMA) on the contralateral side.

The implanted screws have been tested with a one axis compression device (Zwick 1475) with the following load scenario: two consecutive 50 cycles load steps of 100N and 200N [1]. The output of this force driven test is the displacement of the screw's head. Two different setups have been employed: (i) machine's tip is freely acting on the screw (free connection -FC-) and (ii) angle between the machine's tip and the screw is blocked (blocked connection -BC-). A load step is regarded as successful if the migration between two consecutive cycles tends to zero at the end of each 50 cycles, which indicates that the screw has reached an mechanical equilibrium state with the bone.

To reduce the impact of the vertebras' geometry, the screws' migration haven been compared contra-laterally using the migration ratio (MR). MR of vertebrae is defi-

ned as the division of the augmented screw's migration with the non-augmented screw's migration. An MR smaller than one indicates that augmented screws exhibit less migration than the non-augmented ones. To control the relevance of the MR, they have been compared unilaterally to a uniform distribution of 1 with the help of a T-test.

# Results

All the augmented screws survived to both test setups whereas the non-augmented failed the 200N FC load step. Significant differences are observable only for the highest successful load steps for each test setup, as illustrated in Fig. 1. TBC FC. In other word the averaged migration of non-cemented screws are 37% and 58.7% (200N BC test and 100N FC respectively) larger than the one observed for augmented screws. The T-tests (0.039 and 0.007 respectively) put into evidence that the results are statistically smaller than one (P<0.05). The BC 100N migration (MR of 1.34 allow to determine whether augmented or non-augmented screws exhibit less migration because of the too large standard deviation occurring for small load (100N) for the BC setup.

It is observable as well, that the BC induced fewer loads into the vertebrae: even non-augmented screw can withstand 200N load step.



Fig 1: Averaged MR (N=4) for each test setup. All FC-screws failed for the 200 N load steps (cross).

# Conclusion

BC setup induces an internal moment in the screw/tip fixation, which avoids screw's flexural rotation. This will reduce the amount of energy that can be used to deform the bone resulting lower screw migration.

As expected, augmentation of pedicular perforated screws increases their stability in osteoporotic vertebras undergoing large physiological load significantly. Smaller load induce only small differences that are not significant. The large stiffness of PMMA increases the load transfer between screw and cancellous bone, increasing its bearing capacity. Therefore forces acting locally on cortical bone are reduced. These phenomena lead to smaller migration of the pedicular screws.

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O-062 POLY

# POLYMER-BASED ANNULUS SEALING IMPROVES NUCLEUS IMPLANT CONTAINMENT

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# Introduction

The safety of nucleus implants remains an open issue in the treatment of intervertebral disc degeneration. Post-operative migration and subsequent extrusion of the implant through the annulus defect represent a high risk of catastrophic clinical outcomes. This topic is often discussed in the literature for inert nucleus replacement devices and regenerative nucleus implants [1, 2]. In this experiment, the effectiveness of additionally sewing a biointegrative annulus implant into an annulus defect was investigated for improving nucleus implant containment and minimizing this risk.

# Aim

The aim is to determine the effectiveness of sewing a biointegrative annulus implant into an annulus defect for improving nucleus implant containment.

# **Materials and Methods**

Laminectomy, preserving the facet joints, was performed on seven human functional spinal units (FSU's). A reproducible annulus defect of 6 x 6 mm was incised, followed by a standard nucleotomy procedure. Then, nucleus implants were introduced into the disc space. These consist of biointegrative, absorbable polyglycolic acid (PGA), lyophilized with hyaluronic acid. The annulus sealing technique [A] requires placing a PGA-patch adjacent to the inner annulus, fixed by sutures (Polysorb3-0, Syneture) at its four corners according to Fig.1. Unsealed annulus defects served as a control group [B]. FSU's were loaded with an eccentric force of 250 N, introduced on the upper endplate. The lever arm varied between 20–30 mm, which resulted in an overall bending torque of 5-7.5 Nm, as recommended in the literature [3]. The applied loads were adjusted to the individual dimensions of the vertebral cross-sections. Continual revolution of the specimen around its vertical axis resulted in a combination of lateral, dorsal and flexural bending.



Fig. 1: Sealed annulus defect by fixing a PGA patch (blue) with sutures (red) to the inner annular walls.

During application of loads, implant herniation level was determined every 1000 cycles according to the following criteria: I: initial situation after insertion, II: visibility of the implant, III: extrusion of a patch out of the annular circle, IV: extrusion of a patch more than half of its volume out of the annular circle and V: dropping out of the implant which represented the abort criteria. Tests were stopped after reaching 20'000 cycles. Specimens that were already used were tested again; randomization defined whether procedure A or B was performed first.

### Results

Five of totally six sewed specimens withstood 20'000 load cycles, whereas only one of five not sewed specimens terminated successfully. Based on the Mann-Whitney test comparing the withstood cycles, significant increase in stability can be detected for the sewed procedure.

An initial decrease in the extrusion grade in sealed specimens was detected after the test start, followed by a subsequent stabilisation over time (Fig. 3).



Fig. 3: Herniation level during loading. (Curve for method B is slightly displaced for a better viewing).



Fig. 4: Lateral view of a sewed defect through the foramina (left) and dorsal view of an extruded implant.

# Discussion

Sewing a biointegrative annulus implant into an annulus defect improves nucleus implant containment. It remains to be shown whether this annulus sealing technique is also effective in highly degenerated annulus tissue. Furthermore, a minimally invasive implantation device is crucial for application in a clinical setting. The applied test represents a selective method to determine nucleus implant containment.

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O-063

# DYNAMIC NEUTRALISATION SYSTEM COM-PLICATED BY ACCELERATED ADJACENT SEGMENT DEGENERATION

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# Introduction

We report a series of 10 cases from a cohort of 421 Dynesys procedures in which evidence of Accelerated Adjacent Disc Disease (AASDD).

Spinal fusion for degenerative disc disease is known to have inconsistent outcomes. One concern is the possibility of Adjacent segment disease (AASDD) as a result of the altered kinematics. The Dynamic Neutralisation System ( Dynesys) appears to offer an advantage in that it restricts, rather than abolishes movement at the treated segment, and should thereby reduce the problem of AASDD, In the event of failure, it can in addition be removed, returning the spine to the former status quo. Various biomechanical studies confirmed flexibility of Dynesys.

### Method

Ten patients developed new and symptomatic disc disease within segments adjacent to Dynesys. The average age of patients was 49 year with range between 36-70 years. Average post Dynesys to secondary surgery for ASD was 24.7 months. Previous discography and MRI in all cases had shown no evidence of disc disease within these adjacent segements prior to Dynesys. All patients were evaluated preoperatively using Oswestry Disability Index, SF 36 and Visual Analogue Scores together with plain x ray imaging, MRI scanning and discography. Of this cohort Dynesys was indicated to treat single disc level in 7 and two levels in 3

### Results

Incidence of AASDD associated with Dynesys was 2.1%. Further surgical intervention included: Extension of Dynesys 10 Dynesys combined with MIF 2 Dynesys combined with PLIF 2 There was no caudal ASD in our cohort.

# **Discussion & Conclusions**

Dyensys did not prevent the development of accelerated ASD. Evidence from Aylott cadaver studies suggests that Dynesys instrumentation alters the Kinematics of the adjacent segment and increases the excursion. It is unclear whether the small number of AASDD reported here is other than thenatural progression of degenerative change. 95.7 cases did not progress.





# INFLUENCE OF NEURAL TENSION IN MECHANICAL NOCICEPTIVE THRESHOLDS (MNTS) OF LUMBOPELVIC REGION MUSCLES

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# Introduction

Neurodynamic tests are daily regarded as important in orthopedic physical assessment. Some of these, such as passive straight leg raising (SLR) and the slump tests, are used as an usual procedure for the examination of patients with low back pain (LBP). Therefore, changes in neural tension provoked by these tests over differents nerve trunks in lumbopelvic region may alter the nociceptive responses of nearby tissues. Also many authors share the opinion that gluteal musculature may be considered a source of LBP.

The aim of our study was to evidence changes in mechanical nociceptive thresholds (MNTs) of lumbopelvic muscles in different neurodynamic positions.

# **Materials and Methods**

A cross-sectional study was carried out with single-group repeated measurements. Fifty asymptomatic volunteers (22 men, 28 women) were evaluated with algometer in three neurodynamic positions:

1) initial position was defined on lateral position resting on the contralateral lower limb and fixing with a type of stabilizer belt without neural tension, so with knees bent 80°, hips at 90° of flexion and the ankles, feet and spine in neutral; 2) initial position with the homolateral knee in complete extension to add neural tension of sciatic nerve; 3) initial position incorporating maximum craniocervical flexion (chin getting in touch with manubrium sterni) to add neural tension within vertebral canal.

The pressure algometry was tested at one anatomical site on gluteal region 2.5 cm. below iliac crest bone and behind iliotibial band.

One physiotherapist (PT) measured MNTs unilaterally over gluteus medius. Pressure was applied at a uniform rate until a local soft pain was noted; the repeatability of 3 consecutive measurements was evaluated in the three described positions, while a second PT reported the data in kilograms (kg). A third PT was responsible for modifying the knee and craniocervical range of motion.

Student's paired t-test, Student's groups t-test, mean differences and 95% confidence interval were used for statistics with SPSS 11.5 for Windows.

# **Results and Discussion**

The findings revealed significant mean differences (0.522 kg; 95% IC: 0.385-0.659 kg) in algometry measurements (P < 0.0001) betweeen position 1 (mean 3.632 kg; SD 1.235 kg) and position 2 (mean 3.110 kg; SD 1.233 kg), and a mean difference (0.590 kg; 95% IC: 0.412-0.768 kg) significant (P < 0.0001) betweeen position 1 and

position 3 (mean 3.042 kg; SD 1.136 kg). Furthermore, no significant differences between the two different neural tension positions (P < 0.420). Also, it was noted difference significant in b) position (P < 0.029) between males (mean 3.573 kg; SD 1.542 kg) and females (mean 2.746 kg; SD 0.774 kg).

# Conclusions

MNTs of lumbopelvic muscles decrease with neural tension positions.

MNTs decrease is similar with sciatic nerve and vertebral canal neural tension positions.

# Summary

Neurodynamic positions are important procedures to be taken into account in clinical reasoning, both physical therapy diagnosis and treatment.

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# DISRUPTION OF THE SPINAL MUSCLE TENSEGRITY HAS MORE IMPACT THAN COSTOTRANSVERSECTOMY ON EXPERIMENTAL INDUCTION OF SCOLIOSIS

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### Introduction

Costotransversectomy has probed to be a reliable method for induction of scoliotic deformities in animals with research purposes. An alteration of the spinal tensegrity due to resection of bony structures has been recently proposed as the pathogenic mechanism for curve progression. This work was aimed at study the role of paraespinal muscles on spinal tensegrity. Four different models of spinal tensegrity breakage with and without injury of the posterior spinal muscle were investigated.

### Methods

Fifteen minipigs (mean age 6-week) underwent costotransversectomy (CTT) at 5 consecutive vertebral segments. In 4 animals ribs and transverse processes (T7-T11) were removed through a posterior midline approach with complete desinsertion of paraespinal muscles. In other 3 animals, the same bony structures were resected by a posterolateral approach (T6-T10) without desinsertion of paraespinal muscles. Other 4 minipigs underwent rib resection (T7-T11) throughout a thoracoscopic approach avoiding damage of posterior spinal muscles. A final group of 4 animals, a complete desinsertion of the paraespinal muscles was performed from T7 to T11 without removing bony structures and leaving in deep surgical vax attached to the spinous and transverse processes to avoid reinsertion of the muscles after surgery. Thoracic spine deformity was assessed by standard X-rays at the immediate postoperative period, and at 2-month and 4-month follow-up. Anatomic specimens were also macroscopically studied just at sacrifice 5 months after surgery

# **Results and Discussion**

All 4 animals operated on of CTT by midline posterior approach developed structural spinal deformity with curve convexity at the side of rib removal. Mean Cobb angle was found to be 34,6° (27-41). Vertebral rotation was clearly evident in these 4 animals (average rotation, 24 degrees) (Fig. 1). Animals undergoing CTT by posterolateral approach without paraspinal muscle desinsertion did not develop any significant spinal deformity. The same absence of spinal deformity was found in those animals in which rib resection was performed by thoracoscopy without injury of the posterior spinal muscles. All 4 animals undergoing desinsertion of the paraespinal muscles without CTT and application of the surgical vax developed scoliotic curves with a mean Cobb angle of 28° (20-38). Vertebral rotation was less apparent than in the first CTT-group.



Fig 1. Scoliotic curve in an animal with CTT

To our knowledge no previous studies have focussed breakage of the spinal tensegrity by an experimental model in which bony structures are removed with minimal damage of the paraspinal muscles as in our posterolateral or thoracoscopic approach. Furthermore, breakage of the spinal tensegrity depending alone of the muscle-ligamentous structures has never attempted. A new insight on the underlying pathogenic mechanisms of scoliotic curves is given by using this model of spinal tensegrity model. As in smaller experimental animals, CTT was a reliable method for induction of scoliosis in minipigs. In these cases, scoliotic deformity showed a similar appearance than human idiopathic curves. However, in these animals spinal deformity may be due more to the posterior muscles injury than to the bone resection.

# Conclusion

Isolated damage of the posterior muscle-ligamentous structures around the costotransverse joints breaking of the muscles spine tensegrity seems to be mandatory to induce scoliotic deformity. Rib removal alone appeared to have less scoliotic inductive implication. The finding that muscle-ligamentous structures are more decisive than rib resection for curve progression completely questions previous knowledge on scoliosis etiopathogeny.

# BIRTH ADVANCEMENT DIMINISHES CHIARI MALFORMATION IN SURGICAL MIELOMENINGOCELE MODEL IN RABBITS

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# Introduction

Mielomeningocele (MMC) is a congenital malformation of the spine characterized by a defect of closure of the neural tube in the third week of the gestation. Damage of neural elements (spinal cord and encephalon) seems to be progressive during gestation because of amniotic fluid chemical toxicity (direct lesion) (1-6) and continuous leakage of cerebrospinal fluid (collapse of the ventricular system) (7;8).

The aim of our study was to assess the effect of preterm delivery and prenatal corticosteroids administration in the degree of Chiari malformation.

# **Material and Methods**

Seventeen pregnant New Zealand White rabbits underwent laparotomy and hysterotomy at 23rd day of the gestation. Seventy-five out of a hundred and forty-eight foetuses underwent lumbar three levels laminectomy. Dura-mater was opened to expose the neural elements to the amniotic fluid.

Animals were distributed in five groups: group T, foetuses with MMC, delivery at term and no other treatment; group TC, foetuses with MMC, delivery at term and prenatal administration of corticosteroids; group P, foetuses with MMC, delivery preterm and no other treatment; group PC, foetuses with MMC, delivery preterm and prenatal administration of corticosteroids; group C, controls.

Newborns were euthanized in order to analyse the craniospinal junction. The degree of herniation was measured in percentage of decrease between the inferior limit of the skull and the superior limit of the first vertebra.

Statistical analyses comparing means and obtaining the confidence interval of 95% was done among groups.

# Results

Mean survival was of 38% of the foetuses. We obtained 7 newborns alive from group T, 5 newborns alive from group TC, 10 newborns alive from group P, and 6 newborns alive from group PC and 28 newborns alive from group C.

All groups with prenatal delivery or prenatal corticosteroids showed statistically significant minor degree of herniation: group TC IC 95% between 25.7 and 47.2% minor (p=0.000), group P IC 95% between 30.4 and 47.7% minor (p=0.000), group PC IC 95%



Seminario 18:05 - 18:45 h O 066-070

between 32.6 and 55.4 minor (p=0.000). There were no statistically significant differences among groups TC and P (p=0,577), TC and PC (p=0,227) or P and PC (p=0,311).

# Discussion

Despite using a surgical and non congenital model, newborns with MMC showed similar lesions to humans in lumbar area, extremities and encephalon.

Preterm delivery produces lesser Chiari malformation because represents less time losing cerebrospinal fluid and allows precocious closing.

Despite prenatal treatment with corticosteroids is used to accelerate lung maturation in all preterm newborns, both treatments produce separately improvement in the degree of Chiari malformation.

# **Conclusions/Summary**

Preterm delivery and prenatal administration of corticosteroids, together or separately, result in lower degree of Chiari malformation in a model of surgical MMC in rabbit fetuses.

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# SIMPLIFIED PRENATAL COVERAGE OF SURGICAL MIELOMENINGOCELE IN SHEEP ALLOWS REGENERATION OF SEVERAL LAYERS OF SOFT TISSUES

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# Introduction

Mielomeningocele (MMC) is a congenital malformation of the spine characterized by a defect of closure of the neural tube in the third week of the gestation. Damage of neural elements (spinal cord and encephalon) seems to be progressive during gestation because of amniotic fluid chemical toxicity (direct lesion) (1;2) and continuous leakage of cerebrospinal fluid (CSF) (collapse of the ventricular system) (3).

The options to approach the condition include abortion, postnatal reparation, preterm delivery (4) and fetal reparation (5;6). Open fetal surgery reverses hindbrain herniation and protects exposed neural elements from secondary lesion but is associated with complications as preterm labour, amnionitis, abruptio placentae (6;7).

The aim of our study was to assess whether a simple and fast technique of coverage produces the same results as a complete and longer technique of reparation in terms of neural protection, with less complications.

# **Material and Methods**

Twelve sheep's foetuses underwent lumbar three levels laminectomy and opening of the dura-mater on the 75th day of the gestation. Four of them (group MMC) did not receive any treatment. Four of them (group SI) underwent coverage with Silastic® sheet and Coseal® surgical sealant on the 95th day. Four of them (group SM) underwent coverage with Silastic® sheet, Marlex® sheet and Coseal® surgical sealant on the 95th day. Group C was formed by four sham foetuses. At birth, clinical examination included ability to stand and to walk, sphincter continence, swallow problems, malformations, leakage of CSF and percentage of coverage of the MMC area. Animals were euthanized to perform pathologic examination. In the MMC area we studied the degree of neural lesion (percentage of glia/neurons) and the existence, thickness and organization of tissues above the neural elements. In the craniospinal junction we measured the degree of herniation in percentage of decrease between the inferior limit of the skull and the superior limit of the first vertebra.

Statistical analyses included when needed Chi square and comparison of means obtaining the 95% confidence interval.

# Results

None MMC animal were able to stand or to walk nor had sphincter continence. Two of them had ataxia, two had swallow difficulties and one of them had a thorax deformity. All of them showed a wide defect of closure in the lumbar area and continuous leakage of CSF. All animals showed neural damage and no coverage of the medulla. The mean vermis herniation was 75%.

All SI and SM animals were able to stand and to walk and all of them showed sphincter continence. None of them showed deformities or leakage of CSF and showed coverage of the 93% of the defect. All animals showed regeneration of several layers above the medulla: duramater, muscle and skin. They did not show regeneration of bone tissue. The mean vermis herniation was 10%.

# Discussion

Despite using a surgical and non congenital model, newborns with MMC showed similar lesions to humans in lumbar area, extremities and encephalon.

This study provide evidence of the Chiari etiologic theory of continuous leakage of CSF by the MMC area (3) and that coverage reverses the existing herniation.

Clinical situation correlates with pathologic findings. Minor neurological alterations in SI and SM animals can be due to secondary damage of the neural elements between the production and the coverage of the defect.

# **Conclusions/Summary**

In a model of surgical MMC in sheep, a simplified technique of coverage provides enough protection to avoid secondary lesion of the neural elements, to avoid Chiari malformation, and to produce the regeneration of several soft tissue layers, including dura-mater but excluding bone.

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# O-068 ACET

# ACETABULAR INDEX AND PROXIMAL PHYSEAL ANGLE OF THE FEMUR. PRE- AND POST-WEIGHTBEARING STUDY

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# Introduction

The Acetabular Index and the proximal physeal angle of the femur are important in the morphology of the acetabulum and the proximal femur, respectively. Their values appear to decrease with age and it remains unknown whether any correlation exists between them or if weightbearing has influence over them.

# **Material and Methods**

Observational, prospective, longitudinal study of the children hip. X-rays of 30 children (60 hips)(4 boys, 26 girls), were studied (2003- 2006), measuring the acetabular index (AI) and the proximal femoral physeal angle (PFPA). Measurements were taken using a goniometer (error  $\pm$  1°). We included children that presented ultrasound, at 4 months of age, with alpha angles smaller than 50° (Graf type IIa) and cephalic coverage between 33% and 50%. Anteroposterior hip X-rays were taken at 3 months (preweight-bearing) and 4-10 months (post-weightbearing). Statistics: Descriptive t-Test and correlation.

# Results

The AI was 21.5° (19.5° boys, 21.8° girls) pre-weightbearing and 20.9° (20.8° boys and 21° girls) post-weightbearing. The PFPA was 76.5° (75.9° boys and 76.6° girls) pre-weightbearing and 74.9° (75.5° boys and 74.8° girls) post-weightbearing. AI and PFPA decreased pre- and post-weightbearing, 2.8% and 2.1% respectively. The decrease was considered significant in the PFPA (p = 0.02), especially in girls (p = 0.009), and not significant in the AI. Differences were found between sexes: the AI increased in boys (+6.3%) and decreased in girls (-8.3%), and the PFPA decreased in both boys (-0.5%) and girls (-2.3%). The side had no influence. No correlation was found between AI and PFPA, both pre- (r = - 0.15, p = 0.27) and post-eightbearing (r = - 0.24, p = 0.07).

# Discussion

No studies of correlation between PFPA and AI were found in the literature. We did not find correlation between AI and PFPA values, neither in the previous stages to weightbearing, nor in the months after weightbearing occurs.

# Conclusion

The measured angles suffered a decrease after weightbearing but the only significant decrease was that of the PFPA. There is no correlation between AI and PFPA, before or after weightbearing.

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# MECHANICAL STRESS AT THE PROXIMAL FEMORAL GROWTH PLATE IN ADOLESCENTS WITH AND WITHOUT SLIPPED CAPITAL FEMORAL EPIPHYSIS. A COMPARATIVE STUDY USING A PARAMETRIC GEOMETRICAL SUBJECT-SPECIFIC FINITE ELEMENT MODEL

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# Introduction

In a previous work1, our research group developed a parametric geometrical finite element model (p-FEM) of the proximal femur based on subject-specific hip morphology parameters. This model probed to be a useful tool to analyze mechanical stress at the growth plate and to predict therefore the risk of capital femoral epiphysis slippage. In the current work, the parametric model was adapted to the specific hip geometric measurements of a group of patients with slipped capital femoral epiphysis (SCFE). The objective of this work was to analyze the stress distribution in the growth plate of these patients and to evaluate differences for those patients who developed bilateral disease.

# **Material and Methods**

Different geometric parameters were measured in the healthy proximal femur of 18 adolescents (epi-c and epi-post groups) (mean age, 12,1 yr) with unilateral SCFE and in 23 adolescents matched in age (mean 12,2) without hip disease (control group). Five patients developed SCFE in the contralateral side during follow-up (epi-post group), once the measurements were taken in the previous non-affected hip. Geometric measurements were taken from conventional X-ray studies of the hip according to Barrios et al (2005)2 and included, as a main parameters, the physeal sloping angle (PSA), the posterior sloping angle of the physis (L), the neckdiaphysis angle (NDA), the intersection angle, the physeal and femoral neck wide, and the major throchanter height. The p-FEM of the proximal femur used in this work has been previously validated1. The model permits modifications of different geometrical parameters, therefore the X-ray measurements taken from each patient were applied to the model obtaining a subject-specific model for each case. In each model, different mechanical situations such as walking, stairs climbing and sitting were simulated by applying loads on the femoral head corresponding to each own weight. The risk for growth plate failure was estimated by the Tresca, von Misses and Rankine stresses. The stress distributions during these activities in the growth plates were analysed.

# **Results and Discussion**

A similar pattern of stress distribution in the three groups was observed. Nevertheless, the values of these stresses were higher in the epi-post group. So, the 95% confidence interval of the percentage of volume of the growth plate subjected to stresses higher than 2MPa (Fig. 1) was almost similar for the control group and patients with unilateral SCFE. However, those patients who developed bilateral disease during follow-up had statistically significant large physeal areas with more than 2.0 MPa while climbing stairs (p<0.005). These differences could also be observed in the sitting and walking activities but stresses are lower.



Figure 1. Confidence interval (95%) for percentage of volume of the growth plate with a Tresca stress greater than 2MPa while climbing stairs.

These findings was related in part with the higher hip loading derived from the higher weight of SCFE-patients. Stresses were also strongly dependent on the geometry of the proximal femur, especially on the posterior sloping angle of the physis and the physeal sloping angle.

# Conclusions

In spite of simplifications of the developed parametric model, this tool has been able to show the influence of femur geometry in growth plate stresses and to predict the sites where growth plate starts to fail. The models shows important differences between the stresses computed at the healthy femurs of patients with unilateral SCFE and femurs that further underwent bilateral SCFE.

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# FETAL SURGERY OF EXTREMITY AMNIOTIC BANDS IN FOETAL LAMB: LIMB SALVAGE BY INTRAUTERINE RELEASE

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# ABSTRACT

# Introduction

With the use of fetoscopy (minimally invasive surgery), the indications for fetal surgery have been expanded (1). Extremities at risk of amputation by EAB are amenable to foetal surgery (2,3). A previous model of in uterus reparation of moderate EAB has been reported (4). The purpose of this study is to evaluate the feasibility of intrauterine foetal release of amputating EAB(5).

Material and methods: Right limbs of fifteen 60-days gestational age pregnant sheep were ligated with silk suture at the infracondilar level. Left limbs were used for paired comparison. Fetuses were randomized in three groups: early repair group(n=5), late repair group (n=5) and no-repair group (n=5).The limbs of repaired groups underwent foetal release.The limbs obtained from at term foetuses were analyzed morphologically, functionally, radiologically, and histologically. Statistical analysis with paired test was used to compare data.

Results Non-repaired limbs showed amputation or quasiamputation ; the repaired ones did not. However, those late repaired had significantly reduced passive ankle range of motion, shorter limb length, and mild residual changes.

# Conclusions

In uterus release of potentially severe EAB avoids limb amputation and permits its morphofunctional recovery. Early release shows better results.

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# POSTER SESSIONS EORS

Friday, April 25th

# POSTER SESSION 1 Spine

### P-001

# FUNCTIONAL OUTCOME FOLLOWING DYNAMIC NEUTRALISATION SYSTEM FOR THE TREATMENT OF SPONDYLOLISTHESIS WITHOUT ADJUNCT DECOMPRESSION

F. Dakhil-Jerew, S. Haleem, J. Shepperd Conquest Hospital, Hastings, UK

# Introduction

The results of the FDA trial for Dynesys stabilisation implied that the procedure was effective as a method of treatment for this condition. However, all the American cases had adjunct decompressive treatment.. In this study we report the outcome of the first two years following DYNESYS for Spondylolisthesis in two groups of patients; Dynesys alone and Dynesys with fusion.

### Method

Fifty five patients had Dynesys for symptomatic Spondylolisthesis which was indicated for surgical treatment. Average age for group 1 was 51 years with range of 36-85 years whereas in group 2, average age was 59 years with range of 31-79 years. Patients were evaluated preoperatively using ODI, SF36, VAS, plain x-ray, MRI scanning & discography. 33 of the patients underwent Dynesys alone (group 1) while 22 underwent dynesys with fusion (group 2). Forward slipping was graded as GI, GII and GIII and it was recorded in group 1 as 46, 7 and 2respectively whereas in group 2 as 37, 14 and 4 respectively.

Previous decompression surgery was noted in 10 in group 1 and 8 in group 2.





to improve, Subsequently 3 group 1 patients underwent fusion and 12 required removal / revision of Dynesys ( 40% ).

### **Discussion & Conclusions**

Dynesys alone in the treatment of spondylolysthesis resulted in a 45% re-operation rate, and we believe it should not be recommended as an indication.

In the first year following Dynesys, both groups did show

significant improvement in all the four parameters; VAS

(back and leg), ODI and SF36. In group 2 slight deterio-

ration was noted in year 2 and while group 1 continued



# Results

IDAY POSTER SESS

94



# TWO YEARS OUTCOME FOLLOWING DYNAMIC NEUTRALISATION SYSTEM FOR THE TREATMENT OF SPINAL CANAL STENOSIS

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# Introduction

We report the outcome two years following Dynesys for the treatment of Spinal Canal Stenosis. In both the FDA trial and the European multicentre study, stenosis was invariably combined with decompression, invalidating conclusions on the results of Dynesys alone.

# Method

Eighteen patients had symptomatic Spinal Canal Stenosis with root claudication sufficient to justify surgical intervention. Average age of patients was 68 with a range between 44-86 years. Dynesys was applied for the treatment of a single level in 4, two levels in 8, and more than two levels in 6.

Patients were evaluated preoperatively using ODI , SF36, VAS, plain x-ray, MRI scanning & discography. Questionnaires were evaluated at the first and second years.



in a second	Preoperative	1st year	2nd year	
VAS B	69.8	40.1	47.1	
VASL	62.5	39.8	47.1	
SF 36	36	51.9	34.5	
ODI	56.5	44.1	45.6	

# Results

2 patients had undergone previous spinal decompression, and decompression at the time of Dynesys surgery in 7. In the remaining 9 cases, no decompression was used, relying on distraction alone as in the X stop system. In this latter group, stenotic symptoms failed to resolve. Removal of Dynesys was indicated in 3(16.6%).

# **Discussion & Conclusions**

Dynesys alone is not recommended as a treatment for symptomatic spinal stenosis . A separate study is required to address the question of whether Dynesys adjunct improves the back pain outcome compared with decompression alone.



# ACCURACY OF DETECTING PEDICLE SCREW LOOSENING USING PLAIN X RAY

Fras Dakhil-Jerew , Harpal Jadeja , Nick Bowman , D Shah , AdamCohen , Ashraf El-Metwally , Rose Guy , Guy Selmon , John Shepperd

Conquest Hospital, Hastings, UK

# Introduction:

In this study, we report interobserver reliability of X-ray for the interpretation of pedicle screw osteointegration based on the diagnosis of "Halo zone" surrounding the screw.

Dynamic stabilisation system for the spine relies on titanium screw purchase within the pedicle. Decision on osteointegration is important especially when the patient becomes symptomatic following initial good outcome. From our cohort of 420 Dynesys patients, over all incidence of screw loosening was 17%. Only 35% were symptomatic.

### Method:

Lumbar spine X-ray images of 50 patients in two views (AP and lateral) randomly selected from our cohort of 420 Dynesys patients. The images were deployed in a CD-ROM. The authors were asked to review the images and state whether or not each pedicle screw is loose (total of 258 pedicle screws).

Seven observers composed of two expert orthopaedic spine consultant surgeons and one spine expert consultant radiologist and four Specialist Registrars in orthopaedics and radiology.

Data gathered were distributed and presented in tables in the form of descriptive statistics. The evaluation of interobserver agreement was performed by obtaining a Kappa (K) index. For continuous variables comparison, the t test was employed, with a significance level of 0.05.

Percentage of Kappa index for Pedicle screw loosening

**3** Experts

CI (-0.0520, 0.4916)

0.2198

# **Discussion & Conclusion**

Kappa Index among expert assessors was 0.2 which means X-ray is unreliable for the assessment of pedicle screw osteointegration. Validity of X-ray is not applicable as it is unreliable.

We are planning to evaluate a 3D computer reconstruction model based on 2 X-ray views at 45 degree angle to each other which might be sensitive to detect screw loosenina.

3 Experts & 4 SpR

CI (0.0332, 0.2592)

0.1462



# DOES ACCELERATED ADJACENT SEGMENT DISEASE OCCUR FOLLOWING CERVICAL BRYAN TOTAL DISC ARTHROPLASTY: FOUR CASES

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# Introduction

The rationale to use TDA is to restore and maintain normal physiological motion rather than elimination of motion. Other advantages include restoration of intervertebral space height with reduction of strain aiming at elimination of the adjacent segment disease.

We describe 4 patients with a serious complication observed following implantation of the Bryan disc prosthesis in our cohort of 48 patients.

# **Case series**

43 Male presented with neck pain & left brachalgia. MRI showed C5/6 disc prolapse with left C6 root impingement. He underwent C5/6 Bryan TDA in April 2004. After 14 months he became symptomatic and his MRI revealed new C6/7 and C3/4 disc protrusion compressing the spinal canal and the left exit foramen. His symptoms resolved with C3/4 and C6/7 Bryan TDA in January 2006

47 Male presented with worsening gait over 2 years with right brachalgia. On examination he was found to have progressive cervical myelopathy with right C5 radiculopathy. His MRI confirmed severe C5/6 disc degeneration with spinal cord compression. He did very well following C5/6 Bryan TDA in January 2003. After 16 months he had a flare up of left C6 radiculopathy, MRI was done only to show new left C6/7 disc prolapse.

45 Female with 6 years of neck pain with right C5 brachalgia. MRI confirmed C5/6 central disc herniation with cord compression. He was treated with C5/6 Bryan TDA in December 2000. His symptoms were controlled up to 5 years and 7 months when he developed new C6/7 canal narrowing with right C6 radiculopathy. He was successfully treated with C6/7 Bryan TDA

38 Male with worsening of gait over 5 years and progressive cervical myelopathy. His MRI showed severe C5/6 disc degeneration with spinal cord compression C5/6 Bryan TDA was done in August 2003 and after 3 years new C4/5 disc prolapse with C5 radiculopathy was diagnosed and treated with C4/5 Bryan TDA.

# Discussion

In this study, four patients' initial response after surgery was satisfactory. Neck Disability Index and SF36 were significantly improved. On intermediate term follow up, the functional outcome deteriorated and second surgery was necessary. The average time between first and second surgeries was 33 months with a range of 14 - 67 months.

# Conclusion

Bryan TDR did not prevent the development of accelerated ASD. The authors believe that further evaluation of in vivo Bryan® disc is necessary to decide on its actual ROM and hence protection of adjacent levels.



# SACRUM ORIENTATION, INFLUENCES LUMBAR SPINE AND PELVIS MOTION

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# Introduction

Trunk flexion involves the lumbar spine and pelvis movements (1). Kinematic characteristics of the spine and pelvis are one measure proposed to assess lumbar dysfunction (3). Investigations studying spine-pelvis coordination show large inter-individual variations, which makes a good discrimination between chronic low back pain patients and asymptomatic subjects difficult. Most researchers argued methodological issues to explain these differences. Others (2), further, showed that some subjects move more in the lumbar spine than the hip during trunk flexion. In order to extend our knowledge about this matter we brought forward the present investigation. The purpose was to describe the relationship between the orientation of the sacrum at upright position and the range of the lumbar spine and pelvis movement during trunk flexion in free-pain subjects. Methods. Individuals (n=39), were divided into two groups according to whether they have either pelvis (Pelvis/P) or lumbar spine (Spine/S) dominant movements during flexion. Subjects characteristics for P-group (n=18: 11female, 7male) were (age, =23,67±4,94/ range:18-33 years; average weight: 68,5±9,58 kg and height: 1,72±0,06 m) and for S-group (n=21:10 female, 11male),(age,=22,55±2,70/ range:19-27 years; average weight: 66,21±7,89 kg and height:1,69±0,07m). Sacrum orientation at upright position and differential lumbar-pelvic motion during standardized sagittal trunk flexion and re-extension from upright position were measured with an electro-goniometer. It consists of two sensors located at L1 and S1 spinous processes, which detected the magnetic pulses emitted by the source placed at individual hip level (trochanter major). Thus, data (degrees) given by sensors were referred to the hip joint. L1-sensor gives trunk movement, S1-sensor gives sacral inclination (pelvis movement), and lumbar spine movement was obtained subtracting S1 data from L1 data. Positive and negative values indicate flexion and extension, respectively. Results. No differences in subjects' characteristics of the groups were found by the unpaired t-test. Significant differences (]  $\leq .05^*$ , ]  $\leq .01$ ) between groups and sexes were shown by the two-factor Anova (group, sexes, group\*sexes) for the variables.



	Maxi	Maximum range of flexion degrees (± sd)						
	trunk	pelvis	spine					
Р	119,4 (17,1)	71,2(17,0)	48,2(10,6)					
S	116,0 (15,5)	47,2(10,3)	68,8(11,5)					
F	122,2(15,8) *	62,1(20,5)	60,1(15,8)*					
М	112,1(15,8)	55,2(20,5)	56,9(15,8)					

Pelvis group (P). Spine group (S). Female (F). Male (M).

In the pelvis group the sacrum was significantly more horizontal (-10,0  $^{\rm o}$   $\pm$  11,4°) than in the spine group

 $(-29,3^{\circ} \pm 13,49^{\circ})$ . In the Pelvis-group very strong correlation between sacrum orientation and the maximum range of pelvis flexion was found for both of the female (r = 0,85) and male (r = 0,93). The regression model has an R2 value of 0,73 for female and 0,87 for male and can be expressed mathematically, as['range of pelvis flexion'(degrees) = -0,003 [sacrum (degrees)] 3 - 0,12[sacrum (degrees)] 2 - 0,15[sacrum (degrees)] + 90,3, and 'range of pelvis flexion' (degrees) = 0,22 [sacrum (degrees)] 2 + 1,32 [sacrum (degrees)] + 67,05] for female and male, respectively. In the Spine group, sacrum orientation showed a strong correlation with the maximum range of spine flexion for both of them, female (r = 0, 63) and male (r = 0, 66). The regression model has an R2 value of 0, 40 for female and of 0,43 for male and can be expressed mathematically, as ['range of spine flexion' (degrees) = -0,02 [sacrum (degrees)]2 - 2,23[sacrum (degrees)] + 14,47, and 'range of spine flexion' (degrees) = -0,002[sacrum (degrees)]3 - 0,08[sacrum (degrees)]2 - 1,42[sacrum (degrees)] + 54,22 ] for female and male, respectively. The regression models showed random and normal residuals.

### Discussion

The main finding of this study was that sacrum orientations at upright position, in both sexes, explain: for the range of pelvis motion in people whose pelvis movement is dominant during flexion; and for the range of lumbar spine motion in people whose lumbar spine movement is dominant during flexion. These results suggest the influence of the individual morphology on the lumbo-pelvic patterns of movements.

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# AN APPROACH TO THE LUMBAR VERTEBRAE MORPHOLOGY

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The purpose of this current study was to gain understanding of the lumbar spine morphology. The investigation aimed to quantify dimensions of the lumbar vertebrae and to relate to them, across the five vertebral levels. Methods. 60 male human lumbar vertebrae (12 spines), range of age (20-40 years) were digitalized (lateral view) with a Video camera ICD-840P RGB Ikegami, Targa+ Truevision card. High resolution Monitor Mitsubishi14" FA 3435L9ETKL. Camera objective was kept at a constant distance of each vertebra, which was placed on an adjustable base, in order to be balanced. Upper-endplate was levelled to the horizontal spatial plane by means of a level located on it. A line was drawn all along the upperendplate, and, thus vertebra dimensions' were defined and referred to this line. Dimensions (mm) determined were (fig. 1): the length of the whole vertebra (v) and of the spinous process (sp); the anterior / posterior heights (a / p), and the upper / lower endplate lengths (u / I). The inclination angle (i, degrees) of the lower-endplate was further calculated. Data and statistical analyses. All linear dimensions were related to those of the L3. That is to say, for each of the linear measurements L3/L1, L3/l2,-L3/-L4, and L3/L5 ratios were calculated. Significant differences between ratios and angles across levels were shown by the randomized complete blocks test, and the Student-Newman-Keuls as post-hoc test (]  $\leq .05^*$ ,]  $\leq .001^*$ ).

### Results

Average ratios are presented in the figures 2, 4 and 5, and the angles of the lower-endplate inclination in figure 3.Discussion. There is a level-by-level decrease of the anterior bodies' heights ratios (fig.2), which means that there is a progressive relative increase of the anterior bodies' heights from L1 to I5.There is a level-by-level increase of the posterior bodies' heights ratios, which means that there is a progressive relative decrease of the posterior bodies' heights from L1 to L5. Likewise a significant increase was observed for the lower-endplates inclination angles (fig.3), from the L1 to L5 vertebrae. Altogether, these results showed that L1, L2 vertebrae are ventrally wedged (i<0°), whereas L3, L4, L5 vertebrae are dorsally wedged (i>0°) (1). From these results, it could be suggested that this level-by-level vertebral morphology contributes to shape the anterior convexity of the lumbar curvature along with the intervertebral discs (2). On the other hand, L3/L1 and L3/L2 spinous and vertebral lengths ratios were no significant different from L3/L5 and L3/L4, respectively. However, there is a significant and a progressive decrease from L3/L1 to L3/L2; and from L3/L5 to L3/L4 spinous and vertebral lengths ratios (fig5). It shows that lengths of the spinous process and vertebrae define two segments with same trends at the lumbar spine, the upper L1 and L2 segment; and the lower L4 and L5, which join together at L3 vertebra. This agrees with the posterior concavity of the lumbar curvature. Overall, this study shows another form and more precise way of describing the lumbar spine morphology.

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# MECHANICAL PROPERTIES OF SPINAL SEGMENTS WITH HUMIDITY AND TEMPERATURE VARIATION

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### Introduction

In vitro testing of spinal motion segments provides valuable information about the effects of implants and surgical procedures on the biomechanics of the spine. Few studies, however have investigated the effect of varying laboratory testing environments on the outcome of these tests. Differences in testing temperature and moisture conditions may have an important influence on the subsequent mechanical properties.

### **Materials and Methods**

The lumbar spines of 9 sheep were harvested and separated into L1-L2, L3-L4, and L5-L6 for a total of 27 motion segments. Specimens were set in a testing fixture with a fast curing polymer and frozen until testing. One specimen from each spine was tested in either, 1) air at 18°C while wrapped with gauze soaked in Phosphate Buffered Saline (PBS), 2) a PBS bath at 37°C, or 3) at 37°C and 100% humidity generated by PBS. Mechanical testing was performed on a Bionix 858 bi-axial testing machine (MTS Systems, Eden Prairie, MN) in a jig capable of applying pure moments. Specimens were cycled through +/-8000 Nmm in axial torsion, lateral bending, and flexion/extension. Specimens were allowed 90 minutes to acclimatize to the test conditions after thawing and tests were repeated every hour for 6 hours. Each bending mode was repeated for 4 cycles, the last 3 of which were used in calculations. Torque, angle, load, and displacement were recorded at 20 Hz throughout the test. Stiffness was calculated from 5000 Nm to 7000 Nm via a least squares method and the lines extended to the zero intercept to determine the limits of the neutral zone. Additionally the neutral zone stiffness was calculated as the least squares fit of the data in the hysteresis zone. Range of Motion (ROM) was based on the total angular motion from 7000 to -7000 Nmm.

### Results

The neutral zone gradually increased for all tests with time. Neutral zone stiffness was steady for PBS bath and 100% humidity conditions but decreased steadily for tests in air (Figure 1). Stiffness (5000-7000 Nmm) was steady throughout testing but was higher for specimens tested in air, particularly in flexion/extension (Figure 2). ROM increased consistently with each test and was higher for the tests at elevated temperatures.

# Discussion

There are numerous properties that can be determined through mechanical testing, each providing a different insight into the condition of a motion segment.

Temperature and humidity changes do influence the biomechanics of spinal segments. Testing for 6 consecutive hours was accompanied by a steadily increasing ROM. Mechanical properties in lateral bending are sensitive to changes in the disc. The decreasing neutral zone stiffness suggests that moisture is being expelled from the disc during the open air tests, while the moisture content is stable for the other two conditions. The increased stiffness of the tests in the humidity chamber when compared to the PBS bath were unexpected as the nucleus has been shown to swell in PBS [1]. The significance of this result is unknown at this time. The ligaments of the posterior elements act to limit motion in flexion and as such, the decreased stiffness seen at elevated temperatures might be influenced by the thermo-sensitive properties of spinal ligaments [2].

### Figure 1 Neutral zone stiffness for lateral bending

Figure 2 Stiffness (5000 Nmm-7000Nmm) for flexion/extension

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# EORS 2008 · MADRID



### P-008

# FETAL SPINE CELLS FOR INTERVERTEBRAL DISC REGENERATION

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Introduction

Degeneration of the intervertebral disc (IVDD) is thought to be one main cause of low back pain. IVDD begins early in the nucleus pulposus (NP) with decreased cellular content and a loss of proteoglycan and water. Our hypothesis is that matrix synthesis could be stimulated by proteoglycan producing cells. Fetal disc cells could be a promising cell source for regeneration of the degenerated disc. The aim of this study was to investigate the feasibility of using fetal disc cells for disc tissue engineering.

### Method

Fetal spinal column tissues (1 cm) were obtained after voluntary interruption of pregnancy at 14-16 weeks of gestation (n=3). The spinal tissue was cleaned of adherent tissue, dissected and put into culture in tissue culture dishes. Cells were routinely cultured in DMEM with 10% FCS and 200 mM L-Glutamine. Cell proliferation in monolayer was measured with the CellTiter colorimetric method and compared to adult NP cells (individuals aged 30 to 40 years). Consistency of the cell culture was assessed by measuring expression of galectin-3 and HIF-1 by flow cytometry at passages 4 and 6. Sulphated glycosaminoglycan (sGAG) production by fetal spine cells entrapped in alginate beads was identified by alcian blue staining and measured by DMMB assay and normalized to DNA content. mRNA levels of aggrecan, type I and II collagen were measured after 2, 7, 14 and 28 days of culture.

# Results

Isolated fetal cells proliferated more rapidly than adult NP cells and showed consistent culture regarding galectin-3 and HIF-1 expression at passages 4 and 6. Compared to monolayer culture, fetal spine cells in alginate beads portrayed a rounded morphology with a ring of pericellular matrix identified by alcian blue staining. However, some cells did not produce any matrix. Production of matrix was confirmed by an increase in GAG/DNA ratio during culture. mRNA level of aggrecan and type II collagen largely increased during the 28 day culture period whereas mRNA level of type I collagen remained stable.

### Discussion

Fetal spine cells can be cultured in vitro with minimal requirements and the consistency necessary for a potential clinical application. When cultured in a 3-D environment, they synthesize sGAG, which are responsible for the high water content in NP matrix. It will be of interest to investigate the regeneration capacity of the fetal spine cells in an appropriate animal model.

# Acknowledgements

Supported by AO Research Grant 04-S33.

# POSTER SESSION 2 Shoulder

### P-009

# PECTORALIS MAJOR TENDON AS A REFE-RENCE FOR RESTORING HUMERAL LENGTH AND RETROVERSION WITH HEMIARTHRO-PLASTY FOR FRACTURE

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### Introduction

Shoulder hemiarthroplasty is an established treatment for complex proximal humeral fractures but the functional results of these hemiarthroplasties in proximal humeral fractures are often poor and unpredictable. The capacity of restoring proximal humeral anatomy in such these complex fractures is of capital importance to obtain proper placement and secure fixation of the tuberosities to the prosthesis. The purpose of this study was to determine the value of the upper edge of the pectoralis major insertion as a landmark to determine proper height and version of hemiarthroplasties implanted for proximal humeral fractures.

# **Materials and Methods**

The upper edge of the pectoralis major insertion was referenced with a metallic device in 20 cadaveric humerus. A Computed Tomography study was performed in all the specimens. Total humeral length was recorded in all the specimens. The distance between the upper pectoralis major insertion and the tangent to the humeral head was also recorded. The anatomical neck of the humeral head was determined in the axial plane of the CT scan and a perpendicular line was drawn to represent the posterior fin of the prosthesis. To that image, the CT scan slice showing the upper insertion of the pectoralis major was superimposed and the distance of the metallic reference to the posterior fin of the prosthesis was recorded as it was the angle formed by the line connecting the upper pectoralis major insertion with the center of the anatomical neck diameter and with the posterior fin of the prosthesis.

Qualitative variables are presented in absolute and percentage values. Quantitative variables are presented with mean values and standard deviation.

### Results

Mean total humeral length was 32,13 cm. The mean distance from the upper pectoralis major insertion to the tangent to the humeral head was of 5,64. The mean distance from the upper pectoralis major insertion to the tangent to the humeral head represents the 17,55 % of the total humeral length. The mean distance of the upper pectoralis major insertion to the posterior fin of



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the prosthesis was of 1,06 cm. The angle between the upper pectoralis major insertion and the posterior fin of the prosthesis was of  $24,65^{\circ}$ .

### Conclusions

Mean distance from the upper part of the pectoralis major insertion to the top of the humeral head of 5, 6 cm with a 95% confidence interval.

Placement of the prosthesis in the proper retroversion can be achieved by placing the posterior fin 1,06 cm posterior to the upper insertion of the pectoralis major or by placing the posterior fin at 24,65° with respect to the upper insertion line.

Upper insertion of the pectoralis major constitutes a reliable reference to reproduce anatomy in hemiarthroplasties for proximal humeral fractures.

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# MUSCULAR COMPENSATION IN PATIENT WITH MASSIVE ROTATOR CUFF TEAR: SUPERFICIAL ELECTROMYOGRAPHY STUDY

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Shoulder girdle is an extremely mobile joint. It can determine 16000 different positions due to a fine coordination between bony structures and muscles. The extreme mobility that characterizes this joint is strongly dependent on the absence of skeletal blocks, which, in contrast, is also responsible for its poor intrinsic stability. The rotator cuff muscles (supraspinatus, infraspinatus, subscapularis and teres minor) and the scapular muscles provide the stability of the scapulo-humeral joint. Rotator cuff tears alter the equilibrium existing between these components. The deltoid, thus, finding no opposition to its force, causes the upward shifting of the head of the humerus. The condition resulting from this unbalance is the "subacromial impingement syndrome" and leads to an extension the rotator cuff lesion. The clinical counterpart of this vicious circle is increasing pain and progressive movement impairment.

Our work originates from the evidence that not all patients with massive rotator cuff tear show the same symptoms, characterized by pain and progressive loss in range of motion.

Patients with comparable clinical and RMI lesion can present extremely variable symptoms: pain and loss of articular function may range from mild to severe. A "mechanism of compensation" has been postulated by many authors, but its existence still requires evidence. According to this model, the longitudinal muscles of the shoulder (pectoralis major and latissimus dorsi) and the undamaged muscles of the rotator cuff (subscapularis and infraspinatus) would functionally compensate and would be able to supersede the function of rotator cuff and to reduce the symptoms.

The aim of this study was to evaluate muscular activation of the medium fibers of deltoid, the superior fibers of pectoralis major, the latissimus dorsi and the infraspinatus by a superficial electromyographic study (EMG) and the analysis of kinematics in patients with a massive rotator cuff tear.

From 2005 to 2007, we evaluated 30 subjects (12 males, 18 females, mean age 62), 15 of them had paucisymptomatic massive rotator cuff tear (modest pain and preserved movement), and 15 healthy controls.

Patients with a massive tear, diagnosed by clinical testing and MRI, were enrolled in this study and compared to the control group. This study evaluated the maximal isokinetic values in elevation on scapular plane.

A superficial EMG of the deltoid, pectoralis major, latissimus dorsi and subspinatus muscles was performed on the limb with a  $70^{\circ}$  abduction on the scapular plane. In this particular position, the subacromial conflict is at the highest level, making it our test of choice for measuring the activation of the compensatory muscles. The sudy included: 1) evaluation of maximal isokinetic values (performed 10 minutes before the beginning of the test). Every patient performed 2 maximal isometric contractions of 5 seconds of deltoid, pectoralis major, latissimus dorsi and infraspinatus; 2) active test (elevation on scapular plane). Patient was asked to keep the arm in the testing position for a period ranging from 30 seconds to 3 minutes. This exercise was done 3 times for each patient with a pause of 2 minutes between each test.

Data obtained from the affected limb were compared with those obtained in the healthy contralateral limb and with those observed in the control group.

The study showed higher mean values of activation for the deltoid, the infraspinatus, the pectoralis major and the latissimus dorsi compared to the healthy contralateral joint.

Paired t-test showed significant different activations (p<0.05) of these 4 muscles between the pathological joint and the healthy one in the same patient.

The unpaired t-test, after comparing the mean EMG values of the 4 muscles, produced a significant difference (p<0.05) between the experimental group and control group. These muscles (deltoid, pectoralis major, latissimus dorsi and infraspinatus muscles) increase their activity respectively 2, 3, 1,6 and 2 times with respect to healthy subjects.

The linear correlation (p=0,015; r=0,61) between the activation of deltoid and the other muscles allowed to understand the worldliness of muscular activation. In the first phase, it still increases the activity of the healthy rotator cuff muscles; subsequently, latissimus dorsi and pectoralis major also increase their activity.

This study showed that a mechanism of muscular compensation is activated in patients suffering from rotator cuff tear, involving the deltoid and the infraspinatus muscle, as already presented in literature, but also demonstrated the activation of 2 other muscles: the latissimus dorsi and the pectoralis major. It is, therefore, probable that, in these patients, these muscles, which would not normally pull the head of the humerus downwards, adapt in order to compensate for the pathological situation. We believe that these data are valuable in the surgical and rehabilitation planning in patients with a massive rotator cuff tear.

Primary surgery should aim to obtain a functionally reconstruction of the anterior and posterior components of forces, rather than an anatomical reconstruction of the rotator cuff, in order to allow for the muscular compensation of healthy rotator cuff muscles. Moreover, physiotherapeutic programs for massive rotator cuff tears should also include pectoralis major and latissimus dorsi reinforcement.



# AN ANATOMICAL APPROACH TO FUNCTIONAL SEGMENTS WITHIN THE DELTOID MUSCLE

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### Introduction

Physiological studies have shown that the central nervous system controls groups of muscle fibers in a very efficient manner. Within a single skeletal muscle, the central nervous system independently controls individual muscle segments to produce a particular motor outcome. Recent mechanomyographic studies of the deltoid muscle have revealed that the deltoid muscle, commonly described as having only two (clavicular and scapular) or three (anterior, middle and posterior heads) anatomical segments, is composed of at least seven functional muscle segments which all have the potential to be at an important level independently coordinated by the central nervous system.[1][2] This provides the central nervous system with a greater flexibility to fine-tune the activity of the deltoid muscle motor units. An understanding of the functional mechanisms of the deltoid muscle may give an insight into motion patterns of the upper limb in specific clinical situations or for modeling use. The present study was designed to anatomically describe and guantify the different functional segments within the deltoid muscle, based on the branching pattern of the axillary nerve.

### Methods

Forty-two deltoids of 21 embalmed adult cadavers, median age 73 (54-89), were included in the study. The deltopectoral fascia was divided and the humeral insertion of the pectoralis major muscle was sectioned. The axillary artery and major peripheral nerves were retracted medially, and the axillary neurovascular bundle was identified. The subscapularis muscle, the front of the quadrilateral space and the proximal part of the axillary nerve were exposed. In a second stage the external deltoid muscle segmentations were identified according to the fiber directions and the presence of muscle fascial segmentation patterns. The axillary nerve was carefully dissected together with its anterior and posterior branch upon invasion into the muscle. The deltoids were dissected sharply from their origins and insertions. According to the pattern of fiber distribution and the muscle fascial embalmment, the deltoid muscle was carefully splitted internally into different portions, each being innervated by a major branch of the axillary nerve. The position and volume of each segment in relation to the whole muscle were derived.

### Results

In 3 cases the axillary nerve branched out into 8 major divisions, but most frequently into 7 parts. This branching pattern occurred in 22 out of 42 cases (48%). The second most frequent branching pattern was in 6 major divisions (14 out of 42 cases). A division into 5 major branches was seen in 5 of the specimens. Mean values for volume and weight of the different segments are given in table 1. In general, the posterior and anterior peripheral segments seem to have the largest volume. The more central segments within the deltoid muscle are about 20 to 50 % smaller in volume. In nearly all (93%) cases, the central segments were lower in weight and volume compared to the more peripheral segments.



### **Discussion and conclusion**

Based on the innervation pattern of the deltoid muscle, a segmentation in 5 as many as 8 major segments was found. From anatomical point of view this confirms earlier reports of functional differentiation within the deltoid muscle. This confirmation gives a better understanding of the functional aspect of the deltoid muscle in different shoulder movements and may provide a plus in biomechanical modeling of the upper limb.

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# EXCURSION AND STRAIN OF THE BRACHIAL PLEXUS AND PERIPHERAL UPPER LIMB NERVES FOLLOWING REVERSED ARTHROPLASTY OF THE SHOULDER

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# Introduction

The concept of non-anatomic reversed arthroplasty for the treatment of omarthrotic shoulders with severe destruction of the rotator cuff is becoming increasingly popular and has been shown to provide predictable improvement in pain and function. [1] The reversed prosthetic design medializes and stabilizes the center of rotation, minimizes torgue on the glenoid component, and aids in recruiting fibers of the anterior and posterior deltoid to act as abductors. The design lowers the humerus relative to the acromion, restoring and even increasing deltoid tension by lengthening the muscle up to 18% of its original length. [2] Such a surgically created global distraction of muscles is libely to affect nervous structures. When nerves are stretched, the nerve path straightens by longitudinal sliding or excursion of the nerve within its bed. With further tension the nerve excurses by straining its undulated axons. The change in length divided by the initial length is termed nerve strain. Nerve strain of 5-10% impairs axonal transport and nerve conduction. At 8% of elongation the flow of venous blood from nerves starts to diminish and at 15% all circulation in and out of the nerve is obstructed by stretching and strangulation of the intraneural vessels. [3] In the present study we have tried to quantify the amount of excursion and strain of the brachial plexus and peripheral upper limb nerves following reversed shoulder arthroplasty by simulation of the process on a cadaver model.

### Methods

In a formalin-embalmed female cadaver specimen, the brachial plexus was carefully dissected using an anterior approach and injected with an iodine contrast medium (visipaque), glycerine and toluïdine blue to secure proper injection and highlight the nerve tissue on CT imaging. At the same time sixteen 1.2 mm-diameter leaded markers were implanted in the plexus and peripheral nerves at topographically crucial via points for later enhanced recognition on CT reconstructions. After the first session of CT scanning a plastic replica of the Delta reversed shoulder prosthesis ® (DuPuy Orthopaedics, Inc., Warsaw, IN) was surgically placed followed by re-injection of the plexus with the same solution. The preoperative and the

postoperative specimen were studied using a helical CT scan with a 0,5 mm slice increment (Siemens/ volume zoom). The Mimics ® (Materialise NV, Heverlee, Belgium) software package was used for visualization and segmentation of CT images and 3D rendering of the brachial plexus and peripheral nerves. After reconstruction the nerve segment paths were approximated using the draw nerve function. Each segment was exported in STL format and the respective lengths were calculated.



# Results

The starting position before reversed surgery was assigned 0% strain. The percentage change in strain was calculated from the length of the segments divided by the non-operated segment length. After surgery, there was an average increase in nerve strain below physiologically relevant amplitudes. In a few local segments of the brachial plexus an increase in nerve strain exceeding 5-10 % was calculated. The largest increase in strain ( up to 19% ) was observed in a segment of the medial cord.

# **Discussion and conclusion**

To understand nerve dynamics following reversed arthroplasty, we investigated nerve strain and excursion in a cadaver shoulder before and after surgery. Our results support the hypothesis that there can be a clinically relevant increase in strain of the neurovascular structures.

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# THE "CASCADE" MEMBRANE: A NEW PRP DEVICE FOR TENDON RUPTURES. PRELIMINARY EXPERIENCE ON ROTATOR CUFF TENDONS.

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Rotator cuff tears are common soft-tissue injuries that often require surgical treatment. Initial efforts to better tendon healing centered on improving the strength of repair. More recent studies have focused on biologic enhancement of the healing process. Platelet rich plasma (PRP) is a fraction of plasma that has been isolated and used to enhance regeneration in bone and soft tissues. The healing potential of PRP has been attributed to the release of multiple growth factors from the highly concentrated platelets. The "Cascade" membrane is a thin layer of autologous fibrine very rich of platelets obtained by high speed centrifugation of a small quantity of PRP. Authors present 10 patients (average age 45, range 34-68) that underwent surgical repair with arthroscopy and mini-open approach with acromionplasty, subacromial decompression, cuff repair by trans-bone suture and application on the tear of the "Cascade" membrane (A.T. Grade Milano, Italy) that was sutured side-to-side to close the tear. A standard rehabilitation protocol for rotator cuff tears was performed. A MRI 6 months after surgical repair showed complete integrity of the cuff under the application site of the membrane, the ROM after surgery raised up of about 65% (range 25-95%). There is currently no widely accepted treatment for massive, irreparable rotator cuff tears. Allograft reconstruction to span the remaining defect in massive rotator cuff tears will lead to increased functional results; we think that our experience has to be considered as a preliminary report that needs further studies to describe and evaluate its potential in tendon healing.



# POSTER SESSION 3 Tissue engineering/Biomaterials

### P-015

# EFFECT OF A GLASS-CERAMIC OVER A MSCS POPULATION. AN IN VITRO STUDY.

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### Introduction

In the last years, it has appeared a great interest to improve the osteogenic properties of some materials throught the construction of hybrid materials biologically active. This fact has allowed to seed different types of cells [1] onto different materials acting as scaffolds to optimize the repair results [2,3], trying to mimic the structure and the biology of autologous spongy bone. In this work a bioactive glass-ceramic (GC) in the system SiO2-CaO-P2O5 was evaluated as bone substitute biomaterial. In this sense, the capacity of mesenchymal stem cells (MSCs) to adhere, proliferate and differentiate into osteoblast (OBs) with or without GC was investigated. Two types of culture medium, i.e. growth medium (GM) and osteogenic medium (OM), were evaluated.

### **Materials and Methods**

- Material preparation and characterization: The GC was obtained by heat treatment of a bioactive glass (55-SiO2; 41-CaO; 4-P2O5; mol %), obtained by the sol-gel method [4]. Finally pieces of 4.8 mmdiameter and 1.3 mm-height were obtained. - Primary culture. Isolation and culture of MSCs: The adult MSCs were isolated from bone marrow of adult rabbits obtained by direct aspirations of ileac crest. For the isolation, the aspirated material was devoid of erythrocytes and it was centrifugated. After estimating the viability with tripan blue, the cells were plated out in culture flacks with ]-MEM + FCS and they were incubated at standard conditions. - Isolation and culture of osteoblasts OBs): The OBs used as control were obtained by the method of enzymatic digestion as we previously reported [5]. - Characterization of MSCs and OBs: The isolated OBs were identified and characterized through their morphology and characteristics of growth (PCM and SEM), by their capacity of mineralization, production of alkaline phosphatase (ALP) and osteocalcin (OC), as previously reported [5]. For the characterization and differentiation of MSCs, two culture media were used: (a) GM. It was used for cell isolation. It consists of ]-MEM supplemented with of heat inactivated FCS and routin antibiotics, (b) OM. It consists of GM with an osteogenic supplement composed of L-ascorbic acid-2P, Dexametasone and ]-glicerolphosphate. The cells from first subculture were seeded, one half in GM y and the other half in OM. Afterwards, they were detached from the flasks and subsequently seeded for their characterization through optical and SEM, CD90 expression and OC production.

# Pagoda 15:10 - 15:<u>45 h O 015-022</u>

- Behavior of MSCs on GC: For the study of the behavior of isolated MSCs on the GC, two series of 96-well plates were seeded, one plate with GM and the other one with OM. Then 5 x 103 cells were seeded onto each disk. At 24 hours, 7, 15, 21 and 27 days cell adherence and growth were analyzed. The number of cells was evaluated through the XTT assay. After one month OC production and CD90 expression of cells cultured in both media were measured to evaluate the possible differentiation of MSCs into osteoblasts. These measurements were carried out in triplicate. - Statistical analysis: A variance analysis (ANOVA) was carried out with a minimal significance of p<0.05.

### Results

Briefly, in the XTT assay, the absorbance values detected at 24 h were very low. However, the growth of those cells able to attach to the biomaterial was progressing linearly with the time. The number of cells growing in OM was always discretely lower than those obtained in GM, although there were no significant differences between them. The MSCs under the conditions of this study expressed an osteoblastic phenotype characterized by the OC production. Simultaneously a decrease in the marker CD90 expression typical of the MSCs was detected. These two effects took place by either the action of exposing the MSCs to a MO for a long time (1 month), as well as by the effect of the GC. Therefore, a process of differentiation of the MSCs into OBs took place.

### Conclusions

The GC has provided a favourable environment to support adhesion, proliferation and differentiation of MSCs to OBs and an increase of mineralized ExM, even in GM. This effect increased with the combination of GC with OM. This fact would contribute to the quick bond of the material to the receptor bone in vivo. These results make consider the material object of study as a substrate promoter of bone tissue regeneration suitable for bioengineering of bone tissue.

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# OSTEOGENIC POTENTIAL OF CELLS FROM THE MEDIA LAYER OF ARTERY WALL MAY CONTRIBUTE TO GUIDE BONE REGENERATION: A COMPARATIVE STUDY BETWEEN ARTERY AND E-PTFE MEMBRANES.

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### INTRODUCTION

Calcification and ossification have been described in artery wall of end stage renal disease, atherosclerosis, diabetes mellitus and aging1. We previously described the use of cryopreserved arterial allografts as membranes for guiding bone regeneration2. We hypothesize that artery is as good as synthetic membranes (e-PTFE, gold-standard in guided bone regeneration) due to the osteogenic potential of cells from its medial layer.

### Methods

I-Comparative study between artery and e-PTFE: 10 mm mid-diaphyseal radial defects were created in 15 New Zeland rabbits: 10 defects were covered with an e-PTFE membrane and 10 defects with no membrane (control group). Studies: X-rays, CT, MR, morpho-densitometric analysis, electronic and optical microscopy.

II-Cellular demonstration in artery wall: Cryopreserved and fresh rabbit thoracic aorta specimens were studied. Medial layer was isolated and cultured as explants in normal medium. Cells were harvested and added to a 3-D scaffold based on plasmatic albumin in osteogenic medium. Immunocitochemical study was made.

Results: Radial defects surrounded by cryopreserved arterial membranes showed total regeneration in 9 of 10 defects versus 7 of 10 defects in e-PTFE group (no statistically significant differences were detected). No tissue layer was found between bone and artery (Fig. 1B) while a connective tissue layer was observed between e-PTFE and bone (Fig. 1A).



Figure 1: interface bone regenerated- membrane (A: e-PTFE group; B: Arterial group).

Neither radiological nor histological healing were detected in

the control group (statistically significant difference was detected).

Cells cultured had smooth muscle features as they showed immunofluorescence with anti-smooth muscle alpha-actin (Fig. 2A), anti-calponin (Fig. 2B) and anti-vimentin (Fig. 2C) antibodies.



Figure 2: immunophenotype of cells from the media layer. When cells were added to a 3-D matrix, they showed chondro and osteogenic differentiation, as they stained positive for types II (Fig. 3A) and X (Fig. 3B) collagen, alkaline phosphatase (Fig. 3C) and von Kossa.



Figure 3: Chondro and osteogenic features of cells seeded in albumin-based scaffold in osteogenic medium.

Conclusions: Although no statistically significant differences between artery and e-PTFE groups were detected, histological and cellular findings suggest a superiority of cryopreserved arterial allografts when compared with synthetic membranes of e-PTFE, with a contribution of the cellular stock of the medial layer in the healing process.

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# EFFICIENT SEEDING OF SHEEP BONE MA-RROW-DERIVED MESENCHYMAL STEM CELLS (MSC) IN POLY(L-LACTIC ACID) SCAFFOLDS

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Hyaline cartilage is a support tissue with a poor capacity to self repair. In the last years, tissue engineering and cell therapy have focused its efforts in the development of scaffolds that may support the differentiation and the implantation of mesnechymal stem cells (MSC) in the site of lesions performed in femoral cartilage. Among synthetic materials used for the construction of these scaffolds, poly(L-lactic acid) (PLLA) is a suitable option, since some studies have offered promising results. The use of PLLA, nevertheles has an important handicap, as cell seeding easily results in a non uniform distribution and a poor density of cells, wich have been proposed as key steps for the differentiation of MSCs to chondrocytes. In our work we have cultured sheep MSCs, and proved its potentiallity by differentiation to chondrocytes in micromass culture. PLLA scaffolds 1 mm thick and 6 mm in diameter were characterized by determining their porosity and their mechanical properties, and subsequently were used to assay the seeding of MSCs. We measured efficiency and adherence by quantification of DNA, and density and distribution by light microscopy of paraffin sections. Our results describe a simple technique of cell seeding by aspirating cells with a syringe that achieves a uniform distribution and a high density of cells. Finally 3D cultured MSCs were differentiated to cartilage as it is shown by massons trichrome staining and immunohistochemistry to collagen type II in paraffin embedded sections.



# USE OF EX VIVO CELLS TO ENHANCE BONE REPAIR

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# Introduction

Modern tissue engineering methods have proposed ex vivo cell growing technique as a promising solution for treatment of bone fractures or diseases leading to the local deficiency of bone. This experiment was designed to assess the effect of ex vivo-cultured cells in ectopic bone induction model with normaly functioning connective tissue cells.

# **Material and methods**

Bone marrow cells, harvested via puncture of tibial canal of male Wistar line rats, were cultured using traditional method, and differented into osteogenic lineage using chemical stimulus (ascorbic acid, beta-glycerophosphate and dexamethasone).

After differentiation osteoprogenitor cells were transferred into beta-tricalcium phosphate scaffolds using either centrifugation or simple diffusion. Six types of implants (beta-tricalcium phosphate matrixes) were implanted into subcutaneous pouches. In the control-group salineimmersed implants were used; in the group 2 the ex vivo cells were transferred into the implant by diffusion and in the group 3 by centrifuging; in the groups 4, 5 and 6 the implants were processed as in first three groups, respectively, but 12.5 microgram of rhBMP-2 was added to the each implant.

After 21 days the implants were removed and dissected systematically. Hematoxylin-eosin histochemical staining was used. Histomorphometry analysis was performed following the principles of stereology.

2

Ns

\* p<0.001, \*\*p<0.01, ns - statistically insignificant

3

Ns

Ns

4

\*

\*

\*

5

\*

\*

\*

Ns

6

\*

\*

\*

Ns

Ns

Ratio of

tissue

95%

99%

97%

53%

64%

58%

connective

2

Ns

3

Ns

Ns

4

\*

\*

\*

5

\*\*

\*

\*

Ns

6

\*

\*

\*

Ns

Ns

Ratio of

formed

bone

0%

0%

0%

40%

28%

34%

# **Results and discussion**

Main results are present in Table.

Bone formation was found only in the implants where rhBMP-2 was introduced. The other implants consisted mostly of connective tissue and in lesser extent of the unchanged scaffold. However, no distinctive differences were found between the implants where rhBMP-2 only or implants where differentiated cells and rhBMP-2 were introduced. The results show clearly that osteoinduction is crucial in ectopic bone formation if there is no cellular dysfunction present. The inductive effect of rhBMP-2 cannot be compensated by the abundance of the predifferentiated osteogenic cells as shown by the absence of bone induction in the groups 2 and 3 in this model. Table. Average relative volumes of bone and connective tissues and cross-charts of statistical differences between the groups.

Group

1

2

3

4

5

6


# DIFFERENT TECHNIQUES OF INDUCTION OF BONE GROWTH BY USING BETA-TRICAL-CIUM PHOSPHATE MATRIX AND MULTIPO-TENT FEMORAL CANAL CELLS

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# Introduction

This study was carried out to investigate directing and accelerating of bone tissue growth, which are important aspects in modern mending of complicated fracture healing and treating of bone tissue disintegrating diseases. Three components are considered to be necessary for bone tissue engineering: matrix/scaffold, progenitor (stem) cells and inductive agents.

#### Material and methods

We compared the bone growth in six types of implants (beta-tricalcium phosphate matrixes) implanted in subcutaneous pouches or close to the femoral head of male Wistar rats: 1. implants immersed in 0.9% sodium chloride solution (control implants), 2. implants with the progenitor cells from femoral canal, 3. implants immersed in inductive BMP-2 solution, 4. implants with the progenitor cells from femoral canal + BMP-2 solution, 5. implants immersed in inductive BMP-2 solution and implanted closed to the femoral head, 6. implants immersed in inductive BMP-2 solution and implanted closed to the femoral head while leaving the femoral canal opened for better access of the femoral canal cells. All the necessary progenitor cells were taken from the femoral canal during the implantation procedure. Implants were removed 21 days after operation and dissected following principles of stereology. Presence of bone or cartilage or connective tissue was evaluated by hematoxylin eosin histochemistry.

# Results

Bone formation was only found in the implants where BMP-2 was introduced (the other implants consisted mostly of connective tissue). However, no distinctive differences were found between the implants where cells and BMP-2 were introduced and between the implants where just BMP-2 was used. Percentages of the bone tissue out of all the implant were as follows: 0.0% in group 1, 1.2% in group 2, 32,4% in group 3, 42,4% in group 4, 44.4% in group 5 and, 54.9% in group 6. Differences in amount of bone tissue between group 3 and group 2 were statistically significant, the difference was also statistically different between groups 3 and 1 and between groups 1 and 2 (p=0.0013, p=0.0004 and p=0.0525 respectively). In the other cases, the differences between BMP-2 affected implants and implants without BMP-2 were even greater. It was notable, that there was more hyaline cartilage in the implants located close to the opened femoral canal.

#### Discussion

The results show clearly that introduction of BMP-2 is a crucial part in cell transformation to bone cell and formation of the bone tissue. We concluded that presence of osteoconductive matrix and introduction of an osteoinductive agent (e.g. BMP-2) are the main components of designing of bone tissue and introduction of exogenous bone cells is not as important as the first two. However, it was notable that some bone formation can be achieved also by introducing multipotent femoral canal cells exogenously.



# A REVIEW OF PRE-SURGERY MARKING GUIDELINES IN ORTHOPAEDICS

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#### Introduction

Wrong-site surgery is undesirable both for the patient and the orthopaedic surgeon concerned. Guidelines are commonly used to promote safe practice but their effectiveness is largely unknown. We aimed to collate guidelines for preoperative marking in orthopaedic surgery, identify areas of convergence and difference and relate them to previous work on guideline effectiveness.

#### Methods

We performed a systematic search for relevant guidelines (1) by searching Medline with the terms 'correct site', 'wrong site', 'marking', 'surgery', 'orthopaedics' and 'guidelines'; (2) by using the same terms in the Google search engine in English, German and Spanish; (3) from orthopaedic societies and national bodies and (4) through personal knowledge and un-indexed conference abstracts.

#### Results

We found nine different guidelines which came from ten institutions in seven different countries; UK National Patient Safety Agency/Royal College of Surgeons of England, Australian College of Surgeons, Joint Commission on Accreditation of Healthcare Organisations (USA), Canadian Orthopaedic Association, Veterans Health Association (USA), Copenhagen Hospital Corporation, German Coalition for Patient Safety, American Academy of Orthopaedic Surgeons and the New Zealand Orthopaedic Association.

All guidelines had several different aspects, sometimes described as steps, which detailed the specific instructions in the process of accurately marking a patient for surgery. We identified nine different aspects across the nine guidelines (see table).

Aspect of guideline	Number of articles
Consent form indicates side/site	5
Mark with indelible pen	9
Surgeon/senior marks	8
Initials used to mark	4
Patient involved in marking	9
Check mark at every transfer	4
'Time-Out' before 'knife-to-skin'	7
Mark visible after draping	3
Check imaging/equipment	6

Four aspects from the table are common to the majority of guidelines. These can be seen as 'core-steps' in accurately and safely marking a patient for surgery. Marking with an indelible pen may seem obvious but some gui-

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delines make exceptions for paediatric cases and cases where the mark would be on the face. Almost all the guidelines suggest that the operating surgeon should mark patients before surgery. As this is often impractical most of the guidelines suggested that another senior member of the team, who would be present at time of surgery, would be sufficient.

All the guidelines advise that the patient should be involved in the marking procedure confirming side/site as the surgeon places his mark. The final core step is the idea of having a 'time-out' before starting the procedure. Typically this is a short pause before starting the operation in order to confirm patient identity, proposed operation and side/site.

Only one of the 'core steps' is carried out in theatre. The others are carried out in the pre-theatre stage emphasising the importance of identifying and accurately marking patients early in their journey.

Five of the guidelines mention consent and indicate that the confirmation of side/site should begin when the patient is consented, again with the involvement of the patient. Checking that the correctly labelled radiographs and scans are available and confirmation of the presence of the appropriate equipment/implants in theatre are also part of some guidelines.

#### Discussion

Guidelines can only improve care if practitioners are willing to use them. This cannot be assumed (1). Common sense suggests that guidelines should be simple, user friendly and quick to complete. Making guidelines compatible with existing values and not deviating too much from existing routines are recognised to increase their use (2). Specific advice detailing actions/decisions and who is responsible for these is also thought to be effective (2,3). Guidelines issued by practitioners' own professional bodies are likely to have more impact than those from outside the profession. However increasing the number of items a guideline contains makes it more complex but does not necessarily make it better or safer.

#### Conclusion

The four core steps we identified are the basis for any marking guideline, however, neither these steps nor the less frequently recommended aspects have been evaluated in practice and future work should focus on establishing the relative impact of each guideline aspect. In the meantime it is reasonable to assume that incorporating the guidance into clinical orthopaedic practice will further improve safety.

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# EXPERIMENTAL STUDY OF THE MECHANICAL EFFECT IN THE PATHOGENESIS OF AMNIOTIC BAND SYNDROME IN THE RABBIT

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# ABSTRACT

# Introduction

Amniotic band syndrome is a congenital disorder characterized by limb constrictions(1). The disorder lacks precise definition, and its exact pathogenesis is unknown(2). Though there have been advanced theories to explain the origin of the condition, none have been scientifically validated (2,3,4,5,6). The "exogenous" theory, popularized by Torpin, is the most widely accepted (3). It suggests that early amniotic rupture leads to the formation of amniotic strands, which by means of progressive compression induce the formation of extremity bands. In this disorder, histological examination of the excised bands demonstrates them to be composed of fibrous tissue(7). Multiple clinical and experimental data reveals a low plausibility this theory(8).

Our purpose is to assess if an annular external compression in a fetal rabbit limb will produce a band of subcutaneous fibrous tissue characteristic of amniotic band syndrome.

# **Materials and Methods**

We operated on one limb of 10 different lagomorph fetuses, each at 21 days of gestation. The extremity was ligated with a nylon suture at the infracondylar level. At 30 days gestation, each fetus was delivered by caesarean section. Limbs were analyzed histologically using different techniques.

# Results

Histological analysis though showed a compacting of soft tissues but without changes in the cellular structure. No subcutaneous fibrous tissue was found in the mechanically constricted zone. The distal segment showed dilatation of lymphatic vessels and edema of soft tissue.

#### Discussion

Annular external compression in a rabbit fetal limb does not induce the development of new fibrous tissue, and therefore this experimental study does not support a mechanical exogenous pathogenesis for amniotic band syndrome.

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# ASSESSMENT OF AN INERTIAL- AND MAGNETIC-BASED ORIENTATION TRACKER IN LARGE VOLUME CLINICAL APPLICATIONS

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# Introduction

In many fields, such as orthopedics and rehabilitation, the measurement of segments orientation or threedimensional (3D) joint rotation is highly required. Several devices, either based on cameras, magnetic field or ultrasound propagation, are available on the market. Generally, these systems are enough accurate for human motion measurement. Nevertheless, they suffer from a small capture volume, which is certainly a limitation for numerous applications. Moreover, their costs and complexity are prohibitive for routine uses.

In the past years, some authors have proposed to measure body segments orientation through microelectromechanical sensors (MEMS), justifying lower cost and easiness of use. Though successful, these systems had some restriction of use which could be limiting for routine clinical uses.

Recently [1], we proposed an original system fusing two complementary devices to fulfill the lack of real-time orientation measurement in clinical applications. The first device a low cost magnetic tracker, measures the orientation with a limited precision and relatively low sampling rate, offers a small capture volume, and is unable to work in the vicinity of metallic objects. The second device, a 3D gyroscope measures precisely the angular velocity. However, orientation as obtained by the integration of angular velocity involves an important drift. Our system combined both data through an advanced Kalman-based filter and reported promising results but its features in a real environment were not tested. In this study, a long scenario was proposed to fully assess the performances of this new system. Moreover the algorithm was extended with an off-line processing, thus improving the measurements.

#### Methods

During this study, we used an inertial module (Physilog®, BioAGM, CH) including a 3D gyroscope and a magnetic tracker (Liberty®, Polhemus, USA). The performances of the magnetic device were decreased in order to simulate a low level tracker (Minuteman®, Polhemus, USA). The inertial signals and magnetic data were respectively sampled at 240 and 60 Hz. One magnetic marker and the inertial module were rigidly fixed on a plastic plate and calibrated to hold the same measurement axes.

For the evaluation, five healthy young men were enrolled. The plastic plate was strapped on their left thigh and they were asked to perform two times a long scenario (14 minutes). This scenario included various postures (standing, sitting and lying) and activities (e.g., walking and stairs climbing). The movements were realized both, in the vicinity and far from the magnetic source. Finally, different metallic objects were inserted and moved in the capture volume of the magnetic system. An optical motion capture system (VICON®, UK) was used as reference.

#### Results

Figure 1 displays the orientation error angle for the offline version of proposed system and for the magnetic tracker alone. With the real-time system, in the absence of distortion and independently of the activity, we obtained a RMS orientation error of 1.2°. During distortion periods (either due to a metallic object or to an excessive marker-source distances) and also independently of the activity we obtained a slow growing orientation error of about 0.1°/s. When assessing the off-line algorithm even better results were noticed.



Figure 1: Orientation error angle of the magnetic tracker (grey dots) and of the off-line version of the proposed system (black dots) for five minutes of movements including two distortion periods.

#### Discussion

An original orientation measuring system was tested through a long scenario consisting of realistic activities for routine clinical purposes. Moreover, the scenario involved disturbed environment like present in medical centers. The system provided an accurate and real-time measurement of orientation with a high frequency, both during undisturbed and disturbed periods. Moreover, the system allowed a large capture volume and its performances were independent of the activities. As expected, the off-line extension of the algorithm reported even better results. In combination with a functional calibration, this system is very promising for routine measurements of 3D joint rotations. Further developments are necessary to remove the cables and ensure a more convenient use.

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# POSTER SESSION 5 Knee

#### P-026

THE BIOMECHANICAL PROPERTIES OF A TECHNIQUE FOR RECONSTRUCTION OF THE ANTERIOR CRUCIATE LIGAMENT IN A PORCINE KNEE MODEL.

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# Aims

The aims of this study were to evaluate the biomechanical properties and mode of failure of a technique of anterior cruciate ligament (ACL) reconstruction using the Soffix polyester fixation device.

A 2-strand equine extensor tendon graft model was used because a previous study has shown it to have equivalent bio-mechanical properties to that of 4-strand human semitendinosus and gracilis tendon grafts.

#### Method

Ten stifle joints were obtained from 5 skeletally mature pigs, the soft tissues were removed and the ACL and PCL were sacrificed. Tibial tunnel preparation was standardised using the Mayday rhino horn jig to accurately position a guide wire over which an 8mm tunnel was drilled. A 2-strand equine tendon-Soffix graft was used to reconstruct the ACL of the porcine knee using over the top femoral placement with bicortical screw fixation. Mechanical testing of 10 specimens was performed.

#### Results

The mode of failure included 4 midsubstance tendon failures, 3 Soffix failures and 3 failures at the suture-Soffix interface. The mean ultimate tensile load for the ACL reconstruction was 1360 N (standard deviation (SD) =354), elongation to failure of 41 mm (SD=7.5) and a structural stiffness of 35 N/mm (SD=8.1).

# Conclusion

This in vitro study has shown that the technique of ACL reconstruction using the Soffix soft tissue fixation device with a tendon graft placed in the over the top position is biomechanically strong, providing a sufficiently high UTL immediately following reconstruction, therefore allowing early weight bearing and rehabilitation.





# A COMPARISON OF TWO TECHNIQUES FOR KNEE ARTHRODESIS: THE CUSTOM MADE INTRA-MEDULLARY MAYDAY NAIL VERSUS EXTERNAL FIXATION

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# Introduction

The most common indication for a knee arthrodesis is pain and instability in an unreconstructable knee following an infection at the site of a knee arthroplasty. There are many techniques for arthrodesis of the knee, all with limitations. An ideal arthrodesis should achieve a high rate of union with a low complication rate, allow mobility, minimal inpatient stay and a reduction in a need for further treatment.

In this study, we compare the use of the Mayday arthrodesis nail (Orthodynamics, Christchurch, UK) versus external fixation (Orthofix / Hoffman II) in achieving successful arthrodesis of a knee.

# Methods

In Group A, eleven patients underwent arthrodesis with a Mayday Nail (Orthodesign, Christchurch, UK) between 1995 and 2006 in Conquest Hospital, Hastings. In all cases, the indication was a previous history of infected total knee replacements (TKR). Three of these patients had previously had failed attempts at arthrodesis with external fixation devices. In Group B, seven patients underwent arthrodesis using external fixation (Orthofix / Hoffman II). In six patients, the indication was infected total knee replacements, while one patient had an infection post open reduction and internal fixation of a tibial plateau fracture.

The outcomes of these patients were reviewed retrospectively. Union was assessed both clinically and radiologically and defined as lack of movement on examination, with evidence of trabecular bone crossing the site of fusion in two planes on plain radiographs.

#### Results

In the group treated with the Mayday Nail, the mean stay was 22.6 days (range 8 to 45 days), and the mean time to fusion was 4.5 months (range 2 to 9 months). Ten patients went on to confirmed arthrodesis including the patients where the indication was previous failed arthrodesis using external fixation. One patient underwent redo-arthrodesis due to poor fit and instability of the prosthesis, but subsequently united. In this group, six patients had post-operative wound infections. In the group treated with external fixation, the mean stay was 75.9 (range 34 - 122). Only two patients in this group achieved union and the mean time to fusion was 4.25 months (range 4 to 4.5 months). Three went on to

painless pseudoarthrosis and one died. Five patients in this group had continuing post-operative problems with wound infection.

The inpatient stay for the group treated by the Mayday Nail was shorter than the length of inpatient stay for the group treated by external fixation (p<0.01, CI 95). This was statistically significant. The number of patients who successfully united post arthrodesis was greater in those treated using the Mayday Nail than external fixation (p<0.01, CI 95). This was also statistically significant. There was no difference in the time to fusion between the two groups.

# Discussion

Our personal experience would suggest that the customised Intramedullary Mayday Nail is a superior method of achieving arthrodesis compared with external fixation. It achieves a higher rate of union and reduces the length of hospital stay and provides a more predictable limb alignment.



# THE ECONOMIC IMPLICATIONS OF TRANS-FUSION POST PRIMARY TOTAL KNEE AR-THROPLASTY – AN ARGUMENT FOR AUTO-LOGOUS BLOOD RE-INFUSION?

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# Introduction

To review how many patients required allogenic blood after primary total knee replacement surgery. To determine whether autologous re-infusion units will reduce the allogenic blood requirement and hospital stay.

# **Patients and methods**

Retrospectively, 149 patients undergoing primary total knee replacement using vacuum drains were selected. The outcome measures were the need for allogenic blood transfusion and length of postoperative hospital stay.

# Results

Eight percent (n 12) patients received allogenic blood. Patients who were not transfused (n 137) were discharged from hospital 2.6 days earlier. The cost of allogenic blood and extra day bed occupancy were compared with autologous re-infusion system.

The total post-operative transfusion requirement was 28 units of allogenic blood in 12 patients (8%). At £133.99 per unit of allogenic blood, and including the outlay for the drainage systems utilised, the total transfusion cost for this cohort was £4291.44 (£3751.72 + £539.72). (£28.80 per patient)

The cheapest autologous re-infusion system £8951.92 (£60.08 each).The average post operative stay was increased from 5.6 to 7.7 days in patients requiring post operative blood transfusion. Excess bed occupancy in those transfused was (£55 each). The cost saving of employing autologous re-infusion unit (£24.44 each).

# Conlusion

Re-infusion units are found to be more effective method of reducing allogenic blood requirement and afford significant cost savings in primary unilateral knee replacment.

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# DENSITY CALIBRATION IN COMPUTED RADIOGRAPHY

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# Introduction

Obtaining accurate, quantitative information from X-rays would be of immense value in monitoring fracture healing or bone formation. Use of an aluminium (AI) step wedge to provide calibration between X-ray optical density and aluminium equivalent thickness was a suggested method as far back as 1901.1 Since then, authors have attempted to develop this process.2, 3 However, due to non-standardised methods, it is still not used routinely in clinical assessment.

The advent of computed radiography (CR) offers new opportunities to improve step-wedge calibration, taking advantage of the wider dynamic range and direct digitisation of X-ray images. At the same time it poses new problems such as accounting for automatic pre- and post-processing and the analysis of grey level as opposed to optical density.

In this study we perform a thorough assessment of step wedge to grey level calibration.

# **Materials and Methods**

An Al step wedge of ten 5mm thick steps was manufactured. X-rays were taken using a Fuji CR system. We assessed the effect of different X-ray energies, background variation, Fuji processing settings and beam hardening on image quality.

Images of the step wedge and a bone and tissue equivalent knee phantom were taken at various energy and Fuji processing settings. Automatic detection of the steps, performed in Matlab using Canny edge detection and the Hough transform, was used to assess optimum settings for the CR system. Several methods of relating grey level to Al thickness were assessed. These included the log relationship used in optical density systems and methods adapted to digital grey-levels. Additional X-rays of several thicknesses of copper sheet were taken toge-ther with dose measurements to provide a relationship between dose and image grey level.

Background variation due to the anode Heel effect was evaluated by acquiring an "empty field" X-ray at different energy settings and with copper filtering. 1D background profiles along both image axes were created and analysed. The effects of beam hardening were considered using a custom-made phantom modelling various tissue thicknesses. This phantom was also used to assess correcting for soft tissue and bone thickness, where image thresholding was used to identify regions of interest and measure mean grey levels. These values were used to correct the measured grey levels in orthogonal X-rays.

#### **Results and Discussion**

Acquired X-ray images indicate that the size and thic-

kness of the step wedge is sufficient to provide an accurate calibration between grey level and Al thickness. Fitting of a straight line to the log of the net grey level values provided an excellent model of the data, with a measured R2 value of 0.99 (Figure 1).



Images taken at higher energy settings and with wider windowing imaged the widest number of steps (nine). Further testing illustrated the negative effect on accuracy of using fewer steps. X-rays of copper sheeting show that automatic histogram analysis is performed by the Fuji CR system, even on settings claiming to be processing free. Thus it is vital that imaging settings are consistent throughout further patient-based research so that accurate comparisons can be made.

Beam filtering at clinical settings (66kV, 6.3mAs) with a 1.5mm copper filtration was used to assess the Heel effect in patient X-rays. Background variation in the anode-cathode direction was assessed and, as a first approximation, a 1D model was used to correct subsequent X-rays. This step allows grey level measurements that are independent of position in the X-ray image. Correcting for bone thickness, soft tissue and beam hardening further improves measurements extracted from digital X-rays.

# Conclusions

Use of step wedge calibration to provide quantitative information on plain X-rays is possible using digital radiography. However, a thorough assessment of the entire X-ray process is necessary to achieve accurate and comparable information. Correction for factors such as the Heel effect, beam hardening and the contributions of soft tissue and bone thickness are vital in providing clinicians with reliable measurements from plain digital radiographs without altering the diagnostic quality of the images.

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# EXTRACORPOREAL SHOCKWAVE TREATMENT OF EARLY SPONTANEOUS OSTEONECROSIS OF THE KNEE

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#### Purpose of the study

This work reported of eleven cases of early spontaneous osteonecrosis of the knee successfully treated with a novel extracorporeal shockwave treatment (ESWT).

Traumatic and vascular theories have been proposed as a causative factor of the spontaneous osteonecrosis of the knee, but the precise etiology still remains speculative. The lack of blood in some critical areas, such as the subchondral bone of femoral condyles or the tibial plateaus, has been considered the underlying condition of this pathology.

The ESWT, thanks to its neo-angiogenetic effect, can be suggested as an effective conservative treatment for spontaneous osteonecrosis of the knee.

#### **Materials and Methods**

Ten patients (6 men and 4 women; mean age = 65 years) with a medial femoral condyle osteonecrosis of the knee (one bilateral) were evaluated in this work. Their history was negative for steroid therapy, systemic lupus erythematosus, alcoholism, Caisson decompression sickness, Gaucher's disease and hemoglobinopathies. Exclusion criteria was the evidence of a structural collapse of the subchondral bone. Two patients had received a femoropopliteal by-pass within the last year, while others five presented a deficit of the vascular axis of the homolateral lower limb documented by an eco-colordoppler. A clinical evaluation was taken at the diagnosis using KSS, McGill Pain Questionnaire (PPI, NRS, VAS). Plain radiographs, radioisotope bone scan and MRI confirmed the diagnosis of osteonecrosis.

The patients were treated with a cycle of three ESWT performed with 2000 pulses of 0,28 mJ/mm2 with Wolf Piezoson 300 Dornier Meditech with 6,5 MHz ultrasounds for three times in a month.

A clinical evaluation was performed at first and at third month after the treatment and a RMI evaluation was performed at fourth month after the treatment.

#### Results

The clinical evaluation showed a significant improvement of the symptoms (p<0,001) and the articular functionality (p<0,001). MRI of all cases revealed the continuity of the cartilage with a reduction in bone marrow edema and no collapse of the lesion; in one case the total recover up to a normal signal in the subcondral bone was documented.

#### Discussion

The most effective treatment for osteonecrosis lesions without evidence of structural collapse is conservative, with rest and protected weightbearing. In our study, a single cycle of ESWT produced an improvement of the clinical and MRI aspects in eleven cases of spontaneous medial femoral condyle osteonecrosis of the knee. The neo-angiogenetic effect of the ESWT appears to accelerate the time for the symptom remission.

The ESWT might have the potential to curtail the progression of the disease and to avoid the need for surgical treatment.

# EORS 2008 · MADRID



#### P-031

# EFFECT OF LUBRICANT TYPE ON THE WEAR OF UHMWPE TIBIAL INSERTS IN KNEE SIMULATION

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#### Introduction

Hip and knee wear simulators have been used by implant manufacturers and researchers for many years as a performance predictor and comparator for hip and knee implants. The clinical accuracy of these simulators in predicting wear depends heavily on the type of simulator as well as the methodology used. The joint lubricant used in the simulators is one crucial aspect that has been well studied in hip simulators [1-7]. A previous study has shown that protein concentration to wear rate correlation is similar between hip and knee simulations despite the significant difference between contact geometry and articulation mode suggesting it could be standardized for hip and knee simulations [8]. Differences in wear rate were also previously found between Alpha Calf serum (ACS) based lubricants and Bovine Calf serum (BCS) based lubricants in hip simulations. The purpose of this study is to determine what affect these different lubricants have on knee wear simulation.

# **Materials and Methods**

Conventional polyethylene tibial inserts were tested against CoCr femoral knee components in different lubricant conditions (n=6). All tibial inserts were 9mm thick Triathlon design (Stryker Orthopaedics, Mahwah, NJ) and made of conventional PE (N2 packaged ]-sterilized) and were matched with same size femoral components. Two million cycles of wear testing was performed on a six station knee simulator using gait kinematics. Loading and rotation are applied through a superiorly mounted femur (2700N max, +6/-7.5° I/E rotation) with tibial inserts and trays mounted below. 23° of flexion (loaded phase of gait) was applied through a ball and socket joint. The simulator has been previously described [9]. Different dilutions of Alpha Calf serum or Bovine Calf serum (Hyclone Labs, Logan, UT) and deionized water were tested in this study, with protein concentration ranging from 0g/L (water) to 40g/L for ACS and 60g/L for BCS. Gravimetric wear measurements were performed on inserts and lubricant was changed every 0.5 million cycles (mc).

#### Results

The relationship between wear rates and total protein concentration is shown in figure 1 for ACS and BCS. The PE wear rate under ACS lubrication peaks to 28mm3/ mc at 20g/L total protein concentration (TPC) while PE wear under BCS lubrication peaks to 24mm3/mc at 5g/ LTPC. Wear rates for both lubricants decreases as protein

concentration increases beyond its peak. At the standard protein concentration of 20g/L, wear rate using ACS is 39% higher than the wear rates using BCS.

#### Discussion

Lubricant studies have been performed previously on hip and knee wear simulation [1-7]. Lubricant composition such as protein concentration, albumin to globulin ratio, type of serum, and serum turnover rate has proven to be very significant to wear simulation in vitro. A 20g/L TPC lubricant has been chosen as a standard in many wear simulator laboratories based on this research and is used commonly for both knee and hip wear simulation but laboratories still differ in the type of serum used (ACS or BCS). Although neither BCS and ACS can completely replicate joint fluid in terms of A/G ratio, inorganic constituents, hyaluronic acid, or other characteristics, both are commonly used for wear simulations due to availability and similar constituents. Additionally, human joint fluid constituents are not consistent but vary between patients and vary depending on level of joint disease. This study has found a significant difference in wear rates by using these two different lubricant types (Fig 1). Although a comparison between these two lubricants and human joint fluid has not been made, this study shows that the ACS based lubricant at 20g/L will predict the worst case wear rate when considering these two lubricants at various dilutions. Therefore, although this study cannot conclude that ACS based lubricants in knee wear simulation studies more accurately predicts in vivo wear rates of knee implants, this study suggests that ACS diluted to 20g/L should be used for the most aggressive and worst case prediction of wear rates.

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Figure 1 Knee Wear as a Function of Lubricant Protein Concentration



# INTRA-ARTICULAR MIGRATING BONE MARROW EDEMA SYNDROME OF THE KNEE

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# Abstract

Background: Intra-articular shifting of bone marrow edema syndrome (BMES) is a very unusual pattern of disease which has been previously described in only a few cases and may raise the suspicion of an aggressive disease.

# Methods

We reviewed 8 patients (4 female, 4 male) with unilateral BMES located in the knee. The patients were aged 39-56 years (mean 50.2). In all the patients bone marrow edema (BME) found in the primary magnetic resonance imaging (MR imaging) shifted within the same joint, i.e. from the medial to the lateral femoral condyle or to the neighboring bone. Conservative therapy including limited weight-bearing for a period of three weeks was provided for seven patients after initial detection of BMES and one patient underwent surgical core decompression twice.

# Results

MR imaging showed complete restitution in 6 cases and small residual edema in one case. A final MR imaging control was not obtained in one painless patient. In one patient, avascular necrosis of the contralateral hip was evident after 16 months. Improvement of the MR imaging pattern was correlated with the clinical outcome in all patients. All patients became asymptomatic after a mean of 9 months (6-11).

# Interpretation

Intra-articular shifting BMES is a condition seen very rarely. The disease is self-limited so that conservative therapy can be recommended.

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# TAPPING TEST IN PATIENTS WITH PAINFUL BONE MARROW EDEMA OF THE KNEE

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# Abstract

Background: Although bone marrow edema (BME) of the knee is a common phenomenon, physical tests to diagnose this condition have not been investigated thus far. We hypothesized that a mallet test would be useful as a diagnostic aid as well as a screening tool.

# Methods

70 patients (36 female, 34 male) were investigated in this controlled study. Group 1 consisted of patients with painful BME in the knee and group 2 of patients with a painful knee without BME. Pain provoked by a reflex mallet was assessed for each quadrant on a visual analog scale (VAS).

# Results

The VAS score was 3.7 ( $\pm$ 2.1 cm) for quadrants affected by BME (group 1), 1.59 ( $\pm$ 1.44) in non-affected quadrants of the knee affected by BME (group 1) and, 0.85 ( $\pm$ 0.85) in painful knees without BME (group 2). Pain on the tapping test was significantly correlated with the presence of BME in the affected knee (p<0.0001) as well as the affected quadrant (p<0.0001 for the medial femoral condyle and the medial femoral plateau). Implicating a threshold value of VAS 2.0 for a tapping test to be positive in the distinction of BME affected quadrants of group 1 and all quadrants of group 2 sensitivity was 90.4%, specitivity 83.7%, positive predictive value 73.4% and negative predictive value 94.6%.

# Conclusion

The tapping test is a good screening instrument to diagnose BME in the knee.

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# MICROWAVE THERMOGRAPHY AS A NONIN-VASIVE ANALYSIS OF ANTERIOR KNEE PAIN WITH TOTAL KNEE PROSTHESIS.

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# Introduction

Whereas thermography has already been used as a noninvasive assessment of disease activity in some kinds of inflammatory arthritis and as an evaluation of the temperomandibulary joint, it is a new method for objektive pain evaluation in patients with joint prothesis. To our knowledge, no study has tested the correlation between increase of temperature and anterior knee pain with total knee prosthesis yet.

# **Materials and Methods**

In intention to reassess a five to ten years follow up of LCS total knee prosthesis, 137 patients followed an invitation to the authors' institute. Thirteen (n=9.5%) out of these 137 patients suffered from anterior knee pain of the retinaculum patellae and were included in this study. The thirteen patients were compared with thirteen others, not suffering from anterior knee pain. Control group and patients with pain were asked to walk 3 kilometers before entering a room which was cooled down to 20 degrees Celsius. A black 1 times 4.5 cm square stripe was attached on the diameter of the patella. After that, patients were asked to rest for 20 minutes in intention to cool down before thermographic fotos were taken from 90 degrees, 45 degrees, frontal medial and lateral. The evaluation of temperature difference (deltaT) of each side was performed by marking a 1 times 2cm square field rectangular around the black stripe and comparing it with a reference point of the same size 3 cm distal of the field Statistical analysis was performed using a t-test and a p value < 0.05 was considered to be significant.

# Results

The temperature differences between the rectangular field and the reference point (deltaT) increased signifi-



cantly on the medial (p=0.00037) or lateral (p=0.00002) pain side of the knee (see graphic). The thirteen knees with knee pain had significantly higher temperature differences between medial and lateral temperature differences (deltaT), than the knees without knee pain (see graphic).

# Discussion

This study demonstrates that there is a significant correlation between anterior knee pain and an increase of superficial skin temperature around the retinaculum patellae. Our results confirm observations of previous investigators about the increase of temperature with pain around limbs. To our knowledge, this is the first report of an objective assessment of pain of the retinaculum patellae with total knee prothesis. Our results could help making it possible to localize and assess pain more precisely. Microwave thermography as a non-invasive analysis of anterior knee pain with total knee prosthesis will be a useful tool for the future but high costs and long duration of at least 30 minutes per knee will prevent it from becoming routine.

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# CLINICAL PRACTICE GUIDELINE BASED EVIDENCE FOR THE PHYSIOTHERAPY OF PATIENTS WITH ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION WITH HAMSTRING (T4)

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#### Introduction

Anterior knee instability associated with rupture of the anterior cruciate ligament (ACL) is a disabling clinical problem, especially in the athletic individual. Numerous authors have described successful reconstruction of ACL with autograft and allograft. The gracilis and semitendinosus tendon (T4) represent an alternative autograft donor material that may be used for reconstruction of the ACL without disturbance of the extensor mechanism.

The aim of our study was to elaborate a CPG basis of "best evidence" and consensus among expert group that assists physiotherapists to make diagnostic conclusions and therapeutic decisions, to improve the quality and uniformity in care for ACL reconstruction with T4.

#### **Materials and Methods**

The CPG was developed according to international methods of guideline development (Grimshaw 1995, Sackett 2000). The recommendations were constructed combining best evidence from randomized clinical/ controlled trials, prospective studies with the consensus among expert group and practicing physiotherapist.

1) To identify "best evidence" published research a computerized literature search of Medline, Cochrane, PEDro, IME, IBECS and ENFISPO and search of reference lists to find additional studies were realized. The evidence of the different studies selected was evaluate using scale described by the US Preventive Task Force. When no evidence was available, consensus between experts was achieved to develop the guideline.

2) To identify "best clinical experience" and "physiopatologic reasoning" focus group of practicing physiotherapists was used. They reviewed the clinical applicability and feasibility of the guideline, and their comments were used to improve it.

#### **Results and Discussion**

CPG include three phases determined from the evidence, physiopathology reasoning and the biological process of autograft (weeks after the surgery: 2<sup>a</sup>-6<sup>a</sup>, 6<sup>a</sup>-10<sup>a</sup> and 10<sup>a</sup>-16<sup>a</sup>). The patients were given home exercise program and instructions, elevation of the foot to work on knee extension, and ankle range of motion for the first week. A knee immobilizer was used during sleep or when the patient was ambulatory for the first 2 weeks, cryotherapy and crutches. The recommendations that were



included and that were based on the scientific evidence and clinical experience were: In postoperative weeks (2<sup>a</sup>-6<sup>a</sup>) physiotherapy focused on early range of motion of the knee; manual therapy (passive range of motion 0-120° and miofascial techniques), pulsed ultrasound of low intensity with a power of 0.3w/cm2 (1MHz) during 10min/day in tibial tunnel, early active hamstring beginning with static weight bearing co-contractions (closed kinetic chain) and adductors, partial weight bearing with crutches, exercises in the swimming pool and cryotherapy to pain control (30 mi/4 hours). In weeks 6 to 10, full weight bearing, manual therapy (passive range of motion 0-140° and miofascial techniques), hamstring strengthening progress complexity and repetitions of cocontractions, electrotherapy hamstring and guadriceps co-contractions. Starting at week 10, progress to more dynamic activities/movements, proprioceptive work, emphasis on vastus medialis obliguus guad, stationary bike and Theraband squats. In week 12, progress jogging program and plyometric type activities. The patients performed sports-specific exercises by about 31/2 months postoperative.

#### **Conclusions / Summary**

The guideline reflects the current state of knowledge of the effective and appropriate physiotherapy in patients with ACL reconstruction with hamstring. Three phases with different recommendations were included in CPG combining best evidence and consensus amoung group of expert.

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# POSTER SESSION 6 Bone and Cartilage

#### P-036

# TREATMENT OF CARTILAGE DEFECTS OF THE KNEE WITH A CHONDROCYTE SEEDED CO-LLAGEN TYPE I SCAFFOLD: 1-YEAR CLINICAL RESULTS

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# Introduction

Over the last 10 years ACI (Autologous Chondrocyte Implantation) has become an important surgical technique for treating large cartilage defects. The original method published by Brittberg and Peterson in 1994 has been improved by using cell seeded scaffolds for implantation. A variety of scaffold materials are used in clinical practice today. The aim of our prospective study was to evaluate the effectiveness and safety of a matrix based ACI (MACI) with a collagen type I scaffold for repairing cartilage defects of the knee. We present the clinical and radiological results of 23 pts. one year after collagen scaffold based ACI.

#### **Material and Methods**

Out of 39 pts. treated with ACI for cartilage defects of the knee 23 had reached the one year follow up. We documented preoperatively and postoperatively (3, 6 and 12 months) the clinical situation with the IKDC Knee Examination Form. MRI scans were evaluated at all time points.

#### Results

39% of the pts. were female, 61% male. The average age was 33 yrs. (min: 15; max: 49), the average BMI 25,4 (min: 19; max: 36). One third of the cartilage defects were localized retropatellar the remaining on the medial or lateral femoral condyles. The average defect size was 5,4 square-cm. In about 75% of the cases an additional surgical procedure was performed (acl reconstruction, lateral release, meniscal surgery). One major complication (a deep wound infection) occured. The IKDC score improved over time during follow up significantly compared to preoperatively, although no significant difference could be detect between the 6 and 12 moths postoperative examinations. This fact was due to the poor results in the group with retropatellar defects. The average improvement in IKDC score was about 40%. The MRI showed an improvement of the implanted scaffold over time as well.

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# Conclusion

The present study confirms the benefits of ACI in young patients with large cartilage defects of the knee. The matrix based ACI is a safe and surgically less demanding technique then the traditional ACI. Patients with retropatellar defects have a poor outcome compared to femoral defects. We expect a good long term outcome from MACI comparable to that of traditional ACI.



# INCREASED TYPE I COLLAGEN IN UNDAMAGED CARTILAGE OF ANTEROMEDIAL OSTEOARTHRITIS OF THE KNEE

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# Introduction

Anteromedial osteoarthritis (AMOA) is a distinct phenotype of knee osteoarthritis [1]. The arthritic lesion on the tibia is localised to the anteromedial quadrant with preservation of cartilage posteriorly in a crescenteric form. The aim of this study was to investigate the molecular features of the different severities of cartilage damage from adjacent areas, from anterior to posterior, within the AMOA knee.

# Methods

Ten medial tibial plateau specimens were collected from patients undergoing unicompartmental knee replacements. The specimens were prepared for histological and immunohistochemical analysis. Sections of the same cartilage were snap frozen for guantitative immunoassay and Real Time Polymerase Chain Reactions (RT PCR). The sections underwent histological staining, with Safranin-O and H&E, and were OARSI graded [2]. Further sections were used for immunohistochemical staining for Type I and II Collagens, proliferation and apoptosis. The cartilage within the area of macroscopic damage was divided into equal thirds: T1(most damaged), to T3 (least damaged). The area of macroscopically undamaged cartilage was taken as a 4th sample N. Immunoassays were undertaken for Collagen I, Collagen II and GAG content. RT PCR compared gene expression between areas T and N.

# Results

As expected, there was a decrease in OARSI grade across the four areas, with progressively less fibrillation, and more safranin-O staining between areas T1, T2 and T3. Area N had an OARSI grade of 0 (normal).

The Immunoassay for GAG showed decreased levels with the increasing severity of cartilage damage (ANOVA P<0.0001).

There was no significant difference in the Collagen II staining, content or gene expression between areas.

Unexpected results were obtained for Collagen I. The immunohistochemistry showed an increase Collagen I staining, occurring within chondrocyte pericellular areas in the undamaged region (N).

This was confirmed by immunoassays which showed that the Collagen I content of this posterior, macroscopi-

cally and histologically normal cartilage, was significantly higher than the damaged areas (ANOVA P<0.0001). Furthermore, RT PCR showed that there was a significant difference in Collagen I expression between the damaged and macroscopically normal areas. (p=0.04)

# Conclusion

In the AMOA phenotype there are distinct areas, demonstrating progressive cartilage loss. We conclude that in this phenotype Collagen I content is increased in areas of macroscopically undamaged and histologically normal cartilage. These changes seen in Collagen I may represent very early changes of the cartilage matrix within the osteoarthritic disease process, and may be able to be used as an assay of early disease. The changes found with Collagen I expression may also be a therapeutic target for disease modification or treatment.

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# EFFECT OF PULSED LOW-INTENSITY ULTRA-SOUND ON PROTEOGLYCAN METABOLISM AND VIABILITY OF OSTEOARTHRITIC HUMAN CARTILAGE EXPLANTS

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# Introduction

Animal experimental studies indicate that pulsed low-intensity ultrasound might enhance cartilage repair in early stages of osteoarthritis (OA) (4) and to improve healing of osteochondral defects (3). Continuous low-intensity ultrasound was also investigated; its application was reported to stimulate proteoglycan (PG) and collagen synthesis in both human cartilage cell (1) and explant cultures (5).

The purpose of this in vitro study was to determine systematically whether and to what extent pulsed lowintensity ultrasound (1) influences the synthesis and release of PGs, (2) modulates chondrocyte viability within human osteoarthritic cartilage explants, and (3) is affected by the degree of OA alterations.

# **Material and Methods**

Full-thickness cartilage explants of the lateral compartment of the proximal tibia were taken from OA patients undergoing knee replacement surgery. 4-mmdiameter articular cartilage discs were obtained using a biopsy punch. The degree of OA changes of the tibia resp. explants was determined according to Collins (2). Explants with mild or moderate OA alterations were cultured for 2 days in a CO2-incubator under sterile conditions in order to first stabilize the cartilage metabolism at 37°C, 5% CO2 and 95% relative humidity. Then explants were subjected to ultrasound applied in a pulsed-wave form (1:4) on 3 consecutive days using an ultrasound application apparatus specifically designed and constructed to function within an explant culture system under sterile conditions. The parameters intensity (2, 30, 120, 250 mW/cm2), duration of ultrasound treatment (20, 3 x 30 minutes/day) and frequency (0.5, 1.2, 4.7 MHz) were then systematically applied.

PG synthesis was measured by the incorporation of 35SO4 (10  $\mu$ Ci/ml) during the final 22 hours of the experiments. Radiolabeled PGs were determined in papain digested explants and media by separation of free 35SO4 from macromolecular radiolabeled GAGs using size exclusion chromatography. Endogenous PGs were determined by the DMMB-method. Results were normalized by the cartilage wet weight.

The viability of chondrocytes within each of the three different anatomical zones of cartilage explants (su-

perficial, intermediate and deep layer) was determined in separately cultured explants treated with or without ultrasound as already described above. Cell viability was evaluated microscopically using fluorescein diacetate and propidium iodide as described previously in detail (6). At two sites of each of the 3 slices per explant, viable and/ or dead cells, as indicated by a green or red fluorescence, were counted. Results were compared to untreated explants from the same joint. Each experimental condition was repeated five times using explants always obtained from 6 different patients (n=6).

# Results

Neither the degree of OA alterations of explants, nor the various intensities, durations of application or frequencies of ultrasound applied, displayed any significant effect on the synthesis and release of PGs as well as on the viability of explants.

# Conclusions

Pulsed low-intensity ultrasound has no effect on the proteoglycan metabolism and cell viability of mild and moderate OA human knee cartilage.

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# EFFECTS OF HEPARIN ON HUMAN PERIPHERAL BLOOD MONOCYTES-DERIVED OSTEOCLASTOGENESIS

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# Introduction

Osteoporosis, one of the most common diseases in modern aging society, is responsible for severe bone pain, high risk of bone fracture, and limitations in daily activities. Receptor activator of nuclear factor-]B ligand (RANKL) plus macrophage colony stimulating factor (M-CSF)-mediated osteoclastogenesis has been recently implicated in the pathogenesis of this disease. Among other causes, the anticoagulant drug heparin is a notable inducer of secondary osteoporosis, although the molecular pathway underlying this process, particularly in human model, has not been clarified yet.

Recently, we reported the differentiation of two subtypes of osteoclasts starting from human peripheral blood CD14-positive monocytes, respectively fusion regulatory protein-1 (FRP-1/CD98)- osteoclasts and RANKL+M-CSFmediated osteoclasts (1, 2).

In this study, we investigated the effects of heparin on monocyte-derived osteoclastogenesis to clarify the mechanism of heparin-induced osteoporosis.

# Methods

Isolation of monocytes: After informed consent, monocytes were isolated from healthy young volunteer whole blood by Ficoll-Hypaque density gradient centrifugation and monocyte attachment to plastic. Monocytes were cultured in 300  $\mu$ l of ]-minimum essential medium (]-MEM) with 10% fetal calf serum (FCS) at a density of 2x105 cells/ml on plastic 96 well plate dish. All cultures were incubated for 14 days at 37] in a humidified atmosphere containing 5% CO2 in the presence of anti-FRP-1/CD98hc monoclonal antibody or RANKL+M-CSF with/ without various concentrations of heparin. More than three monocyte suspensions were utilized per experiment.

Staining with Giemsa solution: After incubation for 14 days, the cells were dried, fixed with methanol for 20 minutes, and stained with 10% Giemsa solution for 20 minutes.

Fusion index: To estimate the degree of cell fusion, numbers of cells or nuclei within multinucleated giant cells (]3 nuclei/cell) were counted. The fusion index was calculated using the formula fusion index (%) = total number of nuclei within giant cells / total number of nuclei counted x100.

Bone resorption assay: Functional evidence as osteoclasts is the formation of resorption lacunae. In experiments of bone resorption assay, the monocyte suspensions were cultured on dentine slices or mineralized calcium phosphate plates (Ca plate), and one-half of the culture medium was replaced with fresh medium containing osteoclastogenesis stimulating factors every 3 days. After culture for 14 days, pit formation was observed by scanning electron microscopy or light microscopy.

# Results

When monocytes were cultured with osteoclastogenesis relating factors and a high dose of heparin, heparin suppressed osteoclastogenesis. However, a proper quantity of heparin enhanced tartrate-resistant acid phosphatase-positive multinucleated giant cell formation. FRP-1-mediated osteoclasts treated with a proper quantity of heparin formed larger pits on Ca plates. Moreover, lacunae formations of dentin surfaces induced by FRP-1-mediated osteoclasts were enhanced with moderate concentration of heparin. In contrast, heparin did not increase pit formation area on Ca plates and on dentin surfaces by RANKL+M-CSF-mediated osteoclasts.

# Discussion

Heparin osteoporosis was first reported in 1964 (3). Our previous work demonstrated that there are two types of osteoclasts with fundamental differences in bone resorption ability (2). FRP-1-mediated osteoclasts tend to absorb the minerals component of bone, while RANKL+M-CSF-mediated osteoclasts tend to absorb bone organic component. In osteoclastic activity, heparin stimulated monocyte differentiation only to the FRP-1 system, but not to the RANKL+M-CSF system. Our results revealed that in human model, heparin osteoporosis may be dependent on FRP-1-induced osteoclastogenesis and also that the onset mechanism after long-term administration of heparin may be affected by the characteristic bone resorption ability of FRP-1 osteoclasts.

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COMPARING THE SERUM LEVELS OF 25(OH) D3 AFTER 12 MONTHS OF TREATMENT WITH FIXED COMBINATION OF WEE-KLY ALENDRONATE PLUS CHOLECALCI-FEROL 2800UI WITH THESE OF WEEKLY ALENDRONATE PLUS DAILY CALCIUM 500MG AND VITAMIN D 400 UI.

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Recent epidemiological studies have demonstrated that more than half of postmenopausal women with osteoporosis (PWOP) treated with an antiresorptive drug plus calcium (Ca) and vitamin D, have serum levels of 25(OH)D3<30ng/ml. Chronic low levels of vitamin D can contribute to the inefficiency of main antiresorptive treatment. A possible explanation for this phenomenon is the non-compliance with the daily supplementation of Ca and vitamin D. A fixed combination of Alendronate Once Weekly (OW) 70mg plus 2800 UI of cholecalciferol (AL+D) made its appearance in the market two years ago as a solution to this problem.

The current study was designed to assess the efficacy of AL+D versus the old scheme of Alendronate 70 OW plus daily Ca 500mg + 400 UI of vitamin D (AL+S) on serum levels of 25(OH)D3. 100 randomly assigned PWOP treated already for 1 to 5 years with AL+S have changed their treatment to AL+D for one year. Serum levels of 25(OH)D3 (Biomedica.co.at/vitamind) has been measured before and after 12 months and also their BMD (Hologic Delphi), PTH, TSH, serum chemistry and hematology has been recorded for safety reasons. At the end of the study only 83 PWOP (MA=59,9±6,6 yrs) appeared for comparison.

# Our results are as follow:

1) The mean plasma level of 25(OH)D3 under AL+S treatment and before taking AL+D is 24,3 $\pm$ 8,4 ng/mL and

2) The plasma levels of 25(OH)D3 after 12 months of treatment with AL+D are  $33,3\pm9$  ng/mL. The paired t-test has been used to compare the levels of 25(OH)D3 between treatment groups. There is a highly important statistical difference (t=-8.989, df=82, p<0,0001) between treatment groups.

From the above data it can be concluded that fixed combination of AL+D can improve the 25(OH)D3 status over 12 months versus AL+S probably because it assures a better compliance of vitamin D.



# TRABECULAR ANISOTROPY IN OSTEOARTHRITIC BONE

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# Introduction

Many studies pointed out how the bone in osteoarthritis presents changes if compared to normal bone not affected by diseases. Changes in the composition of osteoarthritic (OA) samples were found, related also to a different mechanical behaviour [1]. Studies using histomorphometry suggested that the trabecular structure may change even its orientation in severe OA [2].

The aim of this study was to observe whether trabecular anisotropy calculated in 3D presents differences between severe OA bone and non-pathologic bone.

#### **Materials and Methods**

Twenty two femoral heads were obtained from deceased persons without bone pathologies thanks to a donor program (International Institute for the Advance of Medicine, Jessup, PA, USA). One cylindrical specimen of cancellous bone from the primary compression region of each head was extracted as described in literature [3, 4]. Three dimensional structural parameters, such as bone volume fraction (BV/TV), direct trabecular thickness (Tb. Th\*), structure model index (SMI) and connectivity density were calculated using X-ray microcomputed tomography (microCT). By computing the Mean Intercept Length in the three main directions (MIL1, MIL2, MIL3, ordered by decreasing MIL), the three degrees of anisotropy (DA1=MIL1/MIL3, DA2=MIL2/MIL3, DA3=MIL1/MIL2) were calculated [5, 6].

The OA group consisted of 22 OA bone specimens, selected from an internal database, matching in age and in BV/TV with the control group, so as to reduce the influence of these factors on the trabecular anisotropy. Comparisons in age and structural parameters between the OA and control group were done by a Mann-Whitney test, with the statistical significance set at p=0.05 (a non-parametric test was used because of the data not following a normal distribution).



Parameter	Arthritic	Control	P value
Agea	70 (±9)	70 (±10)	0.707
BV/TV (%) a	29 (±6)	31 (±7)	0.467
Tb. Th*	279 (±47)	266 (±34)	0.453
SMI	0.22 (±0.42)	0.03 (±0.85)	0.481
Connectivity density	4 (±2.1)	3.9 (±2.8)	0.622
DA1	1.59 (±0.13)	1.49 (±0.11)	< 0.05
DA2	1.10 (±0.06)	1.15 (±0.06)	< 0.05
DA3	1.45 (±0.13)	1.31 (±0.08)	< 0.001

Table 1 Comparison in age and structural parameters on trabecular bone specimens between OA and non-pathologic subjects. a BV/TV and age values were used to pair the specimens.

No statistically significant differences were found between OA and controls in age, BV/TV, or in any of the examined structural parameters, except from anisotropy; this parameter presented significant differences in DA1, DA2, DA3 (increases of 7%, decreases of 4% and increases of 11%, respectively). The results of comparisons are summarized in Table 1.

#### Discussion

A different spatial organization for the OA bone is suggested by the differences found in the Degrees of Anisotropy. In particular, as the biggest increases are found in DA1 and DA3, the OA specimens result to be more oriented along the primary compressive direction, that is, the inferior superior direction, than the non-pathologic cohorts. From a biomechanical point of view a similar modification in anisotropy is explained in literature by a model of bone remodeling under uniaxial compression [7]. Such a uniaxial loading scenario can be present in a OA patient; a patient which is able to load his hip in the only position in which he does not feel pain. Thus, the present results suggest a link between the underlying bone mechanics and the modifications found in the trabecular bone structure, which might be driven by the patient's pathology, osteoarthritis.

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#### Acknowledgements

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# EFFECT OF PULSED LOW INTENSITY ULTRASOUND ON HUMAN CHILD CHONDROCYTES

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# Introduction

The purpose of this study was to evaluate how healthy human articular chondrocytes harvested from the ablated polydactylia of very young children responded to PLIUS exposure in an in vitro agarose gel-embedded culture. The effects of different intensities of PLIUS with different durations of PLIUS exposure were also assessed to evaluate the dose response and time course of PLIUS treatment on these early differentiated human chondrocytes.

# **Materials and Methods**

Chondrocytes isolated from young children's articular cartilage of ablated polydactyly were embedded in gel after expansion, and exposed to PLIUS on the third day after embedding. Another group of cells was exposed to sham PLIUS as a control. Different intensities of PLIUS treatment, 18 mW/cm2, 48 mW/cm2, 72 mW/cm2, and 98 mW/cm2 (1.0 MHz, with burst duration of 200 microseconds repeated at 1.0 kHz) were administered for 20 minutes per day, and the medium was replaced twice a week. The cultures were evaluated for aggrecan synthesis by enzyme-linked immunosorbent assay (ELISA), type II collagen production by western blotting or ELISA, and cell proliferation by total DNA measurement.

# Results

The PLIUS was found to increase aggrecan synthesis in a time-dependent manner (Fig. 1). The maximal response was observed at an intensity of 48 mW/cm2 (Fig. 2). After 14 days of exposure at this intensity, the aggrecan synthesis was 214±26 % of control, and type II collagen synthesis was 148.5±8.0% of control. However, PLIUS-treatment revealed no significant influence on cell proliferation, confirming that the stimulation of aggrecan and type ] collagen synthesis by PLIUS was not due to an increase in chondrocyte cell proliferation. In addition, it was found that human chondrocytes harvested from older donors become less responsive to the PLIUS.

# Conclusions

From this in vitro three-dimensional study of cultured human chondrocytes, our findings suggest that PLIUS may be applied to the tissue engineering of cartilage constructs.







# (Fig. 2)

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P-042



# CELL CONCENTRATION AND FENOTIPIC DIFFERENCES BETWEEN MESENCHYMAL CELLS IN HUMAN, SHEEP AND RABBIT.

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# Introduction

Some stroma-derived progenitor cells have demostrated a trinileage potential for osteogenic, adipogenic and chondrogenic differentiation. Progenitor cells with osteochondrogenic potential have been identified within adipose tissue . These cells present diversity of characteristics that can be explained by differences in tissue origin, isolation methods and culture conditions. Mesenchymal stem cells (MSC) have been isolated from many tissues. MSC have been shown to exhibit tissue protective and regenerative properties.

#### Methods

Hoffa's fat samples were obtained from 4 patients (mean age 44 years), 5 rabbits (New Zeland aged 12 weeks) and 5 sheeps (Rasa aragonesa aged 22 weeks). Cells were obtained by means of enzimatic and mechanical digestion. The suspension was centrifuged and washed twice with phosphate buffered saline. The resultant pellet was resuspended and plated in culture medium (37°C, CO2 5%). Cellular markers were studied with specific monoclonal antibodies (CD13, CD44, CD49d, CD90, CD105, CD117).

# Results

Human cells: CD13+ (94-99%), CD44+ (87-99), CD49d (14-70%), CD90+ (92-99%), CD105+ (90-97%), CD 117-BD+ (2-22%).

Sheep cells presented CD13+ (32-70%), CD34-, CD36, CD44+ (90-96%), CD49d (40-80%), CD54+ (50-80%), CD90+ (90-97%), CD105+ (10-25%). CD117-BD+ (48-76%).

Rabbits cells: CD13+ (14-78%), CD44+ (10-80%), CD49d (2-9%), CD90+ (27-92%), CD105+ (2-24%), CD 117-BD+ (15-57%).

Human cells number/mL did not show significant differences between patients, or between P0 0 (14 culture days) (average mean:  $525000 \pm 298956$ ) and P5 (525000), nevertheless the average mean decreased from P5 to P6 (130.000) until P8 (111 culture days) (85.000).

Rabbits cells number/mL did not show significant differences between P0 (673000  $\pm$  379697) and P1 (596000  $\pm$  488740) and decreased in P2 (299500  $\pm$  159161) without any significant change in P8.

Ovine cells number/mL average mean in P0 was 1.370.600 ( $\pm$  802758), this decreased in P1 (420000  $\pm$  95197) however, showed no significant changes in P8 (291875  $\pm$  86394).

# Conclusions

MSC from human, rabbits and sheeps present differences in cellular concentration and markers.



# VISCOELASTIC CHARACTERIZATION OF BOVINE NASAL SEPTUM AS MODEL FOR TMJ DISC MECHANOBIOLOGY

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# Introduction

Animal models have shown that artificially induced temporomandibular joint (TMJ) disc failure (displacement or perforation) affect histology and biochemistry of joint cartilage, leading to osteoarthritic changes. However, it is still unclear whether TMJ discs fail simply due to wear or whether the cartilage is degraded by a biological response to mechanical loading. In order to gain insight into TMJ cartilage mechanobiology, we developed a system to reproduce on live tissue the complex dynamic compression effects that we can accurately measure in vivo. For this purpose we need a tissue sample with a well-defined geometry. As a first approximation we chose bovine nasal septum (BNS) cartilage as a model because it is abundantly available and it can be conveniently shaped without cell or structural damage. Models have already been used in research on other connective tissues such as ligaments [1]. However, little or no information is available on the mechanical properties of the BNS in order to correctly set up the loading experiments. Aim of this study was therefore to determine material properties of the BNS in a viscoelastic model.

# **Materials and Methods**

Cartilage samples were harvested from the central part of BNSs (Fig. 1) of young, healthy animals (average age 18 months) and stored at -25 °C. Prior to testing, the cartilage was thawed at room temperature and then cut into strips of regular thickness. Twenty cylindrical plugs of  $4.68 \pm 03$  mm diameter and  $2.13 \pm 04$  mm thickness were obtained by means of a biopsy punch and equilibrated in phosphate buffered saline (PBS).

Stress-relaxation tests in unconfined compression (Fig. 1) were performed on each sample using a universal testing machine (Zwick/Roell Z010) by placing the sample between two stainless steel plates and applying a 10% strain at a rate of 0.01 mm/s and holding it for 30 minutes. Throughout the measurements, cartilage disks were kept immersed in PBS.



Figure 1: (left) Bovine nasal septum dissected; the sample B2 was used for testing; (right) schematics of the unconfined compression test.

A viscoelastic linear solid model [2] was chosen to characterize the tissue. The relationship between stress ] and the applied strain ]0 can be approximated as:

](t)=ER[1-(1-]s/]e)exp(-t/]e)]]0.

From this expression the relaxed elastic modulus (ER) was determined as ](1800), the time constant ]s and ]e by mean of linear regression, and the instantaneous elastic modulus (EO) as EO=ER(]s/]e).

Stress was estimated from the compressive force data and the initial cross-sectional area. Experimental data were fit to a mathematical model in MATLAB.

# **Results and Discussion**

Experimental results show a high viscoelastic behavior of the BNS, with a maximum average stress of  $0.73 \pm 0.14$  MPa and relaxed stress of  $0.21 \pm 0.03$  MPa.



*Figure 2: Mathematical model fitting the average experimental curve.* 

The numerical model shows good correspondence to the experimental data (R2=0.96) (Fig. 2). The average values for the instantaneous and relaxed moduli were E0= 7.72 MPa and ER= 2.30 MPa. The values of the time constant were ]]=149.2 s and ]]=387.6 s.

The data found is difficult to compare to the values in the literature due to the different methods used, although the order of magnitude of the elastic moduli is the same as the one found for the TMJ disc [3,4]. Further analyses of other BNS regions are ongoing.

# Conclusions

Bovine nasal septum can be modelled as viscoelastic tissue. It appears to be a convenient model to study mechanobiology of the TMJ disc.

Furthermore, this study contributes to the assessment of BNS mechanical properties.

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# Acknowledgments

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# POSTER SESSION 7 Ligament and Tendon



# Pagoda 18:20 - 18:25 h O 045-046

#### P-045

# THE BIOMECHANICAL PROPERTIES OF TAILORED EQUINE EXTENSOR TENDON

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#### Aims

Replacing human cadaveric specimens with fresh frozen animal tissue in biomechanical studies has become increasingly more popular due to the scarcity of young human tissue. The aims of this study were to characterise and compare the biomechanical parameters of tailored strips of equine extensor tendon, with 4 strand young human semitendinosus and gracilis (STG) tendons as an alternative tendon model for testing anterior cruciate ligament (ACL) graft reconstruction techniques using the Soffix Polyester ACL fixation device.

#### Method

Common digital extensor tendons were harvested from normal equine forelimbs and tailored into 5 mm wide, 2 strand equine tendon strips. The doubled equine tendons were overlapped and braided around the buttonholes of a Soffix fixation device and secured with No 2 Ethibond sutures (Johnson & Johnson Ltd). The Soffix-4-strand young human STG tendon complex was prepared in an identical manner. Mechanical testing was performed measuring ultimate tensile load (UTL) and elongation to failure (EF), structural stiffness (SS) was calculated from load extension curves.

# Results

The Soffix-STG and the equine tendon complexes produced a mean UTL of 1186 N +/- 113.89 and 1116 N +/- 208.5 respectively showing no statistically significant difference.

# Conclusions

We conclude that a tailored 5mm wide 2-strand equine extensor tendon strip provides a comparable alternative for in vitro testing of young human four strand STG tendon graft using a Soffix polyester fixation device.



# SCAFFOLD-FREE SUSPENSION OF UNDI-FFERENTIATED MESENCHYMAL STROMAL CELLS (MSCS) ARE ABLE TO REPAIR NOT FULL-THICKNESS DAMAGED TENDON IN RA-CE HORSES.

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# Introduction

Adult bone marrow contains a small population of multipotent cells called mesenchymal stromal cells (MSCs) that show the ability to differentiate in several stromal tissues(1). This findings suggest that MSCs possibly contribute to the regeneration of bone, cartilage, muscle, tendon and adipose tissue. These properties have prompted several authors to evaluate their role in regenerative medicine. In view of possible clinical applications, interesting results in repairing the Achilles tendon have been achieved in rabbit models (2) since 1997. Histological and immunochemical studies in rabbit models have demonstrated the quality of repair (3) even when allogeneic stem cells were employed. A basic problem in tissue repair is the way to administer stem cells to the damaged tissue. Several questions remain: 1) have the cells to be (partially) differentiated or committed to the cell lineage we intend to repair or they should be kept undifferentiated in order to prevent the loss of proliferative potential? 2) Should cells be administered using a scaffold in order to resolve handling troubles, providing a static or dynamic support to cells and possibly sustain the oriented differentiation to the desired lineage? Obviously, there is no simple answer to these points but the understanding of modifications induced by in vitro manipulation, play a key role in view of a possible human clinical application of MSCs in tissue repairing. When directed to tendon defect repair, scaffolds have usually been employed especially considering the specific properties of such tissue as regards resistance, tension, sharing, and elasticity. Whereas there is an obvious indication for the use of scaffolds in the attempt to repair full-thickness defects of tendons or even to fabricate ligament constructs in vitro, their in vivo implant still may have unexpected implications. In fact scaffolds may induce host reactivity and interfere with the expected differentiation of implanted stem cells, for example, inducing ectopic bone formation (4). We hypothesized that the injection of undifferentiated MSCs, without use of any scaffolds, could contribute to healing. In this case we should assume that tissue micro-environment and spatial tendon organization would induce differentiation of MSCs to tenocytes and correctly orient deposition of fibers. To assess this point we attempt to cure, as a clinical model, horses with a pathological core lesion in the superficial digital flexor tendon (SDFT).

# Materials and methods

In this study MSCs were recovered from autologous bone marrow, expanded ex vivo, resuspendend in 1,5ml of autologous serum and re-injected directly into the lesion. Equine MSCs were morphologically characterized. Both clonogenic and osteogenic potential were evaluated. Results of cell injection were evaluated clinically, by ultrasound (US) evaluation of the tendon and by performance results. We treated eleven race horses with autologous MSCs and fifteen horses with standard anti-inflammatory therapy as control group.

# Results

All 11 horses implanted with autologous MSCs exhibited no adverse reaction due to the implantation of the cells. After rehabilitation therapy nine MSC-treated animals recovered from their clinical conditions, had an excellent US image of tendons after a period ranging from 3 to 6 months, and returned to racing with good or even optimal results in the previous category of competition in 9 to 12 months without any re-injuring event. All of them are still active more than 2 years from diagnosis. US studies show initial tendon repair indicated by greater density after only 1 month. Six months after mesenchymal cell injection, tendons appeared to be almost completely repaired. Orientation of fibers revealed using US analysis was correctly parallel to the long axis of the tendon. In contrast, most of horses from the control group showed tendon US images that revealed fibrosis during the healing process, and all of them were re-injured after a median time of 7 months.

# Discussion

Our results show that, in racing horses with an incompletely (not full-thickness) damaged tendon, the scaffold may not be necessary and that excellent results, compared with typical scar-tissue images reported in this pathology, may be achieved by injecting a cell-rich solution directly in the lesion. The tissue microenvironments appear to be able to induce cell differentiation and fiber production, as revealed uisng ultrasound scanning. The correct orientation of fibers strongly suggests that microenvironment and lines of tension/relaxation determine correct tissue morphology. The ability of tissue microenvironments to induce cell differentiation could render unnecessary a partial or total ex vivo differentiation. In our series, no bone deposition was shown, according to US, in the treated tendons, thus confirming our working hypothesis that direct infusion of undifferentiated MSCs could represent a safe therapeutic approach to tendon repair and suggesting that tissue is able to orient cell differentiation correctly, allowing, in parallel, the necessary in situ cell expansion.

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J Orthp Res 22, 998, 2004.



# POSTER SESSION 8 Infection

#### P-047

# "DEAD" SPACE FILLING FOR TREATMENT AND PROPHILAXIS OF INFECTED COMPLICATIONS OF JOINT REPLACEMENT

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# Introduction

The problem of prophylaxis and treatment of infected complications after total joint replacement is relevant today, especially in case of revision procedures. The important factor in successful preventive maintenance and treatment of purulent complications is reduction of socalled "dead" space of the operated joint filled usually with a hematoma.

Traditionally for reduction of this "dead" space various surgical ways and methods, for example, filling of a cavity of a joint with a muscular tissue are used.

Aim of this study is to analyze the Taurolin-Gel 4% application for "dead" space filling in patients with high risk of wound infections after total hip replacement.

# **Materials and Methods**

Follow-up results of 178 operations with Taurolin-Gel 4% use have been studied.

Patients were observed for 2 to 12 years (average 6 years). In research 4 groups of patients have been allocated. 1st group - (46 patients) patients with signs of an early infected postoperative complications (from 5 till 20 days) after total hip or a knee joint arthroplastics. The second group (38 persons) was made by patients with purulent arthritises of joints or with signs of a chronic infection after total joint replacement. All this patient after removal purulent and necrotic tissues carried out the first phase of two-stage revision, consisting in installation of articulating spacer.

3 group included 35 patients in the second phase of two stage replacement - exchange articulating spacer on final endoprosthesis has been executed. 4 group included 59 patients with one stage joint replacement having in the anamnesis different infected complications.

In all above listed cases the articulate cavity during operation was filled Taurolin-Gel 4 %. Taurolin contains the broad spectrum chemotherapeutic and endotoxic agent Taurolidine which is derived chemically from taurine, the endogenous aminosulphonic acid.

Taurolidine has been shown to be remarkably effective against gram-negative infection and particularly against the resistant strains which are responsible for infections in hospitals. Its range of action also includes gram-positive bacteria and pathogenic fungi. Its bactericidal action is not affected by the addition of blood, serum or pus. Pagoda 18:30 - 18:35 h O 047-048

Depending on volume of joint and intramedullary cavity at operations used from 40 to 100 g Taurolin-Gel of 4 %

# Results

In all four groups the total of infection recurrence was observed at 6 patients (3,4 %). Thus in the first group the repeated infection took place only at one patient (2,2 % from total of patients of this group). After performance of the first phase of two stage revision arthroplasty infection relapse is noted at 2 sick (5,3 % from number of patients of the second group), after the second phase the repeated infection is found out also in two cases (5,7 %). The best results have been received in the fourth group - only at one patient (1,7% from the number of the patients of the fourth group) recurrence of a slow chronic infection in 28 months after operation carrying out has been noted.

# Discussion

Taurolin-Gel 4%, inserted into joint cavity, is not only a good antibacterial agent, but it also fills up "dead" spaces in the hip joint and displaces haematoma.

Deleting a hematoma which is the favorable environment for functioning of the bacterial agent, we sharply reduce risk of infectious complication in the postoperative period.

Besides, Taurolin-Gel reduces postoperative blood loss for approximately 30 %, causing mechanical haemostasis by the tamponade.

In difference from filling of a joint cavity with the moved muscular tissue, use Taurolin Gel of 4 % are much easier technically, reduces time of revision intervention, reduces the general traumatic of operations.

# Conclusions

Filling of a joint cavity with Taurolin-Gel 4% after hip and knee replacement is indicated at patients with high risk of infected complications.



# EFFECT OF AGE ON CYTOKINE RESPONSE IN AN EXPERIMENTAL MODEL OF OSTEOMYELITIS.

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# Introduction

Osteomyelitis is a major problem after trauma-induced open fractures and following total joint replacement. The most frequent pathogenic organism in arthroplasty infections is Staphylococcus. The immune response impairment is a frequent finding in elderly people. The aim of this work is to investigate the response of some cytokines and the effect of age on cytokine response and bacteria in an experimental model of osteomyelitis associated with implant.

# Materials y methods

Under anaesthesia with inhalated isoflurane 40 adult male Wistar rats received a stainless steel needle (with an adherent slime producing S. aureus in groups B & D), intramedullarily in the left tibia.

Group A: Young rats (3 months old) + Sterile implant. Group B: Young rats + Sterile implant + S. aureus.

Group C: Old rats (22 months old) + Sterile implant. Group D: Old rats + Sterile implant + S. aureus.

At the end of the experiment, 60 days after surgery, rats were sacrified and implants and tibias were retrieved. Peripherical blood samples were obtained one week previous to surgery (PRE) and previous to sacrifice (PO). Tissues samples were obtained at the end of the experiment. Cytokines (IL-1], IL-2, IL-4, IL-6, IL-10 and IL-12) were determined (ELISA) in blood and in tibia extract. Ribotyping (using enzyme Eco R1), antibiotic susceptibility testing of bacteria in suspension and determination of colony morphology in Congo red agar were applied in order to verify that the strain recovered from implants and tissue was the same as the originally used. The average number of bacteria was estimated (plate count and bacterial ATP quantification). The Wilcoxon, Mann-Whitney U test and a two factorial analysis of variance test were used to compare cytokines levels and bacterial counts (Log cfu). Results were considered to be significant with  $p \leq 0.01$ .

# Results

Infection was detected in all the left tibias in old rats receiving S.aureus, and in seven of the 10 young rats. IL-2 levels increased in blood in the S.aureus group after surgery in old and young rats. Pre and postoperative IL-2 levels in blood were higher in old rats in both groups than in the corresponding groups of young rats.

IL-4 levels in blood were higher in young rats than in old rats before surgery, and in the control groups after surgery. IL-4 levels in blood increased after surgery in the S.aureus group in old rats.

IL-6 levels in tibia were higher in young rats than in old rats. IL-6 levels in blood increased after surgery in the S.aureus group in old rats.

IL-10 levels in blood were higher in young rats than in old rats in the S.aureus group. IL-10 levels in blood increased after surgery in young rats in the S. aureus group. Young rats presented higher levels of IL-10 in blood and tibia in the group of S.aureus than in the control group after surgery.

Old rats in the S.aureus group showed higher IL-12 levels than the young rats of the same group, and that old rats control group.

# Conclusions

Significant differences in tibia infection were found with age. Old rats presented differences with young rats in cytokine response in an experimental model of osteomyelitis, showing an immune response impairment associated with old age.



# ORAL SESSIONS EORS

Saturday, April 26th

# ORAL SESSION 13 Gait and kinematics

# O-071

# A COORDINATE SYSTEM FOR THREE DIMEN-SIONAL DATA ANALYSES IN THE FOOT AND ANKLE.

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Introduction

Complex foot and ankle surgery and reconstruction require accurate preoperative planning. In the foot corrective osteotomies and lengthening procedures are challenging and can be associated with a range of complications (1,2). The aim of planning is to correct only the deformity (3), prevent extensive surgery, reduce post operative morbidity and maintain biomechanical integrity. Knowledge of foot and ankle morphometry is vital to preoperative planning models. To conduct meaningful comparison between different subjects the coordinate system between subjects must be constant (4). There have been a number studies carried out in other joints to define a coordinate frame (4-6). To the authors knowledge there has been no previous description in the literature defining a coordinate system in the foot and ankle for three dimensional analysis.

# Materials and methods

CT images of ten anatomically normal feet were acquired in a 1mm slice thickness using an Ankle Foot Ankle Foot Orthosis (AFO) to hold each foot in an anatomically neutral position. These images were then segmented in Materialise's Interactive Medical Image Control System 10.1 (MIMICS) a general purpose segmentation program for grey value images. These files were then imported to a shape analysis program for biomechanics, Arthron. A coordinate frame was defined in a 3 X 3 identity matrix using the inter-malleolar axis and a fibular diaphyseal centroidal axis in the construction. Centroidal vectors were defined in the metatarsals enabling three dimensional analysis of the forefoot. Correlation of metatarsal length, inter-metatarsal angles, inter-malleolar distance and height was carried out using Pearson product moment correlation coefficient, r.

# Results

Three Dimensional analysis of the forefoot was preformed in the defined coordinate system. The metatarsal length, the inter-metatarsal angles and the inter-malleolar distance were calculated. The morphology of the forefoot was examined in relation to the medial and lateral columns. Metatarsal length had a large correla-

# Aula Magna 10:00 - 11:00 h O 071-077

tion within each column and between the two columns notably in the 3rd (0.525 - 0.965) metatarsal at the columns junction. The 3rd metatarsals also correlated well (-0.583) with the inter-metatarsal angles. There was a weak correlation between the 1st 3rd and the 3rd 5th inter-metatarsal angles directly (in two and three space) however, each had a large correlation with the 1st 5th inter-metatarsal angle (0.734 – 0.950). There was also a large correlation between the individual's stature and the metatarsal length and the inter-malleolar distance.

# Discussion

Three dimensional analysis has significance in preoperative planning and intra-operative navigation software design. We have presented a means defining a coordinate system for three dimensional analyses in the foot and ankle. This coordinate system can now be used for meaningful comparison of data between multiple subjects. We have shown that this coordinate system to be effective in practice in the morphometrical analysis of the normal forefoot. We examined the forefoot in relation to the medial and lateral columns and our study lends support this model. This analysis also demonstrates the importance of maintaining proportion within the forefoot to ensure biomechanical integrity. This next stage in this research is the morphometrical analysis of the mid-foot and hind-foot in the normal foot.

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# REPEATABILITY OF FOOT AND ANKLE COMPLEX KINEMATICS

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# Introduction

Kinematics of foot and ankle complex is a widely accepted criterion in clinical evaluations. Thanks to the recent developments of motion capture systems, multi-segment kinematic assessment of foot and ankle complex was paid more attention [1, 2]. However, since the ranges of rotation of foot joints are rather small, the reliability of these new parameters is questionable. Thus, estimating the repeatability of foot kinematic measurements is of major importance for reasonable and reliable uses. Particularly, achievement of acceptable results for clinical decision makings demands to extract repeatable features either with the use of reflective skin markers or inertial sensors [3]. Indeed, obtaining repeatable parameters in kinematics of foot and ankle depends not only on the measurement system (camera, inertial sensors, etc.) but also on the mathematical tool used to quantify the kinematics. In this study, repeatability of kinematics assessment of multi-segment foot and ankle complex by means of different mathematical descriptors was investigated.

# Methods

21 tiny markers (3 mm diameter) were mounted on dominant anatomical landmarks of the foot and 4 small markers (9 mm diameter) around the knee. Six young healthy subjects (age: 27±3) were asked to walk over a forceplate (Kistler, CH) surrounded by 6 infra-red cameras (Vicon, UK). Marker trajectories were captured during stance phase and 9 to 12 trials per subject were recorded. Foot and ankle complex was considered as 6 rigid segments: 1) Shank, 2) Hindfoot, 3) Mid-foot, 4) Medial forefoot 5) Lateral forefoot 6) Toes. 3D angles between each pair of segments (i.e., 1-2, 2-3, 3-4, 3-5 and 4-6) were calculated based on three prominent methods: a) helical angle, b) joint coordinate system and c) projection of lines representing segments on three anatomical planes. Then, the coefficient of multiple correlation (CMC) was used to estimate the degree of similarity among joint angle patterns.

# Results

The 3D angles between each pair of segments in foot and ankle complex were calculated for all the trials of the six subjects following the three methods (a, b and c). The intra-subject CMC were calculated for each subject and then averaged over the six (Table 1, 2 and 3). In addition, the inter-subjects CMC (Table 1, 2 and 3) were calculated between the mean joints angles patterns of each subject.

# Discussion

Joints angles were calculated for multi-segment foot and ankle complex according to three of the most cited angle description methods. It was observed that all angle calculation methods had comparable repeatability for both intra-subject and inter-subjects kinematics. No significant difference among their repeatability was noticed. Most of angles showed good pattern repeatability both, intrasubject and inter-subjects. Thus, most of multi-segment foot joints angles can be reliably used. Further studies enrolling patients with foot and ankle disease are necessary to investigate the usefulness of these measurements for clinical evaluations.

Table 1.

Method		Helic	al Angl	le (3D)	
Joint Plane	1-2	2-3	3-4	3-5	4-6
Intra-subject	0.89	0.8	0.7	0.75	0.89
Inter-subject	0.82	0.68	0.4	0.1	0.75

Table 2.

Ν	Aethod	Joint coordinate system					
Plane	Joint	1-2	2-3	3-4	3-5	4-6	
	Sagittal	0.89	0.78	0.69	0.85	0.91	
Intra-	Coronal	0.84	0.75	0.8	0.77	0.87	
sub.	Transverse	0.84	0.79	0.75	0.89	0.77	
Inter- sub.	Sagittal	0.83	0.65	0.39	0.76	0.83	
	Coronal	0.67	0.6	0.69	0.62	0.74	
	Transverse	0.83	0.36	0.66	0.8	0.15	

N	Aethod	Projection of segment lines					
Plane	Joint	1-2	2-3	3-4	3-5	4-6	
Intra- sub. Tra	Sagittal	0.89	0.7	0.79	0.85	0.93	
	Coronal	0.89	0.75	0.75	0.77	0,83	
	Transverse	0.55	0.65	0.49	0.76	0.88	
	Sagittal	0.83	0.51	0.68	0.76	0.88	
Inter- sub.	Coronal	0.85	0.59	0.61	0.58	0.43	
	Transverse	0.39	0.53	0.35	0.59	0.73	

Tables 1-3. The average of intra-subject CMC over six subjects and inter-subjects CMC for foot joints (proximal - distal segments) according to three angle calculation methods. 3D Angles are expressed in the Sagittal, Coronal and Transverse planes

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# FUNCTIONAL COMPENSATION OF THE OS-TEOARTHRITIC LEG: DIFFERENCES BETWEEN HIP AND KNEE PATIENTS

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# Introduction

Patients with osteoarthritis (OA) will try to protect their impaired leg. They can either do that by reducing the movement velocity of the leg or by moving asymmetrically and thereby overloading the contralateral leg. In this study, we used the sit-to-stand movement to quantify which strategy OA patients use; reducing the movement velocity (=kinematic) or rising asymmetrically (=kinetic). Also, we were interested if there was a difference in patients with knee OA or hip OA. The first purpose of this study was to assess if there was a difference in asymmetry between knee and hip patients and if a total knee/hip prosthesis would lead to symmetrical loading. The second purpose was to assess the difference in moving velocity between the two groups and the effect of the prosthesis.

#### Methods

Patients on the waiting list for either total knee arthroplasty (TKA) or total hip arthroplasty (THP) were included in this study. The two patient groups were matched according to age and BMI, which resulted in 11 TKA (age=61.5 (sd=9.3), BMI=28.7 (sd=5.0)) and 10 THP patients (age=57.2 (11.3) and BMI=24.9 (sd=4.2)). The subjects were measured pre-operatively, and 1 year post-operatively. The sit-to-stand movement was performed 10 times, with rest in between, from 90° knee flexion from a chair with adjustable height and without armrests. The subjects had to hold their hands at their waist, and their ankles in a straight line under their knees. The feet were separately placed on two forceplates. The asymmetry (=ASYM) was defined as:

$$ASYM = \frac{Peakforce tka}{Peakforce contralateral} (eq 1)$$

The movement velocity was quantified as the maximal knee angular extension velocity (VELOCITY\_KNEE) and was measured with sets of bi-axial accelerometers and a gyroscope on lower and upper leg1. The ASYM and VELOCITY\_KNEE were averages of the 10 rises. Student t-tests were used to assess differences between the THP and TKA groups and the improvement with the prostheses was assessed with a paired t-test.

# Results

Pre-operatively, the ASYM was greater for the THP group than for the TKA group, p=0.015. Both groups showed an improvement after 1 year (p=0.045 for THP and p=0.05 for TKA) and this amount of improvement was not different between the groups (p=0.58). This resulted in a still greater ASYM for the THP group as compared to the TKA group, 1 year post-operatively (p=0.039), see figure 1. Concerning the VELOCITY\_KNEE, there were no significant differences between the THP (pre:mean=99.7, sd=22.3; post:mean=108.6, sd=17.8) and TKA group (pre:mean=86.4, sd=18.3; post:mean=107.0, sd=24.2), both pre-operatively (p=0.15) and 1 year post-operatively (p=0.86). The THP group showed no significant improvement (p=0.19), while the TKA group did improve significantly (p=0.018).



# Discussion

Hip and knee patients differ in how they perform the sit-to-stand movement. Hip patients rose more asymmetrically, both pre and 1 year post-surgery. Asymmetrical joint loading due to osteoarthritis is a risk factor for evolving contralateral osteoarthritis progression2. THP patients do not load their prosthetic leg adequately. We did ask the patients if they were aware of this unloading, but they were surprised that they loaded asymmetrically. The knee patients showed a very symmetrical rising pattern after they received their prosthesis. However, TKA patients tended to rise with a smaller velocity of movement pre-operatively, but they showed a significant improvement in velocity of movement after 1 year.

#### Conclusion

Hip patients change their movement pattern kinetically, whereas knee patients change it kinematically. After placement of a THP, the asymmetrical loading pattern remains with the risk of evolving contralateral OA. Hence, extra attention on asymmetrical movement should be paid during the rehabilitation period of THP patients.

#### References

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# ACCELERATION BASED GAIT TEST TO MONITOR PATIENTS AFTER TOTAL KNEE SURGERY

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# Introduction

In joint arthroplasty in general and in total knee replacement (TKR) in particular, the currently used patient assessment scores like the KSS or Womac suffer from subjectivity, a low ceiling effect and pain dominance. These effects mask functional differences or changes following intervention or during therapy which are important for the demanding patient or the validation of new procedures. Thus objective functional assessment tools are required which can monitor patient performance in time. Previous studies have shown for single time point comparisons that accelerometer based motion analysis system is reliable to analyze gait and to distinguish between different knee pathologies[1,2]. However its use in a follow up study where changes over time need to be monitored has never been reported before. This study investigates whether an objective acceleration based gait test is able to monitor patients after surgery.

# **Materials and Method**

A cohort of 24 patients (11 men, 13 women, avg. age: 72yrs, weight: 85kg, height: 1.69m) operated for osteo-arthritis receiving unilateral TKR (Stryker Scorpio) were monitored for 3 months after surgery. Classic scores including subscores (KSS: function and knee; Womac: function, stiffness, pain; VAS and PDI) as well as a gait test were measured preoperative, at 2 weeks, 6 weeks and 3 months postoperative. Gait was analyzed using a triaxial accelerometer fixed to the sacrum while walking 6 times a 20m distance at preferred speed. Movement parameters like step frequency, step time, step number, vertical displacement, asymmetry and irregularity were calculated based on a peak detection algorithm. Speed and step length were scaled for height. Correlations between scores were tested using Pearson' R and changes with regards to pre-op were evaluated using repeated measurements ANOVA (p<0.05).

# **Results and Discussion**

The average pre- and 3 months post-op KSS (57 and 86) and Womac scores (54 and 22) agreed with other studies showing that the population was a representative patient group[3]. The classic scores were all significantly intercorrelated (Table 1) indicating to a certain degree of redundancy. Significant correlations were shown between several gait parameters and the KSS, PDI and VAS. Most significant correlations between the gait parameters and a classical score were found for the KSS function subscore indicating that this conventional assessment gives the most objective measure of a patient's functional state amongst the classic scores. In contrast, the Womac (sub)scores did not correlate with any of the gait parameters (Table 1). This lack of WOMAC capturing objective changes in gait performance was reported before using another functional test[4].

The post-op recovery profile also showed differences between the standard scales and the gait test (Fig 1). Two weeks after surgery the classic scales reached

10	VAS	KSSFu	Womac <sub>Tot</sub>	Freq	Displ	Asym
VAS	1	.41*	.59*	18	.12	.06
KSS <sub>Fu</sub>	41*	1	60*	33*	32*	23*
Womac <sub>Tot</sub>	.59*	60*	1	07	07	.18
Freq	18	33*	07	1	81*	27*
Displ	.12	32*	.07	81*	1	.17
Asym	.06	23*	.18	27*	.17	1

Table 1: Correlation coefficients b/w scores (\* p<0.05). equal (VAS, PDI, KSS) or better values (Womac 24% improvement) compared to preoperative, while all gait parameters remained worse than preoperative. At 6 weeks all classic scales showed significant improvements (42 to 63%) compared to pre-op, while the gait parameters only just reached pre-op levels. Beyond 6 weeks, the standard scales improved only slightly and almost reached a plateau at 3 months, while gait continued to improve without showing a plateau. This indicated that pure function as measured in gait needs more time to adapt a normal levels than the classic scores weighing pain and having a ceiling. E.g. the cadence for TKR patients improved from 101 steps/minute pre-op and 83 steps/minute two weeks post op to 105 steps/minute at 3 months postoperative, while healthy subjects score 120 steps/min[4].



Fig 1: Follow up of the KSS, Womac and frequency.

This suggests that the classic scales and the gait test cover different dimensions of surgical outcome supporting their combined use to follow up patients. The improvements in standard scales at 2 weeks post-op can be due to patient's satisfaction and the ability to move without pain, while the way they perform activities like walking remains less adequate. For instance patients 2 weeks after surgery walked with smaller step length leading to a higher energy consumption per distance which results in a faster fatigue, which can be a limiting factor in daily life.

# Conclusion

This study showed the clinical validity of the gait test during follow-up and the importance to add a functional assessment tool to complement the standard scales.

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# O-075

# OUTCOME ASSESSMENT IN ORTHOPAEDICS USING A STAIR CLIMBING TEST AND ACCELEROMETER BASED MOTION ANALYSIS: A FEASIBILITY STUDY

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#### Introduction

To clinically diagnose and postoperatively monitor the younger or more demanding orthopaedic patients ('millennium patient') it becomes increasingly important to measure function beyond the capacity of classic scoring systems suffering from subjectivity, pain dominance and ceiling effects. Current methods to objectively assess function are video based gait analysis systems, force platforms, EMG all of which are not suitable for routine clinical application because of their high costs and complexity demanding designated space, personnel and long set-up times.

Inertia based motion analysis using accelerometers is cheap, quick and easy to operate in the clinical environment making it feasible for routine follow-up. Accelerometer derived motion parameters have been clinically validated for normal gait in subjects with knee pathologies[1,2] but gait was identified as not demanding enough to distinguish finer functional differences. Stair climbing is a more demanding common activity of daily life that may produce more sensitive motion parameters for patients with disorders of the lower extremity.

This study investigates whether a stair climbing test with accelerometer derived motion parameters in a group of healthy subjects is clinically feasible and valid to distinguish between demographic differences.

#### **Materials and Methods**

The ascending and descending of stairs was measured in 46 healthy subjects (19m/27f, no orthopaedic pathology, no treatment of muscoskeletal disorder) with a mean age of 39 years (SD 20; range: 21-74) using a triaxial accelerometer (size: 62x41x18 mm; weight: 53g; f: 100 Hz) attached with a belt to the sacrum. The study group was divided in two age groups: young group (15m/16f; mean age 25; SD 3.1; range 21-38) and old group (4m/11f; mean age 67; SD 6.2; range 54-74). Other values recorded were height, weight, BMI, leg length and dominant side. Subjects ascended and descended five stairs two times at preferred, comfortable speed (no handrails allowed). Motion parameters were derived from acceleration peak detection algorithms in Matlab 7.1 (Mathworks, USA): average step time up and down (tup, tdown), the difference between the average step time up and down (tup-tdown), irregularity up and down (irrup, irrdown) defined as the difference between maximum and minimum step times, and asymmetry up and down (asymup, asymdown) defined as the difference between the step times of the dominant and nondominant leg. Group comparison were performed using the t-test and correlation using Pearson's R (p<0.05)





#### Results

Avg. step times were slightly higher ascending (tup=606ms) than descending (tdown=575ms, p<0.05, table 1), a difference seen also in most individuals (39/46). The step time difference between ascending and descending was 31ms with a sign. difference between the young (tup-tdown=47ms) and elderly group taking on average more time to descend (-7ms). All subjects with descending times at least 20ms slower than ascending (6/46) were found in the elderly group (p<0.05, Fig 1).

Irregularity was nearly equal ascending (142ms) and descending (140ms) and not different between age groups. Also asymmetry did not show large differences between stepping up or down or between age groups. However, asymmetry revealed that steps with the dominant leg were of equal or faster speed than the non-dominant leg in 43/46 cases ascending and 39/46 cases descending. The stair test parameters were not significantly correlated to other demographic parameters such as gender, height or BMI.

[ms]	Avg	SD	Min	Max	Young	Old
t <sub>up</sub>	606*	63	470	743	590	638*
t <sub>down</sub>	575*	91	428	843	544	645*
tup-tdown	31	55	-155	103	47	-7*
Irrup	142	51	50	260	140	140
Irr <sub>down</sub>	140	51	50	250	130	150
Asym <sub>up</sub>	49	35	2	138	50	40
Asym <sub>down</sub>	39	29	0	113	30	50

Table 1: Stair climbing parameters [ms] overall and per age group (\* p<0.05).



Fig 1: Difference step time up minus down vs. age.

#### Discussion

Avg. step times up were higher than step times down as expected by the difference in energy expenditure. Individuals with slower step times down were all elderly indicating that a loss of balance, coordination, strength, proprioception or fear of falling compensates the benefits of an energetically less demanding movement. This parameter may be powerful to detect general or bilateral orthopaedic pathologies such as osteoarthritis. Asymmetry clearly identified the strength of the dominant leg indicating its potential as a powerful parameter to detect and monitor unilateral pathologies such as in knee arthroplasty. With a total test duration of <30s and sensitive parameters, the accelerometer assessed stair test seems a functional test suitable for routine clinical follow-up complementing classic scores.

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# A NEW DYNAMIC RSA SET-UP FOR 3D JOINT MOTION ANALYSIS

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#### Introduction

Dynamic roentgen stereophotogrammetric analysis (RSA) showed to be a very accurate method in detecting 3D joint motion1, but at present this technique is based only on custom radiographic equipments. We tested a new dynamic RSA set-up, based on the use of a commercial bi-plane fluoroscopy system. This set-up permits the acquisition of slow passive and active movements of the lower limb, both in supine and weight-bearing position. This method relies on a fully 3D data acquisition, therefore a more homogeneous accuracy in all the directions of motion is to be expected, in comparison with single plane fluoroscopy 2,3 which is characterized by a large out-of-plane error.

# Methods

We used a Biplane Advantx (GE) system, with two 320mm diameter image intensifiers. Image sequences were recorded at 4fps. We utilized a bi-planar calibration cage and a regular grid for the calibration of systematic geometric distortion. All calibration tools were custom made. Custom toolbox (in MATLAB language) were designed for the correction of distortion following the global bi-polynomial technique4; a commercial software (Model-Based RSA 3.0, Medis Specials bv) were used for the reconstruction of 3D position of the markers; custom software were used for kinematics elaboration. We performed in-vitro tests with a phantom and in-vivo tests examining slow passive motions of 5 patients (3 ligament reconstructions, 2 knee replacements). Tantalum markers were implanted in both femoral and tibial epiphyses of each knee. Bias and precision were investigated in terms of errors in dynamic tracking of markers1 and in terms of translational and rotational accuracy3.

#### Results

Dynamic tracking of markers inserted in the phantom object showed a bias of 0.40mm and an inter-marker distance standard deviation of 0.3mm. In-vivo tests showed an average standard deviation of inter-marker distances of 0.3mm, too. From in-vitro tests the mean error in detecting relative motion were not negligible, whereas translational precision was below 0.5mm in all directions and the rotational precision was below 0.3° (Tab.1).

<i>n</i> =27	Tx (mm)	Ty (mm)	Tz (mm)	<b>Rx</b> (°)	<b>Ry</b> (°)	Rz (°)
mean	-0.2	0.0	0.5	0.2	0.4	0.3
SD	0.3	0.2	0.5	0.3	0.2	0.3

Table 1: Errors in relative translations (T) and rotations (R) of two groups of markers within the same phantom object comparing n consecutive frames (y was an in-plane direction for both views).

# Discussion

This study shows the potentiality of a dynamic RSA setup using an available commercial bi-plane fluoroscopy system to provide an interesting method for fully 3D joint motion analysis. Further improvements in terms of reduction of bias of the system may be reached by the use of more precise calibration tools and of different commercial bi-plane fluoroscopic systems, with more suitable specifications for kinematics studies (e.g. with a stricter synchronization of bi-plane acquisitions).

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# THE EFFECT OF STANCE ON STATIC LOADING WITH LEG LENGTH DISCREPANCY

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# INTRODUCTION

Leg length discrepancy (LLD) is a well recognised complication of total hip arthroplasty. Large LLDs can cause abnormal weight bearing, leading to increased wear, aseptic loosening of replacement hips and pain. To compensate for LLDs the patient can either flex the knee of the long leg, or extend the knee and tilt their pelvis. The aim of this project was to investigate how stance affects static limb loading of patients with leg length discrepancy.

# Methods

A pedobarograph was used to measure the limb loading of 20 normal volunteers aged 19 to 60. Each volunteer was asked to stand on the pedobarograph with both feet. A 2 second recording was taken to establish their body weight. Three readings were then taken of the left foot load with the right foot at the same level.

Further readings were then taken with the right foot 3.5 cm lower, to simulate a long left leg, as shown in Fig 1. Readings were then taken with the right foot 3.5 cm higher to simulate a short left leg, as shown in Fig. 2.

Fig 1: Low Right Fig 2 High Right

In each of the LLD positions three readings were taken with the knee flexed and three readings with the knee extended and the pelvis tilted.

# **Results and Discussion**

The results of the 6 sets of measurements are shown in table 1 and figure 3.

The second column of table 1 shows the load through both feet. All remaining columns show the left foot load, with the right foot in various positions, with the knee flexed or pelvis tilted. The % row shows the load through the left leg as a percentage of total body weight. The P row shows the results of a paired t-test between the feet Level position and the LLD positions.

#### Figure 3:- Results

When both feet were at the same level, the left limb

took 54% of the load.

When the Right foot was lower the set up simulated a long left leg. When the left knee was flexed the left leg took 39 % of the load (P < 0.001). When the left knee was extended and the pelvis tilted the left leg took 49 % of the load (P = 0.074).

When the Right foot was higher, the set up simulated a short left leg. When the right knee was flexed the left leg took 65 % of the load (P < 0.001). When the right knee was extended and the pelvis tilted the left leg took 58 % of the load (P = 0.069).

# Conclusion

These results show that weight distribution increased in the shorter limb when leg discrepancy is simulated. The loading is at its greatest when the longer limb is flexed. This loading can be reduced by adopting a tilted pelvis stance. However this may cause pelvic and spinal problems for the patient.

Uneven load distribution is likely to lead to early fatigue when standing and may explain why some patients with limb length discrepancy post arthroplasty have poor outcomes.


#### ORAL SESSION 14 Biomaterials

#### O-078

#### A NEW APPROACH OF MEASURING CELL ADHESION ON IMPLANT SURFACES

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#### Introduction

For orthopaedic implants the adhesive strength of bone cells on implant surfaces is of high interest. In some cases the adherence of cells is desirable, e.g. on endoprosthetic implants, in others, mainly temporarily used implants, e.g. orthopaedic nails, it is not favourable for the cells to attach to the implant.

There are different approaches to measure cell adhesion. The simplest way is the "wash off" principle for short term adherent cells (< 60 min).1 Non-adherent cells will be washed off from the surface and can be counted, but it is not possible to quantify the adhesive strength. The cell attachment forces can be obtained using a centrifuge but only for cells that have bonded to the substrate for a short period of time (<60 min), because the centrifugal forces are not strong enough to detach long time adherent cells. Using micropipettes or atomicforce-micrometers (AFM) it is possible to apply normal and tangential forces in order to detach adherent cells and measure the applied forces. Disadvantageous is the fact that the forces can only be applied to one cell but not to a biofilm.

The aim of the present study was to perform quantitative measurements of the adhesive strength of bone cells on implant surfaces. Based on García et al.1 a new device for microscopy was designed which uses the physical properties of a rotating disc in a fluid and allows for short term as well as long term cell adhesion measurements in a large cell population.

#### **Materials and Methods**

MG-63 cells (human osteosarcoma cell line, CRL-1427, ATCC, Rockville, Maryland, USA), were stained with fluorescent dye, PKH26 (Sigma-Aldrich, St. Louis, MO, USA). Approximately 1500 MG-63 cells were seeded in 2 µl droplets of DMEM with 10 % FCS (Gibco Invitrogen, Karlsruhe, Germany) and 1 % Gentamicin (Ratiopharm, Ulm, Germany) onto a polished TiAl6V4 disc (Ø 30 mm) at defined radial positions. After 20 min of incubation at 37 °C and 5 % CO2 the disc was fully covered with medium and incubated for further 18 h. For measurement of the cell adhesion the disc was mounted onto the shaft of the new device and the chamber was filled with 250 ml DMEM (at a temperature of 37 °C) without FCS and antibiotics (schematically shown in figure 1). The apparatus was adapted for application with a confocal Laser Scanning Microscope (LSM410, Zeiss, Oberkochen, Germany). The shaft can be moved up and down in order to focus the cells with the LSM. For rotation the disc was lifted away from the glass bottom. During rotation shear stress is exerted on the cells, which causes them to detach. The magnitude of the shear stress depends on the rotational velocity and the radial position (r) of the

#### Seminario 10:00 - 10:50 h O 078-083

cells on the disc. The disc was rotated at different velocities for 2 min. After each rotational speed the shaft was lowered and the number of remaining cells at each position was imaged by LSM and analyzed using a software image tool. (UTHSCSA, San Antonio, TX, USA).



#### **Results and Discussion**

At a rotational velocity (vrot) of 2900 rpm more than 50 % of the adherent cells were detached at the outermost radial position (r = 13.5 mm), see table 1. *Table 1: Summary of the results at different radial positions* 

V <sub>rot</sub>	Detachment [%]				
[rpm]	r = 13.5	r = 10.5	r = 7.5	r = 4.5	
2900	60-70	15	2-5	0	
3100	95-98	80	30-40	2-5	
3300	99	95-98	60-70	5-10	

The further the cells are away from the centre of the disc, the higher the shear stress exerted on the cells at a given rotational velocity. According to García et al.1, once more than 50 % of the cells are detached the experiment is successful. Considering ideal laminar flow conditions the results obtained in the experiments calculate to an average shear stress (adhesive strength) of  $d_{m} = 0.79981 \sqrt{(mt^2)}$  approx. 50 N/m2. In comparison to the data assessed by García et al.1 the current results appear too high but bearing in mind that different cells as well as different experimental parameters such as a longer adhesion period were used the results are plausible.

#### Conclusion

The study shows that the adhesion strength can be calculated using the new device. The advantage of this approach is that the same cells can be observed before and after rotation. Moreover, different rotational speeds can be applied to the same cell population. Further investigations using different surfaces and variations of proteins for cell proliferation are carried out.

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#### EORS 2008 · MADRID



#### O-079 THEO

#### THEORETICAL MODEL FOR ORTHOPEDIC IMPLANT USED AS DRUG DELIVERY SYSTEM

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#### Introduction

In this study we assess the innovative concept of orthopedic implant as bisphosphonate-delivery system. This concept relies on the fact that implants failure rate is strongly related to the short-term quality of fixation. Our hypothesis is that the release of bisphosphonate from the implant would protect the peri-implant bone from early osteolysis. The aim of this paper is, first, to develop a comprehensive mathematical model of implants used as bisphosphonate delivery system and, second, to verify it with in vivo experimental data of rats and osteoporotic sheep models. This theoretical framework will be needed in the future for the development of orthopedic implants combined with bisphosphonates.

#### **Material and Method**

The experimental method was developed in [1]. Briefly, titanium cylinders of ø 3mm and length 5mm were coated with hydroxyapatite and loaded with different concentrations of Zoledronate. These implants were then inserted in condyles of rats and sheeps. After 3 weeks for the rats and 6 months for the sheeps, the animals were sacrificed, the condyles extracted, sliced transversally and the bone density (BMD) was measured on the images obtained by backscattered scanning electron microscopy.

The system we analyze here is the trabecular bone surrounding the implant. The different events arising around the implant are distinct components of the global model. Each event is represented by a partial differential equation. The first element is the release and diffusion of the drug into the bone pores where it may fix on the bone material. This diffusion process is well represented by Fick's law of diffusion, with a speciesspecific coefficient of diffusion. The effective diffusion coefficient was estimated with a custom numerical model of diffusion into porous bone. The second element is the biophysical effect of the drug on bone cells. Once it is fixed, the drug inhibits the osteoclasts activity. The effect of the drug was calculated indirectly at the implant surface, where the concentration was known. The model was implemented in a two-dimensional geometry and computed over a distance of 200µm from the implant for the rats and 800µm for the sheep. The effect of bisphosphonate-loaded implants was compared with that of control implants. All computations were realized with Mathematica (Wolfram Research).

#### Results

The rat model was solved numerically over a distance of

200  $\mu$ m from the implant. The relative bone density ](x) was evaluated and compared with in vivo results (figure 1) for doses of 0.2, 2.1, 8.5 and 16 $\mu$ g of Zoledronate per implant and a Zoledronate-free control. The model fits the in vivo data for the control, 2.1 $\mu$ g, 8.5 $\mu$ g and 16 $\mu$ g conditions, with a maximum relative error of 9% on bone density. The model diverges from experimental data for the 0.2 $\mu$ g conditions after 100 $\mu$ m from the implant.



Fig. 1 - Rat model: comparison of mathematical model (lines) with in vivo data (dots) adapted from [1].

For the osteoporotic sheep model, the distance of interest was 800 $\mu$ m from the implant. The relative bone density  $\ddot{u}(x)$  was evaluated and compared with in vivo results (figure 2) for a dose of 2.1 $\mu$ g of Zoledronate per implant compared to control. The model fits the sheep in vivo data for the control and 2.1 $\mu$ g conditions, with a maximum relative error of 10% on bone density.



Fig 2. Sheep model. Comparison of mathematical model (lines) with in vivo results (dots)

#### Discussion

Peter et al have shown that bisphosphonate-delivering implants increase the implant fixation [1] through an increase of density. Our model reflects this pattern with a very good accuracy for most drug concentrations. The model parameters are species-dependent, but the model concepts are not. This mathematical model can be a very useful tool in the future to calibrate and optimize bisphosphonate coated implants for human applications.

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#### Acknowledgments

This work was supported by a grant from the AO Foundation (grant 04-P2), Davos, Switzerland..

#### **DETECTION OF BIOFILM FORMATION** IN STAPHYLOCOCCAL ISOLATES FROM **RETRIEVED ORTHOPAEDIC IMPLANTS**

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Introduction

Biofilm development is a major factor in the pathogenesis of implant-related infections. Several reports studied the development of such structure on different biomaterials. However, there are only a low number of studies that analyzes the ability of clinical isolates of bacteria to develop biofilm in vitro. Here we study such ability in several isolates of Staphylococcus aureus and Coagulase-negative Staphylococcus (CNS) isolated from retrieved orthopaedic implants from patients diagnosed of implant-related infections.

#### Methods

Clinical strains of S. aureus and CNS were isolated by using a sonication protocol from retrieved orthopaedic implants of patients diagnosed of implant-related infection. The strains were frozen until further experiments were performed. Identification of the strains was performed by using a coagulase-conventional test and a commercial system (API-STAPH, bioMérieux, France). Biofilm development was studied using the microtiter plate test (MtP) using polystyrene tissue culture-treated plates (Costar, USA) and crystal violet as dye. The amount of developed biofilm was analyzed at 540 nm optical density (OD) with a spectrophotometer. Confirmation of the biofilm development was obtained by microscopic examination of the micro wells. The experiments were performed by triplicate.

#### Results

Twenty-seven strains (15 S. aureus, 9 S. epidermidis, and one each of S. hominids, S. lugdunensis and S. warneri) were included in the study. Four strains of S. aureus and one strain of S. epidermidis did not develop biofilm in the test, showing OD lectures almost identical to the negative control. The microscopic examination confirms this finding. Among the biofilm-producing strains, an important difference of the amount of biofilm produced was detected. One strain (S. aureus) produced biofilm in greater amount than all other strains, detectable even by visual examination of the plate.





Figure: Biofilm developed by a S. aureus strain. Microscopic examination (x10)

#### Discussion

Biofilm development is considered to have a key role in the pathogenesis of implant-related infections. However, in our study, not all the strains showed the ability to develop biofilm in an in vitro model. Notoriously, 26.7 % of the S. aureus strains were not able to develop biofilm, while only one strain of CNS did not have this ability, although this difference was not significant (p=0.2, Fisher's exact test). Intraspecies differences have also been detected. These findings agree with others (Arciola et al.). There must be other pathogenic factors that are important in the pathogenesis of implant-related infections and need to be studied in order to develop a better strategy for treat these infections.

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#### Acknowledgments

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#### TITANIUM PARTICLES HAVE A HAVE A MORE UNPREDICTABLE EFFECT ON BONE RESORPTION THAN FLUID PRESSURE.

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#### Introduction

The mechanism behind bone resorption adjacent to prosthesis is controversial. A majority of researchers claim that an inflammatory reaction to wear debris particles from the articulating surfaces is the main cause for the bone resorption that unfastens the implant. However, increased intraarticular fluid pressure and factors related to instability and micromotion are important for the early loosening process. The most common model to study particle induced osteolysis is the murine calvarial model. This model has only a transient effect [1]. The osteolysic lesion has peak after 7 days and disappears after 13 days. The size, concentration and volume of particles and the osteoblastic activity are critical for the effect [2]. We have rat model in which bone resorption can be induced both by fluid pressure and particles. Based of earlier observations of particle induced bone resorption we hypothesized that 1) titanium particles cause a transient inflammatory ostelysis in our model, 2)Repeated particle implantation induces more osteolysis. We also compared the bone resorptive potency of particles and fluid pressure.

#### **Materials and Methods**

The rats received a titanium plate at the proximal tibia. A central plug was inserted. After 5 weeks of osseointegration, the central plug was changed to a piston or a hollow plug with 20mg titanium particles. Commercially pure titanium particles with 90 % of particles lesser than 3,6 microns were used in this study (Alfa Aesar, Karlsruhe, Germany). To obtain particles with a size exceeding 10 µm we used a multiple step sedimentation process. The particles were confirmed endotoxin free after 30 minutes in 95% ethanol heating in for 3 hours at 200°C. The pressure piston was subjected to a transcutanous force of 5N. Each episode of pressure comprised 20 pressure cycles at 0.17 Hz, applied twice a day. 60 rats were randomized to 6 groups for particle treatment with 10 rats. One group had particle implantation both at day 1 and 7 (Group 1-6, table 1). Additionally 15 rats were randomized into 3 groups with 5 rats in each groupfor pressure treatment (Group 7-9, table 1). The rats were killed after 5 or 14 days. Bone resorption underneath the piston was evaluated blindedly in hematoxlyin/ eosine stained paraffin sections by the following score: (0) no bone resorption; (1) occational resorption <5%, (2) resorption area covering 5-25% of tissue examined, (3) resorption area covering 25-75%, (4) resorption area covering over 75% of tissue examined. Differences between groups were analyzed by Kruskal Wallis and Mann-Whitney U-tests.

#### Results

Titanium particles induced a highly variable effect after both 5 and 14 days. Many specimens showed no visible resorption at al, and a few showed dramatic osteolysis. After 14 days, the osteolytic effect was significant. This was alre so than titanium particles both after 5 and 14 days (Table1).

Table	1.	Histologic	scoring	of bone	resorption
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Group	Follow -up	Median	Min- max
1. Control no particles	5 days	0	0-1
	5 days	1,5	0-3
3. Particles>10m	5 days	0	0-1
4. Control no particles	14 days	0	0-1
	14 days	3 <sup>a,b</sup>	1-4
	14 days	3 <sup>a,b</sup>	1-4
7. Control no pressure	5 days	0	0-1
8. Pressure	5 days	3 <sup>b</sup>	3-4
9. Pressure	14 days	4 °	4-4

a= p<0.001 compared to controls 14 days; b= p<0.001 compared to particles 5 days; c= p=0.003 compared to particles 14 days

#### Discussion

We found a wide variability the osteolytic response to titanium particles after 5 and 14 days. This is in line with previous studies [3, 4]. Underlying factors such as the amount of particle debris in direct contact to the bone and factors related to the newly formed granuloma might contribute to the osteolytic response. There was lesser variability in fluid pressure induced osteolysis, which might be due to a different signalling pathway [3, 4]. We did not find a transient effect of the particles, which is seen in the mouse calvarial model. This might be explained by the age of the rats since the mouse calvaria model is mostly based on young mice with higher osteoblastic activity [1]. We conclude that titanium particles have an osteolytic effect in this model, but in spite of the massive amount of particles, the effect was less predictable than with pressure.

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#### INCREASING THE CRYSTALLINITY OF CROSSLINKED UHMWPE AFTER POST-IRRADIATION REMELTING

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#### Introduction

The three main requirements for improved performance of ultra-high molecular weight polyethylene (UHMWPE) used in total joint replacement prosthesis are: (1) high wear resistance (2) high oxidation resistance and (3) high mechanical properties. Several studies have now established that radiation crosslinking by applying a dose of 50-100 kGy gamma or electron beam radiation followed by remelting to quench free radicals fulfils the criterion of high wear resistance as well as high oxidation resistance [1, 2]. However, post-irradiation remelting leads to a decrease in several mechanical properties of UHMWPE including fracture toughness and resistance to fatigue crack propagation [3-5], which are deemed important for components in joints where they are subjected to high stresses, such as in tibial components. A major factor associated with low mechanical properties is the low crystallinity and ill-formed crystalline lamellae in such crosslinked UHMWPEs. It is therefore of great value to increase the crystallinity of irradiated, remelted UHMWPE. In this study, we hypothesized that processing methods, which disentangle UHMWPE macromolecules would assist in increasing its crystallinity since disentangled polymer chains would be more readily incorporated into crystalline lamellae, thereby increasing overall crystallinity. The results showed that high-pressure crystallization was more effective than macromolecular orientation in increasing crystallinity of irradiated, remelted UHMWPE.

#### **Materials and Methods**

Extruded rod stock of GUR 1050 UHMWPE (Ticona, Bayport, TX) was purchased from MediTech Medical Polymers (Fort Wayne, IN) and irradiated using gammairradiation to a dose of 50 kGy (Steris, Northborough, MA). The irradiated rod stock was remelted at 170C for 4 hours and cooled. One group of cylinders was placed in a Carver hydraulic pressure, heated to 130C and compressed to compression ratios (CR=final height/initial height) of 1 (no compression), 1.48, 1.85, 2.03, 2.23 and 2.5. The cooled, compressed samples were later remelted for strain recovery. A second group of cylinders machined from the stock was placed in a high-pressure cell, heated to 130, 180, 200, 220 and 240C, subjected to a pressure of 500MPa for 1 hour and then cooled to room temperature followed by pressure release. It must be noted that the 130C samples were only partially melted while the rest were fully melted prior to highpressure crystallization. A Perkin Elmer Pyris 6 differential scanning calorimeter was used to measure the degree of crystallinity for all samples (n=3), using a heat of fusion of 293 J/g. Statistical analysis was conducted using ANOVA (Fisher's PLSD post-hoc test) with a p-value less

than 0.05 used to define significance.

#### **Results and Discussions**

Uniaxial compression of radiation crosslinked UHMWPE did not lead to any statistically significant (p>0.05, ANOVA) change in crystallinity for all compression ratios (see Fig 1). It was also not possible to increase compression ratio further since the samples fractured. Remelting the compressed specimens to remove orientation also did not alter crystallinity significantly. This is probably because the disentangled, oriented chains immediately re-entangle upon remelting even when it is maintained in the melt-state for only a few minutes [6]. In the case of high-pressure crystallization, only the samples crystallized at 240C showed a statistically significant increase (p<0.05, ANOVA) in crystallinity from 46.2% for the untreated control to 56.4%. This is probably due to extended chain crystallization, which occurs via the wellknown hexagonal phase for polyethylene [7].

#### Conclusion

High-pressure crystallization via the hexagonal phase is more effective than macromolecular orientation & strain recovery in increasing crystallinity of irradiated, remelted UHMWPE, which could increase its clinically relevant mechanical properties.



Figure 1. Crystallinity versus compression ratio for irradiated, remelted UHMWPE compressed at 130C.



Figure 2. Crystallinity versus crystallization temperature at a pressure of 500 MPa for crosslinked UHMWPE

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#### INVESCOT O-003

#### A QUANTITATIVE EVALUATION OF ARTICULAR CARTILAGE AFTER MENISCUS REPLACEMENT IN RABBITS

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#### INTRODUCTION

Experimental and clinical studies have documented that meniscal allografts show capsular in growth in meniscectomized knees. However it remains to be established whether meniscal allograft transplantation can prevent degenerative changes after total meniscectomy. In this study, functional changes in articular cartilage after meniscus transplantation in rabbits were evaluated quantitatively.

#### **METHODS**

Thirty rabbits were divided into five groups. Group A and Group C were subjected to meniscectomy. Group B and Group D underwent meniscal transplantation immediately after meniscectomy. Group E had delayed transplantation 6 weeks after meniscectomy. Six nonoperated knees served as controls. Using image analysis with QwinPro software functional changes of articular cartilage were examined 6 weeks (Groups A, B) and 1 year (Groups C, D, E, controls) after surgery by measuring the lactate dehydrogenase (LDH) activity in chondrocytes as a measure of their vitality and the proteoglycan content of the extracellular matrix as a measure of its quality.

#### RESULTS

All experimental groups demonstrated a significant decrease in proteoglycan content of the cartilage as compared with the control group. At 6 weeks and 1 year follow-up, no significant differences were found between the postmeniscectomy group and immediate transplant group. The delayed transplant group showed a significantly decreased proteoglycan content as compared with the postmeniscectomy group. Compared to the control group, no significant differences in cellular LDH activity were found in the postmeniscectomy group and immediate transplant group at 6 weeks and 1 year. However, delayed transplantation caused diminished vitality of chondrocytes. No significant differences were found between the postmeniscectomy group and immediate transplant group at 6 weeks and 1 year. The delayed transplant group showed a significant decrease in LDH activity as compared with the postmeniscectomy group.

#### CONCLUSIONS

It can be concluded that immediate meniscal transplantation in rabbits did not significantly reduce degenerative changes of articular cartilage whereas delayed transplantation leads to even more degenerative changes than meniscectomy.

#### ORAL SESSION 15 Award Papers

#### **O-127**

#### CDNA ARRAY BASED ANALYSIS OF THE GENE EXPRESSION OF CHONDROSARCOMA OF DIFFERENT HISTOLOGICAL GRADES

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#### Introduction

Chondrosarcomas are malignant, hyaline cartilageforming tumours which can be classified according to malignancy through histological grading. Grade 1 chondrosarcomas rarely metastasize whereas in grade 3 chondrosarcoma metastasis is observed in 71% of cases. So far, the molecular processes responsible for the regulation and control of the development and growth of chondrosarcomas have not been elucidated. There is no clear molecular marker for the identification and characterisation of chondrosarcoma. The aim of this project was to identify such marker genes through the comparison of gene expression profiles of chondrosarcoma with normal hyaline cartilage, and through the correlation of expression profiles to patient outcome and histological grading.

#### Methods

The mRNA of 19 chondrosarcomas with different histological grades (6 grade 1, 8 grade 2 and 5 grade 3 chondrosarcoma) and of 8 normal cartilage samples was analysed. Gene expression profiles were assessed on a customised cDNA array including 230 genes with a focus on cartilage- and stem cell-relevant genes. After normalisation the data were analysed using the Cluster and Treeview software (http://rana.lbl.gov/EisenSoftware. htm) and the SAM (Significance Analysis of Microarrays) software. Results from the cDNA array analysis were confirmed by real-time RT-PCR.

#### Results

In the analysed chondrosarcoma samples, cartilage as well as stem cell marker genes were found to be expressed. Gene expression profiles clearly discriminated between normal and neoplastic cartilage, but did not allow any classification of chondrosarcoma according to malignancy. Accordingly, through the comparison of the gene expression profiles of chondrosarcoma and healthy cartilage a high amount of differentially expressed genes was identified: 60 genes higher expressed in cartilage and 13 higher expressed in chondrosarcoma.

#### Aula Magna 13:20 - 14:00 h O 126-130

The genes higher expressed in cartilage included several genes encoding matrix proteins, whereas among the genes higher expressed in chondrosarcoma signalling molecules as the PTH receptor and syndecan 3, which is involved in BMP signalling in the growth plate, were found. Genes differentially expressed between tumours of different grade were identified and correlations were established between gene expression profiles and histological grading. Galectin 1, amongst others, was significantly higher expressed in highly malignant tumours compared with tumours with lower histological grade. The correlation of galectin 1 expression with malignancy could be confirmed at protein level by immunohistological analysis.

#### Conclusions

The comparative analysis of normal cartilage and chondrosarcoma gene expression showed that there are important molecular differences between the matrix of normal and neoplastic cartilage. Our results furthermore confirm that genes implicated in the regulation of the growth plate were expressed in chondrosarcoma. Remarkably, we identified galectin 1 as a marker correlating to malignancy on the level of gene and protein expression. Galectin 1 is functionnally polyvalent molecule involved in several cellular processes. More extended studies would be necessary to establish it as a marker for malignancy in chondrosarcoma.



#### ROLE OF PARATHYROID HORMONE-RELA-TED PROTEIN (PTHRP) ON THE ALTERED BONE FORMATION IN A MOUSE MODEL OF DIABETIC OSTEOPENIA.

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#### Introduction

Osteoporosis is a skeletal disease characterized by a reduced bone mass and deterioration of the remaining bone microarchitecture, making it prone to fracture (1,2). Type 1 diabetes mellitus (DM) is associated with bone loss, but the mechanisms of DM-related osteoporosis are poorly defined (3). A variety of studies show that parathyroid hormone-related protein (PTHrP) acts as a modulator of osteoblast differentiation (4,5). PTHrP is present in osteoblasts (6), and its expression decreases in age-related osteopenia (7). We examined here the putative role of PTHrP on the alterations of osteoblastic function in DM.

#### **Materials and Methods**

In vivo, we used a marrow ablation model in diabetic mice by multiple streptozotocin injections (glycemia > 300 mg/dl). A group of mice were treated with PTHrP (1-36) (100 ng/g/every other day, s.c.) for 2 weeks including the period of bone regeneration (6 days) before sacrifice. One tibia from control and diabetic mice was fixed in 4% p-formaldehído, and then decalcified in formic acid. H/E and Masson stainings were made in 5-µm sample sections. Total RNA was isolated from the other tibia of each mouse, using Trizol (Invitrogen, Groningen, The Netherlands). Gene expression of several osteoblastic markers was analyzed by real-time PCR using an ABI PRISM 7500 system (Applied Biosystems, Foster City, CA). In vitro, mouse osteoblastic MC3T3-E1 cells were grown in differentiation medium (a-MEM with 10% fetal bovine serum, 50 µg/ml ascorbic acid and 10 mM ]-glycerolphosphate) up to 80% confluence, with or without high glucose (HG) (25 mM) (or mannitol, as osmotic control), supplemented (or not) with PTHrP (1-36) (100 nM). In some experiments, anti-PTHrP N-terminal antibody C13 (1:100) or [Asn10, Leu11, D-Trp12] PTHrP (7-34) amide [PTHrP (7-34] (1  $\mu$ M) were also added. Medium and stimuli were replaced every other day. Gene expression was analyzed by real-time PCR after cell total RNA isolation. RANKL secretion was measured in the cell-conditioned medium by ELISA (Biomedica Gruppe, Wien, Austria), detecting free soluble mouse RANKL, following the manufacturer's instructions.

#### **Results and Discussion**

In vivo, DM induced a 10-15% weight loss and a significant decrease (20-40%; p<0.05) in the gene expression of the following osteoblastic factors in the regenerating mouse tibiae: PTHrP, the PTH/PTHrP type 1 receptor (PTH1R), osteocalcin, VEGF and its receptors VEGFR1 and VEGFR2; and in the OPG/RANKL ratio. These changes were related to an increased gene expression of peroxisome proliferator-activated receptor (PPAR) ]. Compared to control mice, the regenerating tibiae of DM mice showed a 5-fold increase in adipocyte number, and a decrease in both osteoblast number and osteoid surface (by Masson's staining). Treatment with PTHrP (1-36) reversed these effects.



In vitro, HG medium induced a decrease (20-40%) in OPG/RANKL ratio (both mRNA and protein) and in the gene expression levels of the PTHrP/PTH1R system and VEGF and its receptors in these cells. Similar effects were obtained by adding a neutralizing anti-PTHrP antibody or the antagonist PTHrP (7-34) to MC3T3-E1 cells in normal glucose medium (5.5mM). The presence of PTHrP (1-36) (100 nM) during cell growth reversed the HG-induced inhibitory effects on OPG/RANKL, the PTH1R and VEGFR1, while it decreased PPAR ], in these cells.

#### Conclusions

A deficit in PTHrP production by osteoblasts seems to be at least in part responsible for the decreased bone formation associated with DM in mice.

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#### IN VITRO TESTING OF A REVISION HIP RECONSTRUCTION WITH IMPACTED TITANIUM PARTICLES

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#### Introduction

We investigated the feasability of using porous titanium particles (TiP) to reconstruct femoral bone defects in revision hip replacement surgery in stead of using morzellized allografts. The following questions were postulated: 1) Is it possible to create a graft layer made of porous TiP in a femoral reconstruction?, 2) Does this graft layer provide adequate initial stability when a femoral stem is implanted in it?, 3) What kind of particles are released from the graft layer after impacting the TiP and subsequent cyclic loading of the reconstruction?

#### **Materials and Methods**

The intramedullary shaft of 7 composite femurs (Sawbones) were reamed to  $\emptyset$  18 mm to simulate cortical thinning. A distal plug was inserted to facilitate the placement of a central guide wire.

The created defects were filled, and impacted, stepwise with 32 grams of large ( $\emptyset$  3.15 - 4 mm) and 9 grams of smaller ( $\emptyset$  2.8 - 3.15 mm) pure, 85% porous TiP. Prior to each impaction step, the TiP were soaked in distilled water to improve adhesion characteristics. After impaction an Exeter hip prosthesis was cemented in the femur.



Figure 1: The experimental setup

All femurs were placed in 7° of anteversion and cyclically axial loaded (0-3000 N) for 300,000 loading cycles at 2 Hz (Figure 1). Subsidence of the stem was measured with radio stereometric analysis (RSA) evaluation at 0, 1,000, 10,000, 50,000 and 300,000 cycles. At the same time intervals 200 ml water was aspired through the whole reconstruction. This water was led through cellulose acetate filters (pore size: 0.45  $\mu$ m) to collect possible

titanium particles.

After the first 3 reconstructions we noticed the "soaking water" came out through the bottom of the plug upon retraction of the guide wire. This water was analyzed in the last 4 reconstructions, since it could contain titanium particles. Both filters and "soaking water" were analyzed with the laser diffraction technique.

After 300,000 loading cycles the Sawbone was cut in the frontal plane and graft thickness, cement mantle thickness and cement penetration were measured at 5 mm intervals.

#### **Results & Discussion**

The TiP were impacted into a > 3 mm (SD 1.43 mm) thick, highly entangled, graft layer. The average cement mantle of > 2 mm (SD 0.86) was seen, although the medial side (1.82 mm) was significantly thinner (p < 0.01, Students t-test) than the lateral side (2.89 mm). Little cement penetration was seen.

An average subsidence of only 0.45 mm (SD 0.04 mm) was measured after 300,000 loading cycles. A fast initial subsidence was seen that gradually diminishing towards the end (Figure 2). These findings are in line with other in vitro and in vivo studies [1-3].



Most particles (87%) in the "soaking water", collected directly after impaction, were smaller than 6  $\mu$ m. These particles can be potentially dangerous because they can induce osteolysis [4]. Analysis of the filters collected during cyclic loading was very clear: none of the filters contained enough particles to be measured by the laser diffraction method. However, it remains unclear whether truly no particles were released or if the reconstruction was not "flushed" adequately.

#### Conclusions

From this study we can conclude that: 1) From a surgical point of view a graft layer of impacted TiP can be constructed, 2) The graft layer is stable enough to initially support an Exeter stem, 3) Titanium particles are released during impaction. These data warrant further animal tests to assess the biological response to these released impaction particles. Also, animal tests should clarify possible particle release upon loading and its effects.

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#### EORS 2008 · MADRID



O-130

#### BONE RESORPTION INDUCED BY FLUID PRESSURE OR TITANIUM PARTICLES: COMPARISON OF INFLAMMATORY PATHWAYS.

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#### Introduction

The response to particulate debris is often considered the main factor behind aseptic loosening [1,2]. However, there is no doubt that mechanical factors such as instability, increased intra-articular fluid pressure and micromotion contribute to loosening [2,3,4]. The particles mediate their effect via macrophages that release proinflammatory cytokines such as TNF-a, IL-6 and IL-1b, and thereby activate the RANKL-RANK system. In a rat model, fluid pressure causes more bone resorption than particles. Does pressure also cause more inflammation, or are other mechanisms involved?

#### **Materials and Methods**

Institutional guidelines for care and treatment of experimental animals were followed. The rats received a titanium plate at the proximal tibia. A central plug was inserted. After 5 weeks of osseointegration, the central plug was changed to either a piston or a hollow plug with titanium particles. Commercially pure titanium particles with 90% of particles lesser than 3,6 microns were used in this study (Alfa Aesar, Karlsruhe, Germany). The pressure piston was subjected to a transcutanous force of 8N. Each episode of pressure comprised 20 pressure cycles at 0.17 Hz, applied twice a day. 39 rats were randomized to 3 groups: Titanium particles (n=13), fluid pressure (n=13) and controls with neither particles nor fluid pressure (n=13). The rats were killed after 3 days. 6 rats in each group were used for histology and the others were used for gene expression. Primers for cat K, RANK, RANKL, OPG IL-1, IL-b, TNF-a, iNOS and COX-2 . The other bone specimens were processed for routine histology with hematoxlyin/eosine.Osteoclasts were defined as multinucleated cells with bone contact. Soft tissue formation underneath the piston or the hollow plug was evaluated qualitatively. Differences between the groups were analyzed by Kruskal Wallis ANOVA and Mann-Whitney U-test.

#### Results

Gene expression: Both particles and fluid pressure induce an elevated expression of osteoclastic genes compared to controls. Particles induced also an elevated expression of IL-6 compared to both controls and fluid pressure. There was a tendency that particles induced more expression of inflammatory genes than fluid pressure.

#### Histology

The controls showed an intact bone surface covered by an organized fibrous callus with osteoid formation. There were no or only few osteoclasts at the bone surface. The particle group showed resorption at the bone surface, covered by a dense connective tissue with macrophagelike cells. The osteoclasts were lining the interface to the soft tissue. In contrast, the pressure group showed resorption cavities spread out inside the bone, filled with loose tissue and osteoclasts.

Target gene	Control	Particles	Pressure
	Median	Median	Median
	Min-Max	Min-Max	Min-Max
	(n=6)	(n=6)	(n=7)
Osteoclastic ge	nes		
RANKL a,b	0,2	12	5
	0,05-2	4-50	1.2-15
RANK a,b,c	0,06	1,4	0,4
	0,04-0,60	0,7-1,6	0,2-0,5
OPG <sup>b</sup>	0,004 0,0-0,2	0,2 0,06-0,5	<b>0,1</b> 0,02-0,3
Cathepsin K <sup>a,b</sup>	0,7	15,3	6,2
	0,05-3	7-302	1-19
RANKL/OPG	24	69	35
	5-130	21-300	0-120
Inflammatory g	enes		
TNF-α	1,5	0,9	0,5
	0,6-1,9	0,6-1,4	0,2-1,7
COX-2	150	160	120
	55-1500	100-620	94-1300
IL-6 <sup>b,c</sup>	0,7	3,8	0,7
	0,1-2,5	2,5-12	0,1-3
IL-1β	1,2 0,6-9	0,8 0,5-2,4	1,1 0,8-8
CatK/TNF a,b	0,5	14	6,6
	0,03-1,8	9-31	0,9-78

a=pressure compared to controls p=0,05-0,002; b particles compared to controls p=0,03-0,002; c=pressure compared to particles p=0,008.

Discussion: Both particle debris and mechanical factors are involved in the loosening process. However, it is still not clear which cells and signalling pathway that are responsible for the bone destruction. Although there was more resorption in the pressure group, there was a lesser inflammatory response. This suggests that pressure-induced resorption is mediated via different pathways [2,3]. This is supported by studies that report different cellular mechanisms of bone resorption in aseptic loosning [4,5].

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#### IN VITRO KNEE KINEMATICS FOLLOWING REMOVAL OF THE CENTRAL ONE-THIRD OF THE PATELLA TENDON IN SHEEP

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#### Introduction

Infrapatellar Contracture Sydrome (IPCS) [1] describes a post-operative complication characterised by a vertical migration of the patella. This condition, referred to as patella infera or patella baja, is induced via 2 non-exclusive pathways; (1) Patella Tendon (PT) shortening and PT adhesion (PTA) formation. Patella infera can have dire implications for both anterior knee pain [2] and mobility [3-4].

The main aims of this study were to investigate how removal of the central one-third of the PT in sheep influences PT length (LT) and the in vitro knee kinematics.

#### Materials and methods

This study was performed on 18 skeletally mature sheep divided into 3, 6, 12 and 24 week groups. All animals underwent an operation on the right knee to remove the central one-third of the PT without reconstruction of the anterior cruciate ligament. The PT defect was not approximated during wound closure. At the time of sacrifice the pelvis-lower extremities complex was isolated from the remainder of the carcass and left in a supine position for approximately 3 hours until rigor mortis set in and transferred to a freezer. Whilst frozen, each complex was sectioned in the mid-sagittal plane and each limb CT-scanned (0.5mm) 10cm either side of the knee joint. Models of the limbs were generated using the dicom output and imported into ProEngineer (PTC, MA) where PT length (LT) was measured.

The specimens were then defrosted and rigidly fixed into a knee loading frame and 50N load applied along the line of action of the rectus femoris muscle using a weight/ cable/pulley system. Knee kinematics were continuously measured throughout the range of motion of the knee using a magnetic tracking system, 3Space IsoTrack II (Polhemus, Colchester, VT). Receivers were attached using custom-designed bone screws (Figure 1).



Figure 1 Receiver assembly

Before and after the tracking experiments the patella receiver assembly was transferred to the femoral bone screw to register the spatial location of the femur. Each leg was then disarticulated and all bones CT-scanned (0.5mm) with the registration block portion of the receiver assemblies engaging the relevant bone implants. DICOM outputs were then used to generate 3D surface representations of the bones and associated registration blocks which were then imported into ProEngineer where body-fixed coordinate systems were created using bony landmarks in accordance with the Joint Coordinate System (JCS) of Grood and Suntay [5]. The necessary coordinate transformations were then obtained from assemblies in which parametric models of the complete receiver assemblies were aligned with datum features based on the surface representations of the registration blocks. Matlab (MathWorks) was used to transform the raw data into translations and rotations as per the JCS. The un-operated side served as the control data for both LT and knee tracking parameters. Statistical analysis (ANOVA) was performed using Matlab with significance set at P<0.05.

#### Results

Removal of the central 1/3 of the PT had no significant effect on LT. As determined from the CT reconstructions, the mean PT length ratio (LT/LC) in the 3 week group was  $1.0028\pm0.0040$  (mean±SD). In the 6 week group this ratio had increased to  $1.0282\pm0.0246$  and had returned to  $1.005\pm0.00347$  in the 12 week group. At 24 weeks, this had increased to  $1.0159\pm0.0217$ . No PTA's were observed.

Removal of the central one-third of the PT was associated with a significant proximal shift of the patella, reflecting the increase in LT between treatment and control groups, and which correlated well with a retardation of patellar flexion (r = 0.880). A significant decrease in medial patellar tilt throughout the entire range of flexion was also observed but was not coupled with changes in tibial rotation. Proximal and lateral tibial shifts were also detected.

#### Conclusion

In our model removal of the central-third of the PT resulted in a condition of patella alta at 6 and 24 weeks postoperatively. The changes in the patellar tracking pattern and LT induced by removal of the central one-third of the PT do not recover 24 weeks post-operatively.

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#### ORAL SESSION 16 Knee Implants

#### O-084

# SOFT TISSUE BALANCE DURING TKR SURGERY: A PROSPECTIVE EVALUATION

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#### Introduction

The implications of residual soft tissue imbalance following TKR surgery has been discussed extensively in recent years. Documentation of the extent of imbalance has been considered in terms of the medial and lateral separation of the joint in full extension and 90° of flexion 1. Similarly, the significance of the angular deviation of the separation gap2 has been studied during the last few years. However, recent work has questioned the need to obtain perfect balance during TKR surgery because the knee is not tensioned equally medially and laterally. Also, others have commented that viscoelastic stress diminishes post operatively and thus the soft tissues relax. Consequently, it remains unclear what levels of residual soft tissue balance are clinically acceptable and which will not increase the risk of biomechanical failure of the TKR in the medium to long term.

#### **Materials and Methods**

One hundred and eighteen patients were recruited to the study consecutively from the top of the waiting lists of two orthopaedic surgeons based at the Derby Hospitals NHS Foundation Trust (TW, DM). Ethical committee approval was gained for the methods used and eligible patients who provided informed written consent were recruited at the preoperative assessment 2 weeks prior to surgery. All the patients completed a WOMAC clinical questionnaire which defined their knee pain and stiffness and their abilities in activities of daily living. Just prior to surgery they were assigned randomly to one of two groups. Soft tissue balance of those allocated to the 'measured' group was measured objectively using a soft tissue balancer3 during surgery. This information was used to guide the release of soft tissues. The soft tissue balance of patients allocated to the 'comparison' group was assessed in the standard manner on the basis of observation and examination. During surgery the soft tissue balance was measured again for both groups following completion of the balancing procedures. No further adjustments were made. The WOMAC clinical rating scale was then repeated at six months post sur-gery by an investigator (ZR) who was blinded to group allocation. The passive range of movement of the knee and alignment of the limb were also measured post operatively. Limb alignment was calculated from X-rays.

#### Results

Sixty of the 118 patients who were recruited to the study were able to complete the trial (34 measured, 26 comparison). The reasons for non-completion included:

failure to attend follow up (n=24), non-standard surgical procedure followed (n=16), patient did not proceed to surgery (n=12), non compliance with randomisation (n=4), death (n=1). The results of the soft tissue balance measurements following balancing procedures for the two groups can be seen in figure 1. Analysis of the post operative Tibio-femoral angle showed that the measured group had a mean value of 7.4° (4.8 SD) and the

#### Aula Magna 14:15 - 15:15 h O 084-090

Figure 1 Soft tissue imbalance in the varus knees following soft tissue releasing procedures.



comparison group 6.5° (4.2 SD) and the post operative range of movement at six months in both groups was comparable. The post operative WOMAC scores for pain and stiffness were also comparable. Differences in the scores for activities of daily living and the total WOMAC score can be seen in figure 2.





#### Discussion

This project considered the effect of measuring soft tissue balance at the time of surgery and using the WOMAC clinical rating scale as an outcome measure. It has shown that the measurement of soft tissue balance will result in a slightly reduced mean level of imbalance in full extension and flexion and a smaller standard deviation about the mean. No difference was seen between the groups for the WOMAC score for the pain or stiffness sections, however, difference was seen in the activities of daily living section and in the overall WOMAC score. This may have been due to improved proprioception4 in the measured group. None of the data presented in this project were statistically significant when compared with a t-test for equal variance. However, the project may be subject to a type 2 error, due to the large number of patients that withdrew from the project.

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#### CONGRUENCY IN THE TIBIO FEMORAL ARTI-CULATION OF FIXED BEARING KNEE PROS-THESES – INFLUENCE ON DELAMINATION RISK, ABRASIVE WEAR GENERATION AND KINEMATICS

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#### Introduction

Total knee arthroplasty (TKA) has become a successful clinical treatment for patients in regard to relief of pain, correction of deformity and restoration of function with promising long term behaviour [Pradhan et al. 2006].

The parameters abrasive wear and delamination are of high relevance for longterm clinical outcomes [d'Lima et al. 2001]. Particle induced osteolysis and subsequent aseptic loosening is responsible for approximately 40 % of necessary revisions in total knee arthroplasty (TKA) [Robertsson et al. 2001].

In TKA the generation of polyethylene wear debris is mainly affected by the factors design of the articulating bearing, contact stresses, kinematics, implant material and surface finish [McEwen et al. 2005].

The objective of our study was to evaluate the in vitro wear behaviour of fixed bearing knee designs in comprehension to the contact mechanics and resultant kinematics for different degrees of congruency.

#### **Material and Methods**

Wear simulator testing on 12 Columbus® and Search® Evolution TKA devices (Aesculap, Germany) has been performed according to ISO 14243-1 under load control and axial loaded reference. The knee replacements were tested in the fixed bearing configurations LC, CR and DD with different degrees of tibio-femoral congruency.

For gravimetric wear assessment the protocol described in ISO 14243-2 has been used, followed by a kinematic analysis of the single test stations.

The articulating contact and subsurface stresses have been investigated in a finite element analysis (FEA) according to Morra et al. 2005.

#### Results

The contact areas are increasing from Search® Evolution LC (144 mm2) to Columbus® CR (235 mm2) and Columbus® DD (279 mm2), whereas the peak surface contact stresses are decreasing from Search® Evolution LC (34.4 MPa) to Columbus® CR (20.9 MPa) and Columbus® DD (18.1 MPa).

The peak von Mises stress magnitudes are decreasing from Search® Evolution LC (20.1 MPa) to Columbus® CR (12.1 MPa)and Columbus® DD (10.6 MPa) (Fig. 1).



Fig. 1: Subsurface stresses for two different degrees of congruency

For the complete test period (5 million cycles) the estimated amount of wear has decreased from Search® Evolution LC (21.4+/-2.3 mg/million cycles) to Columbus® CR (8.9+/-2.9 mg/million cycles) and Columbus® DD (2.2+/-0.7 mg/million cycles) (Fig. 2).



Fig. 2: Gravimetric wear rates for three different fixed bearing knee designs (tibiofemoral congruency)

The wear rates between the knee design configurations differ substantially and statistically analysis demonstrates a significant difference (p<0.01) between the test groups in correlation with congruency.

#### Conclusion

The present study demonstrates the influence of different bearing types on contact stresses, abrasive wear and kinematics for two knee systems under elimination of production, material and sterilization parameters.

#### CROSSLINKED POLYETHYLENE IN KNEE ARTHROPLASTY - SIMULATOR RESULTS OF DIFFERENT MATERIALS

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#### Introduction

Aseptic loosening is one of the main reasons for revision of total joint replacements. A chronic inflammatory adverse reaction to wear particles in the surrounding tissues can lead to osteoclast activation, so that articulating surfaces with low wear rates and a minimum amount of particles are required [1-4]. Compared with conventional ultra high molecular weight polyethylene (UHMWPE) crosslinked polyethylene (XPE) shows a reduced wear rate in a hip simulator [5]. The crosslinking process reduces the mechanical properties of UHMWPE, particularly its fatigue strength. This is achieved by gamma or electronic radiation, followed by heat treatment either above the melting point (remelting) or below (annealing). UHMWPE fatigue occurs more frequently in the knee joint than in the hip joint due to its changing tribocontact areas combined with high weight bearing. This is why crosslinked polyethylene is still controversially discussed for use in total knee prostheses [6].

Is XPE proven appropriate for the use in total knee prostheses in simulator testing? Does the manufacturing process affect the wear properties?

#### Material and Methods

In a knee joint simulator\* different kinds of XPE and a conventional UHMWPE (3 inlays in each case) were tested according to the ISO standard (Tab 1). For 5 million cycles in a fixed bearing knee the gravimetric (mg/year) and the volumetric (mm<sup>3</sup>/year) wear rates were measured and the wear mechanism was analyzed by means of a scanning electron microscope.

Results: All inlays showed signs of abrasion, scratching and wear polishing, but no traces of delamination or other fatigue reactions. All types of XPE produced significantly (p<0.05) lower wear rates than the conventional UHMWPE (Tab 2). Between the different kinds of XPE Inlay A showed significantly (p<0.05) lower wear rates than the other XPEs.

#### Conclusions

Crosslinked polyethylene is suitable for total knee prostheses. Simulator testing showed overall reduced wear rates compared to conventional UHMWPE and fatigue symptoms were not observed, so that a monitored clinical investigation can be recommended. The wear rates vary depending on the manufacturing process. Crosslinked polyethylene manufactured by sequential irradiation and annealing seems to produce still lower wear rates than those manufactured by remelting, at least when used in total knee prostheses.

\* Stallforth-Ungethuem knee joint simulator



ХРЕ, Туре А	Fixed-bearing CR, GUR 1020, 3x30 kGy Gamma, sequential irradiation and annealing, Gasplasma
XPE, Type B	Fixed-bearing ultra-congruent, GUR 1050, 95 kGy E-beam, remelting, EtO
XPE, Type C	Fixed-bearing CR, GUR 1050, 65 kGy E-beam, remelting, Gasplasma
Conventional UHMWPE, Type D	Fixed-bearing congruent, GUR 1050, Gamma

Tab 1: Different kinds of polyethylene used for simulator testings in knee arthroplasty

Inlay		Mean gravimetric wear rate [mg/mil]	Mean volumetric wear rate [mm <sup>3</sup> /mil]	
	A	0.63* (0,47-0,79)	0.67* (0,50- 0,85)	
XPE	в	1.95*(1,45-2,45)	2.1*(1,55-2,62)	
	C	2.9*(2,5-3,3)	3.19*(2,7-3,5)	
UHMWP E	D	8.5(8,1-9,1)	9.1(8,6-9,7)	

Tab 2: Gravimetric and volumetric wear rates of XPE and UHMWPE in total knee arthroplasty (p<0,05)

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#### THIGH-CALF CONTACT: THE EFFECT ON THE PROSTHETIC KNEE LOADING DURING HIGH-FLEXION

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#### Introduction

Recently, high-flexion knee implants have been developed to provide for a large range of flexion (>120°) after total knee arthroplasty (TKA). Since knee forces typically increase with higher flexion angles, it is commonly assumed that high-flexion implants are subjected to larger loads than conventional implants. However, most knee studies focusing on high-flexion do not consider thighcalf contact which occurs during deep knee flexion activities such as squatting and kneeling. Thigh-calf contact is expected to reduce the knee forces in the high-flexion range as the tibio-femoral load shifts from occurring inside the knee towards the thigh-calf contact interface.

The purpose of this study was to analyze the effect of thigh-calf contact on the loading of the knee joint. In a previous study, it was demonstrated that thigh-calf contact is substantial:  $\pm 68\%$  bodyweight (BW) transfers through the contact between thigh and calf on both legs during squatting.1 Hence, in this study we investigated the effect of thigh-calf contact on the prosthetic knee loading during deep knee flexion using a finite element (FE) knee model.



#### **Materials & Methods**

The three-dimensional dynamic FE model utilized in this study consisted of a distal femur, a proximal tibia and fibula, high-flexion components of the PFC Sigma RP-F (DePuy International, Leeds, UK), a quadriceps and patella tendon and a non-resurfaced patella (figure 1). Both tibio-femoral and patello-femoral contact were defined in the model. Non-linear elastic-plastic material properties were used to model the polyethylene.2 Knee flexion was simulated by application of the ground reaction force to the ankle and releasing the quadriceps tendon incrementally. Thigh-calf contact characteristics from a typical individual having an average body mass index (BMI = 22.3 kg/m2) were included in the knee model. Finally, a squatting movement was simulated using the knee model.







#### **Results and Discussion**

Thigh-calf contact considerably reduced both the joint forces and the polyethylene stresses during deep knee flexion (figure 2). At maximal flexion (155°), the compressive knee force computed by the knee model decreased from 4.89 to 2.90 x BW. In addition, the maximal joint force shifted from occurring at maximal flexion to the flexion angle at which thigh-calf contact initiated ( $\pm$ 130°). At maximal flexion, the Von Mises stress and contact stress at the tibial post decreased from 25.89 MPa to 15.86 MPa and from 49.32 MPa to 28.06 MPa, respectively.

#### Conclusions

The current study confirms that thigh-calf contact considerably reduces the loading of the knee in the highflexion range. Both the joint forces and the polyethylene stresses reduced considerably when thigh-calf contact was included in the knee model. Furthermore, average knee patients having a high BMI (>25 kg/m2) and fairly obese leg segments benefit relatively more from thighcalf contact as the reducing effect caused by the softtissue compression initiates at lower flexion angles.

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#### Acknowledgments

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#### TRACTION FORCES IN DEEP KNEE BENDING OF ROTATING PLATFORM TOTAL KNEE IMPLANTS AND IMPLICATIONS FOR WEAR

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#### Introduction

This computational study examines a rotating-platform TKA design in a weight-bearing functional activity (deep knee bending) to explore theoretical differences in wearrelated contact parameters.

#### Methods

A multibody dynamics program (LifeMOD/KneeSIM, Biomechanics Research Group, Inc., San Clemente, CA) was used to simulate two cycles (9-sec) of knee bending. A PFC Sigma® rotating platform (RP) posterior cruciate retaining total knee with a curved insert, (DePuy, Warsaw, IN) was subjected to two cycles of deep knee bending up to 130 degrees of flexion. The rotating platform model (Free RP) included experimentally determined torsional frictional behavior for the insert-tray bearing as a function of axial load and rotational speed. The analysis was repeated with the exact same implant design, but with the insert locked (Fixed RP) to the tray to prevent internal-external (IE) rotation (a theoretical TKA design). IE rotation and surface traction (frictional) forces were calculated over the contact patch and averaged at the center of pressure in the medial and lateral compartments.

#### **Results and Discussion**

When the insert was free to rotate (Free RP) the insert rotated with the femur until about 40 degrees of flexion, after which it lagged slightly (Fig. 1). When the insert was fixed to the tray (Fixed RP) the maximum IE rotation was reduced from 8.5 to 5 degrees.



Fig.1. IE rotation of the tibia relative to the femur (+INT) (red open circles for free-RP and solid black line for fixed RP) and of the insert relative to the tray (+EXT) (blue dot-dash lines). Output for two cycles.

Cross-wise surface traction forces were greater for the Fixed RP than the Free RP design in both medial and lateral compartments (Fig. 2). The knee experiences combined rolling and sliding between the femoral component and insert and this leads to normal and traction forces in the contact region [1]. The traction forces arising from rolling and sliding may cause delamination [2], especially if they are in a



Fig. 2. Traction forces for the Fixed RP (solid) and Free RP (dotted) in the insert reference frame in the antero-posterior (AP), supero-inferior (SI), and medio-lateral ML directions in the medial (red) and lateral (blue) tibio-femoral compartments during the second knee bend cycle from 0 to 130 to 0 degrees.

direction cross-wise to the main direction of motion of the contact patch, in accordance with the strain-softening effect proposed as a mechanism of wear for multidirectional motion [3]. Even though the amount of cross motion in TKA designs has been shown to be limited [4], the present study indicates that cross-wise traction forces are greater in a theoretical TKA design which is restrained from rotation at the RP bearing.

#### Conclusions

These theoretical results lend support to the notion that a rotating platform design may reduce wear by reducing cross-shear traction forces between the femoral component and the tibial insert.

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## BISPHOSPHONATES REDUCE MIGRATION OF KNEE PROSTHESES

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#### Background

In a previous randomized studiy using Röntgen Stereometric Analysis (RSA), we showed that oral bisphosphonates reduce the mean migration distance during the first 6 months. The difference persisted up to 4 years (1). In a similar randomized study, bisphosphonates applied locally at the operation had a similar effect (2). However, these studies compared mean values between groups. Although statistically significant, the magnitude of the difference was only 0.1 mm. Does this small difference matter? It would matter if the small difference in mean value reflects an important reduction of the number of patients who migrate excessively. The present study addresses this question by use of frequency analysis.

#### Methods

The patients from the 2 previous studies were combined for analysis, and designated as bisphosphonate (n=44) or control treated (n=49) per protocol. The migration vector lengths were assumed to be a compound of log-normal distributions. The frequency analysis determined if the observed frequency distributions were best described as a single, or a sum of 2 or more lognormally distributed subgroups. We analysed the migration vector (for the center of the rigid body) by use of a new set of algoritms for frequency distribution analysis called Rmix (3).

#### Results

After 6 months, the control patients had formed 2 subgroups, one comprising 85% of the patients, with a mean migration distance of 0.14 mm, and the other with a mean of 0.34 mm. The dichotomy in 2 groups was statistically significant (p=0.016).

After 2 years, the dichotomy persisted (p=0.027). One subgroup comprised 73% of the patients, with a mean migration distance of 0.15 mm, and the other had a mean of 0.34 mm (Figure 1).

In the bisphosphonate-treated patients, no dichotomies could be found. The distribution of the migration vector length appeared similar to the larger and less migrating subgroup among the controls, with a mean of 0.13 mm at 6 months and 0.17 mm at 2 years.

#### Discussion

The risk of aseptic loosening for cemented knees is extremely small in this material, which had the normal age for idiopathic osteoarthritis. In young and physically active patients the risk may be considerable. However, the initial fixation and its biology should be similar. The smaller and more migrating subgroup among our control patients may be at risk of loosening, and would have run a high risk if they were young and active. This subgroup did not appear with bisphosphonate treatment

In a larger material of cemented acetabular cups we found a similar dichotomy, and were able to show that the larger group was completely stable, whereas the smaller group apparently comprised the "true" migrators. We have not demonstrated this for the knees, but because there are two distinct postoperative courses, and the patients fall into one or the other, it is likely that the course which involves more migration is ominous, if combined with high physical activity.

#### Summary

In previous comparisons we found a slight decrease in mean value with bisphosphonates. The present analysis shows that this reflects the disappearance of a small subgroup with large migration.



Figure 1. Frequency distribution of the length of the migration vector (mm) from postop to 2 years. Histogram indicates observations. Curves indicate the estimated distributions under the assumption that the material consists of one or more groups with lognormal distribution. Triangles indicate the mean of the 2 subgroups. Dichotomy significant, p=0.027

#### References

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#### REALLY OBJECTIVE CLINICAL OUTCOME OF A NEW ULTRA CONGRUENT POSTERO-STABILIZED TOTAL KNEE ARTHROPLASTY

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#### Introduction

In order to address the more specific needs of the young and active patients suffering of severe knee osteoarthritis, a new total knee arthroplasty (TKA) has been designed at our University Hospital. The FIRST knee prosthesis (Free Insert in Rotation Stabilized in Translation, Symbios SA) is an ultra congruent, postero-stabilized total knee arthroplasty with a mobile bearing expecting to reduce significantly polyethylene wear, to improve the range of motion and the overall stability of the knee while ensuring a physiological ligament balance.

Gait analysis has proven to give really objective outcome parameters after lower limb surgery. Using an ambulatory device, our goal was to compare subjective and really objective results of this new TKA with standard models used all over the world.

#### **Materials and Methods**

A clinical prospective monocentric cohort study of 100 consecutive patients undergoing a FIRST TKA for primary osteoarthritis is currently done. All the patients have already been included (mean age of the cohort is 70,2  $\pm$  8,1 years (47-88) and mean BMI is 27.5  $\pm$  5.1 kg/m2 (21-42)). Follow-ups were done at 6 weeks, 4.5 months, 1 year and 5 years. Data included subjective evaluations (EQ-5D and WOMAC scores), semi-objective questionnaires (KSS score and radiography evaluation) and really objective gait parameters from 6 walking trials of at least 30 meters long, performed at different speeds with an ambulatory gait analysis system (Physilog®, BioAGM CH). The outcomes of 32 FIRST TKA after one year of follow-up are reported here and compared to the results of a randomized controlled clinical trial performed in the same center just before this study and comparing 29 NexGen® postero-stabilized TKA (Zimmer Inc) with a fixed bearing to 26 NexGen® postero-stabilized TKA with a mobile bearing using the same methods.

#### Results

Statistically significant improvements were noted between the pre-operative and the 3 months and 6 months follow-ups in terms of subjective and semi-objective scores for all types of prosthesis (EQ-5D, WOMAC and KSS scores). No statistically significant differences were observed between the 6 and 12 months follow-ups for the same scores in the three groups.

As for the ambulatory gait analysis, the comparison of several temporal and spatial gait parameters at different walk paces (slow, normal and fast) showed significant differences between the types of prosthesis: the gait cycle time of the FIRST TKA was improved at normal, slow and fast walk compared to both NexGen® TKAs

but only statistically significantly at normal speed.

Shorter double-support periods were obtained for all speeds of walk with the FIRST TKAs. This better improvement was statistically significant at normal and slow speed walk compared to the both NexGen® TKAs (mobile and fixed-bearings). The normal walking speed was significantly higher with the FIRST TKAs (cf figure and table). Significantly faster swing speed of the operated knee was observed for the FIRST TKAs when the patient was walking normally.



Figure: Average speeds (m/s) chosen by the patients in different types of walk.

	NexGen® mobile bearing		FIRST		
	Mean	SD	Mean	SD	р
Normal	1.11	0.17	1.19	0.13	0.004
Slow	0.76	0.13	0.83	0.12	0.002
Fast	1.44	0.19	1.59	0.25	0.001

Table: Average speeds (m/s) chosen by the patients in different types of walk.

The extension (in terms of range of motion when walking) of the operated knee was significantly improved for all three types of walk in favour of the FIRST TKAs compared to both NexGen® TKAs. The stride lengths of the patients were also significantly improved for the FIRST TKAs when the patient was walking normally in comparison with the 2 other designs. Finally, significantly better coordination scores2 were observed with the FIRST TKAs at normal walk when compared to NexGen® fixed-bearing TKAs, while the differences were not significant in comparison with the group of NexGen® mobile-bearing TKAs.

#### Conclusions

This new total knee arthroplasty, based on an ultracongruent, postero-stabilized and mobile bearing insert showed very encouraging clinical outcomes: similar subjective and semi-objective results were obtained in comparison with widespread TKA designs; statistically significantly better objective gait outcomes appeared after one year of follow-up for the FIRST TKAs. The validity of these positive results will have to be confirmed by the 5 years results of the FIRST TKAs.

#### ORAL SESSION 17 Knee soft tissues

#### **O-091**

#### ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION IMPROVES, BUT DOES NOT RESTORE, NEUROMUSCULAR ACTIVITY AROUND THE KNEE

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#### Introduction

Anterior cruciate ligament (ACL) injury is the first cause of knee instability. There is not enough evidence for the best therapeutic option, as operative and non-operative treatments of anterior cruciate ligament (ACL) injuries are often associated with a lack of proprioception and a persistent muscle weakness of unclear origin.

#### Material and methods

This study in the cat experimentally compares in the long-term both neural and muscular activity in the knee articular nerves (PAN and MAN), guadriceps and hamstrings, in the chronic unstable knee and the reconstructed knee. Experimental section of ACL in 24 cat's knees was followed by stable reconstruction in 6 knees and unstable reconstruction in 8 knees, leaving the other ten knees unstable without reconstruction. Electrical activity from muscles and nerves was registered with Ni-Cr electrodes. Mean firing activity and peristimulus time histograms (PSTH) for each structure were obtained. Secondly, it evaluates the neuromuscular response changes due to the graft's mechanical competence, comparing stable and unstable reconstructed knees. Two different grafts were evaluated in the reconstructed knee, pediculated extensor digitorum longus (a) and free bone-tendonbone from patellar tendon (b). Statitiscal analysis consisted in Mann-Whitney's test with Bonferroni adjustment between groups, and a two-way ANOVA to evaluate the separate effect of graft type and graft competence.

#### Results

We found an increased periarticular muscle activity during anterior tibial translation in chronically unstable knees. Both reconstructed and non-reconstructed unstable knees lose the fast reactive activity in the articular nerves. When stability was recovered after reconstruction, knees showed a more adjusted, although incomplete, muscular reaction. No differences were observed among grafts, but their mechanic competence was determinant in the neuromuscular firing activity.

#### Aula Magna 15:30 - 16:10 h O 091-095

#### ANTERIOR TIBIAL TRANSLATION 30 3 Mean firing activity (units/bin) 2.5 2 1.5 1 0.5 0 MAN OUA HAMS PAN 0.4 -0.35 0.3 PSTH slope 0.25 0.2 0.15 0.1 0.05 0 OUA HAMS MAN PAN Control 🖾 Long-term stable, reconstructed knees (SR) Dong-term unstable, reconstructed knees (UR) Long-term unstable, non-reconstructed knees (UNR) Dotted line: comparison between controls and SR, or UR, or UNR Solid thin line: comparison between SR and UR or UNR Solid thick line: comparison between UR and UNR

#### Discussion

ACL injured knees in the cat, with or without reconstruction, display confirmed abnormalities in neuromuscular reaction in the long-term, while to regain stability with a competent graft in the reconstructed knee is crucial to lessen this anomalous reaction.

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#### THE BIOMECHANICAL EFFECT OF MULTIPLE BONE – TENDON GRAFT HARVESTING ON PATELLAR FRACTURE RISK.

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#### Introduction

Graft choices for revision anterior cruciate ligament (ACL) reconstruction and complex ligament reconstructions of the knee are controversial. Allograft ACL grafts have the innate risk of viral and bacterial disease transmission; furthermore availability is limited in many countries. Synthetic grafts have also become unpopular due to the increased re – ruptured rate. The aim of our study was to analyze the biomechanical effect of harvesting bone plugs from both the distal and proximal poles of the patella, to simulate a simultaneous harvesting of a Bone – Patellar Tendon – Bone and Quadriceps Tendon – Bone grafts, in a transverse stress environment.

#### **Material and methods**

60 Bovine Patellae were analysed. They were divided into 4 groups – based on the residual bone bridge (percentage of total length of patella) remaining after bone plug resection. 0 - 10%, 11 - 20%, 21 - 30% and >30%. All patellae were tested in a modified 4 – point bending environment, to a maximum load of 10,000N, in a customized designed jig. This method simulates the axial bending stress on the patella during knee flexion. All dimensions of the patellae were recorded including Depth of patella at bone resection and wall thickness adjacent to plug resection site.

#### Results

All patellae with a 0% bone bridge fractured (Ultimate Tensile Strength/UTS) at a mean Tensile Force of 5863N (Range 3140 – 8730N). There was a subgroup of incomplete fractures – extra-articular fractures – which fractured at 6542N (Range 5085 – 9180N). The remaining specimens failed to fracture. Comparing the UTS and the patellar dimensions, using Weibull's Statistical Analysis we demonstrated that less than 60% bone plug resection carried a very low probability of fracture.

#### Discussion

This study demonstrates the safe criteria for bone – tendon graft harvesting from both the proximal and distal poles of the patella. With regards to a normal human patella, a 40% bone – bridge is approximately a 20mm bone – bridge. We conclude that the simultaneous harvesting of Bone – Patellar Tendon – Bone and Quadriceps Tendon – bone grafts from a patella has no significant increase in the fracture risk of the patella.



#### BIOMECHANICAL PROPERTIES OF FOUR METHODS OF FIXATION USED FOR HAMSTRING ACL GRAFTS

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#### Aims

The aims of this study were to evaluate the biomechanical properties and mode of failure of 4 methods of fixation used for hamstring tendon ACL grafts. The fixation methods investigated included titanium round headed cannulated interference (RCI) screws, bioabsorbable RCI screws, Endobuttons and Bollard fixation. It has been previously shown that a 2 strand tailored equine tendon-Soffix graft has equivalent biomechanical properties to a 4 strand human hamstring tendon-Soffix graft, therefore this model was used for the graft in the study.

#### **Materials and Method**

32 stifle joints were obtained from skeletally mature pigs, the soft tissues were removed and the ACL and PCL were sacrificed. Tibial tunnel preparation was standardised using the Mayday Rhino horn jig to accurately position a guide wire. An 8 mm cannulated reamer was then used over the guide wire to create the final tibial tunnel. A back radiusing device was then placed into the tibial tunnel to chamfer the posterior margin of the tunnel exit to prevent abrasion and fretting of the graft. A 2 strand equine tendon-Soffix graft was then introduced into the tibial tunnel and secured with one of the four fixation methods. The proximal part of the graft was attached to the cross head of the materials testing machine using the Soffix. Five of each method of fixation were tested mechanically to failure and three of each method were cyclically loaded for 1000 cycles between 5 to 150 N, followed by 2000 cycles at 50 to 450 N.

#### Results

The mean ultimate tensile loads (UTL) were: titanium RCI screw = 444 N, bioabsorbable RCI screw = 668 N, Endobutton = 999 N and Bollard = 1153 N. The mode of failure for all RCI screws involved tendon slippage past the screw. Two Endobutton failures were encountered and one Bollard pull out occurred. Under cyclic loading conditions the titanium and bioabsorbable RCI screws failed rapidly after several hundred 5 to 150 N cycles due to tendon graft damage and progressive slippage. Both the Bollards and Endobuttons survived 1500 cycles at 50 to 450 N, with less tendon slippage occurring.

#### Conclusion

Titanium and bioabsorbable RCI screws provide poor initial fixation of tendon grafts used for ACL reconstruction, having significantly lower UTL's than both Endobutton and Bollard fixation. Under cyclic loading titanium and bioabsorbable RCI screws fail rapidly due to progressive tendon slippage, whereas Bollards and Endobuttons survive cyclic loading. Both Bollard fixation and Endobuttons provide sufficiently high UTL's and survive cyclic loading to allow early postoperative mobilisation and rehabilitation. Caution must be used in the early postoperative period when using interference screws to secure a hamstring tendon graft because progressive tendon slippage may result in excessive graft elongation and early clinical failure.

#### EORS 2008 · MADRID



#### O-094

#### IN-VIVO KINEMATIC QUANTIFICATION OF TRANSLATIONAL AND ROTATIONAL LAXITIES IN ANATOMICAL DOUBLE-BUNDLE ACL RECONSTRUCTION USING PIVOT-SHIFT TEST

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#### Introduction

The pivot-shift clinical test is commonly used for the gualitative dynamic evaluation of the translational and rotational knee instability and can be a useful indicator in the prediction of later ostheoarthitis [1]. With the aim of controlling the static antero-posterior knee instability as also tibial subluxation (highlighted with pivot-shift test) many surgeons have started performing anatomical double-bundle (DB) reconstructions, thus trying to reproduce with the surgery the anatomy and complex functions of the native ACL [1]. In fact the literature suggests that an anatomical DB ACL reconstruction has some biomechanical advantages [2,3]. Although different studies reported, at a mid term follow up, the superior results of the DB bundle reconstruction with respect to the Lachman's test and pivot-shift phenomenon after, they did not provided quantitative assessment about the global laxity. The objective of this study was thus to quantify intra-operatively the improvements in knee stability and the restore of knee kinematics due to an anatomical DB reconstruction [3].

#### **Materials and Methods**

Fifteen patients (32.8±7.6 y) with isolated anterior cruciate ligament injury, that consecutively underwent anatomical DB ACL reconstruction, were included in this preliminary study. To evaluate the joint laxity and kinematics we used an optical navigation system focused in kinematic acquisitions [4]. After tunnel drilling and before graft fixation, the operating surgeon performed manually clinical tests at maximum force: valgus/varus (VV) rotation at 0° and 30° of flexion, internal/external (IE) rotation at 30° and 90° of flexion, antero/posterior (AP) displacement at 30° and 90° of flexion and pivotshift test. Anatomical double-bundle ACL reconstruction was, then, performed [2] and the same kinematic tests were re-acquired. The surgeon was blinded on test results; the whole set of the kinematic data was off-line elaborated. Statistical analysis was performed comparing data derived from stress tests performed before and after reconstruction (fig. 1). For what concerns pivot-shift test we analysed the decomposition of three different parameters with respect to flexion/extension angle: AP translation, IE and VV rotations. For each decomposition we evaluated the areas included by the curves (the 'hysteresis' of the joint due to positive pivot-shift) and the difference in the peaks before and after the surgery at a specific flexion angle. A typical result is shown in fig. 2. Comparisons between pre- and post-op levels of laxity and of pivot shift were made using paired Student's ttest (p=0.05).

#### **Results and Discussion**

The differences in static laxity values before and after anatomical DB reconstruction is shown in fig. 1. All laxity were significantly reduced by the reconstruction (p<0.01).



Figure 1. Static laxity test.

More interesting results have been obtained with the analysis of pivot-shift test: coupled peaks in AP translation, at  $25.0\pm1.8^{\circ}$  of flexion, are reduced from  $-11.3\pm4.7$ mm to  $-3.1\pm3.1$ mm (p<0.01) after reconstruction as also in IE rotation are reduced from  $10.8\pm4.7^{\circ}$  to  $2.6\pm4.9^{\circ}$  (p<0.01) after surgery. The analysis of the area highlighted a huge recovery of the dynamic stability of the joint, from 211.5mm\*deg to 57.3mm\*deg (p<0.01) (Fig. 2).



Figure 2. Example of pivot-shift decomposition.

#### Conclusions

The navigation protocol, applied to anatomical DB ACL reconstruction, allowed a quantitative evaluation of knee global kinematics before and after surgery: all ACL-deficient knees showed a positive pivot-shift test before the surgery with huge value in the subluxation of the tibia; anatomical DB seems to eliminate both static anterior/posterior instability (Lachman test) and to control pivot-shift (subluxation of the lateral femoral condyle) reducing tibial translation and controlling tibial rotation.

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#### EFFICACY AND COMPLIANCE OF A QUADRICEPS FEMORIS NEUROMUSCULAR ELECTRICAL STIMULATION PROGRAM IN SUBJECTS WITH SEVERE KNEE OSTEOARTHRITIS

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#### Introduction

Quadriceps femoris muscle (QFM) weakness has been implicated in the development of knee osteoarthritis (OA ) and predicts functional ability after total knee arthroplasty (TKA).(1,2) The putative mechanisms responsible for QFM weakness following TKA include sarcopenia, disuse atrophy and failure of voluntary muscle activation (arthrogenic muscle inhibition).(2)

Neuromuscular electrical stimulation (NMES) devices apply transcutaneous electrical current to the neuromuscular junction and surrounding muscle fibres causing muscle contraction by circumventing the neural inhibition feedback loop. As a rehabilitation tool, NMES has been shown to reduce extensor lag, length of hospital stay, and significantly improve walking speed 12 weeks after knee surgery.(3,4) There is little published data on the efficacy of NMES as a treatment modality in knee OA.

#### Aim

To evaluate the efficacy and compliance of a homebased NMES training programme in restoring QFM strength and knee function in a cohort with radiologically confirmed GradelII-IV knee OA.

#### **Patients and Methods**

Sixteen patients (10 women and 6 men) with Grade III or IV knee OA on plain radiology according to Kellgren-Laurence classification were recruited and randomised (single blind) into a control (n=6) or intervention (n=10) group. The two groups were similar in terms of age (65.5  $\pm$  6.8 vs. 61.8  $\pm$  9.0; mean  $\pm$  SD) and BMI (29.7  $\pm$  2.1 vs.33.2  $\pm$  5.6). Exclusion criteria included morbid obesity (BMI>40), uncontrolled hypertension, anticoagulant therapy, neurological disorders, inflammatory arthritis, implanted pacemakers or defibrillators, dermatological conditions affecting the thigh, recent participation in an exercise or strength training program, inability to walk unassisted, and severe cognitive impairment.

NMES was applied using a portable garment based stimulator (Kneehab II, Bio-Medical Research, Galway, Ireland) for 20 min/day, 5 d/wk for 8 weeks. The initial 2 weeks were used to familiarize the patients with stimulator and to adjust stimulation intensity until an effective level was achieved.

Isokinetic and isometric QFM strength were determined at baseline, week 2, week 5 and week 8 using a Biodex

dynomometer. QFM function was assessed using a 25 metre timed walk test (TWT), timed stair-climb test (SCT), and timed chair-rise test (CRT) at baseline and week 8. Subjects in the intervention group recorded the duration and maximal stimulation intensity of each session in a log book. In addition, and unknown to participants, the Kneehab II software also recorded and stored the total treatment time and average stimulation intensity for the last 4 sessions. Statistical analysis was performed using ANOVA and independent t-test's where appropriate.

Results: The timed SCT decreased from 16.9 sec to 13.4 sec (p<0.01), and the timed CRT decreased from 9.0 sec to 6.6 sec. (p<0.01) in the NMES group at week 8 compared to week 0.

Isometric QFM strength was significantly higher in the NMES group at weeks 2, 5 and 8 than week 0. Compared to week 0, isokinetic hamstring strength increased significantly in the NMES group at week 2, week 5 and week 8 5 and isokinetic QFM strength increased at week 5 (p<0.05) and week 8 (p<0.01).

Patient recorded compliance was 99.5% (range, 97.1%-100%). The overall usage recorded on the stimulator was variable ranging from 69.7% to 114.8% (96.1%  $\pm$  13.2; mean  $\pm$  SD).

#### Conclusion

The use of a portable home-based NMES program for 8 weeks resulted in significant improvements in QFM strength and function in patients with severe knee OA. The compliance rate was excellent.

NMES may have a role as a treatment modality in patients where TKA is medically contraindicated or declined by the patient. Further considerations for NMES include preoperative strengthening (prehabilitation) and its application in younger patients as a temporising therapy delaying an inevitable TKA, although further study is required.

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**ORAL SESSION 18** 

# Shoulder 1

#### INFLUENCE OF BONE DENSITY ON THE PULLOUT STRENGTH IN DIFFERENT SUTURE ANCHORS FOR ROTATOR CUFF REPAIR

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#### Introduction

O-096

Absorbable suture anchors have become more and more important in rotator cuff surgery due to their easy revisability. In osteoporotic bone however they are thought to be of minor primary stability. Purpose of the present study was to compare different absorbable and non-absorbable suture anchors in their pullout strength depending on bone density. Two screw anchors and one tilting anchor were tested.

#### **Methods**

The absorbable screw anchor SPIRALOK 5,0mm (DePuy Mitek, Raynham, MA, USA), the titanium screw anchor Super Revo 5mm (Linvatec, Largo, FL, USA) and the tilting anchor UltraSorb (Linvatec, Largo, FL, USA) were tested, each anchor representing a different material and/or design.

On the basis of bone density measurement by means of CT-scans a healthy and a osteopenic group of cadaveric human humeri were formed. Each type of anchor was inserted in the greater tuberosity six times. Three suture anchors were placed in the greater tuberosity with a distance between the sites of insertion of approximately 10 mm. The different suture anchors were inserted according to the manufacturers instructions in an angle of 45° to the diaphysis of the humerus. The anchors were tested with the suture material supplied by the manufacturer.

An incremental cyclic loading with an electromechanical testing machine (model Z010/TN2A, Zwick, Ulm, Germany) was performed, starting with a load of 75 N for 50 cycles. Until failure of the anchor fixation system the tensile load was gradually increased by 25 N after every 50 cycles. The ultimate failure loads, the anchor displacements and the modes of failure were recorded.

#### Results

Six non-osteopenic bones (0,109±0,026 g/cm3) and six osteopenic bones (0,041±0,020 g/cm3) were used. The level of significance between the bone density of the healthy and the osteopenic bones was p<0,05 as well for the trabecular bone as for the cortical bone area (Mann-Whitney-U-test).

Modes of failure varied depending on bone mineral density and anchor design. Rupture of the suture material at the eyelet accumulated with the Super Revo titanium



#### Seminario O 096-101 14:15 - 15:05 h

anchor whereas the SPIRALOK and UltraSorb anchors displayed rupture of the suture material independently from the eyelet. In the osteopenic group the number of anchor pullouts clearly increased. In the non-osteopenic bone group the absorbable suture anchor SPIRALOK achieved a significantly better pullout strength (274 N) than the titanium anchor Super Revo (188 N) and the tilting suture anchor UltraSorb (192 N). There was no significant difference between those three suture anchors in the osteopenic bone group.

#### Discussion

The present study demonstrates that absorbable suture anchors do not have lower pullout strengths than metal anchors. Depending on their design they can even outmatch metal anchor systems. Considering the advantages of absorbable suture anchors like the higher patient acceptance, minimized artifacts in postoperative imaging, a more simple revision surgery and a comparable pullout strength, preference should be given to the SPIRALOK 5,0mm in young patients. The results of our study suggest that the anchor design has a crucial influence on primary stability, whereas the anchor material is less important.



# A SINGLE STAGE INSERTION NOVEL DESIGN SUTURE ANCHOR

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#### Introduction

Suture anchors are widely used to secure tendons and ligaments to bone during both arthroscopic and open surgery. However, single stage insertion suture anchors, i.e. anchors that could be inserted without predrilling of the bone, are not currently available although they would be highly advantageous by eliminating the difficulties associated with identifying drill holes prior to anchor insertion. This study reports the in vitro characteristics of a new design of suture anchors that are suitable for single stage insertion, comparing their performance with another range of commercially available suture anchors. Aims: We aimed to record the impact needed for insertion of the new design of suture anchors, and to compare their pull out strength with another range of commercially available suture anchors. We also recorded whether the new suture anchors could be inserted without running an unacceptably high risk of complication, such as fracture of the surrounding bone.

#### Materials and methods

The force required to insert the new design of suture anchors was investigated using an impact hammer capable of recording, for subsequent analysis, the number and force of each of the hits. The anchors were inserted in a consistent manner into animal (porcine) bone at sites analogous to common anchor sites used in clinical practise. Pull out strength was assessed using a digital force gauge after tying the suture to create a secure loop. Thereafter, force was applied steadily until either the anchor or the suture failed and compared with a popular range of commercially available suture anchors (Mitek).

#### Results

Our initial investigations using prototype designs for small, medium and large anchors compared favourably with the Mini-mitek, GII, and Superanchor range of Mitek anchors. Essentially the most common point of failure for each of the suture anchor families was the suture itself with both suture anchor systems performing similarly. In addition, similar pull out strengths were demonstrated for both the Mitek and new design of suture anchors when loaded parallel, or at 90°, to the line of anchor insertion.

#### Conclusion

The new design of single stage suture anchors have an equivalent pull out strength compared with a popular commercially available family of suture anchors, but in addition have the significant advantage of being suitable for single stage insertion in many clinical settings. This promising family of suture anchors still need to be evaluated in the clinical setting.

#### EORS 2008 · MADRID



#### O-098

#### BIOMECHANICAL TESTING OF A NEW KNOTLESS SUTURE ANCHOR COMPARED WITH ESTABLISHED ANCHORS FOR ROTATOR CUFF REPAIR

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Introduction

Absorbable suture anchors have become more and more important in rotator cuff surgery due to their easy revisability. Today a great variety of suture anchors is available for rotator cuff repair. One of the recently introduced anchors on the market is the Bioknotless RC (absorbable suture anchor, DePuy Mitek), a press-fit anchor whose special feature is the knotless reconstruction of the ruptured rotator cuff. Arthroscopic knotting is a technically demanding and time-consuming procedure and therefore encourages the development of knotless anchors in shoulder surgery. In addition, a possible subacromial impingement can be avoided by omitting the knot.

We compared the new knotless anchor (Bioknotless™ RC, DePuy Mitek) with established absorbable and titanium suture anchors (UltraSorb™ and Super Revo 5mm™, Linvatec).

#### Methods

The absorbable pressfit anchor Bioknotless RC (DePuy Mitek, Raynham, MA, USA), the titanium screw anchor Super Revo 5mm (Linvatec, Largo, FL, USA) and the tilting anchor UltraSorb (Linvatec, Largo, FL, USA) were testedIn the present study six human cadaveric shoulder bones were extracted from corpses whose mean age at the time of death was 74 years (range: 45-93 years). Each anchor was tested in the greater tuberosity 6 times. Three suture anchors were placed in the greater tuberosity with a distance between the sites of insertion of approximately 10 mm. The different suture anchors were inserted according to the manufacturers instructions in an angle of 45° to the diaphysis of the humerus. The anchors were tested with the suture material supplied by the manufacturer.

An incremental cyclic loading with an electromechanical testing machine (model Z010/TN2A, Zwick, Ulm, Germany) was performed, starting with a load of 75 N for 50 cycles. Until failure of the anchor fixation system the tensile load was gradually increased by 25 N after every 50 cycles. The ultimate failure loads, the anchor displacements and the modes of failure were recorded.

#### Results

The anchor displacement of the Bioknotless<sup>TM</sup> RC (15,3 $\pm$ 5,3 mm) after the first cycle with 75 N was significantly higher than with the two other anchors (Super Revo 2,1 $\pm$ 1,6 mm, UltraSorb: 2,7 $\pm$ 1,1 mm). The ultimate failure loads of the tested anchors were comparable. The differences between the three suture anchors were not significant: Bioknoteless RC 150 $\pm$ 57 N, Super Revo

#### 150±42 N, UltraSorb 151±40 N (p>0,05).

Modes of failure variied. Rupture of the suture material at the eyelet occurred more frequently with the Super Revo titanium anchor, a well known problem whereas which is contributed to the sharp metallic adges. Bioknoteless RC and UltraSorb showed a tendency towards anchor pullout.

#### Discussion

Our results do not confirm the higher pullout strength of metal anchors, which was found in other studies. We observed comparable pullout strengths of all tested suture anchors, independent of the anchor material. Our mean specimen age of 74 years is appropriate for the clinical situation since the rotator cuff tear is usually a degenerative that rather occurs in old age.

Knotless anchors have only been commercially available for a short time. They facilitate surgery by eliminating the technically challenging step of arthroscopic knot tying. The decisive disadvantage of the Bioknoteless RC is its unsatisfactory press-fit-anchorage. It behaves, as does the tested UltraSorb anchor, by becoming dislocated after the first pull and only afterwards blocking itself firmly in the trabecular bone. After the applicator of the Bioknoteless RC has been removed, a re-tightening or checking of the fixation is not possible. The initial displacement of the Bioknoteless RC of a mean of 15,3 mm is clinically significant for rotator cuff repair and jeopardizes the repair.

Because of the high initial displacement and the possibly adherent gap formation between tendon and bone, we recommend the use of the Bioknotless RC in a zone of minor tension only, for instance as a second-row anchor in double row technique for rotator cuff repair. The Bioknotless RC is not appropriate for rotator cuff repair, if it is used on its own.



#### MECHANICAL PROPERTIES OF GLENOID CAN-CELLOUS BONE

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#### Introduction

Total shoulder arthroplasty is a well-established and widely accepted method of treatment for a variety of shoulder disorders, loosening of the glenoid prosthesis is the main complication in total shoulder arthroplasty [Boileau, 2002; Kelly, 1994; Wirth, 1996], it is highly dependent on the quality of the glenoid cancellous bone. Very little is known about mechanical properties of this cancellous bone. The objectives of this study were to determine the mechanical properties (elastic modulus and strength) of glenoid cancellous bone in the axial, coronal and sagittal planes including regional variation using a uniaxial compression test. To our knowledge, this kind of study was not done before.

#### Methods

Eleven scapulas were obtained from six fresh-frozen, unembalmed human cadavers (mean age 88 years). Eighty two cubic cancellous bone specimens of 6x6x6 mm3 were used for mechanical testing in the three planes. The test was a uniaxial compression along each direction, Elastic modulus and strength were determined from the stress-strain curve. Apparent density was also calculated.

#### **Results- Discussion**

The study showed significant differences in the mechanical properties with anatomic location and directions of loading. Young modulus and strength were found to be significantly higher at the posterior part of the glenoid with the weakest properties at the antero-inferior part.

Cancellous bone was found to be anisotropic with higher mechanical properties in the latero-medial direction (perpendicular to the articular surface of the glenoid).

The apparent density was on average equal to 0,29 g/ cm3 with the higher values at the posterior and superior part of the glenoid.

Good correlation between apparent density and elastic modulus was found only in the sagittal plane but not in the coronal and axial plane, the overall correlation was low ( $r^2 = 0,22$ ) which emphasizes the role of trabecular bone architecture in predicting mechanical properties [Ciarelli, 1991].

The mechanical properties determined in this study provide input data for finite element method analyses and may help to assist in uncemented shoulder prosthesis design.

#### References

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#### BIOMECHANICAL EFFECT OF DOUBLE-ROW COMPARED WITH SINGLE ROW REPAIR

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#### Introduction

**O-100** 

A high number of primary cuff repairs fail to obtain persistent integrity of the cuff as has been showed by several clinical studies including postoperative imaging. The most common complication affecting functional outcome of cuff repairs is the structural failure of the repair. Double-row configuration has been developed to address the increase of the tendon to bone footprint. The objective of this study is to analyze the changes in the force needed to raise the arm caused by using a single or a double-row configuration of cuff repair.

#### **Material and Methods**

A cadaveric study was performed using 5 fresh-frozen shoulders. A supraspinatus tear was created in all specimens beginning 0.5 cm from the biceps tendon and including all the supraspinatus at its insertion site. Repairs were performed using standardized open approach. Specimens were prepared with a single and a doublerow configuration of anchors placed 1cm apart each one and starting 1 cm posterior to the bicipital tendon. Sutures were fixed to a digital dynamometer placed at the superior scapular angle to ensure reproducible tendon to dynamometer distance. Continuous traction was applied and registered to elevate the humerus to 30° and 45° of anterior elevation with the aid of a goniometer. Experiment was repeated 3 times for each configuration and angle of elevation on each specimen. The paired Student t test was used to compare the difference between single and double-row configuration at 30° and 45° of anterior elevation. The significance level was set at p=0.05.

#### Results

There were significant differences between the force needed to raise the arm to  $30^{\circ}$  with the single-row (4,76 kg) configuration and the double-row (6,94) (p<0,001). There were significant differences between the force needed to raise the arm to  $45^{\circ}$  with the single-row configuration (10,32 kg) and the double-row (15,93) (p<0,008). There were also significant differences when comparing the mean increase of force needed to raise the arm from  $30^{\circ}$  to  $45^{\circ}$  between the single and the double-row configuration (p<0,012).

#### Conclusions

This study demonstrates that the force needed to raise the arm to  $30^{\circ}$  and  $45^{\circ}$  is significantly higher for the double than for the single-row configuration.

The quality of the tendon margin should be taken into account when choosing between double and single-

row configuration. If the repair is done to a frayed and degenerated tendon, the surgeon has to imbalance the benefits of the double-row repair with the fact that the tendon suture will have to resist and increased force in active movement.

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# **ORAL SESSIONS - SATURDAY**

#### O-101

#### RECONSTRUCTION OF MASSIVE ROTATOR CUFF LESIONS WITH A SYNTHETIC INTERPOSITION GRAFT: FIVE TO TEN YEAR FOLLOW-UP AND BIOMECHANICAL ROTIONALE

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#### Introduction

Treatment of massive rotator cuff tears still present a major challenge in shoulder surgery. Direct repair of the native rotator cuff tendons to the proximal humerus is impossible because of retraction and inelasticity of the tendons. Conventional techniques for soft tissue release are often insufficient and the remaining tendon edges, altered by chronic degeneration, show inferior tissue quality and are not suited for secure primary repair.

Only a small number of papers are available describing the technique and outcome of synthetic grafting for the treatment of massive rotator cuff lesions. Moreover, only a limited number of patients is described, only short term results are available and there are important differences in patient selection, technique and used synthetic materials. Some of the used synthetic materials have lead to disastrous results, making the use of synthetic grafts in shoulder surgery very controversial. [1]

In the present prospective study, we report about our long term experience with massive rotator cuff tears treated by means of a nonresorbable transosseously fixated patch combined with subacromial decompression.

#### Methods

From December 1996 until August 2002, a total of 40 patients were treated with a synthetic interposition graft and subacromial decompression and included in the present study. (Figure 1) All included patients had preoperative ultrasonographic evidence of a primary massive full-thickness tear that was thought to be irreparable by simple suture.



Prior to surgery, all patients received maximal conservative treatment. When conservative failed after 3 months, an open surgical approach was scheduled. In all the included patients, it was impossible to conventionally reattach the tendon edges to the greater tuberosity with the arm in less than 30° abduction.

Informed consent was obtained in all patients and they were evaluated preoperatively and postoperatively using the Constant and Murley score, SST-test, DASH questionnaire, ultrasonography and radiography. All radiographic imaging was fluoroscopic controlled and digital phosphor plates were used, allowing DICOM measurements.

The nonparametric Wilcoxon signed ranks test was used to analyze data. The level of statistical significance was set at an alpha level of p < 0.05. All data were analyzed with the SPSS statistical package release 12 (SPSS, Inc., Chicago, IL).

#### Results

The patients consisted of 22 men and 17 women aged 51–80 years (mean, 67 years). They were followed up for a mean of 7.2 years. Their mean preoperative Constant and Murley score improved (P<0.001) from 25.7 preoperatively to 72.1 postoperatively and remained 69.6 at the latest follow-up. Substantial pain relief and improvement in the performance of activities of daily living were obtained. Anatomically, the repair resulted in a mean acromiohumeral interval of 8.6 mm. At the latest follow-up, only one patient presented with a severe omarthosis likely needing a reversed shoulder arthroplasty.

#### **Discussion and conclusion**

Restoring a massive rotator cuff tendon defect with a synthetic graft combined with subacromial decompression can give significant and lasting pain relief and improvement of range of motion and strength with few complications.

#### References

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# ORAL SESSIONS

ORAL SESSION 19 Shoulder 2

#### O-103

#### ROLE OF ULTRASONOGRAPHY IN SHOULDER PATHOLOGY: CONSISTENCY WITH CLINICAL AND OPERATIVE FINDINGS?

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#### Background

Shoulder disorders are common. Main causes of shoulder pain and/or functional deficit are adhesive capsulitis (frozen shoulder) and impingement and/or rotator cuff disease. Ultrasonography has a proven role in assessing, identifying and classifying pathology of the rotator cuff. It helps clinicians in making decisions about ongoing management of the condition. Ultrasonography is well tolerated, cost-effective and non-invasive. Its disadvantages include a long learning curve and reduced sensitivity in patients who are obese or who have severely restricted shoulder movement. Ultrasound has sensitivity and specificity rates of 80% and 100% respectively.1 Most patients with painful shoulder being referred to a district general hospital outpatient clinic will be seen by one of the consultant orthopaedic surgeon with interest in upper limb. Most of the patients will be referred for shoulder ultrasonography to aid diagnosis and management. All the ultrasonography results will then be reported by one of the radiologists with special interest in musculoskeletal system. This study was carried out to evaluate consistency of ultrasonography with clinical and operative findings.

#### Methods

Retrospective case note review of patients that attended orthopaedic outpatient clinic and underwent ultrasonography of shoulder between 1st of June-31st December 2006. Data of patients that underwent ultrasonography of shoulder was identified from the radiology department computer system. Further information was then determined from the medical notes with regards to scan results, additional investigations and further followup for clinical management of patients.

#### Results

58 patients, 36 male and 22 female attended the orthopaedic outpatient clinic with painful shoulder and underwent ultrasonography of shoulder during period of study. Mean age of patients is 55. 33 patients had ultrasonography of right shoulder, 20 patients had ultrasonography of left shoulder while 5 patients had ultrasonography of both shoulder. 79% (50/63) of the ultrasonography results were consistent with clinical diagnosis. 17 patients had normal scan results and were discharged fully. 25 patients with clinical and radiologi-



#### Seminario 15:25 - 16:15 h O 102-107

cal diagnosis of biceps tendon tear, calcifying tendinosis and partial/full thickness rotator cuff tear were treated conservatively. 19% (4/21) of patients with diagnosis of calcifying tendinosis had decompression surgery. 38% (8/21) of patients with diagnosis of partial/full thickness rotator cuff tear had decompression surgery + rotator cuff repair. The degree of rotator cuff tear in operative findings for 6 out of 8 patients (75%) that underwent decompression surgery +/- rotator cuff repair were consistent with ultrasonography findings. 4 patients had inconclusive ultrasonography of shoulder and had magnetic resonance imaging to further confirm the pathology.

#### Discussion

Ultrasonography is a non-invasive and cost effective investigation in aiding the diagnosis of painful shoulder. It adds value into subsequent management of patient. Sensitivity of ultrasonography in detecting shoulder pathology is 75% from this study. However, successful use of ultrasound to examine the shoulder depends on the operator, machine, and patient factors. Knowledge of the relevant anatomy and pathologic appearances and experience in performing the technique are required of operators.

#### Conclusion

Ultrasonography should be used as the first line of investigation in aiding the clinical diagnosis and management as it is non-invasive and cost effective. Orthopaedic surgeon can then make better decision in deciding whether to follow-up patient further or discharge them fully based on history, clinical examination and radiological diagnosis.

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#### A LARGER GLENOSPHERE TO IMPROVE THE MOBILITY OF REVERSED SHOULDER PROSTHESIS

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#### Introduction

The medial displacement of the glenohumeral centre of rotation is the main feature of reversed shoulder prostheses. It increases the moment arm of the deltoid, which balance for deficient rotator cuff muscles [1]. However it also induces mechanical impingements between bone and implants. The most important impingement occurs at the inferior side of the glenoid during adduction, but the posterior impingement also limits external rotation and may produce a notch [2]. Several ideas have already been proposed to reduce impingements and improve mobility of reversed prosthesis [3]. To extend the external rotation, it has been suggested to increase the size of the glenosphere, but there is still no measured evidence of this benefit. The aim of the study was thus to measure the allowed passive range of motion in the three glenohumeral angles and compare the mobility of a 36 mm glenosphere to a 42 mm.

#### Methods

CT data of a normal cadaver shoulder were segmented (Amira) to obtain a dense set of points delimiting the bone surface. A precise geometric model of the scapula, clavicle and humerus was then built (Geomagic). This model was then re-imported into Amira to assess the precision of the reconstruction, by direct comparison of the reconstructed bony surface with the original CT slices. The bones were then imported into a CAD software (Solidworks), which was used to perform the bone resection, to position the prosthesis and to measure the impingement positions. The Aequalis reversed prosthesis was used for this study. The original glenoid and humeral components were positioned according to manufacturer recommendations. The glenoid base plate was positioned inferiorly. Two glenosphere sizes were compared: 36 mm and 42 mm. The ISB standards were used to measure the three glenohumeral rotation angles: plane of elevation, elevation and axial rotation (). For these 3 angles, glenohumeral positions were tested every 10 degrees, providing a 3D mobility table to characterize the complete mobility of each glenosphere size.



Figure 1. The 32 mm and 42 mm glenospheres

#### Results

The 3D mobility table was analysed through 2D graphs of 2 angles while the third angle waswas fixed to 0 degree (neutral)vs. elevation plana larger glenosphere increased both adduction and abduction for all elevation planes . When the elevation angle was fixed at 10 degrees (fig. 2), there was a clear increase of the external rotation, but also of internal rotation. The gain of axial rotation was less important as elevation increased.



Figure 2. At a fixed elevation angle, dark X represent available positions of both the 36 mm and the 42 mm, while light X represent additional positions provided by the 42 mm.

#### Discussion

Reversed shoulder prostheses displace the rotation centre towards the medial side, inducing impingements and scapular notches. This occurs not only at the inferior part of the glenoid, but also with the anterior and posterior glenoid, the coracoid, the acromion and the spine of the scapula. The increase of the glenosphere diameter reduced the inferior impingement and also improved external and internal rotation. This study showed that a 3D analysis of the impingement problem in the 3 rotation angles is necessary to understand and improve the reversed shoulder prosthesis design.

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#### Acknowledgements

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#### EORS 2008 · MADRID



#### 0-106 GLEN

#### GLENOHUMERAL CONTACT PRESSURE: REVERSED VS. ANATOMIC SHOULDER ARTHROPLASTY

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#### Introduction

Reversed prostheses are being increasingly used as a satisfying solution for glenohumeral arthropathy associated with partial or severe rotator cuff deficiency [1]. Despite reported complications, this non-anatomical implant provides indeed a significant improvement of pain relieve and mobility. The biomechanics of this implant is based on two main features: it is semi-constrained and it medializes its rotation centre. The constraint restores the lost stability, which was provided by the rotator cuff muscles, while the centre medialization increases the deltoid moment arm and thus the muscular strength, which was also diminished by the rotator cuff deficiency. Although the general mechanism of this prosthesis implant is known, the biomechanical gain is not clearly quantified. The aim of this study was thus to analyse the glenohumeral contact pressure of a reversed prosthesis during active abduction, and to compare to an anatomic prosthesis.

#### Methods

The study was conducted by a 3D finite element model of the glenohumeral joint including 6 muscles: anterior, middle, and posterior deltoid, supraspinatus (SS), subscapularis and infraspinatus combined with teres minor. Glenohumeral joint stability was achieved by the compressive force of the muscles wrapping around the humerus, allowing for natural humeral head translation. Abduction was simulated in the scapular plane by a muscle activation algorithm. Scapulohumeral rhythm was set to 2:1. Arm weight was 37.5 N. A reversed prosthesis was compared to an anatomic one (Tornier, France). With the reversed implant, rotator cuff muscles were deactivated. Bone and metal parts were rigid, while polyethylene components were elastic. For both prostheses, the following quantities were calculated during the entire range of abduction: distribution of the contact pressure on the articular surface, maximum and average (contact force/contact area) contact pressure, equivalent contact force amplitude, direction and application point. Besides, the muscle forces and moment arms were also calculated.

#### Results

With the anatomic prosthesis, classical results were retrieved: joint contact force was maximal at approximately 90 degrees of abduction, reaching 86% of the body weight. With the reversed prosthesis, the contact force was 50% lower and the global muscular force was also

approximately 50% less, but the overall deltoid force was only reduced by 20%. The moment arm of each deltoid part was up to 20 mm higher with the reversed design, particularly at the beginning of abduction. The centre of the glenohumeral contact area was also very different for each design. Classical results were retrieved with the anatomic design. With the reversed implant, the contact centre on the glenoid side (metal glenosphere) moved continuously from the inferior part towards its centre during abduction. Conversely, on the humeral side (polyethylene cup), the contact centre remained located in the same inferior position during the entire range of abduction. At 90 degrees of abduction, the maximum (resp. average) contact pressure was 1.2 PMa (resp. 0.5 PMa) with the reverse prosthesis, vs. 19.0 MPa (res. 7.9 MPa) with the anatomic one.



Figure 1. Contact stress pattern (light grey) on the polyethylene component of anatomic (first row) and reversed (second row) prosthesis, at 0, 30, 60, 90, 120, 150 degrees of abduction in the scapular plane

#### Discussion

The reverse prosthesis medializes the rotation centre, which increases the deltoid moment arms, and thus reduces the overall muscle force required for elevation. In this numerical study, this mechanism was reproduced. The contact force and contact pressure were quantified and compared to an anatomic prosthesis. The model confirmed that abduction with a reversed prosthesis can be performed without rotator cuff muscles, and even with a weaker deltoid, but produced very different contact pattern. Because of a lower contact force and a higher contact area, the glenohumeral contact pressure dropped considerably. This should be associated to a much lower lever of wear, assuming that impingements are avoided.

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#### Acknowledgements

This study was partly supported by Tornier SAS (Montbonnot, France).

#### ORAL SESSION 20 Cartilage and Meniscus

#### **O-108**

#### SECRETION OF MMP3 BY EXPANDED ARTICULAR CHONDROCYTES PREDICTS ECTOPIC CARTILAGE FORMATION CAPACITY IN VIVO

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#### Introduction

Monolayer expansion of human articular chondrocytes (HAC) is known to result in progressive dedifferentiation and loss of stable cartilage formation capacity in vivo. For optimal outcome of chondrocyte based repair strategies, HAC capable of ectopic cartilage formation may be required. A positive correlation between mRNA expression of certain molecules by expanded chondrocytes and their ectopic cartilage formation capacity was reported before [1]. Unfortunately, mRNA molecules are unstable, their detection by PCR is difficult to standardize, and sometimes mRNA expression does not correlate with protein production and cellular phenotype. Thus, the aim of this study was to establish appropriate quality control measures capable to predict the ectopic cartilage formation capacity of HAC from culture supernatants. This strategy would avoid the waste of cells for quality control purposes, in order to improve cell therapy and tissue-engineering approaches for the repair of joint surface lesions.

#### **Materials and Methods**

Standardized culture supernatants (n=5) of freshly isolated HAC and chondrocytes expanded for 2 (PD2) or 6 population doublings (PD6) were screened for 15 distinct interleukins, 8 MMPs and 11 miscellaneous soluble factors by a multiplexed immunoassay. Cartilage differentiation markers like COMP and YKL-40 were determined by ELISA. Corresponding HAC were subcutaneously transplanted into SCID-mice and their capacity to form stable cartilage was examined histologically 4 weeks later.

Results and Discussion: While freshly isolated chondrocytes (PD0) generated stable ectopic cartilage positive for collagen type II, none of the PD6 transplants formed cartilaginous matrix. Loss of ectopic stable cartilage formation capacity between PD0 and PD6 correlated with a drop of MMP3 secretion to <10% of initial levels, while changes for other investigated molecules were not predictive. In order to challenge the competence of an MMP3 decline below 10% to predict the loss of the capacity for ectopic cartilage formation, PD2 chondrocyte cultures were screened before transplantation. Chondrocytes



### 17:00 - 18:20 h O 108-116

from three donors were identified for which MMP3 levels dropped below 10% of initial levels already at PD2. Consistent with our predictions, these PD2 cells failed to produce a collagen type II and proteoglycan-rich matrix while PD2 chondrocytes with MMP3 levels ≥20% (20-79%) synthesized cartilaginous matrix. This indicates, that MMP3 levels of cultured chondrocytes, independent of the number of cell doublings and the time in culture, predicted ectopic cartilage formation.

#### Conclusions

Loss of stable ectopic cartilage formation capacity in the course of HAC dedifferentiation can be predicted by determination of relative MMP3 levels demonstrating that standardized culture supernatants can be used for quality control of chondrocytes dedicated for cell therapeutic approaches.

Figure 1. Ectopic cartilage formation declines with chondrocyte expansion. Consecutive sections of ectopic explants were stained with a monoclonal anti-human collagen type II antibody or Alcian Blue. A-C: Freshly isolated chondrocytes (A) and cells expanded for PD2 (B, MMP3 level ≥20%) formed ectopic cartilage in vivo, chondrocytes expanded for PD6 formed only a fibrous explant (C). D-E: In situ hybridization for human specific genomic Alu repeats on sections prestained for collagen type II. Human nuclei stained black in collagen type II positive PDO (not shown), PD2 (D) and in collagen type II negative PD6 explants (E). Adjacent mouse tissue (asterisk in E) was negative. F-I: Predicted loss of ectopic transplant formation by PD2 cells with low relative MMP3 levels. Freshly isolated chondrocytes (F, insets show transplants of the other two donors) produced cartilaginous matrix in vivo. Cells from screened donors with MMP3 levels below 10% already at PD2, failed to build up ectopic cartilage (G,H: staining shown for 2 representative donors at PD2; I: staining shown for one representative donor at PD6).



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#### 0-110

#### ATTENUATION OF PAIN AND INFLAMMA-TION IN ADJUVANT-INDUCED ARTHRITIS BY SELECTIVE INHIBITION OF PROTEASOME

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#### Introduction

Inflammatory pain and tissue destruction is initiated and propagated by the production of proinflammatory mediators. Nuclear factor-kappaB (NF- ]B) is a key transcription factor involved in the expression of these proinflammatory mediators1. Ubiquitin Proteasome System (UPS) play significant role in activation of NF- ]B. Inhibitors of proteasome suppress the activation of NF-]B and production of proinflammatory mediators. Inflammation causes up regulation in the expression of the pronociceptive sensory neuropeptides in the ankle joints. The aim is to study is the effect of proteasome inhibition on inflammation and pain in the rat model of adjuvant arthritis and to explore a link between immune and nervous system during autoimmune disease.

#### **Materials and Methods**

Induction of arthritis: The study included 36 female Lewis rats, body weight 150-170 g. The animals were housed 4/cage and according to the Karolinska Institute protocol. Arthritis was induced in 24 rats by heat killed Mycobacterium butyricum in paraffin oil (0.1 mg/ml) injected into the base of the tail under anaesthesia. At the onset of arthritis rats were injected subcutaneous daily for two weeks with vehicle 10% DMSO or proteasome inhibitor MG 132 (1mg/kg bw) solubilised in 10% DMSO according to manufacturer's advice.

Mechanical pain test: Mechanical nociceptive thresholds were measured as described previously by Randall and Selitto. An increasing force at a constant rate was applied to the hind paw.

Radiological assessment: To assess the degree of bone and joint changes in the arthritic rats, imaging was done with a dental X-ray machine.

Immunohistochemistry: Rats were perfused and fixed with Zamboni. Bilateral ankle joints were dissected and demineralization. Immunostaining was performed according to the biotin-avidin system (Vector Laboratories Inc., USA). The sections were incubated with 10% normal serum before incubation overnight with antibody against SP (Santa Cruz, USA).

Electrophoretic mobility shift assay (EMSA): NF- ]B activity was studied by this assay. Frozen ankle joints were homogenized before dissolving in buffer supplemented with protease inhibitors. Binding reactions was performed with 32P-labelled oligonucleotide representing B binding sites of the HIV enhancer. The reaction mixtures were separated on native gel.

#### observed in adjuvant arthritic rats treated with proteasome inhibitor MG 132 compared to untreated groups (Fig 1A). Our results also indicated a significant reduction in the activity of transcription factor NF-kB in ankle joints after treatment with MG 132 as analyzed by Electro mobility shift assay (Fig 1B). Similarly, radiographic analysis demonstrated a



Fig 1: A) pain test. B) EMSA. Results are means  $\pm$ SD reduction in soft tissue swelling and joint destruction of the ankle joint (Fig 2 A) and marked reduction in the expression of SP in the joints of rats treated with proteosome inhibitor was observed. (Fig 2B)



Fig 2: A) Radiological analysis and B) Expression of SP-LI Discussion: Our results indicate pivotal role of proteasome system in chronic rheumatoid arthritis. Inhibition of this system reverses the behavioural manifestations of inflammatory pain as well as the associated neurochemical and morphological changes produced by chronic inflammation. The effects of proteasome inhibitor on inflammatory pain may be mediated through several cellular mechanisms; direct suppression of osteoclasts activity, altereing synthesis or release of pro-inflammatory cytokines and/or indirectly stimulating the nerve degeneration.

#### Conclusion

Proteasome play significant role in regulating pain and inflammation in joint diseases and can be good candidate for pharmacotherapy.

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#### Results

Significant reduction of pain in the affected joints was



#### SPONTANEOUS CHONDROGENIC MSC-DIFFERENTIATION IN A PORCINE ARTICULAR CARTILAGE DEFECT

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#### Introduction

Mesenchymal stem cells (MSC) have recently evoked interest as a promising alternative cell source for the treatment of articular cartilage defects. However, common protocols for in vitro induction of chondrocytes from MSCs induced typical features of hypertrophic chondrocytes, such as expression of collagen type X and MMP13. This may implicate a risk for graft instability as seen in an ectopic cartilage formation assay where calcification and microossicle formation occurred in differentiated MSC constructs [1]. This indicates that, possibly, MSC should better not be set to path to become chondrocytes before transplantation into cartilage defects. So far it is however unclear whether MSC transplanted into a cartilage defect undergo spontaneous differentiation in the absence of hypertrophy. The aim of the present study was to provide a molecular characterization of spontaneous MSC differentiation in full thickness cartilage defects in a large animal model with a special emphasis on upregulation of hypertrophic markers. We hypothesized that the orthotopic environment in the knee joint provides a distinct guidance of MSC compared to chondrogenic in vitro induction and may inhibit the expression of hypertrophic markers in the transplanted or naturally attracted repair cells.

#### **Materials and Methods**

MSC isolated from bone marrow of Göttinger minipigs were expanded in monolayer before autologous transplantation into a full thickness cartilage defect. All animals were operated in general anaesthesia on both hind legs to generate ø6mm chondral defects that were covered with a collagen type I/III membrane. In one group autologous MSC were transplanted underneath the collagen matrix, in the second group no MSC were transplanted. Animals were randomly assigned to one, three, or eight weeks follow-up before both hind limbs were obtained for further investigation (n=4 samples at one week, n=4 at three weeks, n=6 at eight weeks). All procedures were performed according to the German Animal Welfare Act and the experi-mental design was approved by the animal rights pro-tection authorities. The repair tissue was divided for histological analyses and for quantitative gene expression analysis for Col2A1, Col10A1, aggrecan (AGC), MMP13, and ]-actin for normalization.

#### **Results and Discussion**

Defect filling and integration into surrounding cartilage tissue was poor to moderate after 1 and 3 weeks indicated by clefts present between the implanted collagen membrane and subchondral bone and surrounding cartilage. In addition no sign of cartilaginous matrix production as indicated by negative safranin-O staining was visible for both groups. At 8 weeks regenerative tissue was integrated into the surrounding tissue in 6 out of 6 in the MSC group and in 5 out of 6 regenerates in the MSC-free group. A safranin-O positively stained neocartilage was detectable in 4 tissue regenerates out of 6 in the MSC group compared to 2 out of 6 in the MSC-free group. This staining correlated to immunohistology for collagen type II and was accompanied by a better histological grading score in the MSC group. At 1 and 3 weeks after surgery only marginal Col2A1 mRNA levels (approx. 2 % ]-actin) and no AGC expression (<1%) were detectable in both groups. At 8 weeks Col2A1 and AGC levels had strongly increased (~400-fold and ~8-fold, respectively) consistent with the histological examination. Higher median Col2A1 expression levels within the MSC group compared to the MSC-free group, however, did not reach statistic significance due to high donor variability. This indicates that 3 weeks were not sufficient to induce reliable collagen type II expression in MSC that contribute to cartilage repair. Whether implanted MSC directly contribute to regenerate after 8 weeks or provide secreted molecules (e.g. growth factors) for other invading cells, remains to be answered in further studies. Hypertrophic maker induction (Col10A1 and MMP13) was similar in both groups 8 weeks after surgery with expression levels between 20 and 40% ]-actin. Immunostaining for collagen type X was restricted to the lower third of regenerative tissue close to the subchondral bone in both groups, while collagen type II staining was detected from superficial to deep zone.

#### Conclusions

Our data provide molecular evidence for spontaneous differentiation of MSC in cartilage and show that the expression of hypertrophic markers is not a specific feature of in vitro chondrogenesis but rather a common phenomenon in early phases of cartilage repair. However collagen type X was inhibited in the upper, collagen type II positive, cartilaginous zone and restricted to deep zone neocartilage regenerates close to the subchondral bone. Whether by remodelling of defect filling tissue collagen type X positive areas will further diminish or even disappear from repair cartilage at later stages has to be evaluated in a longer follow-up study.

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#### 0-112

#### EXTRACORPOREAL SHOCK WAVES DOWN-REGULATETHEEXPRESSION OF INTERLEUKIN-10 AND TUMOR NECROSIS FACTOR-ALFA IN OSTEOARTHRITIC CHONDROCYTES.

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#### Introduction

The purpose of this study was to investigate the effects of extra corporeal shock waves (ESW) therapy on the metabolism of healthy and osteoarthritic human chondrocytes, and particularly on the expression of IL-10, TNF-] and ]1 integrin.

#### **Materials and Methods**

Human adult articular cartilage was obtained from 9 patients (6 male and 3 females), with primary knee osteoarthritis (OA), undergoing total joint replacement and from 3 young healthy donors (HD) (2 males, 1 female) with joint traumatic fracture. After isolation, chondrocytes underwent ESW treatment (electromagnetic generator system, MINILITH SL1, STORZ MEDICAL) at different parameters of impulses, energy levels and energy fluxes. After that, chondrocytes were cultured in 24-well plate in DMEM supplemented with 10% FCS for 48 hours and then ]1 integrin surface expression and intracellular IL-10 and TNF-] levels were evaluated by flow-cytometry.

#### **Results and Discussion**

At baseline, osteoarthritic chondrocytes expressed significantly lower levels of ]1 integrin and higher levels and IL-10 and TNF-] levels (1). It has been recently reported that ESW may be useful to treat OA in dogs (2), and veterinarians have begun to use ESW also to treat OA in horses (3). Following ESW application, while ]1 integrin expression remain unchanged, a significant decrease of IL-10 and TNF-] intracellular levels was observed both in osteoarthritic and healthy chondrocytes. IL-10 levels decreased at any impulses and energy levels, while a significant reduction of TNF-] was mainly found at middle energies.

#### Conclusions

Our study confirmed that osteoarthritic chondrocytes express low ]1 integrin and high TNF-] and IL-10 levels (4,5). Nonetheless, ESW treatment application downregulate the intracellular levels of TNF-] and IL-10 by chondrocytes, suggesting that ESW might restore TNF-] and IL-10 production by osteoarthritic chondrocytes at normal levels thus potentially interfering with the pathologic mechanisms causing cartilage damage in OA and representing the theoretical rationale for using ESW as therapy of OA.

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#### ARTHROSCOPIC SECOND GENERATION AUTOLOGOUS CHONDROCYTE IMPLANTATION COMPARED WITH MICROFRACTURE IN THE KNEE. A PROSPEC-TIVE COMPARATIVE STUDY.

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#### Background

Various approaches have been proposed to treat articular cartilaginous lesions that are plagued by inherent limited healing potential; however orthopedic surgeons still consider these lesions to be challenging treatment scenarios.

#### Methods

80 active patients with a mean age 29.8 years and grade III-IV cartilage lesions of the femoral condyles or trochlea were treated with arthroscopic second generation Autologous Chondrocytes Implantation Hyalograft C and Microfracturing (40 patients in each group). All patients achieved a minimum five year follow-up and were prospectively evaluated. The group treated with Hyalograft C had significantly more patients who underwent previous surgery and less traumatic cases compared to the Microfracture group. No significant difference was found between groups regarding the age, patient's sport activity level, presence of associated surgery, defect size, and location.

#### Results

Both groups showed statistically significant improvement of all clinical scores from the preoperative interval to 5 year follow-up. When comparing the two groups, better improvement of the IKDC objective (p<0.0005) and subjective (p=0,003) scores were observed in the group treated with Hyalograft C at the 5 year follow-up. The return to sports at 2 years was observed to be similar in both groups and remained stable after 5 years in the Hyalograft C group, whereas worsening was observed in the microfracture group. In both groups, older patients had more difficulties when attempting to return to the pre-injury sport activity level. However, the patient's age has not influenced the clinical outcome evaluated with the IKDC objective and subjective scores.

#### Conclusions

Both methods have shown satisfactory clinical outcome at medium - term follow up. Better clinical results and sport activity resumption was noted in the group treated with second generation autologous chondrocyte transplantation. This method may be used for the treatment of large femoral condyles cartilage lesions in the young active population, but long-term and randomized controlled studies will be needed to confirm these findings.





#### 0-114

#### COMP, MENISCUS AND OSTEOARTHRITIS

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#### Introduction

Meniscus injury is one of the causes of secondary osteoarthritis (OA). Cartilage oligomeric matrix protein (COMP) is a major component of the extracellular matrix of the musculoskeletal system1. Although COMP abnormalities are associated with several pathological conditions, its normal function remains unclear.

This study was undertaken to evaluate the changes occurring in meniscus from the knees of anterior cruciate ligament (ACL) transected rabbits during the early stages of OA development, especially regarding COMP changes.

#### **Materials and Methods**

Ten skeletally mature white New Zealand male rabbits underwent ACL transaction of the right knee joint. Left knee joints were used as controls. Animals were sacrificed at 4 and 12 weeks post-surgery. Meniscal tissues were processed for histology and immunohistochemistry.

The number of cells and positive cells were counted per high-power field (HPF). Anti-COMP antiserum was obtained according to Hauser et al.2 with minor modifications3. Monoclonal Ki67 antibody was used to find out cells undergoing active division. TUNEL reaction was used for the study of apoptosis. Alcian blue staining was used to study glycosaminoglycans. Staining intensity of extracellular matrix was evaluated as follows: 0 (none), 1 (weak), 2 (intense) and 3 (very intense).

#### Results

At 4 weeks post-ACL section 2/5 of the medial menisci presented with incomplete vertical posterior tears, while all lateral menisci were no altered. At 12 weeks post-ACL section 5/5 of the medial menisci and 2/5 of lateral menisci presented tears.

At 4 weeks postsurgery menisci showed: a weak increase of cells with a significant increase of cells undergoing active division; an increase in the number of apoptotic cells; glycosaminoglycans staining was increased and COMP staining was weakly increased. At 12 weeks postsurgery cells per HPF reverted to normal number; the number of cells undergoing active division decrease below normal; whereas the number of apoptotic cells was still elevated; glycosaminoglycans staining was more elevated than at 4 weeks postsurgery and COMP staining of extracellular matrix remain elevated.

Areas of large and abundant cell clusters were seen post-ACL around menisci tears.

#### Conclusions

After ACL transaction, extracellular matrix changes and altered cell distribution occur early in the meniscus. Cellular division as well as apoptosis occur early too. Elevated concentrations of Cartilage Oligomeric Matrix Protein after ACL transection might indicate meniscus changes early in osteoarthritis process.

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#### O-115

### EXPERIMENTAL INVESTIGATION OF ULTRASONIC KNEE MENISCUS RESECTION

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#### Introduction

High power low frequency ultrasound in the range 20-60kHz has wide ranging clinical applications in surgical and medical instruments for biological tissue cutting, ablation or fragmentation, and removal [1]. Surgical applications have been described in orthopaedic surgery, angioplasty, neurosurgery, ophthalmic surgery, urology, hepatobiliary surgery, dentistry and oral-maxillofacial surgery. Despite widespread clinical application and common device operating characteristics, mechanisms of tissue failure, removal and damage have not been adequately evaluated [1]. In particular, the relationship between applied force and amplitude of distal tip displacement as determinants of cutting effect and tissue damage has not been clearly defined. Recent clinical studies have highlighted the potentially deleterious thermal [2] and mechanical [3] effect of ultrasonic energy in residual tissue.

This study aims to evaluate ultrasonic tissue resection as an alternative to mechanical shaver and electrosurgical resection in the knee. We aim to investigate factors influencing material removal rate [4] (MRR), cutting rate (CR) and thermal damage for meniscus tissue resection using an experimental 20kHz ultrasonic ablation device.

#### **Materials and Methods**

An experimental force controlled testing rig was constructed using a 20kHz ultrasonic probe suspended vertically from a load cell (500N) in a materials testing machine. Ex-vivo bovine meniscus samples were harvested from knee joints of freshly slaughtered 12-15 month old animals and cut into uniform 16mm discs. The tip of the probe was aligned so that it moved vertically downwards into the tissue. Effect of variation in force (2.5-4.5N) and amplitude of distal tip displacement (242-494µm peak-peak) settings on material removal rate (MRR) and cutting (CR) was analysed. Time-discrete temperature elevation in the meniscus was measured by embedded thermocouples, infrared thermography and histology. The experiment was designed using a response surface quadratic model with both input variables treated as continuous, using Design-Expert v.7.1.3 (Stat-Ease Inc., Minneapolis, MN). Statistical analysis was conducted using SPSS v.11.0 (SPSS Inc., Chicago, IL).

#### Results

Sharp differences in tissue removal rate are observed for different combinations of parameter settings. As either force (2.5-4.5N) or amplitude (242 $\mu$ m to 494 $\mu$ m) increases, there is a linear increase in MRR (Mean±SD:

 $0.94\pm0.44$  to  $8.8\pm1.13$ mg/s) [Figure 1]. A corresponding increase is observed in CR for increases in force and amplitude (Mean±SD:  $0.08\pm0.04$  to  $0.65\pm0.13$ mm/s). Maximum MRR and CR is obtained for a force setting of 4.5N of and amplitude setting of 494µm. There is an inverse relationship between both force and amplitude, and temperature elevation, with higher force and amplitude settings resulting in less thermal damage. Maximum (mean) temperatures of  $89.7\pm20.6^{\circ}$ C and  $56.6\pm2.9^{\circ}$ C were recorded in residual tissue at 2mm and 4mm from the probe-tissue interface respectively.





#### Discussion

Although high power low frequency ultrasound is capable of meniscal resection, key limitations of this technology are low MRR rate and thermal damage. The mechanism of removal is primarily thermal, with tissue temperatures reaching potentially dangerous levels. Control of user force and amplitude of tip displacement settings in ultrasonic instrument design can maintain temperature peaks below critical temperatures of thermal necrosis during operation.

Conclusion/ Summary:

High power low frequency ultrasonic technology warrants further evaluation as an alternative to radiofrequency and mechanical instruments for knee meniscus resection.

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# ORAL SESSION - FRII

**ORAL SESSIONS - SATURDAY** 

#### O-116 STEM CELLS PROMOTE MENISCAL HEALING IN THE AVASCULAR ZONE. EXPERIMENTAL STUDY IN RABBITS

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Various studies have demonstrated that menisci heal in the vascular region but do not heal in the avascular area. Experimental studies of the promotion of meniscal healing in the avascular area have involved the application of fibrin clot, fibrin glue to the injured area, as well as the construction of an access channel to the vascular region, all of them with poor results. We try to show that the use of stem cells may promote meniscal healing in the avascular area.

Twelve New Zealand white rabbits with a mean weight of 3 kg were used. The medial meniscus of both knees was approached, and was performed a longitudinal tear in the avascular area in the anterior horn with a mean length of 0,5 cm. All the tears were sutured with one vertical stitch of nonabsorbable suture. In each rabbit a solution with 100.000-1.000.000 stem cells from the fat was introduced in one of the knees, and the other one was used as a control. The rabbits were killed at 12 weeks, and a macro-microscopic study of the meniscus was done, and also an inmunohistochemistry study for the stem cells.

The incidence of healing was better in those menisci with the stem cells solution. Three totals and three partial healing were obtained in the stem cells group and none in the control group. The inmunohistochemistry showed that the stem cells were in the repair zone.

We think that stem cells will be very useful in the treatment of the lesion in the avascular area of the meniscus. 1. Arnoczky, S P and R F Warren. "The microvasculature of the meniscus and its response to injury. An experimental study in the dog." The American Journal of Sports Medicine 11.3 (1983): 131-41.

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#### ORAL SESSION 21 Hand, wrist, elbow, fractures, other

#### O-117

#### CLINICAL OUTCOME OF 34 IMPLANTATIONS OF A CEMENTLESS SEMI-CONSTRAINED TRAPEZIOMETACARPAL JOINT PROSTHESIS

An observational prospective cohort study with vitamin C prophylaxis

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#### Introduction

Osteoarthritis of the trapeziometacarpal joint can be treated non-operatively or by different surgical procedures. These are known to lead to complications, complex regional pain syndrome (CRPS) type I being one of many. We investigated prospectively our clinical results after total joint arthroplasty under vitamin C prophylaxis.

#### **Materials and Methods**

First web opening (°)

VAS daily activities

VAS satisfaction

VAS pain

Patients with trapeziometacarpal joint arthritis stage II or III (according to Dell) and no benefit from non-operative therapy were selected to undergo joint arthroplasty [1]. Visual analogue scale (VAS) scores for pain, daily activities (ADL) and satisfaction were taken pre- and postoperatively, together with first web opening [2]. Vitamin C 500 mg daily was started two days prior to surgery during 50 days as prophylaxis for Complex Regional Pain Syndrome (CRPS) [3].

Postoperative treatment consisted of a bandage with collar and cuff for 5 days, a NSAID and physical therapy if necessary. Follow-up was at 5 days, 2 weeks, 6 weeks with X-ray, 6 months and 12 months with X-ray.

Mean (SD)

preop postop

76.3

1.3

8.6

8.9

58 5

7.5

4.1

2.1

#### Results

We performed 34 arthroplasties for first carpometacarpal arthritis in 29 patients (23 females and 6 males) with a mean follow-up of 39 months. Mean age was 61 years.

17:00 - 18:20 h

The degree of osteoarthritis according to Dell was stage II in 13 cases, stage III 20 times and in one case there was a traumatic trapezio-metacarpal dislocation.

Operation was performed in day care under general or regional anesthesia. We implanted a cementless prosthesis type Roseland (total trapezio-metacarpal joint prosthesis; Depuy International Ltd, Leeds, England) [4]. This prosthesis is hydroxy-apatite coated and semiconstrained.

First web opening increased with 17.80 and there was a significant improvement for pain, ADL and satisfaction as well.

Difference (95% CI)

(postop - preop)

13.0 - 23.6

-5.7 - -6.8

3.8 - 5.2

5.8 - 7.7

Seminario

O 117-125

P value

0.000

0.000

0.000

0.000



#### VARIATION IN THE ROTATIONAL AXIS MO-VEMENT OF THE WRIST DURING ULNA TO RADIAL DEVIATION

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#### Introduction

The carpal bone arrangement can be described as a matrix of two rows and three columns. There are various theories as to how the bones within the matrix move during ulna to radial deviation. One theory suggests that there are two types of wrist movement, namely Row & Column [1].

The aim of this study was to investigation how the rotational axis of the wrist moves as the hand goes from full ulna to full radial deviation.

#### Methods

Ulna to radial deviation was assessed in 50 normal wrists in 25 normal subjects aged 19 to 57. Movement was measured with a Polhemus Fastrak (TM) magnetic tracking system. The system has translational and rotational measurement accuracies of 1 mm and 1 degree respectively. Subjects placed their palms on a flat wooded stool and had movement sensors attached over their 3rd metcarpal and distal radius. These sensors then recorded movement as the hand moved from full ulna to full radial deviation.

#### **Results and Discussion**

The mean range of movement was 45 degrees (SD 7). In full ulna deviation the wrist rotational axis was in the region of the lunate. As the hand moved towards radial deviation, the axis moved distally. At the end of the movement the mean distal displacement was 21 mm (SD 15). In 32 wrists the distal displacement was accompanied by mean displacement towards the ulna of 12 mm (SD 8). In 18 wrists the distal displacement was accompanied by a mean displacement towards the radius of 8 mm (SD 5).

#### Conclusion

The rotational axis position indicates how the wrist is moving during radial deviation. In early movement, when the axis is proximal, there is a high degree of sideways translation. In later movement, when the axis is distal, there is more rotational movement. In some cases the axis moved distally and toward the radius, whereas in other cases it moved distally and toward the ulna. This spectrum of movement may support the theory of 2 types of carpal movement. i.e. Column movers and row movers [1].

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#### O-120

#### BIOMECHANICAL ANALYSIS OF ELBOW JOINT LOADING DURING DIFFERENT TYPES OF OPEN KINETIC CHAIN EXERCISE

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#### Introduction

Various strengthening program, such as open-chain and close-chain kinetic exercises, are used for sports activity and post-traumatic rehabilitation. Inadequate training may result in injuries to the upper extremities. Bench press is one of the most popular weight training open kinetic chain exercises for the upper extremity. Nonetheless, there is very little data available regarding to the biomechanical analysis of the open kinetic chain exercise of the upper extremity. In order to treat and prevent these injuries, there is a need to further understand the loading mechanism of the upper extremity. Therefore, the purpose of this study is to investigate the effect of different hand position on elbow joint loading during an open kinetic chain exercise.

#### **Materials and Methods**

Thirteen male subjects volunteered in this study. Their average age was 26 years, with an average height of 170.6 cm, and average weight of 70.3 Kg. With both hand in neutral position, each subject was asked to perform bench-press type1, (normal shoulder width), and bench-press type2. (150% shoulder width). A Motion Analysis System (Motion Analysis Inc., Santa Rosa, CA, U.S.A.), two Kistler force plates (Model 9281B, Kistler Instruments AG, Winterthur, Switzerland), and computers were used to collect data.

#### Results

A cycle of the bench press exercise was expressed in the change of elbow flexion (Fig. 1). After normalization, the elbow joint force (Table 1), and the elbow joint moment (Table 2) were shown.



Figure 1: Change of elbow flexion angle during a cycle.

Ld : Hand closest to body.

Lu : Hand most distant from body.

Table-1 Elbow Loading Force during 2 Types of Bench

Press

Elbow Force	Type 1 Mean (SD)	Type 2 Mean (SD)	P
Axial force	14.28 (1.1)	14.53 (1.5)	0.29
Medial/Lateral force	-4.6 (4.6))	-6.04 (2.9)	0.018 *
Anterior / Posterior force	-2.63 (2.7)	-5.21 (1.3)	0,017 *

Unit: % Body Weight; ( "\*" is p < 0.05), ( "\*\*" is p < 0.01)

Table-2 Elbow Moment during 2 Types of Bench Press

Elbow Moment	Type 1 Mean (SD)	Type 2 Mean (SD)	P	
Varus / Valgus	8.61 (5.4)	12.72 (4.5)	0.016 *	
Flexion / Extension	-12.89 (6.2)	-15.03 (5.0)	0.014 *	
Supluation / Pronation	0.97 (2.0)	1.17 (1.4)	0.018 •	

Unit: N-m ; ( "\*"is p < 0.05) , ( "\*\*"is p < 0.01)

In the type 2 open-chain exercises, the antero-posterior and medial-lateral shearing forces around the elbow joint were 198% and 131% higher than the type 1, respectively. The valgus-varus, the flexion-extension and the pronation-supination moment were 148%, 117% and 121% higher than the type 1 bench press exercise, respectively.

#### **Discussion and coclusions**

In conclusion, the loading biomechanics of the elbow joint differs with two different hand positions during open kinetic chain exercise. As shown in this study, keeping the distance of both hands as shoulder width may reduce the elbow joint loading during bench-press exercise. The database established in this study will warrant a better understanding of the loading mechanics in the upper extremity. Furthermore, these data will be valuable reference in clinical treatment and rehabilitation.

#### References

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#### Acknowledgements

This study was supported by the National Science Council in Taiwan.

#### 0-121

#### CONVERSION OR CONTINUING EXTERNAL FIXATION FOR TREATMENT OF OPEN TIBIAL FRACTURES

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#### Background

The treatment of Open tibial fractures is still an orthopaedic challenge, full of complications and many times the use of external fixator which has been known as a nonunion machine is obligatory with a high incidence of pin track infection and other complications.

#### Objective

comparison between the use of external fixation as a definitive method of treatment or change it later to internal fixation or casting.

#### **Materials & Methods**

Between June 2004 and July 2006 in a randomized controlled trial we studied sixty-seven young patients with type IIIA and IIIB open tibial fractures, treated with half pin AO external fixation. All of the fractures were due to motor vehicle injury any patient with concomitant neurovascular, abdominal or other organ injuries were excluded from the study. The average time between accident and surgery was 12-48 hours.

Twenty of the patients between (6-8 weeks) converted to internal fixation , in twenty-five of them between(16-20 weeks) external fixator removed and treatment continued with casting, and in twenty-two of them the fixator continued until union. The patients followed up for 10-16 months and evaluated according to union time, union rate, infection, range of motion, malunion, nonunion, nerve injury, and reduction.

#### Results

There was a meaningful difference only in the union time and superficial infection between first group and other two groups. (P-value 0.001). There was not any significant difference in superficial and deep infection, knee flexion limitation, ankle dorsiflexion limitation, malunion or nonunion between groups.

#### Conclusion

We can consider the conversion of external to internal fixation as a safe, effective , less complicated and more acceptable method for treatment of open tibial fractures. (references 1-26)



#### O-122

#### THE NUMBER OF DISTAL LOCKING CROSS SCREW REQUIRED FOR SUFFICIENT STABILISATION OF FEMORAL FRACTURES USING INTRAMEDULLARY NAILING SYSTEM

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#### Introduction

The indications for intramedullary nail fixation of fractures of the femoral shaft have been greatly expanded by techniques of interlocking nailing. Shortening and malrotation are well controlled with interlocking fixation that is now generally accepted that interlocking nailing is the treatment of choice for comminuted fractures of the femoral shaft, including extreme distal locking fractures. However, distal locking screw fixation remains the most technically demanding and problematic portion of the procedure. Distal locking fixation, using two cross screws, may be responsible for as much as one-half of the exposure of the surgeon's hands to radiation during the procedure.Some studies have shown, one distal locking screw is sufficient to provide adequate stability compared to two distal locking screws1, there by reducing the duration of surgery and surgeons exposure to radiation.

#### Objective

This biomechanical study was undertaken to compare the effectiveness of using one distal locking cross screw instead of two cross screws in femoral fractures fixed with intramedullary nailing (IMN) system.

#### Materials

A composite model made from a stainless steel IMN (12mmx1mm), with similar dimensions to clinically used IMN systems, was connected to a load cell Instron 1822 materials testing machine (Instron Ltd., High Wycombe, UK). Axial forces, upto 2kN (3times body weight) and torque force upto 10N was applied; to reproduce the forces experienced during weight bearing2, or until a maximum displacement of 1 mm was reached. A displacement of 1 mm was chosen, as a fracture will not heal if there is excessive deflection3. The distal locking end of the intramedullary nail was secured using a variety of stainless steel cylinders of dimensions 50mmx5mm, 75mmx5mm and 100mmx3mm of equal heights to represent the proximal femoral diaphysis, diaphyseometaphyseal junction and distal femoral metaphyseal respectively. These dimensions are comparable to the dimensions of the average femur. The distal locking end of the intramedullary nail was attached to the centre of the cylinder with a dedicated single or two rods (5mm diameter), made from stainless steel and titanium, to represent the distal locking cross screw.

Results: In the 50mmx5mm cylinder, the mean stability of fracture model using either single or two screws were similar. But in the 75mmx5mm and 100mmx3mm cylinders, the mean stability of the fracture model significantly decreased (50%) with single distal locking cross screw fixation when compared to two distal locking cross screws fixation. Similarly, stainless steel alloy provided more stability compared to titanium alloy cross screws in 75mmx5mm and 100mmx3mm cylinders. However there was no difference between the cross screws performance for 50mmx5mm when comparing both the alloys.

#### Conclusion

As shown in this experiment, femoral shaft (diaphyseal) fractures fixed with shorter intramedullary nail had the same stability for one or two distal locking cross screws. However fractures fixed with longer intramedullary nails, to fix diaphyseo-metaphyseal junction fractures and extreme distal femoral fractures, single distal locking cross screw fixation provide poorer fracture stability compared to two distal locking cross screws fixation. We recommend that all distal locking fractures be treated with two distal locking stainless steel cross screws to provide better stability of fracture fixation.

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ORAL SESSIONS - SATURDAY





#### 0-123

#### CLINICAL PRACTICE GUIDELINE BASED EVIDENCE FOR THE PHYSIOTHERAPY OF PATIENTS WITH CALCANEAL FRACTURES REPARED WITH VIRA® SYSTEM

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#### Introduction

Although modern operative intervention for calcaneal fractures has improved the outcome in many patients, there still is no real consensus on treatment, operative technique, or postoperative management.

Vira® is a system for reconstruction-arthrodesis of severe calcaneal fractures, consisting of a nail with holes and screws for fastening to the talus. Treatment of closed calcaneal fractures with Vira® System has excellent results, with less impairment, shorter hospital stays, and better functional outcomes than those following nonoperative treatment or open surgical repair.

The aim of our study was to elaborate a clinical practice guidelines basis of "best evidence" and consensus among expert group that assists physiotherapists to make diagnostic conclusions and therapeutic decisions, to improve the quality of care and to provide uniformity in care of conservative treatment interventions for severe calcaneal fractures.

#### **Materials and Methods**

The CPG was developed according to international methods of guideline development (Grimshaw 1995, Sackett 2000). The recommendations were constructed combining best evidence from randomized clinical/ controlled trials, prospective studies with the consensus among expert group and practicing physiotherapist based on disease related impairments (loss of mobility and force, pain, ) and disabilities (activities dailing living (ADL), walking...).

To identify "best evidence" published research a computerized literature search of Medline, Cochrane, PEDro, IME, IBECS and ENFISPO and search of reference lists to find additional studies were realized. The evidence of the different studies selected was evaluate using scale described by the US Preventive Task Force. When no evidence was available, consensus between experts (physiotherapist and orthopedic surgeons) was achieved to develop the guideline.

To identify "best clinical experience" and "physiopathology reasoning" focus group of practicing physiotherapists was used. They reviewed the clinical applicability and feasibility of the guideline, and their comments were used to improve it.

#### **Results and Discussion**

CPG include three phases determined from the physiopathology and biomechanical reasoning of surgical system (weeks after the surgery: 2ª-5ª, 5ª-14ª, 14ª-+/-24<sup>a</sup>). Unfortunately, evidence related to the treatment of severe calcaneal fracture was sparse and often of poor methodologic quality. The recommendations that were included: early onset (2<sup>a</sup> week after the surgery) with early mobility and loading, manual therapy (articular and miofascial techniques), walking in swimming pool, continuous electromagnetic fields of 99Hz with an intensity of 99 Gaussian during 30min/day; electrotherapy of the intrinsic muscles of the feet (80Hz; 8:12, 20 mi), a program of active exercises of the feet (dorsiflexion and plantarflexion, not supination and pronation) and resistive exercises of triceps surae muscle (7<sup>a</sup> week), criotherapy and anti-inflammatory positions. The CPG also includes a program of home exercises that the patient will develop from the following days to the surgery to the beginning of physiotherapy program.

#### **Conclusions / Summary**

The guideline reflects the current state of knowledge of the effective and appropriate physiotherapy in patients with Vira® System after calcaneal fractures. Nine recommendations were included in CPG combining best evidence and consensus amoung group of expert.

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#### ANTI-RESORPTIVE/CANCER TREATMENTS IMPROVE RAT FEMURS PROPERTIES WITH TUMOR-INDUCED OSTEOLYSIS

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#### Introduction

The mechanisms of the metastatic spread of cancer to bone is still a question that needs to be addressed and a requirement for establishing guidelines for monitoring the response of metastases to treatment [Mundy, 1997]. This pilot study investigates the efficacy of two treatments (Anti-Resorptive: Ibandronate, and Anti-Cancer: Paclitaxel) of tumor induced osteolysis in terms of geometrical and biomechanical parameters, to establish guidelines for monitoring the response to anticancer treatment.

#### Methods

A male adult rat femur model for tumor-induced osteolysis using W256 cancer cells was adapted from a previous study [Kurth, 2001]. An open-knee surgery was done on the right knee and 2×106 cancer cells suspended in saline were injected through a hole drilled at the femoral intercondylar notch. Of the 30 rats (approx. 350g) implanted with cancer cells, 12 were untreated (Canc), 9 received Ibandronate (Iban) [Kurth, 2001], and 9 received Paclitaxel (Pac) [Stearns, 1996]. An additional 12 rats underwent a sham operation (Cont), where only saline was injected.

cross-sectional area (CSA) of the cortical bones (at 25% of distal femur length) [Kurth, 2001], and microstructure data of trabecular bones, such as trabecular thickness (Tb.Th), number (Tb.N), separation (Tb.Sp), bone volume density (BV/TV), and bone surface density (BS/BV) [Kurth, 2007]. Subsequently, a non-destructive 3-point bending test, limiting the force to a predetermined yielding strength, was done to assess the elastic mechanical property of the same femur.

#### Results

Taking intra-species variability into consideration, parameters of the implanted right femur were always compared to those of the nonimplanted left femur of the same animal. Contra-lateral differences in percentage from different treatment groups were summarized in Figure 1 and Table 1.



Figure 1: Difference in Stiffness between the Paired (intact vs. operated) Femurs at 10-day Intervals.

Paired Differences (%)	Group, after 30 days (20 days for Pac)				
	Cont	Canc	Iban	Pac	
BV	0.08	10.80	-0.13	5.35	
CSA	10.19	16.18	3.63	12.54	
Tb.Th	-20.66	0.13	-15.82	-3.2	
Tb.N	7.41	20.75	1.96	-16.22	
Tb.Sp	-2.73	-5.10	28.85	15.89	
BV/TV	-0.89	14.87	-16.69	-11.16	
BS/BV	10.68	10.68	-7.26	7.53	

Table 1: Paired Difference (%) in Geometrical Parameters of the Rat Femurs.

#### Discussions

Although having different mechanisms, both Ibandronate and Paclitaxel have the potential in preserving the structural integrity of cortical and trabecular bones, and improving the mechanical properties, as in this bone metastasis model. While Ibandronate results in improvements to the geometry and microarchitecture, paclitaxel seems more effective in maintaining the stiffness (Young's modulus) of the bone. Further studies with a larger number of animals involved will be carried out to validate this claim.

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#### Acknowledgement

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0-125

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Recently more investigations concentrated on the role of cytokines in the mechanism of back pain. Several cytokines, including Interleukin 6 (IL-6),

THE ROLE OF TNF-A IN PATIENTS WITH

CHRONIC LOW BACK PAIN – A PROSPECTIVE

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COMPARATIVE LONGITUDINAL STUDY

IL-8, tumor necrosis factor (TNF) are thought to influence nociception or pain. To date, there have been no studies of the production of inflammatory mediators in blood from patients with low back pain. In this prospective longitudinal clinical study with a matched pair design we evaluated the role of TNF- ] and its clinical relevance in patients with chronic low back pain.

#### Methods

120 patients with chronic low back pain of at least 3 months duration with clearly defined inclusion and exclusion criteria underwent a 3 weeks inpatient multidisciplinary therapy. Patients were age and sex matched to a healthy control group (n=84). Patients and controls were prospectively followed for 6 months. At 4 fixed time points blood samples were taken and TNF- ] levels compared in both groups: at beginning of the study (T0), at 10 days (T1), 21 days (T2), and at 6 months (T3), respectively. Pain level (visual analogue scale) and clinical function (Roland Morris score) were assessed in the patient group and correlated to TNF- ] levels.

#### Results

At T0 (57,6% vs 12,3%) and at all other time points, there was a significant higher amount of TNF- ] positive patients compared to the control group. In the patient group there was a significant reduction of TNF- ] positive patients from T0 to T1 (57,6% vs 39,4%), but after this period, TNF- ] levels remained constantly high without further change until the final follow up at 6 months. In the healthy control group the amount of positive TNF- ] levels remained constant over the entire period.

There was a significant improvement of pain and function in the patient group from T0 compared to T1 without further significant change at the following time points. A significant correlation of TNF- ] levels with pain or clinical function could not be detected in these patients.

#### Discussion

As a conclusion, patients with chronic low back pain show a significantly higher amount of TNF- ] positive levels compared to healthy control persons, at the beginning of the therapy as well as throughout a prospective period of 6 months. TNF- ] seems to play an important role in these chronic pain patients. However, pathophysiology of this process, the clinical relevance of TNF-] and especially its part in a potential therapy regimen in these patients, need to be further examined and defined in additional studies.

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# POSTER SESSIONS EORS

Saturday, April 26th

#### POSTER SESSION 9 Hand, foot, fractures, tumor

#### P-049

#### ASSESSMENT RESULTS OF PRIMARY EXTENSOR TENDON REPAIR OF THE HAND WITH REGARD TO THE ZONE OF INJURY

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#### Abstract

#### **Backgrand:**

Extensor tondon lacerations are much more common than flexor tendon injuries. The outcome of this lesions depends on mamy factors including severity of initial trauma, coexisting lesions, of the hand, site of the laceration, experience of the surgeon and post operative rehabilitation.the aim of our study was to evaluate the results of primary ext.tendon repair with regard to the zone of injury.

#### **Materials and Methods**

During a period of 28 months, 32 patients with open extensor tendon laccerations were repaired by modified kessler technique using 4-0 nonabsorbable suture. After tendon repair, immobilization with a volar splint was applied for 4-weeks and physiotherapy was carried out. Patients were followed –up for a mean of 12 months. we used the 5 extensor tendon zones and results were assesed using Miller's rating system, table 1. patents with closed tendon ruptures or concomitant hand fracture were excluded.

#### Pagoda 10:00 - 11:05 h O 049-062

#### Findings

Seventy two extensor tendons were repaired. the mean age of patients was 24.6 years (17-46 y). excellent and good resalts were obtained more in zone 5(88/4%) and zone 3 (84%). the out come was worse when tendon repair was performed in the zones 1, 2 and 4. Table 2. No in fection was seen.

Conclusion:

We found a strong correlation between the site of the repair and outcome, with more excellent and good results distal to ext. retinaculum (Zone 3), and above wrist (Zone 5). This indicates the warse results when the tendon repair was done at or near DIP joint (zone 1), in the region of complex extensor mechanism (zone 2) or beneth the extensor retinaculum (zone 4).

Table	1:	Miller's	classification	system
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Total flexor Loss (Degree)	Total extensor lag (Degree)	
0	0	
20>=	=<10	
12-45	11-45	

Table 2: Results of tendon ropair with respect to the zone of injury

Zone	No. tendons	Excellent	Good	Fair	Poor
1	5 (6.9%)	2(40%)	0	1(20%)	2(40%)
2	9 (15.5%)	3(33.3%)	2(22.2%)	2(22.2%)	2(22.2%)
3	25 (34.7%)	10(40%)	11 (44%)	3 (12%)	1 (4%)
4	7 (9.7%)	1(14.2%)	2 (28.5%)	1(14.2%)	3(42.8%)
5	26 (36%)	14(53.8%)	9 (34.6%)	2 (7.6%)	1(3.9%)



#### EORS 2008 · MADRID



#### SHORT TIME RESULTS OF THE EATON LITTLER LIGAMENT RECONSTRUCTION OF THE PAINFUL UNSTABLE THUMB SADDLE JOINT

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#### Introduction

Pain free function of the thumb carpometacarapal joint is essential for manual work. This study should evaluate the results of the Eaton littler ligamnet reconstrucction in which a slip of the flexor carpi radialis tendon (FCR) weaved through the first metacarpal and around the abductor pollicis longus and back to the FCR.

#### **Material and Methods**

In our 8 patients (10 surgeries) we had two times a posttraumatic instability and 8 times a rhizarthrosis I°. We evaluated subjective satisfaction, pain, clinic and radiological outcome.

#### Results

All patients would underwent the operation again. The mean DASH score was 17,43, the VAS under stress 1,29 and in rest 0.

The pinch and key grip strentgh were excellent (3,98kg, 7,18kg). The loss of ROM was low.

Radiologically there was no progression of the Eaton Littler rhizarthrsois stadium.

#### Coclusion

Our experience with the Eaton Littler procedure for stabilisation of the hypermobile painful thumb saddle joint were positive. The subjective satisfaction of the patients and the objective clinical and radiologiacl results could confirm this impression.







#### SHORT TIME RESULTS OF TOTAL REPLACEMENT OF THE THUMB SADDLE JOINT IN RHIZARTHROSIS

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#### Introduction

Rhizarthrosis is very common. Among the different treatment options, the implantation of a prosthesis is an alternative. This study reports short time results of the lvory prosthesis.

#### Material and Methods

We examinated 21 patients with an average age of 57,2 years which underwent total replacement of the CMC I joint between 2005 and 2007. We evaluated subjective satisfaction (DASH score), clinical and radiological outcome.

#### Results

The clinical results show good pain relief, good ROM and excellent strength. Radiological there were no signs of implant loosening. As complications we saw one posttraumatic fracture and one tendovaginitis De Quervain.

#### Conclusions

The advantage of a total replacement of the CMC I joint, compared to the standard resection arthroplasty, is faster rehabilitation and preservation of the length of the thumb and better strength.



#### INVESTIGATING THE POTENTIAL ADVAN-TAGES OF A NEW DESIGN OF SMALL JOINT ARTHROPLASTY USING FEA ANALYSIS

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#### Introduction

The role of small joint arthroplasty in treating patients with advanced destructive arthritis affecting the small joints of the hand, providing relative pain free hand function, has been well established. Current existing joint designs, principally flexible silastic spacers, satisfy the initial requirements but commonly lack durability1. In particular all flexible silastic joints are prone to early breakage with subsequent loss of function due to their anatomical shape, abrasion against bone and constant loading of the central section of the flexible implants. Hence the current implants are restricted for use primarily in severe arthritis and are unsuitable for treating patients with moderate degrees of arthritis.

#### Aim

The aim of our new small joint design is to overcome many of the deficiencies of the flexible silastic designs while maintaining their main advantage of stabilising joint alignment throughout the flexion range.

#### Materials

The design (WO04/017861) is essentially a cross between a flexible spacer and a surface replacement, whereby the spanning flexible spacer is located within the long axes of direct load bearing metacarpal and phalangeal 'housings'. The flexible spacer has a regular shape, is not subjected to direct longitudinal loading, does not come in contact with the surrounding bone, and flexion / extension is spread along 60% of its length. We have investigated a number of parameters, using finite element analysis (FEA), focussing principally upon the load bearing and wear properties of the new design to both statically and dynamically applied loads with reference to the test protocol developed by the Durham group.

#### Results

Detailed FEA of the new joint design has highlighted the extreme potential durability of the housings and the internal flexible spacer. Our results suggest that the wear characteristics of both housings manufactured from PEEK (Polyetheretherketones) using an injection moulding process may result in the generation of considerably less wear debris compared with conventional alloy / plastic articulations. In addition, modern medical grade polyurethanes would appear to have better load bearing and wear characteristics than existing silastic materials.

#### Conclusions

Clearly, if our FEA findings were to be reproduced with biomechanical testing, we would be well placed to introduce durable and readily affordable

small joint arthroplasties that may well resolve our current difficulties of treating patients with moderate joint disease in addition to being a realistic alternative for patients with advanced destructive small joint arthritis.

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#### HALLUX RIGIDUS: MAL-ALIGNMENT OF THE CENTRE OF ROTATION OF THE 1ST METATARSOPHALANGEAL JOINT OR INTRINSIC PLANTAR MUSCLE TIGHTNESS? A BIOMECHANICAL STUDY.

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#### Introduction

The foot is a very complex structure acting as the platform for all gait patterns. At present, little is known about the exact biomechanics of the foot due to the difficulties in modelling all of the components of the foot simultaneously and accurately1,2. This has made it virtually impossible to develop a complete understanding of the aetiology of many diseases of the foot including hallux rigidus.

We hypothesize that sagittal plane incongruency of the rotation of the 1st Metatarsophalangeal joint, or an increase in the tension of the intrinsic plantar structures may be responsible for the development of hallux rigidus.

#### **Materials & Methods**

Ground reaction forces and kinematic data from gait analyses together with anthropometric data from MRI scans of a 24 year old male were used to create a Mimics model of the articulation of a normal 1st Metatarsophalangeal joint during a gait cycle. The centre of rotation pattern was calculated by Affine Transformational Matrices. Finite element analysis was performed on the model and on similar models with the hypothesized; (a) incorporated incongruence, (b) an increased tension in the Flexor Hallicus Brevis and (c) an increased tension in the plantar fascia.

#### Results

The results demonstrated a minor increases in the peak contact stresses with increasing tension of the Flexor Muscle, mean maximum articular cartilage stress of 4.34MPa (Range 4.32 – 4.39). This non significant increase in the Joint Stress did not cause an abnormal stress environment within the Joint ( p-value = 0.6477, Wilcoxon matched-pairs signed-ranks test). A 30% increase in the medial band of the Plantar Fascia resulted in an significantly abnormal joint stress environment with the maximum articular cartilage stress increasing to 7.3MPa ( p-value = 0.0015, paired t-test), resulting in doubling the load through the 1st MTP joint compared to the normal physiological loads, fig 1.

#### Discussion

This study demonstrates important biomechanical evidence which supports the optimum surgical procedure for treating Hallux Rigidus, Moberg's and Dorsal Cheilectomy. While it is known Hallux Rigidus has a multifactorial aetiology, the authors feel the above study demonstrates an important inherent aetiology.

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#### ILOPROST FOR THE TREATMENT OF BONE MARROW EDEMA IN THE HINDFOOT

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#### Abstract

Bone marrow edema (BME) is a rare cause of pain in the foot.

We reviewed 19 patients with unilateral bone marrow edema of ischemic, stress or osteoarthritic origin located in the hindfoot treated with the vasoactive prostacyclin analogue iloprost. Iloprost has a potency to dilate arterioles and venules and to reduce capillary permeability. All these rheological factors of the terminal vascular bed are discussed to be of pathogenetic importance for bone marrow edema syndrome. The patients' mean age was 61,5 years (25-76) and the duration of symptoms lasted 19 weeks before the therapy started. Bone marrow edema was located 9x in the talus, 3x in the calcaneus, 3x in the navicular bone and 2x in the cuboid. 11 cases were estimated to have a primary ischemic origin, the other 8 ones to be secondary to an activated osteoarthritis or to mechanic stress. Our therapy consisted of a series of five infusions with 20 µg (50 µg in the first six patients) of iloprost given over 6 hours on 5 consecutive days each. During and after treatment partial weight bearing was requested for up to 3 weeks depending on the pain level at the start of therapy. Mazur's foot score was used to assess function before and 3 months after therapy.

During this time, the score improved from a mean of 54,9 (range 23-73) before to 87,8 points (47-100) 3 months after therapy, with the best results in ischemic lesions with an improvement from 56,2 to 93,9 points and inferior results in patients with osteoarthritic edema as well as edema due to stress with a change in the score from 53 to 79,3 points. Plain radiographs were graded according to Mont with grade I lesions before and after therapy, indicating that in all patients no subchondral fracture or collapse occurred. Magnetic resonance imaging showed complete recovery of the bone marrow edema within 3 months in 12 patients (9x ischemic, 3 osteoarthritic or stress), 3x partial regression (1x ischemic, 2x osteorthritic or stress) and no change in 4 cases with bone marrow edema due to activated osteoarthritis.

We conclude that the parenteral application of the vasoactive drug iloprost might be a viable method in the treatment of bone marrow edema of different origins but especially in ischemic ones. In edema secondary to osteoarthrosis or stress, therapy effect with iloprost is of a symptomatic character depending on the grade of the basic disease.

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#### RESECTION ARTHROPLASTY WITH AND WITHOUT CAPSULAR INTERPOSITION FOR TREATMENT OF SEVERE HALLUX RIGIDUS

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#### Abstract

Resection arthroplasty - known as 'Keller procedure'- is used for treatment of severe hallux rigidus. As a modification of this procedure, resection arthroplasty is combined with cheilectomy and interposition of the dorsal capsule and extensor hallucis brevis tendon, which are then sutured to the flexor hallucis brevis tendon on the plantar side of the joint (capsular interposition arthroplasty).

In this study the clinical and radiological outcome of 22 feet treated with interposition arthroplasty were investigated and compared to 30 feet on which the Keller procedure was performed. The mean follow-up period was 15 months.

No statistically significant difference was found between both groups concerning patient's satisfaction, clinical outcome and increase in range of motion of the first metatarsophalangeal joint. At follow-up, patients who had undergone interposition arthroplasty did not show statistically significant better AOFAS forefoot-scores compared to the Keller procedure group. A high rate of osteonecrosis of the first metatarsal head was found in both groups. These radiological findings did not correlate with the clinical outcome at follow-up.

In conclusion, no significant benefit in clinical or radiological outcome was found for capsular interposition arthroplasty compared to the Keller procedure.

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#### MULTIPLE ROLES FOR INTERLEUKIN-6 (IL-6) IN FRACTURE HEALING

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#### Introduction

A role for the cytokine IL-6 in addition to inflammation in fracture healing was earlier indicated by IL-6-related activity in rat femoral fracture callus (1) and increased mRNA in fractured femoral bone in patients (2). IL-6 can recruit mesenchymal cells and stimulate osteoclast formation, suggesting potential roles in bone formation and turnover in fracture healing. Support for this hypothesis came from the recent distraction study in rat tibia by Cho and colleagues (3). The authors found immunostaining of osteoblasts and chondrocytes for IL-6 on day 7 post-fracture, the only day observed before distraction. The aim of our study was to investigate the time-course of expression of the IL-6 protein by cells in fracture healing in a rat model.

#### **Materials and Method**

A closed fracture of the lower right limb was induced in male Wistar rats, the tibia being stabilised with an intramedullary pin. The tibia was obtained from six animals at each of 1, 3, 7, 14 and 28 days post-fracture, decalcified, paraffin-embedded and thin sections of 6-8µm were cut. Immunohistostaining of the sections was undertaken with an IL-6-specific polyclonal antibody and colouring agent, being counterstained with haematoxylin. Controls consisted of IgG in place of the antibody. The cell type and degree of positively stained cells was counted under x400 magnification in areas of interest. Seven squares (0.3125mm) in the callus adjacent to the cortex on both sides of the fracture, 2 squares in the cortex both sides of the fracture and 2 vertical squares directly above the fracture were evaluated. Data from each defined region was combined for all animals from each time-point.

#### **Results and Discussion**

One day after fracture significant staining of inflammatory cells was observed (34%). Their number and staining declined by day 3 and were virtually absent on day 7, by which stage the inflammatory phase has normally ended. Additionally on the first day some cells within the periosteum, distal to the fracture were positive, where intra-membranous bone formation directly arises. Staining of 26% of osteocytes was seen within the cortex on day 1, which may contribute to stimulation of osteoclast formation for the removal of necrotic bone at the fracture ends. Some fibroblastic cells (6%) were also stained, which could be involved in chondrogenesis. Chondrocytes appeared by 3 days, of which 23%

were stained, suggesting a role for IL-6 in endochondrial ossification. At day 3 staining was seen throughout the expanding periosteum. Bone at this time was starting to form distal to the fracture, with staining of some osteoblasts (3%) associated with its synthesis. By day 7 the callus was greatly expanded, with extensive calcified cartilaginous tissue proximal to the fracture, where the majority of the chondrocytes were stained (72%). Distal to the fracture woven bone was rapidly being laid down by osteoblasts, with significant staining of these cells (42%). The amount of new bone in the callus increased by day 14, as did the percentage of stained osteoblasts (56%). From day 7 osteocytes that were forming within this bone showed increased staining (5%, up to 27%) day 14), potentially stimulating remodelling. Staining of this cell type reached 43% by day 28, whereas for osteoblasts it had declined (39%), suggesting remodelling may be overtaking formation. As bone replaced cartilaginous tissue within the callus, most of the latter being removed by day 28, a parallel decline in staining of chondrocytes occurred (10% above the fracture, absent elsewhere in the callus).

#### Conclusions

IL-6 appears to be involved throughout the fracture healing process. In addition to the initial inflammatory response, IL-6 also plays a role in bone formation, both intra-membranous and endochondrial ossification. Staining of osteocytes early in the cortex and later within the newly laid down bone in the callus suggests the involvement of IL-6 also in bone removal and remodelling. The level of staining of each cell type appears to reflect the degree of activity of cells with respect to production of related tissue.

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#### A NEW RADIOLOGICAL ALIGNMENT JIG TO OVERCOMING THE CHALLENGES OF INSER-TING DISTAL LOCKING SCREWS

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Introduction

The current techniques used for locking the distal end of intramedullary nails with cross screws remain a technical operative challenge for many clinicians. The surgeon uses his / her experience and judgement to locate the distal holes in the intramedullary nail, relying heavily on the use of two dimensional intra operative X-ray images (fluoroscopy) to undertake a three dimensional task. As a result, a large number of X-ray images are frequently required, significantly increasing the radiation exposure to both the patient and the operative team1. Also there is an overall proportional increase in the operating time.

#### Aim

We aimed to develop a simple new radiological alignment jig that would allow the accurate placement of distal locking cross screws in an intramedullary nailing, with minimal radiation exposure and without having to visualise the distal screw holes.

#### Materials and method

Laboratory tests were conducted using plastic femora (Sawbones Limited) fixed with intramedullary nails. Tests were performed three times using each of the different femoral intramedullary nails (Russell-Taylor, Smith & Nephew) investigating whether the length or diameter of the nail had any influence upon the accuracy of distal screw insertion. After successfully concluding the laboratory tests, a limited clinical study was conducted using the new alignment jig to insert distal locking screws in patients.

#### Results

Both the bench tests and limited clinical study were 100% successful and permitted the clinician to identify the distal holes correctly without needing to visualise the distal screw holes radiologically.

#### Conclusion

Our initial bench tests and clinical study show that the new alignment jig allows simple and accurate insertion of the distal locking screws with minimal radiological guidance. It also has considerable potential to reduce the overall operating time.

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204

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#### EORS 2008 · MADRID



#### CLINICAL AND BIOMECHANICAL EVALUATION OF LOCKING COMPRESSION PLATING IN COMMINUTED OLECRANON FRACTURES

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#### Introduction

New concepts in plate fixation have led to an evolution in plate design for olecranon fractures. The purpose of this study was (1) to compare the stiffness and strength of a contoured Locking Compression Plate (LCP) with a conventional plating method (one-third tubular plate) in a cadaveric comminuted olecranon fracture model with standardized osteotomy, and (2) to evaluate the LCP fixation method in a prospectively included group of patients with complex olecranon fractures using validated outcome scores.

#### **Materials and Methods**

In the biomechanical study, five matched pairs of cadaveric elbows were randomly assigned for fixation by either LCP or a conventional plating method. Specimens were mounted to a custom-made testing bench and subjected to cyclic loading until failure occurred while measuring gapping at the osteotomy site. In the clinical study, twenty-one patients treated with LCP for complex olecranon fractures had a mean follow up of 20 months (3-39 months) and functional and patient rated outcome were evaluated.

#### Results

In the biomechanical study, there was no significant difference in fixation stiffness and strength between one third tubular plating and LCP (p>0,05). In the clinical study, the mean time to union of the fracture was 6 months (2-28 months). According to the Mayo Elbow Performance Index (MEPI) most patients had a good or excellent outcome. No patients reported difficulty with activities of daily living. Physical capacity showed minimal loss of stability and strength. Six patients had their hardware removed.

#### Conclusion

Technical ease of application and advantageous features of the LCP -such as unicortical screw fixation and improved holding power in osteopenic bone- make it a good alternative implant for comminuted olecranon fractures.





#### SIRT1 ACTIVATION INDUCES APOPTOSIS OF HUMAN OSTEOSARCOMA CELLS

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#### Introduction

Recently, the longevity gene sirt1 was found to be highly expressed in several types of mammalian tumors (3). Upregulation of sirt1 expression has also been correlated with the developement of chemotherapy resistance in human osteosarcoma (1). The present study aimed to test the effects of sirt1 activation on growth and survival of osteosarcoma cells.

#### **Materials and Methods**

Normal human osteoblast cell line HNOst and four osteosarcoma cell lines HOS, MG-63, SaOS-2 and U-2OS were used in the study. Cells were cultured in ]-MEM supplemented with 10% FBS, 1 mM L-glutamine and 100 g/ml gentamicin at 37°C in a humidified atmosphere containing 5% CO2. Sirt1 activation was mediated by two activators, resveratrol and isonicotinamide, as well as by nutritional restriction elicited by L-asparaginase. Cell growth was measured on cells growing in 96-well plates by WST-1 assay (Roche Molecular Biochemicals). Flow cytometric analysis of apoptosis was performed on cells culturing in 6 well plates after staining with Annexin-FITC and/or propium iodide using an Annexin V kit (Caltag Laboratories, Burlingame, CA, USA).

#### **Results and discussion**

Instead of promoting cell survival, both resveratrol and isonicotinamide decreased cell growth and induced cell apoptosis dose dependently in all four osteosarcoma cell lines. Such inhibition effects on cell survival were relatively minor on normal human osteoblasts. Although the osteosarcoma cell lines responded variably to L-asparaginase alone the pro-apoptotic effects of resveratrol were significantly enhanced with the presence of L-asparaginase.

Both resveratrol and isonicotinamide are activators of the mammalian nuclear NAD-dependent protein deacetylase sirt1. The mechanism of sirt1 activation by resveratrol is not known in detail but it has been proposed that, as for some other polyphenols with trans-stilbene structure, it induces a conformational change in sirt1, which lowers Km for both the acetylated substrate and NAD (2). Isonicotinamide was supposed to enhance sirt1 deacetylase activity by competing with naturally presented nicotinamide, which inhibits deacetylation by chemical reversal of a covalent reaction intermediate (5). Besides activation by potential agonists, sirt1 expression can also be up-regulated under nutritional stress (4). The enzyme L-asparaginase can deprive L-asparagine through hydrolysis of L-asparagine into L-aspartic acid and ammonia. Unlike normal tissue many tumors including

osteosarcoma has been shown to be lack of enough asparagine synthetase and have to rely on external sources of L-asparagine to keep up with their rapid growth (6). Thus, by addition of L-asparaginase the tumor cells would suffer more severe nutritional stress than normal tissue.

We demonstrated herein that sirt1 activators elicited pro-apoptotic effects in osteosarcomas. We also supposed that induction of sirt1 overexpression by nutrition restriction could further enhance the sensitivity of osteosarcomas to sirt1 activators so as to magnify the antitumor effects. Further studies aimed to confirm the role of sirt1in the anti-osteosarcoma effects are undertaken now in our group. Although our study can not elucidate the complicated relationship between sirt1 and cancer development our results supported the hypothesis that sirt1 could be a potential target used in osteosarcoma chemotherapy.

#### Summary

Our results demonstrated that activation of sirt1 by resveratrol and isonicotinamide induced apoptosis of osteosarcoma cells. This anti-tumor effect can be further enhanced by nutritional restriction elicited by L-asparaginase. Our findings suggested sirt1 could be a potential target for future therapy of osteosarcoma.

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## SOFT TISSUE SARCOMAS: EVALUATION OF A NEW ASPIRATION-CYTOLOGY-SYSTEM

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#### Introduction

In several countries fine needle aspiration (FNA) biopsy of soft tissue tumours is regarded as a standard procedure.

However, various problems using FNA compared to core needle biopsy have been reported. Less cell amount, blood and other non tumour tissue aspirated and cells torn out of their environment lead to problems in histological diagnose. The aim of this study was to measure the number and the vitality of cells harvested by two new needle systems (Thyrosampler®, ACD Medical Innovation, Vienna, Austria) in comparison with the conventional fine needle system (C-FNA). The innovation of the new system is aeration after aspiration by a valve, so that undesired aspiration of blood, debris, and cells from outside the tumour during withdrawal of the needle is minimized.

#### **Materials and Methods**

In a blinded setting, 45 punctures from fresh pig thyroid glands were made and analyzed - 15 for each needle (conventional needle C-FNA, single-needle with air valve T-ONE and multi needle system with air valve T-THREE). The measurement was done according to the manufacturer's recommendations for CASY (CASY® technology, Reutlingen). The aspirated cell material was evacuated into 10ml Casyton (cell-culture liquid, CASY® technology) and calculated with the CASY (CASY® technology) cell counter. Total cell amount and amount of vital cell was counted and recorded. Statistical analysis was performed using t-test (p<0.05 was considered significant).

#### Results

With each system, 15 punctures each were aspirated and the cells counted. With the T-ONE System the amount of vital cells was 688%, the amount of total cells 521% higher then using the C-FNA system. With the T-THREE System the amount of vital cells was 901%, the amount of total cells 798% higher then using the C-FNA system.

The mean difference between C-FNA and T-ONE was significant regarding total number of cells (p=0.03) as well as number of vital cells (p=0.032). The difference between T-ONE and T-THREE was not significant, neither regarding total number of cells (p=0.35) or number of vital cells (p=0.6).



#### Discussion

The needle systems with the air-valve led to a significantly higher cell amount in needle aspiration biopsy. According to the requirement of cytological diagnosis of soft tissue sarcomas more cell volume could be harvested, which is a well-defined benefit.



#### CORRELATION BETWEEN VEGF, PDGF, FGF1, TGFBETA2,TNFALFA, KI-67 AND P53 AND MALIGNANCY IN CARTILAGINEOUS TU-MOURS

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#### AIM

Tumoral neoangiogenesis is correlated with malignancy and development of metastasis. The aim of the study was to assess the angiogenesis and proliferation index of benign and malignant cartilaginous tumours, usually considered non vascularized and with a scarce capability of developing metastasis

#### **Materials and Methods**

Twenty-one cases of cartilaginous tumours were retrospectively analyzed. Of them 8 cases were benign and the remaining 13 were malignant (5 low grade and 8 high grade). Tumours were localized to upper limb, lower limb and pelvis. Hand and foot chondroma were excluded due to particular behaviour of tumoral cells. For all patients age, sex, localization, symptoms, type of treatment, complication, recurrence and survival rate were collected. Average follow up after surgery was 74,71 months. Diagnosis were confirmed by analyzing clinical data, imaging and histology on samples stained with haematoxylin and eosin. VEGF, PDGF, FGF1, TGFbeta2,TNFalfa, Ki-67 and p53 were measured in order to detect a possible correlation between proliferation angiogenesis and malignancy. Statistical analysis was performed using Fisher test to correlate different group of patients (benign, malignant low grade and high grade) and markers expression. Kaplan-Meier method measured the disease free survival rate and log rank test measured the differences

#### Results

Interesting were the results obtained with VEGF, because a statistic significant difference was measured regarding VEGF expression beween benign and malignant lesion (p=0.023) and between benign and high grade chondrosarcoma (p=0.001) and between low grade and high grade malignant tumours (p=0.007). In particular VEGF expression was correlated with grading (p=0.001). Local recurrence was correlated with Ki-67 (p=0.035), TGF] (p=0.007), PDGF (p=0.007) e p53 (p=0.0455) expression. An over expression of p53 and ki-67 was observed only in 3 cases of high grade malignant tumour. It was interested that these patients developed local recurrence and one of them dead 7 months after diagnosis, showing a possible correlation between marker expression and poor prognosis.

#### Discussion

On the basis of results obtained Authors suggest an diagnostic therapeutic algorithm in case of cartilaginous tumour. In case of benign tumour follow up or eventually curettage should be the treatment. In case of chondrosarcoma it is very important to assess the angiogenetic pattern of tumour, because in VEGF negative chondrosarcoma a curettage with local adjuvant may be considered the choice treatment; in case of VEGF positive chondrosarcoma a wide excision and therapy with VEGF inhibitors may be considered; finally in case of expression of PDGF, TGFbeta2, Ki-67 and/or p53 wide excision and aggressive chemotherapy should be the choice treatment.



#### POSTER SESSION 10 Hip

#### P-063

#### A CASE SERIES OF NINETY NINE HYBRID METAL-ON-METAL HIPS – BIRMINGHAM RE-SURFACING CUP AND BIRMINGHAM MODU-LAR HEAD.

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#### Background

Total hip arthroplasty has been an indication for severe/ end-stage osteoarthritis of the hip. Selection of implants is paramount in such cases which can be patient dependent or surgeon dependent or a combination of both. Birmingham Hip resurfacings (BHR) have been a popular mode of treatment for younger and more active patients with arthritis of the hip. However the use of hybrid hip arthroplasty system with a Birmingham hip resurfacing cup and modular head with a variety of cemented or uncemented stems is less well described in the literature.

#### AIMS

To determine the early Results of THR with BHR Cups and Modular heads with a variety of different stems, both cemented and uncemented.

#### Methodology

We analysed consecutive hybrid hip arthroplasties (cementless BHR cup and a variety of cemented or uncemented stems) with modular heads performed by a single surgeon between 2000 and 2007 with an average of 2.5 yrs (range from .5 to 6.4 years) Follow-up.

All patients who received a Modular head with Birmingham hip resurfacing cups were included in this study.

Patients were standardized for age, sex and demography. All surgery was done through a standard posterior approach and mobilized between 4 and 12 hours from surgery and planned to be discharged the following day unless delayed by social or pre-existing medical circumstances.

We evaluated radiographic changes and clinical outcomes in all patients at the most recent follow-up. A modified DeLee and Charnley method was used to identify lucent areas around the acetabular component. The acetabulum was divided into 3 zones, Zones 1, 2 and 3.

The femoral stems were assessed radiographically using a modified Gruen technique. Clinical assessment was undertaken to determine hip pain and hip function.

#### Results

A total number of 99 hybrid hips were included in the study in 93 patients.

There were 52 females and 41 males with an average age of 69.9, age ranging from 47 to 88 (standard de-

#### Pagoda 14:15 - 15:20 h O 063-076

viation of  $\pm$  7.9). The average BMI was 28.8 (range from 18.7 to 140.9 SD  $\pm$  12.9).

There were 57 right and 42 left surgically treated hip arthroplasties of which 6 patients had bilateral consecutive hybrid hip arthroplasties.

5 hips were revised to hybrids after # NOF of Birmingham hip resurfacings. One other hip was revised with Brimingham hip resurfacing cup and centrepulse revision stem and cables. 3 patients had dysplasia cups of which one was for revision of the total hip replacement (mentioned above) the other two were for asymmetric acetabulum and lack of roof cover respectively. In the latter patient acetabular reamings as bone graft was used to fill the roof defect. In all 3 patients, the dysplasia cup was secured well to the ilium with 2 screws.

Of the 99 hips, 93 were primary hybrid hip arthroplasties, reasons for surgery included 89 for osteoarthritis, 4 for rheumatoid arthritis, 5 patients for revision BHR with #NOF and 1 revision for failed THR.

Medical co-morbidities included 4 patients with noninsulin dependant diabetes, 2 with mild renal faliure, 8 with stable cardiac problems and one patient morbidly obese.

None of the patients in the case series developed infection, deep veinous thrombosis or pulmonary embolism.

None of the patients had dislocations until the most recent follow up.

No resurfacing cups or prosthesis (stems) were revised for loosening and no loosening of components were identified at the most recent follow-up and all patients were mobilising well.

#### **Clinical relevance**

Hip Resurfacing procedures are gaining popularity in the younger individuals with arthrosis of the hip. Some patients who are fairly independent and active fall short of satisfying the criteria for a hip resurfacing and one of our authors (LK) preferred the option of the BHR cup with modular head and a compliment of stems. This metal on metal option with large heads would ideally increase stability and reduce wear patterns with the prospect of increasing longevity of total hip arthroplasties.

In those patients who have an active and independent lifestyle where a hip resurfacing may be contraindicated, a hybrid hip arthropolasty with a modular head would be a reasonable option.



#### DO NON STEROIDAL ANTI INFLAMMATORY DRUGS CAUSE ENDOPROSTHETIC LOOSE-NING?

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#### Background

Total hip arthroplasty is commonly performed for endstage osteoarthritis of the hip to alleviate pain, stiffness and deformity and improve mobility and quality of life.

Pain relief plays an important role in the intra/post operative stages in order to achieve an almost pain free post operative recovery period and mobilise the patient as early and safely as possible in order to get them back into the community and avoid undesirable post surgical complications.

Recent papers have suggested that NSAID use following total hip arthroplasty may have the potential to adversely affect prosthetic fixation. Other animal studies have suggested that NSAIDs impair fracture healing 3-5 and clinical studies have emerged stating NSAIDs inhibit spinal fusion and retard healing of femoral diaphysial fractures. Other clinical and randomised control studies have also stated NSAIDs as playing role in the prevention of HO suggesting they may have an effect on bone metabolism .

#### AIMS

To determine if the use of Intraoperative and early post-operative use of NSAIDs lead to endo-prosthetic loosening.

This paper presents a consecutive case series of x total hip arthroplasties in which NSAIDs were used both by oral administration and periarticular infiltration for post op pain control.

#### Methodology

A series of 99 total hip arthroplasty patients were assessed for signs of clinical or radiological loosening. All patients received a BHR cup and Birmingham modular heads and a variety of cemented and uncemented stems.

We looked at a total of 99 consecutive hybrid hip joint replacements (cementless cup and cementless or cemented stem) that were performed in 93 patients between 1996 Dec and Jan 2006 by a single surgeon LK. The patients were retrieved from the joint reconstruction data base where prospective information was entered.

Inclusion criteria included all patients irrespective of age or sex who had a cementless or cemented total hip arthroplasty (primary and revision) were recruited into the study.

Those patients who had intra-operative fractures or been on long term steroids or disease modifying drugs for inflammatory arthropathies like rheumatoid arthritis were excluded from the study. Patients who had contraindications for the use of NSAIDs were also excluded.

All surgery was conducted by a single surgeon (LK) and

all anaesthesia and pain management was conducted by a single physician anaesthetist (DK). A standard posterior approach used in all cases.

Local anaesthetic mixture (Ropivacaine-Ketorolac (30mg) -Adrenaline or RKA mixture ) was infiltrated into the joint capsule and surrounding tissues after placement of the acetabular component, and thereafter into the different muscle layers in the thigh around the components. A total of 150 to 200 mls of this mixture was injected and a further 50 mls injected through a catheter left insitu upto 24 hrs after surgery before discharge.

Radiographic analysis was carried out using the Hodgkinson criteria to predict acetabular component loosening and used a modified system adopted by Persson et al to determine femoral component loosening.

All patients were mobilising atleast between 4-12 hours post surgery.

#### Results

Of the 99 hybrid hips, 57 were right and 42 were left hip arthroplasties and 6 patients had bilateral consecutive hips done. 5 were performed for revision of fractured necks of femur in Birmingham hip resurfacings and one total hip arthroplasty revised to a hybrid and the remaining 92 were primary hybrid hip arthroplasties. The arthroplasties were performed for Osteoarthritis (89), RA (4), and others (6).

No components were revised for failure of loosening, No dislocations were noted in this series or any deep wound infection or pulmonary embolisms.

At the most recent follow-up no components were found to be loose requiring revisions.

#### **Clinical relevance**

The use of high dose local infiltration NSAIDs in the intraoperative and early post operative phase does not seem to affect prosthetic fixation atleast during short to mid term follow up of hip joint arthroplasties. However randomized double blind studies should be conducted to determine the effects of deep local infiltration NSAIDs on long-term prosthetic fixation in hip arthroplasties.

#### EORS 2008 · MADRID



#### P-065

#### RELATIONSHIP BETWEEN OSTEOPOROSIS AND LIVING/WORKING ENVIROMENT

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Osteoporosis can be caused by many miscellaneous factors. These factors include medical, lifestyle and socioeconomic variables, the latest being not well studied and defined in international bibliography. From these there are the factors regarding the working environment (house or office) and the living environment (urban or countryside). Our hypothesis is based on the fact that women living in an urban environment or working in an office environment should have lower Bone Mineral Density (BMD) and thus, greater fracture possibility because of their lower level of physical activity, greater alcohol/coffee consumption and increased smoking frequency compared to women living in the countryside or women housekeeping.

In order to find whether this hypothesis is true, a population based observational retrospective study has been performed. The fracture rate of 4616 postmenopausal osteoporotic women (PMOW) (mean age=64,1±9,3 years) from 160 centers all over Greece has been compared with the two aforementioned possible risk factors. Descriptive statistics like the mean±SD and frequencies were used to present the data. In order to assess for relationships between categorical variables the chi-square (]2) test was performed. Statistical analysis was conducted using the software SAS, version 9.1 and statistical significance was established as 5%.

The results are as follow: 1) 16,2% of these PMOW had a history of fracture and for 80,3% of them was a hip fracture. 2) 84,1% of PMOW lived in urban environment and had lower fracture rate than women living in the countryside (p<0,05). 3) 47,2% of the PMOW worked at home and had lower fracture rate than women working for more than 20 years in an office environment (p<0,0001).

It can be concluded that more fracture-susceptible PMOW are those working in an office environment and also living in the countryside. It can be assumed that the first is related with lower BMD and the second with the more 'fall-prone' nature of the country environment.

#### EORS 2008 · MADRID



#### P-066 A NEW CERAMIC COMPOSITE FOR USE IN TOTAL HIP ARTHROPLASTY

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Demand for ceramic bearings is increasing rapidly because of excellent clinical results. Alumina offers advantages such as chemical resistance, excellent bioinertness and tribology. However, alumina has limited strength, therefore the applications are restricted to certain designs. Zirconia materials have been used clinically for ten years, they reveal problems due to poor hydrothermal stability. Thus, there is a strong need for new bearing material that combine strength and stability.

The new ceramic named Alumina Matrix Composite (AMC) uses the following principle of transformation toughening: Firstly, the dispersing of small particles of Y-TZP Zirconia in the alumina matrix and secondly the reinforcement by introduction of an anisotropic crystal like whiskers. This process dissipates the crack energy that is associated with an increase of strength. The examination of the tribological situation of AMC, especially under challenging conditions of hydrothermal ageing and under severe micro separation, shows the aptitude of this material in wear applications.

Alumina Matrix Composite offers a better mechanical resistance than alumina while maintaining the structural stability and equivalent tribological qualities. This is a material that has been very thoroughly evaluated and tested as a permanent implant material for the last 9 years. The results of this evaluation and testing process have been included in the manufacturer's Master File at the Food and Drug Administration and approved. Its first clinical use in the United States was in June of 2000. Since its introduction, the Alumina Matrix Composite described in this article has been implanted in more than 65,000 patients around the world.



#### SINGLE NUCLEOTIDE POLYMORPHISMS IN GENES FOR IL-2, IL-6 AND TNF- : INFLUENCE ON OSTEOLYSIS AND SURVIVAL OF TOTAL HIP ARTHROPLASTY

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#### Introduction

Total hip arthroplasty (THA) is the most effective treatment method for end-stage osteoarthritis of the hip [1]. However, THA life-in-service is limited predominantly by aseptic loosening and osteolysis (OL). Both are causally linked to prosthetic surface wear generating a massive number of prosthetic particles. These are believed to lead to increased activity of both osteoclasts and the bone family of proteinases together with suppression of osteoblasts at the bone-implant interface. The above events are orchestrated by the pro-inflammatory cytokines, the most important of which seem to be: TNF-alpha, IL-1, M-CSF and RANKL/RANK/ OPG [2]. However, these purported mechanisms cannot explain the differences in survival of THA and size of OL among patients with the similar wear rates. The aim of this study was thus to determine the potential role of cytokine gene polymorphism (single nucleotide polymorphism, SNP) in the development of OL around THA, risk for revision and survival of THA.

#### **Materials and Methods**

In this case-control association study we investigated patients with severe OL around THA (n=116). All were Caucasian, all had a single type of cementless THA and the surgery was done at a single institution. The control groups included (a) patients with the same THA and mild OL (n=89) and (b) healthy people without THA (n=151). Severity of OL (bone defects) was determined according to the Saleh et al. classification [3]. Overall, 22 SNPs were genotyped by polymerase chain reaction with sequence specific primers (PCR-SSP). All specimens were collected after written informed patient consent and approval of the local Ethics Committee.

#### **Results and Discussion**

The results showed an association of the TNF-238\*A allele with severe OL (odds ratio, OR=6.59, p=0.005), higher risk of revision (OR=infinity, p=0.017) and poorer survival of THA (p=0.022). In addition, carriers of the IL-6-174\*G allele were more frequent among the patients with severe OL (OR=2.51, p=0.007). Finally, the genetic variant IL-2-330\*G was associated with lower risk for THA revision (OR=0.44, p=0.02), protection from seve-

re OL (OR=0.55, p=0.043) and longer survival of THA (p=0.018). SNP in the genes for pro-inflammatory cytokines may have altered function and/or expression and this could influence susceptibility to the above complications. In fact, previous studies have described the potential role of SNP in prosthetic failure due to aseptic loosening or OL [4, 5]. Our study replicates the data for TNF-alpha SNP albeit direct comparison between studies cannot be made due to protocol heterogeneity. On the other hand, this is the first piece of evidence on the potential role of SNP in genes for IL-6 and IL-2 in the pathogenesis of OL and premature failure (only for IL-2).

#### Conclusion

At least in a Czech population, genetic variants of the pro-inflammatory cytokine TNF-alpha and IL-6 confer susceptibility to severe OL and risk of premature THA failure. Conversely, SNP in the IL-2 gene may protect carriers from development of severe periprosthetic OL and risk of early revision.

#### Summary

This study further supports the concept of genetic susceptibility to periprosthetic OL and premature failure of THA.

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#### EORS 2008 · MADRID



#### P-068

#### EDGE LOADING JOINT FORCE GENERATES DISLOCATING FORCE INFLUENCED BY ACETABULAR LINER RIM CAPTURE WALL HEIGHT

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#### Introduction

Clinical studies have shown that the acetabular poly liner rim capture wall height is related directly to the hip joint stability1, 3. When comparing the dislocation rates between a 0mm wall and a 1mm wall, there was a significant decrease in the dislocation rates with the 1mm wall (1.5% to 2%) compared with the 0mm wall (11.4% to 26%) 1, 3. The elevated rim liner also showed lower dislocation rate2, 4. The mechanisms of dislocation were experimentally and computationally verified by inducing the femoral neck impingement. However there was no data available to date for the joint stability just under a rim-directed loading force alone. The purpose of this study was to investigate the effect of rim capture wall height to the tangential or dislocating force (DF) induced by single rim-directed joint force.

#### Materials and methods

FEA: (30) 3-D CAD model assemblies consisted of CoCr femoral heads and corresponding 10mm thick generic UHMWPE acetabular bearings. Each head size of 22, 28, 32, 36, 40 and 44mm had different capture wall cylinders of 0, 0.5, 1, 1.5 and 2mm. (Fig.1) Models were developed by Pro/Engineer Wildfire v2.0 and imported to ANSYS Workbench v11.0 as one-half of the symmetrical assembly. The cup liner was auto-meshed to 0.76mm and the femoral head was to 2.5mm size. The kinetic coefficient of friction of 0.02 was applied to the acetabular liner interface with the femoral head. The backside of the acetabular liner was constrained in all degrees of freedom to simulate the complete fixation of the liner. The nonlinear elastic modulus of UHMWPE was selected from experimental data. The published data were used for CoCr heads. The joint load of 2,446N was applied through the femoral head center to the mid point of the capture wall. The femoral head was constrained except for the loading direction. The reaction forces against the femoral head to prevent the femoral head from dislocating were obtained in the FEA analysis. This force was in the opposite direction but equal in value to the DF. The femoral head reaction force was recorded.

Experiment: The results of curve trend were verified by the physical testing of actual 28mm ID UHMWPE acetabular liners which were 30KGry sterilized in nitrogen. One liner with 0mm capture wall and other with 1.5mm were fixed in the corresponding shells which were mounted in the fixture secured on the MTS testing machine. A 28mm CoCr head was mounted on the main axial actuator and was seated in liner ID at mid point level of capture wall. The interface between head and liner ID was lubricated by bovine serum. A horizontal load was applied against the acetabular shell fixtures peaked at 2,446N with 50N/s ramping by an side actuator. The reaction forces against the head (DF) along main axis were recorded.

#### Results

The highest DF was 1,269N per 2,446N of rim loading force for the 0mm capture wall and 22mm head. The lowest DF was 171N per 2,446N force for a 2mm capture wall height and a 44mm head. The DF decreased as the capture wall and head size increased. When the capture wall was higher than 1mm, the DF was reduced more than 50%. The DF distribution curve are shown in Fig. 2. Two experimental data points of actual 28mm ID liners with 0 and 1.5mm capture wall heights were consistent with the trend of DF curve from FEA. Conclusions and discussion:

In addition to the traditional hip joint dislocation parameters of impingement, subluxation and head jump distance, this study identified a new intrinsic dislocation force DF induced by the rim-directed joint loading force. The study suggests that the hip joint loading force alone can generate a DF component as high as 51% of the loading force. A capture wall height above 1mm can effectively reduce it to less than 25% of the joint force. The larger head diameter resulted in less DF generation. The DF was likely caused by the wedge effect between the deformed polyethylene bearing and the femoral head. The capture wall allows the femoral head to be separated from the spherical bearing surface, thus reducing the wedge effect. Our observation of the stabilizing effect trend of the capture wall was consistent with reported clinical data1, 3. However, the increased height of the capture wall also reduces the range of motion. It is therefore necessary to minimize the capture wall height. This study suggested the larger femoral head has the advantage of reducing the DF in all capture wall heights and this effect is more effective when combining with the capture wall. The result of this study should provide the guidance to improve acetabular poly liner design for better joint stability.

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# THE INFLUENCE OF ACETABULAR SHELL RIM SUPPORT ON THE POLYETHYLENE LINER

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#### Introduction

High tensile stress in the acetabular cup liner rim has been considered as a contributing factor of the UHMWPE liner failure. It becomes more critical for some early generation highly cross linked polyethylene material due to the reduced mechanical strength. Also as the clinical use of larger femoral heads increase, the available poly to resist loads diminishes accordingly. It has been reported that increased tensile stress in polyethylene liner rim are present in vertically placed acetabular cups1. To date however, there has been no data of the stress in the liner when it is assembled in different shells. The objective of this study was to investigate the effect of back side metal support on the stress level at the rim of polyethylene liner in vertical loading angle.

#### **Materials and Methods**

Twelve 3-D CAD model assemblies consisted of: A) CoCr femoral heads in 22, 28, 32, 36, 40 and 44mm diameters. B) Corresponding 22, 28, 32, 36, 40 and 44mm ID with generic 45.7mm OD N2VAC UHMWPE acetabular liners and C) Generic Ti-6Al-4V 52mm OD / 45.7mm ID hemispherical acetabular shell with and without 2mm high integrated rim.(Fig1a&b) One-half of the assembly models were imported from Pro/Engineer Wildfire v2.0 to ANSYS Workbench v10.0. in symmetry boundary condition. The material properties were determined experimentally for UHMWPE and obtained from published data for CoCr and Ti alloy. Each component was meshed with 10-noded, tetrahedral elements (type SOLID92). The finite element mesh of the UHMWPE liner and acetabular shell was refined in the vicinity of the edge load application. Bonded contact (surface contact element type CONTA174 and target contact element type TARGE170) were assumed at the acetabular liner to shell interface, while frictionless sliding contact was considered at the femoral head to acetabular liner interface. The backside of the acetabular shell was constrained in all translational degrees of freedom. A load of 2,450N was applied through the femoral head center to the edge of the UHMWPE insert to simulate the rim loading condition for vertically placed acetabular cup without head subluxation. Maximum principal stresses at the UHMWPE liner rim of the articulating surface were evaluated with and without the supporting rim for different femoral head sizes and liner thicknesses.

#### Results

For rim unsupported conditions, the peak maximum principal stresses at rim of the UHMWPE liners were ten-

sile stress patterns for all poly thickness. While the maximum principal stresses at the rim ID surface were tensile when poly thickness was below 5mm and the average stresses were tensile when poly thickness was bellow 9mm. (Fig 2) For rim supported conditions, stresses were in all compressive patterns. Stress levels in both cases were below the yield strength of UHMWPE (19MPa) in this model.

#### **Discussion and Conclusion**

The rim back support changed the stress pattern to compressive, a preferred stress pattern to avoid fracture, for all poly thicknesses. In the no rim support condition, the average stress was tensile when poly thickness was bellow 9mm. The actual stress level in the poly could be much higher considering the locking mechanism detail but should follow the same trend discovered in this study. These stress pattern trend could become of increasing concern with the shrinking unsupported poly thicknesses associated with the use of larger femoral heads.



Loading conditions for 40mm head assembly with no rim support 1a and with rim support 1b



Fig. 2, Maximum principal stress at rim as a function of poly thickness

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#### ABRASION OF CERAMIC FEMORAL HEADS AND ITS EFFECTS ON PE WEAR

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#### Introduction

Various advanced materials have been introduced for use in total hip replacements (THR) to enhance implant performance. Excessive wear debris may result in osteolysis of the femoral stem and lead to failure [1,2]. In vivo head roughening is one source of accelerated wear and has been replicated as a severe testing model [3-7]. Zirconia reinforced alumina femoral (Biolox Delta, Stryker, Mahwah, NJ) is significantly harder and may be more scratch resistant than CoCr as a femoral head. X3, a sequentially crosslinked polyethylene, has shown improved wear characteristics, retained mechanical strength, and excellent oxidation resistance [8-10]. These properties may result in a higher tolerance to femoral roughness and result in less wear against new as well as roughened femoral heads.

Due to the difficulties in replicating third body wear in vitro, abrasive conditions will be simulated by artificial roughening of the femoral head. A diamond scratch method previously described will be used [11]. The resistance of different femoral heads to this aggressive abrasion, as well as the abrasion's effect on wear of PE will be assessed.

#### **Materials and Methods**

Acetabular inserts of two PE materials were used in this study. All samples are identical in design (28mm Trident, Stryker) and differ only in material (conventional PE n=12 and X3 n=8, Stryker). Conventional PE samples were machined from GUR 1050 material, nitrogen packed, and gamma irradiation sterilized (30kGy). X3 samples were machined from sequentially crosslinked and annealed material and gas plasma sterilized [8].

Two types of femoral heads were tested: ten CoCr (LFIT, Stryker) and ten Delta femoral heads. Half of these samples were unmodified. The remaining samples were abraded using a controlled scratching system [11]. Although previous retrieval reviews have found femoral head scratches to range from 0.3 to 1.3 um PV [12], an internal review of seven retrieved femoral heads (1 mo to 14 years in vivo) found more severe scratching. The average PV was 1.8 um with the most severely damaged head having an average PV of  $3.5\pm3.1$  um (Zygo NewView 6000 at 100X magnification). A 30N load was found to simulate these scratches.

Hip simulation (MTS, Eden Prairie MN) was run for 2 million cycles (mc) using physiological orientation (50° cup inclination) and a 23° biaxial rocking motion to simulate the walking gait [13,14]. Dynamic loading with a maximum of 2450N was applied at 1Hz. Alpha Calf serum (Hyclone Labs, Logan UT) diluted to 50% with DI water and EDTA was used as a lubricant [15]. The serum solution was replaced and cups were weighed every 0.5mc. Results: Average PV was 7.1um for CoCr and 0.4um for Delta heads after exposure to an identical scratching procedure. Wear rates under control conditions were statistically indifferent against either CoCr or Delta for both conventional PE (p=0.31) and X3 (p=0.53). Under abrasive conditions, the alumina bearings exhibited a clear advantage over CoCr against both PE materials (65-97% reduction, all p<0.007).

#### Discussion

Femoral head roughening is a clinically observed phenomenon that is suspected to cause increased wear of acetabular inserts. A computer controlled abrasion system was used to evaluate relative abrasion resistance of CoCr and Delta ceramic femoral heads. These heads were then used in wear simulation testing to determine the effect of this on wear of conventional and HCPE acetabular inserts. After scratching, the CoCr wear rates increased significantly against both UHMWPE inserts. On the contrary, scratched Delta heads wore at the same rate as pristine ones. The surface damage correlated with this (96% lower PV for scratched Delta versus CoCr). HCPE showed a significant reduction in wear against both CoCr and alumina and in either condition (all p<0.012). In fact, the HCPE acetabular cup against a roughened CoCr head is statistically indifferent from control (non abrasive) CoCr and Delta heads against conventional PE (p=0.21 and p=0.90).

This study demonstrates that HCPE has a clear wear rate advantage over conventional polyethylene regardless of femoral head material and abrasive condition. This study also shows that Delta heads are less susceptible to aggressive abrasive roughening. X3 has shown to be the primary factor on wear in this study. Secondary to the PE choice, a Delta femoral head demonstrates superior abrasion resistance producing lower wear against PE. Under these conditions, a Delta femoral head with an X3 acetabular liner showed the least wear.

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#### PAIN MANAGEMENT WITH ILOPROST IN POSTPARTAL WOMEN WITH BONE MARROW EDEMA SYNDROME OF THE FEMORAL HEAD

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#### Abstract

#### Rationale

Bone marrow edema syndrome (BMES) of the femoral head in pregnant women is a very rarely seen disease with disabling pain in the hip, beginning in the second or third trimester and persisting after parturition.

Methods: We treated 4 postpartal women (6 hips) presenting femoral head BMES with infusions of the prostacycline analogue iloprost (20  $\mu$ g for 5 days) followed by 3 weeks of partial weight-bearing.

#### Findings

Symptoms regressed rapidly during and after therapy. After 4 weeks all patients were asymptomatic with no limitations in ambulation. In the MRI assessment, complete regression of BMES could be detected in three patients and minor residual BMES in the femoral neck of one patient (one hip) after 3 months. Pain did not recur in any patient at a mean follow-up of 31 months (14-43 months)

#### Interpretation

The vasoactive drug iloprost has good analgesic potency in the treatment of postpartal women suffering from BMES and accelerates the natural course of the disease.

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#### CLINICAL OUTCOME OF TOTAL HIP REPLA-CEMENT WITH CEMENTED AND UNCEMEN-TED INTRA OPERATIVELY MANUFACTURED PROSTHESIS STEM.

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#### Introduction

Outcome of total hip replacement is mostly evaluated in terms of pain relief and improvement in motor function (1). We report the follow-up of a cohort (n=86) treated with intra-operatively manufactured prosthesis stem up to 1 year post-operatively. Aspects of physical health (i.e. changes in pain and gross motor functioning) as well as changes in mental health are documented using 3 patient-administered questionnaires.

Materials and methods

All patients were treated with custom-made implants. The average age at operation was 64.3 years ( $\pm$  11.8). The majority of the patients suffered from primary coxarthrosis (n=68), followed by congentital hip dysplasia (n=10) and avascular necrosis (n=8). 30 subjects received an uncemented prosthesis. In 56 patients a cemented prosthesis was used. The average age of the two groups differed significantly (p<0.01); 53.9 y (±7.6y) and 69.8 y (±11.3y) for respectively uncemented and cemented THP. Patients were evaluated pre-operatively and postoperatively at 6 weeks, 3 months, 6 months and 1 year. Three patient-administered questionnaires were used: Harris Hip Score (HHS) (2) Hip disability and osteoarthritis outcome score (HOOS) (3) and SF-36, multi-purpose, short-form health survey (4). Differences between subsequent time points and between the 2 groups were evaluated statistically using a paired student's t-test.

#### Results

In the total group, a significant increase in total HHS is found between each of the evaluation points (p<0.01). A significant increase of HHS is found for the complete study group up to 1 year after THR. In the group receiving a cemented prosthesis HHS increases up to 3 months after intervention and in the uncemented group HHS is still increasing after 1 year. (p<0.05)

Subjects with uncemented THP present significantly higher HHS scores 6 months and 1 year postoperatively (p<0.05). No significant differences in HOOS subscores between subjects with cemented and uncemented THP for subsequent time points were found. The scores related to Pain and Symptoms increased significantly 6 weeks after THP (p<0.01). At later evaluation points, no further increase was found.

The scores related to sports and recreation (Sport/Rec) increased significantly up to 3 months after THP (p<0.01).

The score related to Activities of daily living (ADL), as well as the score related to Quality of Life (QQL) continued to improve significantly up to 6 months after surgery (p<0.01).

The quality of life evaluation (SF36) showed no significant difference between the 2 groups. The physical component summary (PCS) increased significantly up to 3 months after surgery (p<0.01)

The mental component summary (MCS) did not change significantly after THR.

#### Discussion

The results of this prospective study indicate an improvement of the scores obtained with the 3 questionnaires. The difference noted in HHS between patients with cemented and uncemented stem fixation may be due to the selection of the fixation technique that is based on the intra-operatively observed bone quality, which is often directly related to the patient's age. The results of the HOOS score confirm the findings of the HHS. Not all patients responded to the questions relative to recreation and sport of the HOOS score. Quality of life is an important indicator for success as perceived by the patient. In this study a rapid improvement of QoL is observed (3 months) and there is little change at 6 and 12 months. The observed decrease in the mental component of the SF-36 at 3 months may partly be explained by incomplete questionnaires. The literature reports that patients find pain and functionality more important than the other components of the QoL SF-36 evalutation (5) and it is well documented that the patient's expectations prior to surgery may seriously impact the perceived QoL (6).

In clinical research, care should be taken to limit the burden of patient self-administered questionnaires. In order to improve the patients' cooperation and thus the accuracy of the responses, questionnaires should be as concise as possible with minimal overlapping topics.

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# FIXATION MODE OF AN INTRA-OPERATIVE MANUFACTURED CUSTOM MADE PROSTHE-SIS STEM INFLUENCES OUTCOME OF TOTAL HIP REPLACEMENT

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# Introduction

Success of a total hip replacement is commonly assessed by the Haris Hip Score(1) (HHS), which provides information on pain reduction and regained mobility. Radiographic images provide information relative to the stability of the prosthesis. Interpretation is based on a combination of the knowledge of clinical parameters, such as time elapsed since surgery and comparison with baseline surgery. The ARA (Agora Roentgenographic Assessment) scoring system starts from a total of 6 points, and gives negative points (from 1 to 4) for any of the "adverse" signs observed (2).

In our centre we use the intraoperatively manufactured prosthesis since 1989(3); because this is prior to the introduction of hydroxyapatite coating, the initially performed THR were done with uncoated prostheses. After introduction of the hydroxyapatite coating that resulted in a better bone ingrowth at the interface prosthesis/ bone, our prosthesis stems were coated.

We retrospectively evaluated the clinical and radiographic outcome of 3 patient cohorts.

# Materials and methods

All subjects received an intra-operatively custom made stem prosthesis.

Group 1: Uncoated stem prosthesis fixated with trochanteric osteotomy.

Group 2: Uncoated stem cementless implant

Group 3: Cementless hydroxyapatite coated stem prosthesis

Clinical assessment is commonly performed using HHS, pre-operatively and at each follow-up visit.

Radiographic imaging is performed pre-operatively, within 2 weeks postoperatively and at each follow-up visit. Baseline data are the pre-operative HHS and first radiography postoperatively. These data are compared with the data of the latest follow-up visit.

RX's are scored according to the ARA score.

#### Results

Records were analysed for 83 patients in group 1, with a mean follow-up period of 93 months. In group 2, 35 patients were followed for 105 months and 54 patients from group 3 were followed for 41 months. In the 3 groups the HHS at follow-up was > 75, this means an improvement of minimum 25 points for group 1 and 2 (baseline HHS for group 2 was not available)

The mean ARA scores at follow-up were 1.6; 1.7 and 5.3 for respectively group 1; 2 and 3

# Discussion

Clinical outcome, assessed with the HHS is comparable in the three studied cohorts.

The ARA score is indicating poor outcome for the uncoated prosthesis, regardless of the type of fixation, while the coated prosthesis group has a good to excellent ARA score.

These findings tend to confirm the superiority of the hydroxyapatite coated prosthesis. However, the duration of follow up of the cohort with a hydroxyapatite coated prosthesis is much shorter than for the other two groups. Therefore the performance of the uncoated prostheses can not be compared with the performance of the coated prosthesis.

The results of this retrospective analysis confirm those of others that clinical performance, which is mainly judged by the patient, because pain is the most important subscore, is not a reliable predictor for potential problems with the stability of the prosthesis. Therefore regular radiographic control and systematic scoring of the X-ray imaging is required to detect potential problems early.

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# PER-OPERATIVE ASSESSMENT OF THE PRI-MARY STABILITY OF HIP PROSTHESES BY VIBRATION ANALYSIS

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#### Introduction

In total hip replacement, survival rate as well as functionality is directly related to the long term fixation stability of the prosthesis stem (1). Besides the design, material composition and surface characteristics of the implant, the initial per-operative fixation of the stem in the femoral bone has a critical influence on its long term fixation stability. Nowadays objective intra-operative assessment of primary stem stability is a challenge, surgeons having to rely mainly on their clinical experience. Excessive press-fitting of a THR femoral component can cause intra-operative fractures with an incidence of up to 30 % in revision cases (2). In a previous study (3-5) we demonstrated the feasibility and validity of a vibration analysis technique for the assessment of the femur-stem fixation in vitro. In this paper a non invasive vibration analysis technique for the mechanical characterization of the primary bone-prosthesis stability is presented.

#### Materials and methods

The vibration analysis technique was applied for the peroperative assessment of fixation stability in 30 THR patients who obtained an intra-operatively manufactured, hydroxyapatite coated, cementless prosthesis.

The surgeon inserts the implant in the femoral canal through repetitive controlled hammer blows. After each blow, the frequency response function (FRF) of the implant-bone structure is measured directly on the prosthesis neck in the range 0-10 kHz. The hammering is stopped when the FRF graph does not change noticeably anymore. Extra blows will not improve the stability of the prosthesis but will increase the fracture risk.

#### Results

Thirty cases of non cemented stems were studied in vivo. In twenty six out of thirty cases (86.7%), the correlation coefficient between the last two FRFs was above 0.99 when the surgeon stopped the insertion. In the other four cases, when the surgeon decided to stop the insertion because of suspected bone fragility, the final correlation coefficient attained lower values.



#### Conclusion

During the insertion of an intra operatively manufactured prosthesis in a femur, the changes of boundary conditions and implant stability between subsequent stages are reflected by the FRF evolution as observed peroperatively. The higher resonance frequencies are more sensitive to the stability change than the lower frequencies. This observation is in accordance with the work of Qi et al. (6). For non cemented stems, the correlation between successive FRFs can be used as a criterion for the detection of the insertion endpoint. Moreover, the FRF analysis can be used to detect dangerous situations during surgery like stem blockage and fracture risk. The per-operative experimental study should be completed and validated by an appropriate post-operative followup of the patients.

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# MODULAR TAPERED STEM IN HIP REVISION SURGERY

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## Introduction

The main objective in hip revision surgery is to ensure implant stability and restore articular function. Nevertheless, it is often difficult to achieve a satisfactory result in the femoral component, particularly when large bone defects are present. The use of monoblock tapered stems has shown very good results, with an implant survival rate of 95% at 14 years of follow-up as reported by Bohm and Bischel1.

However several studies have underlined some problems due to this kind of implant2,3,4,5,6. In particular a too valgus neck, a short offset, may result in a high risk of dislocation. In addiction monoblock stems make the control of limb lenght difficult, and potentially increase the risk of subsidence or intraoperative fracture, particularly at the beginning of the learning curve7.

So different kind of modular tapered stems with distal fixation have been developed to allow a more userfriendly restoration of limb-lenght discrepancy and an indipendent proximal control of offset and anti-retroversion.

The Restoration® Modular (Striker, Orthopaedics) is a modular tapered stem that allows good distal fixation and, thanks to its modularity, restoration of correct limb length and an appropriate proximal muscular balancing, thus providing good implant stability.

#### Materials and methods

We assessed 64 hip revisions performed on 63 patients (25 men, 38 women) with a mean age of 62 years (range 31-82). Indication for treatment was: aseptic loosening (42 cases) septic loosening (18 cases) and periprosthetic fracture (4 cases). Revision was partial in 8 cases and total in 56 cases. According to the Paprosky classification for bone defects, femoral defects type I (2 cases), type II (20 cases), type IIIA (25 cases) and type IIIB (13 cases); periprosthetic fractures were all type B2 according to the Vancouver classification.

In all cases we used a Cone-Conical assembled stem and a lateral approach to the hip, which was combined with a trans-femoral osteotomy in 19 cases, in order to remove a well-bonded cement mantle and/or distal cement plug or in case of cementless painful well-fixed stems. A preventive cerclage cable was used in 10 patients in case of very thin cortex. We used the minimum size stem in most of the cases.

#### Results

Mean follow-up was 20 months (range 6-36). Shortterm complications included hip dislocation (1 case), recurrent infection (1 case), stem subsidence > 5 mm (1 case). Mean Harris Hip Score improved from 43 (range 10.9-73.7) to 81.9 (range 41.9-96.9) (t test p<0.0005), while limb lenght discrepancy improved in 97% of cases with symmetry in 76%. Altogether we observed good or excellent results in 85% of the cases. The most recent radiographic follow-up showed a good distal implant fixation in all cases and a satisfactory proximal osteointegration in 79% of the cases.

#### Conclusions

In our experience the use of modular revision stems is an effective alternative in hip revision surgery when there are large femoral defects or periprosthetic fractures that make the implant instable at the metaphysis and isthmus. Distal fixation ensures good primary stability of the implant and therefore reduces failures, especially in the short term. Furthermore, modularity enables the implant to be tailored to the patient, allowing restoration of the limb length and correct muscular balancing. Nevertheless, further studies are necessary to clarify the characteristics of such devices in the mid and long term on larger samples of patients.

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## RADIOSTEREOMETRIC EVALUATION OF A SYNTHETIC HYDROXYAPATITE GRAFT EXPANDER IMPACTION GRAFTING REVISION HIP ARTHROPLASTY

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# Introduction

Impaction allografting is an established method of restoring deficient bone during revision arthroplasty of the hip. Synthetic graft materials designed to augment pure allograft have been developed, and while numerous tests have been made on the mechanical performance of these materials in the laboratory1,2, their performance in-vivo has still to be established.

This randomized study uses Radiostereometry (RSA) to compare the migration of the implants, graft material and cement following impaction grafting in patients with and without the addition of a graft expander.

#### **Materials and Methods**

Patient inclusion criteria included: acetabular and or femoral defects from aseptically loosened primary THR undergoing cemented revision with impaction grafting; age 55-80 years; initial diagnosis of osteo arthritis; good health with reasonable daily activity level. Exclusion criteria included: previous surgery for inflammatory arthritis; renal impairment; revision for peri-prosthetic fracture; local radiation therapy of the hip; immuno-suppressive condition or recent high dose steroid treatment.

For the treatment of defects patients were randomized to two groups, receiving either pure allograft or a 50% mixture with a porous hydroxyapatite material (IG-Pore, ApaTech Ltd). Allograft was prepared from fresh frozen femoral heads or tibial plateaux. Cartilage and soft tissue were thoroughly removed.

An antero-lateral approach was used. Defects were impacted with the graft material. The RSA Ogee Charnley UHMWPE cup (Depuy Int. Ltd., Leeds, UK) was implanted into the acetabulum and the Exeter stem prostheses (Stryker Howmedica Ltd) implanted into the femur using antibiotic Simplex cement (Stryker Howmedica Ltd).

Tantalum markers (8-12) were inserted in a well spread pattern into both the pelvis and femur. 10 markers were inserted during manufacture in the cup. To observe movement of the graft, single markers were inserted into small pieces of graft before impaction: 3-4 for the pelvis and 3-6 for the femur. Finally the femoral cement mantle was also marked: two markers were attached to the stem centralizer, and after stem insertion two were placed into the proximal cement medially and two laterally.

RSA examinations were preformed supine, postop before weight bearing, and then at 1,6,13,26,52 and 104 weeks. A uniplanar setup was used and the films were scanned and analysed using local software and UMRSA version 6.0 (RSA Biomedical AB, Sweden).

The femur markers were used as a reference for the femoral head, cement and graft. The pelvic markers were used as a reference for the movement of the cup and acetabular graft markers. The cup was used as a reference to assess wear (penetration of the head).

For this RSA analysis to the 2 year followup, a total of 26 patients (14 allograft and 12 mixed) were available for the pelvis, and 18 patients (10 allograft and 8 mixed) for the femur. The Mann Whitney U test was used (SPSS 15) to determine differences at specified time points from the 1 week exam for any parameter between the two graft groups.

## Results

No significant differences were seen in the migration of the cup, nor in the pelvic graft markers. Cup wear was also similar between the groups.

The femoral head moved posterior and distally in both groups, this appeared greater for the allograft group but not significantly so.

Femoral graft markers showed a greater distal movement from 0 to 26 months (p < 0.05).

Significantly higher distal movement of the cement markers near the prosthesis stem tip was seen at all time points (p < 0.05).

The proximo-lateral cement markers moved medially for the allograft but not for the mix (difference p < 0.01 all time points). At 2 years this movement reached a median (IQR) of 0.4 (0.2 - 0.9) mm for allograft and 0.0 (-0.1 - 0.1) mm for the mix group.

The proximo-medial cement markers migrated medially and distally, however there was no difference between the groups.

# Discussion

Observation of medial movement of the proximo-lateral cement markers for the allograft group is very interesting and requires further investigation. The lack of an equivalent movement of the medial markers indicates a possible rotational movement the cement mantle.

The differences observed for the femur certainly indicate an increased support was achieved with the addition of the IG-PORE.

A concern has been raised that there may be an increase in third body wear from particle of the hard ceramic bone substitute being liberated into the joint space2. Our results do not support this, since no difference in wear was observed between the groups, however it would be prudent to follow larger of patients before reaching any firm conclusions.

#### Conclusions

Mechanical stability appears to have been increased with the addition of 50% graft expander. This is in agreement with laboratory findings both with this product (1) and with an alternative (2).

While this increased mechanical stability is probably beneficial in the short term, it remains to be seen whether there will be changes at 5 to 10 years due to different osseo-integration characteristics with IG-PORE bone substitute compared to allograft.

#### **References:**

1. Munro NA, Downing MR, et al., Hydroxyapatite Graft Substitute Reduces Subsidence in a Femoral Impaction Grafting Model. Clinical Orthopaedics & Rel Res. 2007 Feb;455:246-52. 2. Blom AW, Grimm B, et. al., Subsidence in impaction grafting: the effect of adding a ceramic bone graft extender to bone. Proc IMECH, J. Eng. in Med., 2002, 216 (4):265-270