ARCTIC ENVIROMENT IN DEFIANCE TO FAST-TRACK OPERATIONS ON HIPFRACTURES - A CHALLENGE ENLIGHTED

Elisabeth Charlotte Hansen[1], Steen-Erik Christensen[1], Ane Simony[2], Frank Damborg[1], Stig Andersen[3,4]

[1]Queen Ingrids Hospital, Department of Orthopedic Surgery, Nuuk, Greenland, *[2]Sygehus Lillebælt, Ortopædkirurgisk Afdeling, Kolding, Denmark*, *[3]Queen Ingrids Hospital, Medical Department, Nuuk, Greenland*, *[4]Aalborg University Hospital, Geriatric Department, Aalborg, Denmark*

Introduction: Most western countries have implemented fast-track hip fracture aiming at surgery within 24 hours, since the mortality rate hereafter rises markedly.

In Greenland, it is not achievable to operate within 24 hours. Arctic people live in sparsely populated areas and Greenland's population is scattered along the vast coastline. All patients must be chartered to Nuuk by airplane which can take up till several days to weeks, due to logistics and the Arctic weather. This presents a challenge regarding adhering to western guidelines. The operative delay may be acceptable though, as it is the impression that the Greenlandic population survives and endures better than patients of western populations.

However, as data are lacking, we aimed to describe mortality among hip fracture patients in Greenland taking frailty and comorbidities into account.

Method: All patients with ICD-10 codes DS720, DS721 and DS722 from 2018-2022 were identified as 261 patients diagnosed with hip fractures. Variables including time of diagnosis, time to operation, reasons for delay, ASA-score, Charlson Comorbidity index, time of death, and other possible confounding variables were analyzed. Primary outcome was mortality rates at 30-day post-OP and 1-year post-OP.

Results: The average time from fracture to operation was 91.4 hours. In the Danish Cohort (DC) 70,6 % of patient were operated within 24 hours. Overall, 30-day mortality was 9,9 %, and 1-year mortality was 29,4 %, compared to the DC with 10,8 % 30-day mortality and 28,3 % 1-year mortality.

Multivariate regression was conducted, showing no statiscal significant increase in mortality, despite extended delay.

Conclusion: 0

With no increase in death, the authors find it justifiable that patients in Greenland endure longer delays than the western population. The influence on further adverse effects needs to be investigated as well as causes of survival, but perhaps the Arctic people unveil mechanisms for raised survival among other populations.

DOES SHAPE SYMMETRY EXIST IN THE LUNATE BONE? TOWARDS DEVELOPMENT OF A PATIENT-SPECIFIC LUNATE IMPLANT

Nazli Tümer[1], Johan van der Stok[2,3], Rui Lima[1], Ian Blom[2], Gerald Kraan[1,2]

[1]Technical University, Delft, Netherlands, *[2]Reinier Haga Orthopaedic Centre, Zoetermeer, Netherlands*, *[3]University Hospital Limerick, Limerick, Ireland*

Introduction: Kienböck's disease is generally defined as the collapse of the lunate bone, and this may lead to early wrist osteoarthritis. Replacing the collapsed lunate with an implant has regained renewed interest with the advancing technology of additive manufacturing, enabling the design of patient-specific implants. The aims of this project are (1) to determine how accurate it is to use the contralateral lunate shape as a template for patient-specific lunate implants, and (2) to study the effects of shape variations wrist kinematics using 4D-computed tomography (CT) scanning.

Methods: A 3D statistical shape model (SSM) of the lunate was built based on bilateral CT scans of 54 individuals. Using SMM, shape variations of the lunate were identified and the intra- and inter-subject shape variations were compared by performing an intraclass correlation analysis. A radiolucent motor-controlled wrist-holder was designed to guide flexion/extension and radial/ulnar deviation of *ex vivo* wrist specimens under 4D-CT scanning. In this pilot, three shape mode variations were tested per specimen in two specimens were. After post-processing each CT, the scapholunate angle (SLA) and capitolunate angle (CLA) were measured.

Results: The shape of the lunate was not symmetrical, defined as exceeding the intra-subject variation in five different shape modes. The FE tests show a generalized increase in scapholunate and capitolunate angle when using lunate implants, and comparing variation of shape modes showed that shape mode 3 has a significant effect on the measured angles ($p<0.05$).

Discussion: The design of patient-specific lunate implants may prove to be challenging using a 'mirror'-design as it will lead to a degree of shape asymmetry. The pilot study, to determine the effects of those shape variations on wrist kinematics suggest that the degree of shape variation observed indeed may alter the wrist kinematics, although this needs to be further investigated in study using more specimens.

BONE PEG-IN-BONE TECHNIQUE FOR LONG BONE NON-UNIONS: A RETROSPECTIVE REVIEW

Ajit Chalak[1], Sushmit Singh[2], Sachin Kale[1]

[1]D Y Patil Medical College Hospital and Research Centre, Navi Mumbai, India, *[2]Warrington and Halton Teaching Hospitals NHS Trust, United Kingdom*

Introduction: The non-union of long bones poses a substantial challenge to clinicians and patients alike. The Ilizarov fixation system and Limb Reconstruction System (LRS), renowned for their versatility in managing complex non-unions. The purpose of this retrospective study was to assess the outcomes of acute docking with the bone peg-in-bone technique for the management of non-unions of long bones. The study seeks to evaluate its effectiveness in achieving complete bony union, preserving limb length and alignment, correcting existing deformities, and preventing the onset of new ones.

Method: A retrospective analysis of 42 patients was done with infected and non-infected non-unions of long bones who received treatment at a tertiary care hospital between April 2016 to April 2022. We utilized the Association for the Study and Application of Methods of the Ilizarov (ASAMI) scoring system to assess both bone and functional outcomes and measured mechanical lateral distal femoral angle (mLDFA) for the femur and the medial proximal tibial angle (MPTA) for the tibia.

Result: In our retrospective study involving 42 patients, a total of 30 patients had post debridement gap of >2 cm and average gap of 4.54 cm (range 1 - 13 cm) and therefore underwent corticotomy and lengthening. The average external fixation time was 6.52 (range 4 – 11 months) and average external fixation index of 2.08 (range 0.4 – 4.5 months/cm). The ASAMI scoring system showed bone result of 38 excellent, 3 good and 1 fair. Functional result of 40 excellent and 2 good outcomes. The post op mLDFA and MPTA were in normal range except in 3 patients which not statistically significant.

Conclusion: In conclusion, the use of acute docking provides several advantages such as promoting early fracture healing, increasing stability, shortening treatment time, reducing the number of surgical procedures and reduced number of complications.

BIENNIAL EXPERIENCE OF ROBOTIC TECHNOLOGIES, ARTIFICIAL INTELLIGENCE AND TELEREHABILITATION IN KNEE PROSTHETICS: ANALYSIS, CORRELATIONS AND FUTURE PROSPECTS

Rocco Maria Panzera[1,2,3]

[1]Università Cattolica del Sacro Cuore, Italy, *[2]Azienda USL Toscana Sud Est, Italy*, *[3]Fondazione Poliambulanza Istituto Ospedaliero, Italy*

Introduction: Orthopedics is experiencing a significant transformation with the introduction of technologies such as robotics and apps. These, integrated into the post-operative rehabilitation process, promise to improve clinical outcomes, patient satisfaction, and the overall efficiency of the healthcare system. This study examines the impact of an app called Mymobility and intra-operative data collected via the ROSA® robotic system on the functional recovery of patients undergoing robot-assisted knee arthroplasty.

Method: The study was conducted at a single center from 2020 to 2023. Data from 436 patients were included, divided into “active” patients (active users of Mymobility) and “non-active” patients. Clinical analyses and satisfaction surveys were carried out on active patients. The intra-operative parameters recorded by ROSA® were correlated with the Patient-Reported Outcome Measures (PROMs) collected via Mymobility

Result: Intra-operative data showed significant correlations with PROMs for the 48 active patients, highlighting the importance of parameters such as medial joint space and ligament laxity. No significant differences were observed between the sexes, but a positive correlation was detected between age and PROMs. The data analysis indicated that an increased medial joint space and reduced ligament laxity are associated with better PROMs. The adoption of Mymobility remained limited, with only 10% of patients fully utilizing the app. Critical factors have been identified to improve recruitment, engagement, and overall experience with the platform.

Conclusion: The integration of technologies such as Mymobility and ROSA® in post-operative rehabilitation offers numerous advantages, including the objectification of data, active patient involvement, and personalized care. Challenges remain related to costs, patient compliance, and demographic limitations. Nevertheless, these technologies represent a milestone in modern peri-operative management, being able to improve clinical outcomes and the quality of care.

THE ROLE OF REPEAT POST-OPERATIVE RADIOGRAPHS IN PREDICTING REVISION SURGERY FOLLOWING PRIMARY KNEE ARTHROPLASTY USING MACHINE LEARNING

Sevasti Panagiota Glynou[1], Omar Musbahi[2], Justin Cobb[2]

[1]Department of Surgery and Cancer, Imperial College London, White City Campus, London , United Kingdom, *[2]Department of Surgery and Cancer, Imperial College London, White City Campus, London, United Kingdom*

Introduction: Knee arthroplasty (KA), encompassing Total Knee Replacement (TKR) and Unicompartmental Knee Replacement (UKR), is one of the most common orthopedic procedures, aimed at alleviating severe knee arthritis. Postoperative KA management, especially radiographic imaging, remains a substantial financial burden and lacks standardised protocols for its clinical utility during follow-up.

Method: In this retrospective multicentre cohort study, data were analysed from January 2014 to March 2020 for adult patients undergoing primary KA at Imperial NHS Trust. Patients were followed over a five-year period. Four machine learning models were developed to evaluate if post-operative X-ray frequency can predict revision surgery. The best-performing model was used to assess the risk of revision surgery associated with different number of X-rays.

Result: The study assessed 289 knees with a 2.4% revision rate. The revision group had more X-rays on average than the primary group. The best performing model was Logistic Regression (LR), which indicated that each additional X-ray raised the revision risk by 52% ($p<0.001$). Notably, having four or more X-rays was linked to a three-fold increase in risk of revision (OR=3.02; $p<0.001$). Our results align with the literature that immediate post-operative X-rays have limited utility, making the 2nd post-operative X-ray of highest importance in understanding the patient's trajectory. These insights can enhance management by improving risk stratification for patients at higher revision surgery risk. Despite LR being the best-performing model, it is limited by the dataset's significant class imbalance.

Conclusion: X-ray frequency can independently predict revision surgery. This study provides insights that can guide surgeons in evidence-based post-operative decision-making. To use those findings and influence post-operative management, future studies should build on this predictive model by incorporating a more robust dataset, surgical indications, and X-ray findings. This will allow early identification of high-risk patients, allowing for personalised post-operative recommendations.

USE OF THE TROCHANTERIC FIXATION NAIL ADVANCED (TFNA) MAY INCREASE THE RISK FOR NAIL BREAKAGE AND EARLY BREAKAGE TIME COMPARED TO OTHER FREQUENTLY USED IMPLANTS

Leevi Karjalainen[1], Miika Lähdesmäki[1], Antti Ylitalo[1], Antti Eskelinen[2], Ville M Mattila[1], Jussi Repo[1]

[1]Tampere University Hospital, Tampere, Finland, *[2]Coxa Hospital for Joint Replacement, Tampere, Finland*

Background: Cephalomedullary nails are widely used for fixation of unstable pertrochanteric fractures. In 2018, the Depuy Synthes Trochanteric Fixation Nail - Advanced (TFNA) implant was introduced at a level I academic trauma center. Thereafter, the TFNA swiftly replaced the older implant models used at the time. Subsequently, clinical concerns were raised about the use of the TFNA due to reports of nail breakage. The purpose of this study was to investigate whether the concerns raised about the performance of the TFNA were valid and to assess long-term outcomes.

Methods: The data consisted of 2397 patients who had undergone a proximal femoral hip fracture procedure between 2014 and 2020. Data were handpicked from patient records. TFNA was compared with TFN, PFNA, Gamma3, and Intertan regarding nail breakage, breakage time and long-term outcomes.

Results: After exclusion a total of 23/1667 (1.4%) nails broke during the follow-up period. The TFNA broke the most often with 15 cases (2.0%), followed by the Gamma3 with five cases (1.1 %) and the PFNA with three cases (1.3%). Overall, the mean (SD) nail breakage time was 233 (147.8) days. However, for the TFNA, PFNA, and Gamma3, the mean breakage times were 176.8 days (109.9), 419 days (108.6), and 291.8 (153.4), respectively. In cox regression analysis we observed significant reduction in nail breakage when using PFNA with adjusted hazard risk of 0.081 [95% Ci, 0.011-0.576, p=0.011].

Conclusions: In our data, the TFNA had a slightly higher risk for nail breakage when compared to the PFNA and the Gamma3, with a risk difference of 0.7% and 0.9%, respectively. On average, the TFNA broke nearly four months earlier than the Gamma3 and more than eight months earlier than the PFNA. It should be noted, however, that implant breakage is a relatively infrequent complication.

AI-BASED AUTOMATED VARUS/VALGUS ALIGNMENT MEASUREMENT IN STANDARD KNEE RADIOGRAPHS

Dominic Cullen[1,2], Peter Thompson[1], David Johnson[3], Claudia Lindner[1]

[1]The University of Manchester, United Kingdom, *[2]Northern Care Alliance NHS Foundation Trust, United Kingdom*, *[3]Stockport NHS Foundation Trust, United Kingdom*

Introduction: Accurate assessment of alignment in pre-operative and post-operative knee radiographs is important for planning and evaluating knee replacement surgery. Existing methods predominantly rely on manual measurements using long-leg radiographs, which are time-consuming to perform and are prone to reliability errors. In this study, we propose a machine-learning-based approach to automatically measure anatomical varus/valgus alignment in pre-operative and post-operative standard AP knee radiographs.

Method: We collected a training dataset of 816 pre-operative and 457 one-year post-operative AP knee radiographs of patients who underwent knee replacement surgery. Further, we have collected a separate distinct test dataset with both pre-operative and one-year post-operative radiographs for 376 patients. We manually outlined the distal femur and the proximal tibia/fibula with points to capture the knee joint (including implants in the post-operative images). This included point positions used to permit calculation of the anatomical tibiofemoral angle. We defined varus/valgus as negative/positive deviations from zero. Ground truth measurements were obtained from the manually placed points. We used the training dataset to develop a machine-learning-based automatic system to locate the point positions and derive the automatic measurements. Agreement between the automatic and manual measurements for the test dataset was assessed by intra-class correlation coefficient (ICC), mean absolute difference (MAD) and Bland-Altman analysis.

Result: Analysing the agreement between the manual and automated measurements, ICC values were excellent pre-/post-operatively (0.96, CI: 0.94-0.96) / (0.95, CI: 0.95-0.96). Pre-/post-operative MAD values were 1.3°±1.4°SD / 0.7°±0.6°SD. The Bland-Altman analysis showed a pre-/post-operative mean difference (bias) of 0.3°±1.9°SD/-0.02°±0.9°SD, with pre-/post-operative 95% limits of agreement of ±3.7°/±1.8°, respectively.

Conclusion: The developed machine-learning-based system demonstrates high accuracy and reliability in automatically measuring anatomical varus/valgus alignment in pre-operative and post-operative knee radiographs. It provides a promising approach for automating the measurement of anatomical alignment without the need for long-leg radiographs.

Acknowledgements: This research was funded by the Wellcome Trust [223267/Z/21/Z].

STUDY TO EVALUATE NON OPERATIVE MANAGEMENT OF STABLE ANKLE FRACTURES AT A UNIVERSITY HOSPITAL.

Satya Sudhakara Bhat[1], Naveen Joseph Mathai[1], Ram Raghavendra[1], Paul Hodgson[1]

[1]*Cardiff and Vale university Health Board , United Kingdom*

Introduction: As per national guidelines for Ankle fractures in the United Kingdom, fractures considered stable can be treated with analgesia, splinting and allowed to weight bear as tolerated. The guidelines also suggest further follow-up not mandatory. This study was aimed at evaluating the current clinical practice of managing stable ankle fractures at a university hospital against national guidelines.

Method: The study was undertaken using retrospectively collected data, the inclusion criteria being all adults with stable ankle fracture pattern treated non-operatively between December 2022 and April 2023. Collected data included age of patient, date of injury, type of immobilization, number of clinical visits and any complications.

Results: 41 cases were identified and analyzed. The mean age of the cohort was 49.8 years (Standard deviation 20.01). Twelve percent (n = 5) were reviewed in clinic, treated and discharged as stable Weber B type fracture pattern as per national guidelines after the first visit. About 52% (n = 21) were seen in clinic twice before discharge, first visit between 1-2 weeks and the last clinic visit between 5-7 weeks . About a third of patients (30%, n = 12) were seen in clinic on more than two occasions. At the first clinic visit 87% (n = 36) were given a boot and allowed to weight bear as tolerated. Two patients were diagnosed with deep vein thrombosis/pulmonary embolism during the treatment duration. Three patients had extended duration of follow up for ongoing symptoms. None discharged after first or second visit needed surgery for displaced or malunited fracture.

Conclusion: Patients discharged from clinic after first or second visit did not need any further surgery. As per national guidelines, patients deemed stable weber B lateral malleolus fracture pattern after weight bearing radiograph can be treated safely with a weight bearing walking boot with no further follow up.

COMPLICATIONS FOLLOWING INTRAMEDULLARY NAILING OF DIAPHYSEAL FEMUR FRACTURES IN A LEVEL I TRAUMA CENTER IN FINLAND

Miika Lähdesmäki[1], Antti Ylitalo[2], Rasmus Liukkonen[1], Viivi Suominen[1], Leevi Karjalainen[1], Ville M Mattila[2], Jussi Repo[2]

[1]Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland, *[2]Unit of Musculoskeletal Surgery, Department of Orthopaedics and Traumatology, Tampere University Hospital, Tampere, Finland*

Introduction: We aimed to study the rates of both surgical and medical complications associated with femoral diaphysis fracture fixation with intramedullary nailing including all fracture mechanisms. Additionally, we investigated whether the trauma energy has an impact on the complication risk.

Method: In this retrospective cohort study, the health records of 491 patients with 503 femoral fractures, who underwent surgery between May 2007 and May 2022 in Tampere University Hospital, were reviewed. Patients who underwent a primary operation with a reamed rigid intramedullary nail for a diaphyseal femoral fracture and whose follow-ups were organized at the same hospital district, were included. Based on those criteria, 57.5% were included for analysis (279 patients with 289 fractures). The complications were then recorded by chart review. To investigate the impact of trauma energy on complication risk, we compared complication proportions in high- and low-energy groups and calculated odds ratios.

Result: The crude percentage of 30-day mortality was 2.1% (6 of 289) based on information obtained from the patients' records. The overall proportion of complications was 22.5%. The risk of any medical complication was 2.8%, whereas the risk of surgical complication was 19.8%. The risk of complications was nearly twice as high in high-energy fractures compared to low-energy fractures, with an odds ratio (OR) of 1.92, 95% CI 1.03-3.75. The risk of reoperations was significantly increased in high-energy traumas (OR 2.46, CI 1.25-5.24).

Conclusion: This study reveals a 2.1% risk of thirdy-day mortality and a 22.5% risk of overall complications, predominantly of a surgical type. The complication risk, especially the risk of surgical complications, is higher among the patients with fractures caused by high-energy injury compared to low-energy fractures, highlighting the importance of timely identification of those complications for providing better postoperative care.

3D SPHEROID CULTURE OF CHONDROCYTES TO STUDY THE INTERACTION OF CELLS AT THE CHONDRO-OSSEOUS BORDER OF ENCHONDRAL OSSIFICATION

Elnaz Enderami[1], Melanie Timmen[1], Richard Stange[1]

[1]*Institute of Musculoskeletal Medicine, University of Muenster, Münster, Germany*

Introduction: Cartilage comprises chondrocytes and extracellular matrix. The matrix contains different collagens, proteoglycans, and growth factors produced by chondroprogenitor cells that differentiate from proliferating to hypertrophic chondrocytes. In vitro chondrocyte growth is challenging due to differences in behaviour between 2D and 3D cultures. Our aim is to establish a murine 3D spheroid culture method using chondrocytes to study the complex interaction of cells on the chondro-osseous border during enchondral ossification.

Method: Primary chondrocytes were isolated from the knee of WT new-born mice and used to form 10,000 cell number spheroids. We used the ATDC5-chondrocyte cell line as an alternative cell type. Spheroids were observed for 7, 14, and 21 days before embedding in paraffin for slicing. Alcian blue staining was performed to identify proteoglycan positive areas to prove the formation of extracellular matrix in spheroids. Collagen type 2, and Collagen type X expression were analyzed via quantitative real-time PCR and immunohistochemistry.

Result: Alcian blue staining showed increasing matrix formation from day 7 to day 14 and proliferative chondrocytes at early time points. Both cell types showed increasing mRNA expression of Collagen type 2 from day 7 to day 21. Collagen type X positive staining starting from day 14 on confirmed the development of hypertrophic stage of chondrocytes. ATDC5 cells exhibited a slower progression in chondrogenic differentiation compared to primary chondrocytes.

Conclusion: In chondrocyte spheroids, we observed proceeding differentiation of chondrocytes reaching hypertrophic phase. Primary chondrocytes showed faster development than ATDC5 cell line. Overall, spheroid culture of chondrocytes could be a good basis to study the interaction of different cells types of the chondro-osseous border by combination of chondrocytes with e.g., endothelial cells and osteoblasts within the spheroid. Those organoid cultures might also help to reduce animal experiments in the future, by mimicking complex regeneration procedures like bone growth or fracture healing.

DFG(German Research Foundation)

EVALUATING THE BIOMECHANICAL EFFICACY OF 2.5-MM AND 2.0-MM DOUBLE PLATING AGAINST 3.5-MM SINGLE PLATING IN ULNA SHAFT FRACTURE FIXATION: A CADAVERIC STUDY

Ivan Zderic[1], Moritz Kraus[1], Luke van Rossenberg[1], Luise Puls[1], Tatjana Pastor[2], Boyko Gueorguiev[1], Geoff Richards[1], Hans Christoph Pape[3], Torsten Pastor[4]

[1]AO Research Institute Davos, Davos, Switzerland, *[2]Bürgerspital Solothurn, Solothurn, Switzerland*, *[3]University Hospital Zürich, Zürich, Switzerland*, *[4]Cantonal Hospital Lucerne, Wolhusen, Switzerland*

Introduction: The main postoperative complications in fixation of ulna shaft fractures are non-union and implant irritation using currently recommended 3.5-mm locking compression plates. An alternative approach using a combination of two smaller plates in orthogonal configuration has been proposed. The aim of this study was to compare the biomechanical properties of a single 3.5-mm locking compression plate versus double plating using one 2.5-mm and one 2.0-mm mandible plate in a human ulna shaft fracture model.

Method: Eight pairs human ulnar specimens with a standardized 10-mm fracture gap were pairwise assigned for instrumentation with either a single 3.5-mm plate placed posteriorly, or for double plating using a 2.5-mm and a 2.0-mm mandible plate placed posteriorly under the flexor muscles and laterally under the extensor muscles. All constructs were initially non-destructively biomechanically tested in axial compression, torsion, and bending, which was followed by cyclic torsional loading to failure. Interfragmentary movements were monitored by means of optical motion tracking.

Result: There were no significant differences between the two plating techniques for axial stiffness ($p=0.335$), torsional stiffness in supination ($p=0.462$), torsional stiffness in pronation ($p=0.307$), medio-lateral bending stiffness ($p=0.522$), and antero-posterior bending stiffness ($p=0.143$). During cyclic torsional loading over the first 3000 cycles, there were no significant differences between the two plating techniques for shear displacement across the fracture gap, $p=0.324$. The numbers of cycles until clinically relevant failure of 5° angular deformation were 1366±685 for double plating and 2024±958 for single plating, which was statistically non-significantly different, $p>0.05$. The constructs treated with both plating techniques failed due to bone breakage at the most distal screw.

Conclusion: From a biomechanical perspective double plating of ulna shaft fractures using a 2.5-mm and a 2.0-mm locking mandible plate demonstrated equivalent fixation strength as conventional plating using a single 3.5-mm locking compression plate.

BONE-TO-CARTILAGE INTERFACES: ADVANCING 3D PRINTED NANOCOMPOSITES FROM NATURAL-DERIVED LOW-VISCOUS BIOMATERIALS

João Maia[1], Miguel Bilo[1], Ana Sofia Silva[1], Rita Sobreiro-Almeida[1], João Mano[1]

[1]*University of Aveiro, Aveiro, Portugal*

Introduction: Ink engineering can advance 3D-printability for better therapeutics, with optimized proprieties. Herein, we describe a methodology for yielding 3D-printable nanocomposite inks (NC) using low-viscous matrices, via the interaction between the organic and inorganic phases by chemical coupling.

Method: Natural photocurable matrices were synthesized: a protein – bovine serum albumin methacrylate (BSAMA), and a polysaccharide – hyaluronic acid methacrylate (HAMA). Bioglass nanoparticles (BGNP) were synthesized and functionalized via aminosilane chemistry. The functionalization of BSAMA, HAMA, and BGNP were quantified via NMR. To arise extrudable inks, 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC) and N-Hydroxysuccinimide (NHS) chemistry was used to link innate carboxylic groups of BSAMA/HAMA and amine-functionalized BGNP. Different crosslinker and BGNP amounts were tested. Visible light photopolymerization is performed, using lithium phenyl-2,4,6-trimethylbenzoylphosphinate. The NC's rheological, mechanical, and biological behavior was evaluated before 3D extrusion printability.

Result: All composite formulations effectively immobilized and homogeneously dispersed the BGNP, turning low-viscous materials (< 1 Pa) into shear-thinning formulations with tunable increased elastic/viscous moduli (50-500 Pa). More pronounced increments were found with increasing EDC/NHS and BGNP concentrations. The resulting inks produce robust and stable scaffolds successfully retrieved after post-print photocrosslinking (1-5 kPa). Bioactivity in simulated body fluid and in vitro assays using adipose-derive stem cells revealed a similar calcium/phosphate ratio to that of hydroxyapatite, and increased viability and metabolic activity. BSAMA and HAMA demonstrated distinct natures not only in printability but also in overall cellular performance and mechanical properties, making these ideal for interfacial tissue engineering.

Conclusion: This strategy demonstrated being effective and reproducible to advance nanocomposites for 3D printing using different types of biomaterials. Further, we envision using both inks to produce hierarchical constructs via extrusion printing, better mimicking bone-to-cartilage interfaces.

Acknowledgements: FCT grants (DOI:10.54499/2022.04605.CEECIND/CP1720/CT0021), (BI/UI89/10303/2022), (PRT/BD/154735/2023); EU's Horizon 2020 research and innovation programs InterLynk (Nº953169) and SUPRALIFE (Nº101079482) projects; CICECO-Aveiro Institute of Materials projects (DOI:10.54499/UIDB/50011/2020), (DOI:10.54499/UIDP/50011/2020), and (DOI:10.54499/LA/P/0006/2020), financed by FCT/MCTES(PIDDAC).

BONE-IMPLANT PRIMARY STABILITY PREDICTION BY CBCT-BASED FINITE ELEMENT SIMULATIONS

Antoine Vautrin[1], Raphael Thierrin[2], Patrik Wili[2], Benjamin Voumard[2], Cedric Rauber[2], Samuel Klingler[3], Vivianne Chapuis[3], Peter Varga[1], Philippe Zysset[2]

[1]AO Research Institute Davos, Davos-Platz, Switzerland, *[2]ARTORG Centre for Biomedical Engineering Research, University of Bern, Bern, Switzerland*, *[3]School of Dental Medicine, University of Bern, Bern, Switzerland*

Introduction: Achieving an appropriate primary stability after implantation is a prerequisite for the long-term viability of a dental implant. Virtual testing of the bone-implant construct can be performed with finite element (FE) simulation to predict primary stability prior to implantation. In order to be translated to clinical practice, such FE modeling must be based on clinically available imaging methods. The aim of this study was to validate an FE model of dental implant primary stability using cone beam computed tomography (CBCT) with *ex vivo* mechanical testing.

Method: Three cadaveric mandibles (male donors, 87-97 years old) were scanned by CBCT. Twenty-three bone samples were extracted from the bones and conventional dental implants (Ø4.0mm, 9.5mm length) were inserted in each. The implanted specimens were tested under quasi-static bending-compression load (cf. ISO 14801).

Sample-specific homogenized FE (hFE) models were created from the CBCT images and meshed with hexahedral elements. A non-linear constitutive model with element-wise density-based material properties was used to simulate bone and the implant was considered rigid. The experimental loading conditions were replicated in the FE model and the ultimate force was evaluated.

Result: The experimental ultimate force ranged between 67 N and 789 N. The simulated ultimate force correlated better with the experimental ultimate force (R^2=0.71) than the peri-implant bone density (R^2=0.30).

Conclusion: The developed hFE model was demonstrated to provide stronger prediction of primary stability than peri-implant bone density. Therefore, hFE Simulations based on this clinically available low-radiation imaging modality, is a promising technology that could be used in future as a surgery planning tool to assist the clinician in evaluating the load-bearing capacity of an implantation site.

Acknowledgements:

Funding: EU's Horizon 2020 grant No: 953128 (I-SMarD).

Dental implants: THOMMEN Medical AG

ACCURATE PREDICTION OF PEDICLE SCREW LOOSENING USING HOMOGENIZED NON-LINEAR FINITE ELEMENT MODELS

Dominic Mischler[1], Florian Kessler[2], Philippe Zysset[2], Peter Varga[1]

[1]AO Research Institute Davos, Davos, Switzerland, *[2]University of Bern, Bern, Switzerland*

Introduction: Pedicle screw loosening in posterior instrumentation of thoracolumbar spine occurs up to 60% in osteoporotic patients. These complications may be alleviated using more flexible implant materials and novel designs that could be optimized with reliable computational modeling. This study aimed to develop and validate non-linear homogenized finite element (hFE) simulations to predict pedicle screw toggling.

Method: Ten cadaveric vertebral bodies (L1-L5) from two female and three male elderly donors were scanned with high-resolution peripheral quantitative computed tomography (HR-pQCT, Scanco Medical) and instrumented with pedicle screws made of carbon fiber-reinforced polyether-etherketone (CF/PEEK). Sample-specific 3D-printed guides ensured standardized instrumentation, embedding, and loading procedures. The samples were biomechanically tested to failure in a toggling setup using an electrodynamic testing machine (Acumen, MTS) applying a quasi-static cyclic testing protocol of three ramps with exponentially increasing peak (1, 2 and 4 mm) and constant valley displacements. Implant-bone kinematics were assessed with a stereographic 3D motion tracking camera system (Aramis SRX, GOM). hFE models with non-linear, homogenized bone material properties including a strain-based damage criterion were developed based on intact HR-pQCT and instrumented 3D C-arm scans. The experimental loading conditions were imposed, the maximum load per cycle was calculated and compared to the experimental results. HR-pQCT-based bone volume fraction (BV/TV) around the screws was correlated with the experimental peak forces at each displacement level.

Result: The nonlinear hFE models accurately (slope = 1.07, intercept = 0.2 N) and precisely (R^2 = 0.84) predicted the experimental peak forces at each displacement level. BV/TV alone was a weak predictor (R^2<0.31).

Conclusion: The hFE models enable fast design iterations aiming to reduce the risk of screw loosening in low-density vertebrae. Improved flexible implant designs are expected to contribute to reduced complication rates in osteoporotic patients.

CHONDROGENESIS IN 3D PRINTED HYDROGEL SCAFFOLDS SUPPLEMENTED WITH BIOACTIVE GLASS SPHERES

Priv.-Doz. Dr. Clemens Leo Gögele[1], Nils Fleischmann[1], Dr. Silvana Müller[2], Tanja Liesenberg[2], Gina Pizzadili[1], Prof. Dr. Sven Wiltzsch[2], Prof. Dr. Thorsten Gerdes[3], Kerstin Schaefer-Eckart[4], Prof. Dr. Armin Lenhart[2], Prof. Dr. Gundula Schulze-Tanzil[1]

[1]Institute of Anatomy and Cell Biology, Paracelsus Medical University Nuremberg, Nuremberg, Germany, *[2]Faculty of Materials Science, TH Nürnberg Georg Simon Ohm, Nuremberg, Germany*, *[3]Keylab Glastechnologie, University Bayreuth, Bayreuth, Germany*, *[4]Bone marrow Transplantation Unit, Medizinische Klinik 5, Klinikum Nürnberg, Nuremberg, Germany*

Introduction: Articular cartilage has a low self-regeneration capacity. Cartilage defects have to be treated to minimize the risk of the onset of osteoarthritis. Bioactive glass (BG) is a promising source for cartilage tissue engineering. Until now, conventional BGs (like BG1393) have been used, mostly for bone regeneration, as they are able to form a hydroxyapatite layer and are therefore, less suited for cartilage reconstruction. The aim of this study is to study the effect of 3D printed hydrogel scaffolds supplemented with spheres of the BG CAR12N to improve the chondrogenesis of mesenchymal stem cells (MSCs).

Method: Based on our new glass composition (CAR12N), small BG spheres (25-40 µm) were produced and mixed with hydrogel and primary human (h) MSCs. Grid printed scaffolds were cultivated up to 21 days in expansion or chondrogenic differentiation medium. Macroscopical images of the scaffolds were taken to observe surface changes. Vitality, DNA and sulfated glycosaminoglycan (GAG) content was semiquantitatively measured as well as extracellular matrix gene transcription.

Result: It was possible to print grid shaped hydrogel scaffolds with BG spheres and hMSCs. No significant changes in scaffold shape, surface or pore size were detected after 21 days in culture. The BG spheres were homogeneously distributed inside the grids. Vitality was significantly higher in grids with CAR12N spheres in comparison to those without. The DNA content remained constant over three weeks, but was higher in the sphere containing scaffolds than in those without BG spheres. GAG content in the grids increased not only with additional cultivation time but especially in grids with BG spheres in chondrogenic medium. Aggrecan and type II collagen gene expression was significantly higher grids cultured in the chondrogenic differentiation medium.

Conclusion: This developed 3D model, is very interesting to study the effect of BG on hMSCs and to understand the influence of leaking ions on chondrogenesis.

IMPACT OF TRANSFORAMINAL LUMBAR INTERBODY FUSION ON ROD LOAD: A COMPARATIVE BIOMECHANICAL ANALYSIS BETWEEN A CADAVERIC INSTRUMENTATION AND SIMULATED BONE FUSION

Maximilian Heumann[1], Chencheng Feng[1], Lorin Benneker[2], Maarten Spruit[3], Christian Mazel[4], Jan Buschbaum[1], Boyko Gueorguiev[1], Manuela Ernst[1]

[1]AO Research Institute Davos, Davos, Switzerland, *[2]Sonnenhof Spital, Spine Unit, University of Bern, Bern, Switzerland*, *[3]Sint Maartenskliniek, Orthopedics Center, Spine Unit, Nijmegen, Netherlands*, *[4]Institute Mutualiste Montsouris, Paris, France*

Introduction: In daily clinical practice, progression of spinal fusion is typically monitored during clinical follow-up using conventional radiography and Computed Tomography scans. However, recent research has demonstrated the potential of implant load monitoring to assess posterolateral spinal fusion in an in-vivo sheep model. The question arises to whether such a strain sensing system could be used to monitor bone fusion following lumbar interbody fusion surgery, where the intervertebral space is supported by a cage. Therefore, the aim of this study was to test human cadaveric lumbar spines in two states: after a transforaminal lumbar interbody fusion (TLIF) procedure combined with a pedicle-screw-rod-construct (PSR) and subsequently after simulating bone fusion. The study hypothesized that the load on the posterior instrumentation decreases as the segment stiffens due to simulated fusion.

Method: A TLIF procedure with PSR was performed on eight human cadaveric spines at level L4-L5. Strain sensors were attached bilaterally to the rods to derive implant load changes during unconstrained flexion-extension (FE), lateral bending (LB) and axial rotation (AR) loads up to ±7.5Nm. The specimens were retested after simulating bone fusion between vertebrae L4-L5. In addition, the range of motion (ROM) was measured during each loading mode.

Result: The ROM decreased in the simulated bone fusion state in all loading directions ($p \leq 0.002$). In both states, the measured strain on the posterior instrumentation was highest during LB motion. Furthermore, the sensors detected a significant decrease in the load induced rod strain ($p \leq 0.002$) between TLIF+PSR and simulated bone fusion state in LB.

Conclusion: Implant load measured via rod strain sensors can be used to monitor the progression of fusion after a TLIF procedure when measured during LB of the lumbar spine. However, further research is needed to investigate the influence of daily loading scenarios expected in-vivo on the overall change in implant load.

CASPASES-1/-8 AND CHONDROCYTES: DRUG TARGET EFFECT AND OSTEOARTHRITIS PATHOLOGY

Jian Mei[1], Anja Pasoldt[1], Eva Matalova[2], Susanne Graessel[1]

[1]Dept. of Orthopedic Surgery, Experimental Orthopaedics, Centre for Medical Biotechnology (ZMB), Bio Park 1, Regensburg, Germany, *[2]Institute of Animal Physiology and Genetics, Czech Academy of Sciences, Brno, Czech Republic*

Introduction: Osteoarthritis (OA) is a prevalent joint disorder characterized by cartilage degeneration, inflammation, and pain. Current treatments provide only symptomatic relief, necessitating novel molecular targets. The caspase family, known for its roles in apoptosis and inflammation regulation, may additionally influence crucial processes for cartilage homeostasis such as differentiation and proliferation. However, the specific roles of individual caspases in OA pathogenesis remain unclear. This study aims to investigate the involvement of the caspase family in OA and as potential targets for therapy, with a focus on caspase-1 and -8.

Method: Chondrocytes from both healthy and OA donors were cultured in 2D and 3D culture models and stimulated with TNF-α or IL-1β. The expression and activation of caspase-1 and -8 was assessed using RT-PCR, ELISA. Transcriptome analysis of OA and healthy cartilage samples, along with Mendelian randomization (MR) analysis were conducted to explore the involvement of caspase family in OA and to assess its potential as therapeutic targets.

Result: Higher expression levels of caspase-1, -8 were observed in OA cartilage compared to healthy cartilage. TNF-α stimulation increased their expression in both healthy and OA chondrocytes, while IL-1β had limited impact. Caspase-8 expression was causally associated with knee OA in MR analysis, suggesting a potential therapeutic target. The caspase-1 inhibitor VX-765 mildly reduced chondrocyte viability, with no significant effect in the presence of TNF-α. While the caspase-8 inhibitor Z-IETD-FMK exhibited slight enhancements in cell viability, these improvements were not statistically significant. Nevertheless, its effectiveness significantly increased in the presence of TNF-α.

Conclusion: This study highlights the involvement of caspase-1 and caspase-8 in OA pathology, with caspase-8 emerging as a potential therapeutic target for knee OA treatment. Further investigation into the roles of caspase-1 and -8 in OA pathophysiology, including the efficacy and potential side effects of their corresponding inhibitors, is warranted.

Acknowledgements: Funding Inter-Action/Inter-Excellence project (BTHA-JC-2022-36/LUABA22019)

IMAGE SEGMENTATION OF ECTOPIC BONE FORMATION USING A DEEP CONVOLUTIONAL NETWORK: ANALYSIS PROTOCOL AND MATERIAL

Kristian Kjærgaard[1], Ming Ding[1], Marjan Mansourvar[2]

[1]Odense University Hospital, Odense, Denmark, *[2]Technical University of Denmark, Lyngby, Denmark*

Introduction: Experimental bone research often generates large amounts of histology and histomorphometry data, and the analysis of these data can be time-consuming and trivial. Machine learning offers a viable alternative to manual analysis for measuring e.g. bone volume versus total volume.

The objective was to develop a neural network for image segmentation, and to assess the accuracy of this network when applied to ectopic bone formation samples compared to a ground truth.

Method: Thirteen tissue slides totaling 114 megapixels of ectopic bone formation were selected for model building. Slides were split into training, validation, and test data, with the test data reserved and only used for the final model assessment. We developed a neural network resembling U-Net that takes 512x512 pixel tiles. To improve model robustness, images were augmented online during training.

The network was trained for 3 days on a NVidia Tesla K80 provided by a free online learning platform against ground truth masks annotated by an experienced researcher.

Result: During training, the validation accuracy improved and stabilised at approx. 95%. The test accuracy was 96.1 %.

Conclusion: Most experiments using ectopic bone formation will yield an inter-observer or inter-method variance of far more than 5%, so the current approach may be a valid and feasible technique for automated image segmentation for large datasets. More data or a consensus-based ground truth may improve training stability and validation accuracy.

The code and data of this project are available upon request and will be available online as part of our publication.

INCIDENCE, AND TREATMENT TRENDS OF TROCHANTERIC FRACTURES IN GERMANY—A COHORT STUDY COVERING 1.16 MILLION FRACTURES IN 15 YEARS

Yannick Rau[1], Jasper Amtsfeld[2], Nils Reimers[2,3], Lina Behrends[4], Nico Hinz[1], Arndt Peter Schulz[1,4]

[1]BG Klinikum Hamburg, Hamburg, Germany, *[2]Stryker Trauma, Kiel, Germany*, *[3]Faculty of Engineering Queensland University of Technology, Queensland, Australia*, *[4]Fraunhofer IMTE, Lübeck, Germany*

Introduction: Hip fractures, with a global age-standardised incidence rate (per 100,000 population) of 187.2 (2019), are a major public health problem. With a 7.71 billion population worldwide in 2019, hip fractures, in general, are affecting around 14.43 million people per year globally.

We aim to provide a nationwide epidemiological analysis of trochanteric fractures and their respective surgical treatments. In this study we research the epidemiology of trochanteric and subtrochanteric fractures, as well as their most common kinds of osteosynthesis, on a nationwide scale in Germany.

Method: Data was retrieved from the national database of the German Ministry of Interior. ICD-10-GM and OPS-data from the period of 2006-2020 were analyzed, all patients with trochanteric/subtrochanteric fractures were included. Patients were grouped by age/gender and linear-regression was performed to calculate statistically significant correlations between variables/incidences.

Result: 985,104 trochanteric and 178,810 subtrochanteric-fractures were reported during the analyzed period. This calculates to a mean incidence of 80.08±6.34 for pertrochanteric and 14.53±1.50 for subtrochanteric fractures per-million-inhabitants. In both fracture-types, a distinct dependence of incidence on age can be seen. Incidence rates equally rise in both sexes through the age groups with an increase of about 288-fold from those under 60 to those over the age of 90 in pertrochanteric fractures. Intramedullary nailing was the most common kind of treatment for both fracture types with augmentative cerclages on the rise throughout the whole period. Dynamic compression screws were decreasing in frequency.

Conclusion: We found an ongoing increase of incidence among the elderly and an increase in intramedullary nailing as well as augmentative cerclages. Not only could we show an age-dependence of the incidences, but also a sex-dependence that seems to remain consistent in its development. While younger males (<60 years) are at a higher risk than their female peers, older females are at significantly higher risk than their male peers.

UNRAVELING OSTEOARTHRITIC REMODELING: MATRIX METALLOPROTEINASE -2,-3,-7 AT THE CORE OF PERICELLULAR MATRIX PROTEOLYSIS

Marina Danalache[1], Felix Umrath[1], Rosa Riester[1], Maik Schwitalle[2], Farshid Guilak[3], Ulf Krister Hofmann[4]

[1]Department of Orthopedic Surgery, University Hospital of Tübingen, Tübingen, Germany, *[2]Winghofer Medicum, Rottenburg am Neckar, Germany*, *[3]Department of Orthopedic Surgery, Washington University, St Louis, United States*, *[4]Department of Orthopedic, Trauma, and Reconstructive Surgery, RWTH Aachen University Hospital, Aachen, Germany*

Introduction: Chondrocytes are enveloped within the pericellular matrix (PCM), a structurally intricate network primarily demarcated by the presence of collagen type VI microfibrils and perlecan, resembling a protective cocoon. The PCM serves pivotal functions in facilitating cell mechanoprotection and mechanotransduction. The progression of osteoarthritis (OA) is associated with alterations in the spatial arrangement of chondrocytes, transitioning from single strings to double strings, small clusters, and eventually coalescing into large clusters in advanced OA stages. Changes in cellular patters coincide with structural degradation of the PCM and loss of biomechanical properties. Here, we systematically studied matrix metalloproteinases (MMPs), their distribution, activity, and involvement in PCM destruction, utilizing chondrocyte arrangement as an OA biomarker.

Methods: Cartilage specimens were obtained from 149 osteoarthritis (OA) patients, and selected based on the predominant spatial pattern of chondrocytes. Immunoassays were employed to screen for the presence of various MMPs (-1, -2, -3, -7, -8, -9, -10, -12, -13). Subsequently, the presence and activity of elevated MMPs were further investigated through immunolabeling, western blots and zymograms. Enzymatic assays were utilized to demonstrate the direct involvement of the targeted MMPs in the PCM destruction.

Results: Screening revealed increased levels of MMP-1, -2, -3, -7, and -13, with their expression profile demonstrating a distinct dependency on the stage of degeneration. We found that MMP-2 and -3 can directly compromise the integrity of collagen type VI, whereas MMP-3 and MMP-7 disrupt perlecan.

Conclusions: Presence of both pro- and active forms of MMP-2, -3, and -7 in OA-induced patterns, along with their direct involvement in collagen type VI and perlecan degradation, underscores their crucial role in early PCM destruction. Given the early stages of the disease already exhibit heightened MMP expression, this understanding could inform early targeted therapies aimed at arresting abnormal PCM remodelling.

Acknowledgments: Faculty of Medicine of the University of Tübingen (grant: 2650-0-0).

BIOMECHANICAL ASSESSMENT OF A NOVEL PEDICLE SCREW SYSTEM USING FINITE ELEMENT ANALYSIS

Mohammadjavad (Matin) Einafshar[1], Elie Massaad[2], Ali Kiapour[2]

[1]Aalborg University, Aalborg, Denmark, *[2]Massachusetts General Hospital, Harvard Medical School, Aalborg, Denmark*

Introduction:The biomechanical behavior of lumbar spine instrumentation is critical in understanding its efficacy and durability in clinical practice. In this study, we aim to compare the biomechanics of the lumbar spine instrumented with single-level posterior rod and screw systems employing two distinct screw designs: paddle screw versus conventional screw system.

Method: A fully cadaveric-validated 3D ligamentous model of the lumbopelvic spine served as the foundation for our comparative biomechanical analysis[1]. To simulate instrumentation, the intact spine was modified at the L4L5 level, employing either paddle screws or standard pedicle screws (SPS). The implants were composed of Ti-6AL-4V. Fixation at the S1 ensured consistency across loading scenarios. Loading conditions included a 400-N compressive load combined with a 10 N.m pure bending moment at the level of L1, replicating physiological motions of flexion-extension, lateral bending and axial rotation. We extracted data across various scenarios, focusing on the segmental range of motion at both implanted and adjacent levels.

Result: In the flexion of L4L5, the applied force ranged from -29.2 to 29.3 N in the paddle screw, while it ranged from -25 to 25 N in the PS system. Similarly, the extension of L4L5 ranged from -3.1 to 2.6 N in the paddle and ranged from -4.5 to 3.9 N in the SPS system. In terms of stress distributions on the screw, stress concentrations decreased in several cases in the paddle design compared to the SPS systems.

Conclusion: The paddle screw enhanced the range of motion overall in both the upper adjacent segment (L3L4) and the lower adjacent segment (L5S1) compared to the conventional SPS system. The stability of the aimed segment was increased by 33% on average with the paddle screw compared to conventional PS. Increasing the stability of the host segment decreases the possibility of non-union and the rate of fusion failure [2].

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A MACHINE LEARNING-BASED MODEL FOR "IN-TIME" PREDICTION OF PERIPROSTHETIC JOINT INFECTION

Weishen Chen[1], Xuantao Hu[1], Puyi Sheng[1]

[1]The First Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China

Introduction: Previous criteria had limited value in early diagnosis of periprosthetic joint infection (PJI). Here, we constructed a novel machine-learning (ML)-derived, "in-time" diagnostic system for PJI and proved its validity.

Method:We filtered "in-time" diagnostic indicators reported in the literature based on our continuous retrospective cohort of PJI and aseptic prosthetic loosening (APL) patients. With the indicators, we developed a two-level ML model with 6 base learner including Elastic Net (EN), Linear Support Vector Machine (LSVM), Kernel Support Vector Machine (KSVM), Extra Trees (ET), Light Gradient Boosting Machine (LGBM) and Multilayer Perceptron (MLP)), and 1 meta-learner, Ensemble Learning of Weighted Voting (ELWV). The prediction performance of this model was compared with those of previous diagnostic criteria (International Consensus Meeting in 2018 (ICM 2018), etc). Another prospective cohort was used for internal validation. Based on our ML model, a user-friendly web tool was developed for swift PJI diagnosis in clinical practice.

Result:A total of 254 patients (199 for development and 55 for validation cohort) were included in this study with 38.2% of them diagnosed as PJI. We included 21 widely-accessible features including imaging indicators (X-ray and CT) in the model. The sensitivity and accuracy of our ML model were significantly higher than ICM 2018 in development cohort (90.6% vs. 76.1% , P=0.032 94.5% vs. 86.7%, P=0.020), which was supported by internal validation cohort (84.2% vs. 78.6%; 94.6% vs. 83.3%).

Conclusion:Our novel ML-derived PJI "in-time" diagnostic system demonstrated significantly improved diagnostic potency for surgical decision-making compared with the commonly-used criteria. Moreover, our web-based tool greatly assisted surgeons in distinguishing PJI patients comprehensively.

MATRIX MAYHEM: INVESTIGATING THE EFFECTS OF PERICELLULAR PROTEOLYSIS ON BIOMECHANICAL PROPERTIES AND CALCIUM SIGNALING IN ARTICULAR CARTILAGE

Jule Nieuwstraten[1], Farshid Guilak[2,3], Marina Danalache[1]

[1]Laboratory of Cell Biology, Department of Orthopedic Surgery, University of Tuebingen, Tuebingen, Germany, *[2]Department of Orthopedic Surgery, Washington University, St. Louis, United States*, *[3]Shriners Hospitals for Children, St. Louis, United States*

INTRODUCTION: Within articular cartilage, chondrocytes reside within the pericellular matrix (PCM), collectively constituting the microanatomical entity known as a chondron. The PCM functions as a pivotal protective shield and mediator of biomechanical and biochemical cues. In the context of Osteoarthritis (OA), enzymatic degradation of the PCM is facilitated by matrix metalloproteinases (MMPs). This study delves into the functional implications of PCM structural integrity decline on the biomechanical properties of chondrons and impact on Ca^{2+} signaling dynamics.

METHOD: Chondrons isolated from human cartilage explants were incubated with activated MMP-2, -3, or -7. Structural degradation of the pericellular matrix (PCM) was assessed by immunolabelling (collagen type VI and perlecan, n=5). Biomechanical properties of chondrons (i.e. elastic modulus (EM)) were analyzed using atomic force microscopy (AFM). A fluorescent calcium indicator (Fluo-4-AM) was used to record and quantify the intracellular Ca^{2+} influx of chondrons subjected to single cell mechanical loading (500nN) with AFM (n=7) .

RESULT: Each of the three MMPs disrupted the structural integrity of the PCM, leading to attenuated fluorescence intensity for both perlecan and collagen VI. A significant decrease of EM was observed for all MMP groups ($p<0.005$) with the most notable decrease observed for MMP-2 and MMP-7 ($p<0.001$). In alignment with the AFM results, there was a significant alteration in Ca^{2+} influx observed for all MMP groups ($p<0.05$), in particular for MMP-2 and MMP-7 ($p<0.001$).

CONCLUSION: Proteolysis of the PCM by MMP-2, -3, and -7 not only significantly alters the biomechanical properties of articular chondrons but also affects their mechanotransduction profile and response to mechanical loading, indicating a close interconnection between these processes. These findings underscore the influence of an intact pericellular matrix (PCM) in protecting cells from high stress profiles and carry implications for the transmission of mechanical signaling during OA onset and progression.

SAME-DAY DISCHARGE TRENDS IN TOTAL HIP ARTHROPLASTY: A NATIONWIDE ANALYSIS OF 235,393 PATIENTS AND 25,388 SAME-DAY DISCHARGES

Halil Bulut[1,2], Daniel Tomey[1]

[1]Houston Methodist Hospital, United States, *[2]Istanbul University Cerrahpasa, Türkyie*

Introduction: The concept of same-day discharge has garnered increasing significance within orthopedic surgery, particularly in hip and knee procedures. Despite initial concerns surrounding the absence of prolonged hospital care, a burgeoning body of evidence highlights numerous advantages associated with same-day discharge, ranging from mitigating in-hospital infections to offering substantial financial and psychosocial benefits for both patients and healthcare providers. In this study, we aim to scrutinize the trends in same-day discharge specifically within the realm of total hip arthroplasties.

Method: This retrospective analysis delves into the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) database spanning from 2017 to 2021. Leveraging patient data sourced from the ACS NSQIP database, we sought to elucidate patterns and shifts in same-day discharge practices pertaining to total hip arthroplasties.

Result: The preoperative analysis illuminated several notable disparities between patients undergoing same-day hip arthroplasty and those necessitating hospitalization. Notably, same-day hip patients skewed younger, comprising 48.3%females compared to 55.6% in hospitalized hip patients. Furthermore, a lower prevalence of medical comorbidities such as diabetes mellitus (8.5% vs.12.9%), current smoking (9.3% vs. 12.2%), and severe COPD(1.9% vs. 4.1%) was observed among same-day hip group. Operatively, same-day hip surgeries boasted shorter durations, averaging 83.9 minutes, in contrast to the 92.3minutes for hospitalized hip procedures. Postoperatively, same-day hip patients exhibited significantly diminished rates of 30-day readmissions (1.7%vs. 3.5%), procedure-related readmissions (1.0%vs.2.1%), reoperations (1.1%vs.1.9%), and mortality (0.02% vs. 0.04%). Moreover, the prevalence of the same-day discharge concept experienced a remarkable ascent from 2016 to 2021, with rates escalating from 1.5% to 25.6% of all total hip arthroplasties over a span of just six years.

Conclusion: In conclusion, same-day discharge is a feasible and safe option for selected THA patients.

TIE2-ENHANCED NUCLEUS PULPOSUS CELL-DERIVED EXTRACELLULAR VESICLES ENHANCE DEGENERATIVE DISC CELL VIABILITY IN VITRO

Luca Ambrosio[1,2], Jordy Schol[2], Clara Ruiz-Fernández[2], Rocco Papalia[1], Gianluca Vadalà[1], Vincenzo Denaro[1], Daisuke Sakai[2]

[1]Campus Bio-Medico University of Rome, Italy, *[2]Tokai University School of Medicine, Japan*

Introduction: Intervertebral disc degeneration (IDD) is a progressive process affecting all disc tissues, namely the nucleus pulposus (NP), annulus fibrosus (AF), and cartilaginous endplates (CEPs). Several cell-based therapies have been proposed to replenish the disc cell population and promote tissue regeneration. However, cell-free therapeutics have been increasingly explored due to potentially higher advantages and cost-effectiveness compared to cell transplantation. Recently, extracellular vesicles (EVs) isolated from healthy $Tie2^{+}$-NP cells (NPCs) have shown promising regenerative outcomes on degenerative NPCs (dNPCs). The aim of this study was to assess the effect of such EVs on all disc cell types, including AF cells (AFCs) and CEP cells (CEPCs), compared to EVs isolated from bone-marrow derived mesenchymal stromal cells (BM-MSCs).

Method: NPCs harvested from young donors underwent an optimized culture protocol to maximize Tie2 expression ($NPCs^{Tie2+}$). BM-MSCs were retrieved from a commercial cell line or harvested during spine surgery procedures. EV characterization was performed via particle size analysis (qNano), expression of EV markers (Western blot), and transmission electron microscopy. dNPCs, AFCs, and CEPCs were isolated from surgical specimens of patients affected by IDD, culture-expanded, and treated with $NPCs^{Tie2+}$-EVs or BM-MSC-EVs ± 10 ng/mL IL-1b. EV uptake was assessed with PKH26 staining of EVs under confocal microscopy. Cell proliferation and viability were assessed with the CCK-8 assay.

Result: Upon characterization, isolated EVs exhibited the typical exosomal characteristics. $NPCs^{Tie2+}$-EVs and BM-MSC-EVs uptake was successfully observed in all dNPCs, AFCs, and CEPCs. Both EV products significantly increased dNPC, AFC, and CEPC viability, especially in samples treated with $NPCs^{Tie2+}$-EVs.

Conclusion: $NPCs^{Tie2+}$-EVs demonstrated to significantly stimulate the proliferation and viability of degenerative cells isolated from all disc tissues. Rather than the sole NP, EVs isolated by committed progenitors physiologically residing within the disc may exert their regenerative effects on the whole organ, thus possibly constituting the basis for a new therapy for IDD.

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Maximilian Heumann[1], Chencheng Feng[1], Lorin Benneker[2], Maarten Spruit[3], Christian Mazel[4], Jan Buschbaum[1], Boyko Gueorguiev[1], Manuela Ernst[1]

[1]AO Research Institute Davos, Davos, Switzerland, *[2]Sonnenhof Spital, Spine Unit, University of Bern, Bern, Switzerland*, *[3]Sint Maartenskliniek, Orthopedics Center, Spine Unit, Nijmegen, Netherlands*, *[4]Institute Mutualiste Montsouris, Paris, France*

Introduction: In daily clinical practice, progression of spinal fusion is typically monitored during clinical follow-up using conventional radiography and Computed Tomography scans. However, recent research has demonstrated the potential of implant load monitoring to assess posterolateral spinal fusion in an in-vivo sheep model. The question arises to whether such a strain sensing system could be used to monitor bone fusion following lumbar interbody fusion surgery, where the intervertebral space is supported by a cage. Therefore, the aim of this study was to test human cadaveric lumbar spines in two states: after a transforaminal lumbar interbody fusion (TLIF) procedure combined with a pedicle-screw-rod-construct (PSR) and subsequently after simulating bone fusion. The study hypothesized that the load on the posterior instrumentation decreases as the segment stiffens due to simulated fusion.

Method: A TLIF procedure with PSR was performed on eight human cadaveric spines at level L4-L5. Strain sensors were attached bilaterally to the rods to derive implant load changes during unconstrained flexion-extension (FE), lateral bending (LB) and axial rotation (AR) loads up to ±7.5Nm. The specimens were retested after simulating bone fusion between vertebrae L4-L5. In addition, the range of motion (ROM) was measured during each loading mode.

Result: The ROM decreased in the simulated bone fusion state in all loading directions ($p \leq 0.002$). In both states, the measured strain on the posterior instrumentation was highest during LB motion. Furthermore, the sensors detected a significant decrease in the load induced rod strain ($p \leq 0.002$) between TLIF+PSR and simulated bone fusion state in LB.

Conclusion: Implant load measured via rod strain sensors can be used to monitor the progression of fusion after a TLIF procedure when measured during LB of the lumbar spine. However, further research is needed to investigate the influence of daily loading scenarios expected in-vivo on the overall change in implant load.

THE PREOPERATIVE GAIT PATTERN IS ASSOCIATED WITH MIGRATION OF TOTAL KNEE ARTHROPLASTY – AN EXPLORATORY RADIOSTEREOMETRY STUDY WITH 2 YEARS FOLLOW-UP

Emil Toft Petersen[1,2,3], Karina Nørgaard Linde[1,3], Carl Christian Holkgaard Burvil[1,3], Søren Rytter[1,2,3], Daan Koppens[1,2,3], Jesper Dalsgaard[4], Torben Baek Hansen[3,4], Maiken Stilling[1,2,3]

[1]AutoRSA Research Group, Orthopaedic Research Unit, Aarhus University Hospital, Aarhus, Denmark, *[2]Department of Orthopedic Surgery, Aarhus University Hospital, Aarhus, Denmark*, *[3]Department of Clinical Medicine, Aarhus University, Aarhus, Denmark*, *[4]Department of Orthopedics, Gødstrup Regional Hospital, Gødstrup, Denmark*

Introduction: Knee osteoarthritis often causes malalignment and altering bone load. This malalignment is corrected during total knee arthroplasty surgery, balancing the ligaments. Nonetheless, preoperative gait patterns may influence postoperative prosthesis load and bone support. Thus, the purpose is to investigate the impact of preoperative gait patterns on postoperative femoral and tibial component migration in total knee arthroplasty.

Method: In a prospective cohort study, 66 patients with primary knee osteoarthritis undergoing cemented Persona total knee arthroplasty were assessed. Preoperative knee kinematics was analyzed through dynamic radiostereometry and motion capture, categorizing patients into four homogeneous gait patterns. The four subgroups were labeled as the flexion group (n=20), the abduction (valgus) group (n=17), the anterior drawer group (n=10), and the tibial external rotation group (n=19). The femoral and tibial component migration was measured using static radiostereometry taken supine on the postoperative day (baseline) and 3-, 12-, and 24-months after surgery. Migration was evaluated as maximum total point motion.

Result: Of the preoperatively defined four subgroups, the abduction group with a valgus-characterized gait pattern exhibited the highest migration for both the femoral (1.64 mm (CI95% 1.25; 2.03)) and tibial (1.21 mm (CI95% 0.89; 1.53)) components at 24-month follow-up. For the femoral components, the abduction group migrated 0.6 mm (CI95% 0.08; 1.12) more than the external rotation group at 24 months. For the tibial components, the abduction group migrated 0.43 mm (CI95% 0.16; 0.70) more than the external rotation group at 3 months. Furthermore, at 12- and 24-months follow-up the abduction group migrated 0.39 mm (95%CI 0.04; 0.73) and 0.45 mm (95%CI 0.01; 0.89) more than the flexion group, respectively.

Conclusion: A preoperative valgus-characterized gait pattern seems to increase femoral and tibial component migration until 2 years of follow-up. This suggests that the implant fixation depends on load distributions originating from specific preoperative gait patterns.

DOES A NOVEL INTRAOPERATIVE NAVIGATION PLATFORM ALLOW TO RETAIN NATIVE KNEE FUNCTION FOLLOWING TOTAL KNEE ARTHROPLASTY?

Orcun Taylan[1], Thomas Louwagie[1], Maciej Bialy[1,2], Geert Peersman[1,3], Lennart Scheys[1,4]

[1]Institute for Orthopaedic Research and Training (IORT), KU Leuven, Leuven, Belgium, *[2]2Institute of Physiotherapy and Health Sciences, The Jerzy Kukuczka Academy of Physical Education, Katowice, Poland*, *[3]ZNA Stuivenberg, Antwerp, Belgium*, *[4]Division of Orthopaedics, University Hospitals Leuven, Leuven, Belgium*

Introduction: This study aimed to evaluate the effectiveness of a novel intraoperative navigation platform for total knee arthroplasty (TKA) in restoring native knee joint kinematics and strains in the medial collateral ligament (MCL) and lateral collateral ligament (LCL) during squatting motions.

Method: Six cadaver lower limbs underwent computed tomography scans to design patient-specific guides. Using these scans, bony landmarks and virtual single-line collateral ligaments were identified to provide intraoperative real-time feedback, aided in bone resection, implant alignment, tibiofemoral kinematics, and collateral ligament elongations, using the navigation platform. The specimens were subjected to squatting (35°-100°) motions on a physiological *ex vivo* knee simulator, maintaining a constant 110N vertical ankle load regulated by active quadriceps and bilateral hamstring actuators. Subsequently, each knee underwent a medially-stabilized TKA using the mechanical alignment technique, followed by a retest under the same conditions used preoperatively. Using a dedicated wand, MCL and LCL insertions—anterior, middle, and posterior bundles—were identified in relation to bone-pin markers. The knee kinematics and collateral ligament strains were analyzed from 3D marker trajectories captured by a six-camera optical system.

Result: Both native and TKA conditions demonstrated similar patterns in tibial valgus orientation (Root Mean Square Error (RMSE=1.7°), patellar flexion (RMSE=1.2°), abduction (RMSE=0.5°), and rotation (RMSE=0.4°) during squatting ($p>0.13$). However, a significant difference was found in tibial internal rotation between 35° and 61° ($p<0.045$, RMSE=3.3°). MCL strains in anterior (RMSE=1.5%), middle (RMSE=0.8%), and posterior (RMSE=0.8%) bundles closely matched in both conditions, showing no statistical differences ($p>0.05$). Conversely, LCL strain across all bundles (RMSE<4.6%) exhibited significant differences from mid to deep flexion ($p<0.048$).

Conclusion: The novel intraoperative navigation platform not only aims to achieve planned knee alignment but also assists in restoring native knee kinematics and collateral ligament behavior through real-time feedback.

Acknowledgment: This study was funded by Medacta International (Castel San Pietro, Switzerland).

AN OSTEOPOROTIC CO CULTURE STUDY: DOES ADDING CERAMICS IMPROVE THE OSTEOGENIC POTENTIAL OF POLYMER SCAFFOLDS?

Samuel Tiplady[1], Christiane Heinemann[2], Benjamin Kruppke[2], Krishna Manda[1], Susan Clarke[1], Alex Lennon[1], Eneko Larrañeta[1], Fraser Buchanan[1]

[1]Queen's University Belfast, Belfast , United Kingdom, *[2]Technische Universität Dresden, Dresden, Germany*

Introduction: The incidences of fragility fractures, often because of osteoporosis, are increasing. Research has moved towards bioresorbable scaffolds that provide temporary mechanical stability and promote osteogenesis. This research aims to fabricate a 3D printed composite Poly (l-lactic-co-glycolic acid)-strontium doped tricalcium phosphate (PLGA-SrTCP) scaffold and evaluate in an in vitro co culture study containing osteoporotic donor cells.

Method: PLGA, PLGA TCP, and PLGA SrTCP scaffolds were produced using Fused Filament Fabrication (FFF). A four-group 35-day cell culture study was carried out using human bone marrow derived mesenchymal stem cells (hMSCs) from osteoporotic and control donors (monoculture) and hMSCs & human monocytes (hMCs) (Co culture). Outcome measures were biochemical assays, PCR, and cell imaging. Cells were cultured on scaffolds that had been pre-degraded for six weeks at 47°C prior to drying and gamma sterilisation.

Result: 3D printed scaffolds were successfully produced by FFF. All groups in the study supported cell attachment onto the scaffolds, producing extracellular matrices as well as evidence of osteoclast cell structures. Osteoporotic cells increased CTSK activity and CAII activity and decreased ALP activity compared to controls. In control cultures, the addition of bTCP and bTCP/Sr to the PLGA reduced TRAP5b, CAII and ALP activity compared to PLGA alone. The addition of Sr did not show any differences between donors.

Conclusion: This study details suitability of 3D printed polymer scaffolds for use in bone tissue applications. Both composite and pure polymer scaffolds promote osteogenesis in vitro. The introduction of ceramic filler and ion doping does not beneficially effect osteogenic potential and can reduce its ability compared to pure polymer. This study suggests the behaviour of control and osteoporotic cells are different and that osteoporotic cells are more prone to bone resorption. Therefore, it is important to design bone scaffolds that are specific to the patient as well as to the region of fracture.

COMPARATIVE EFFECTIVENESS OF SILVER-COATED IMPLANTS IN PERIPROSTHETIC INFECTION PREVENTION: A SYSTEMATIC REVIEW AND META-ANALYSIS

Halil Bulut[1], Sefa Giray Batibay[2], Enes Kanay[3], Korhan Özkan[3]

[1]Istanbul University Cerrahpasa, Türkyie, [2]umraniye training and research hospital, Türkyie, [3]Acibadem Atasehir Hospital, Türkyie

Introduction: Despite the implementation of numerous preventive measures in recent years, the persistent challenge of periprosthetic infections remains. Among the various strategies, metallic modification of implants, particularly with silver, has emerged as a promising avenue. Silver's antimicrobial properties, coupled with its low human toxicity, render it an appealing option. However, ongoing debate surrounds its comparative efficacy in infection prevention when contrasted with titanium-coated prostheses.

Methods: The PubMed database was systematically searched up to March 2024. Studies in English that met predetermined inclusion/exclusion criteria and utilized "Megaprosthesis AND infection" and " silver-coated AND infection " as key terms were included. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses(PRISMA) statement guided the article selection process.

Results: From a pool of 1892 potential papers after literature screening, 11 studies with a total of 1419 patients were meticulously selected for analysis. Among these patients, 638 were treated with silver-coated implants, while 781 received titanium-coated implants, resulting in 166 recorded cases of infection. Remarkably, the infection rate stood at 9.2% for the silver-coated group, contrasting with 13.4% for the titanium-coated group. The subsequent analysis unveiled a notable discrepancy in proportions (P difference = -0.0473, 95%CI: -0.088 to -0.006), signaling a statistically significant decrease in infections within the silver-coated cohort. Furthermore, the I2 statistic, denoting heterogeneity in effect sizes, stood at 21.8% (95%CI: 0.0-66.9), indicating a modest degree of variability among the studies.

Conclusion: In conclusion, our systematic review and meta-analysis shed light on the potential of silver-coated implants in mitigating periprosthetic infections. Despite the persistent challenge posed by such infections, our findings suggest a statistically significant decrease in infection rates among patients treated with silver-coated implants compared to those with titanium-coated ones.

THE EFFECTS OF SYNCHRONIZED AND NON-SYNCHRONIZED TELEREHABILITATION PROGRAMS IN THE CHRONIC NON-SPECIFIC LOW BACK PAIN

Rayan AHMED TAWFEK[1], ELİF TUĞÇE ÇİL[1]

[1]*Yeditepe University, Istanbul, Türkyie*

Introduction: This study aimed to assess the effectiveness of synchronized and non-synchronized telerehabilitation programs in managing chronic non-specific low back pain (CNLBP).

Method: This was a randomized, controlled clinical trial carried out on 72 (31 females, 41 males; mean age 41.26±10.97 years) individuals with CNLBP. Participants were randomly assigned to three groups: synchronized telerehabilitation Group (STG) (n = 24), non-synchronized telerehabilitation Group (NSTG), (n = 24), and a control group (CG) (n = 24). Sociodemographic characteristics were collected by special form designed by researchers. Numerical visual analogue scale measured pain levels and Roland Morris Disability Questionnaire and Oswestry Disability Index assessed disability. While fear of movement was evaluated with Tampa Scale for kinesiophobia, quality of life was determined by SF-12. Patients underwent a patient education program before starting treatment protocols. Core stabilization, and stretching exercises were demonstrated to Group 1 as real time (twice a week for 12 weeks). The same exercises program was given to Group 2 as pre-recorded videos (12 weeks) and Group 3 used a digital book (PDF file).

Result: Pain levels, disability status, fear of movement, and quality of life showed improvement at week 12 in all groups ($p<0.05$). Post hoc Turkey test revealed superiority for Group 1, followed by Group 2.

Conclusion: A real-time synchronized telerehabilitation demonstrated superiority over a non-synchronized telerehabilitation program in improving pain, disability status, fear of movement, and quality of life. The study recommends further research on telerehabilitation for low back pain and other health-related concerns.

THE POTENTIAL OF STRAIN SENSORS ON A POSTERIOR INSTRUMENTATION TO ASSESS HEALING OF TRANSOSSEOUS FRACTURES IN A LUMBAR VERTEBRA: A CADAVERIC STUDY

Maximilian Heumann[1], Alina Jacob[1], Boyko Gueorguiev[1], Geoff Richards[1], Lorin Benneker[2]

[1]AO Research Institute Davos, Davos, Switzerland, *[2]Sonnenhof Spital, Spine Unit, University of Bern, Bern, Switzerland*

Introduction: Transosseous flexion-distraction injuries of the spine typically require surgical intervention by stabilizing the fractured vertebra during healing with a pedicle-screw-rod constructs. As healing is taking place the load shifts from the implant back to the spine. Monitoring the load-induced deflection of the rods over time would allow quantifiable postoperative assessment of healing progress without the need for radiation exposure or frequent hospital visits. This approach, previously demonstrated to be effective in assessing fracture healing in long bones and monitoring posterolateral spinal fusion in sheep, is now being investigated for its potential in evaluating lumbar vertebra transosseous fracture healing.

Method: Six human cadaveric spines were instrumented with pedicle-screws and rods spanning L3 vertebra. The spine was loaded in Flexion-Extension (FE), Lateral-Bending (LB) and Axial-Rotation (AR) with an intact L3 vertebra (representing a healed vertebra) and after transosseous disruption, creating an AO type B1 fracture. The implant load on the rod was measured using an implantable strain sensor (Monitor) on one rod and on the contralateral rod by a strain gauge to validate the Monitor's measurements. In parallel the range of motion (ROM) was assessed.

Result: The ROM increased significantly in all directions in the fractured model ($p \leq 0.049$). The Monitor measured a significant increase in implant load in FE ($p=0.002$) and LB ($p=0.045$), however, not in AR. The strain gauge detected an increased implant load not only in FE ($p=0.001$) and LB ($p=0.016$), but also in AR ($p=0.047$). The highest strain signal was found during LB for both, the Monitor, and the strain gauge.

Conclusion: After a complete transosseous disruption of L3 vertebra the load on the implants was significantly higher than in the intact respectively healed state. Innovative implantable sensors could be used to monitor those changes allowing the assessment of healing progression based on quantifiable data rather than CT-imaging.

NAIL VERSUS PLATE IN TIBIOCALCANEAL ARTHRODESIS : A BIOMECHANICAL STUDY

Mehar Dhillon[1,2], Kajetan Klos[3], Mark Lenz[4], Ivan Zderic[2], Boyko Gueorguiev[2]

[1]PGIMER, India, Chandigarh, India, *[2]AO Research Institute Davos, Switzerland, Switzerland*, *[3]Gelenkzentrum Rhein-Main, Germany, Germany*, *[4]Jena University Hospital, Germany*

Introduction: Tibiocalcaneal arthrodesis with a retrograde intramedullary nail is an established procedure considered as a salvage in case of severe arthritis and deformity of the ankle and subtalar joints [1]. Recently, a significant development in hindfoot arthrodesis with plates has been indicated. Therefore, the aim of this study was to compare a plate specifically developed for arthrodesis of the hindfoot with an already established nail system [2]

Method: Sixteen paired human cadaveric lower legs with removed forefoot and cut at mid-tibia were assigned to two groups for tibiocalcaneal arthrodesis using either a hindfoot arthrodesis nail or an arthrodesis plate. The specimens were tested under progressively increasing cyclic loading in dorsiflexion and plantar flexion to failure, with monitoring via motion tracking. Initial stiffness was calculated together with range of motion in dorsiflexion and plantar flexion after 200, 400, 600, 800, and 1000 cycles. Cycles to failure were evaluated based on 5° dorsiflexion failure criterion

Result: Initial stiffness in dorsiflexion, plantar flexion, varus, valgus, internal rotation and external rotation did not differ significantly between the two arthrodesis techniques ($p \geq 0.118$). Range of motion in dorsiflexion and plantar flexion increased significantly between 200 and 1000 cycles ($p < 0.001$) and remained not significantly different between the groups ($p \geq 0.120$). Cycles to failure did not differ significantly between the two techniques ($p = 0.764$).

Conclusion: From biomechanical point of view, both tested techniques for tibiocalcaneal arthrodesis appear to be applicable. However, clinical trials and other factors, such as extent of the deformity, choice of the approach and preference of the surgeon play the main role for implant choice.

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Acknowledgements: This study was performed with the assistance of the AO Foundation.

EFFECTS OF LOW DOSE BMP-2 AND IMMUNOMODULATION TARGETING IL-1ß ON FRACTURE HEALING IN A FEMUR DEFECT MODEL IN RATS

Maria Schröder[1], Lena Gens[1], Daniel Arens[1], Nico Giger[1], Dominic Gehweiler[1], Dirk Nehrbass[1], Ivan Zderic[1], Stephan Zeiter[1], Martin Stoddart[1], Esther Wehrle[1]

[1]AO Research Institute , Davos, Switzerland

Introduction: Immunomodulation represents a novel strategy to improve bone healing in combination with low doses of bone morphogenetic growth factors like BMP-2. This study aims to investigate the effect and timing of monoclonal anti-IL-1ß antibody administration with 1µg BMP-2 on bone healing over 14 weeks in a rat femur segmental defect model.

Method: 2 mm femoral defects were created in 22-27 weeks-old female Fischer F344 rats, internally fixed with a plate (animal license: GR/19/2022) using established protocols for analgesia and anesthesia. Animals (n=4/group) received either a collagen sponge, a collagen sponge+1µg BMP-2 (InductOs, Medtronic) or a collagen sponge+1µg BMP-2 with a monoclonal anti-IL-1ß antibody (BioXCell, 10 mg/ml), administered intravenously under anesthesia every third day until day 15, from day 0 or 3. *In vivo* micro-CT was performed after surgery and at 2, 3, 4, 6, 8, 10 and 14-weeks post-OP. Mechanical properties of the operated femurs were assessed by 4-point bending (Instron5866) and compared to contralateral femurs (one-way ANOVA, GraphPad Prism8). Histopathological analysis was performed semi-quantitatively on Giemsa-Eosin-stained sections (Olympus BX63) using a six-grade severity grading scale.

Result: Operated femurs with BMP-2 reached an average stiffness of 91±37% of contralateral femurs, femurs in IL-1ß groups 105±11% (day 0) and 111±12% (day 3). Administration of anti-IL-1ß+1µg BMP-2 led to faster cortical bridging (3/4 femurs bridged by week 4 for day 0, 4/4 for day 3) than 1µg BMP-2 alone (0/4 by week 4). Micro-CT results confirmed histopathological evaluation, as collagen sponge alone led to non-union, complete bicortical bridging was observed for 3/4 femurs in the BMP-2 group and for 4/4 femurs in the IL-1β groups after 14 weeks.

Conclusion: Anti-IL-1ß had a beneficial effect on late fracture healing with faster cortical bridging and new bone formation than 1µg BMP-2 alone.

Acknowledgments: AO foundation. We thank Andrea Furter, Alisa Hangartner and Thomas Krüger for technical support.

DEVELOPING A SMALL ANIMAL TRAUMA MODEL FOR FEMORAL HEAD OSTEONECROSIS

Zeynep Bal[1,2], Nobuyuki Takakura[1,2]

[1]WPI Immunology Frontier Research Center, Osaka University, Osaka, Japan, *[2]Research Institute for Microbial Diseases, Osaka University, Osaka , Japan*

Introduction: Femoral head osteonecrosis (FHO) is a condition in which the inadequate blood supply disrupts osteogenic-angiogenic coupling that results in diminishment of femoral perfusion and ends up with FHO. The insufficient knowledge on molecular background and progression pattern of FHO and the restrictions in obtaining human samples bring out the need for a small animal trauma model to research FHO aetiology. Hence, this study aims to develop a mouse trauma model to elucidate the molecular mechanisms behind FHO.

Method: Left femoral head was dislocated from the hip joint, ligamentum teres was cut, and a slight circular incision was done around the femoral neck of 8-week-old male C57BL/6J mice to disrupt the blood supply to femoral head. Right hip joint was left unoperated as control. Animals (n=5 per time point) were sacrificed on 2-3-4-6-8-10-12 weeks, and ex-vivo µCT was taken to assess bone structural parameters. Haematoxylin/eosin (HE)- and immunohistochemical-staining (IHCS) for CD31 and EMCN were done to observe histology and marrow-specific H-type vascular structures, respectively.

Result: µCT assessment showed trabecular bone loss and decreased BV/TV from 2 to 8 weeks in FHO side. HE staining displayed the increased number of empty lacunae was observed in FHO side as early as 24h after operation. By 4th week, IHCS results displayed the invasion of the epiphyseal plate by H-type blood vessels in FHO side, while the epiphyseal plate was observed intact in control side. Also, by 6th week the HE-staining showed the presence of bone marrow necrosis and bone fat accumulation in FHO side.

Conclusion: Trabecular bone loss, increased number of empty lacunae, bone fat imbalance and bone marrow necrosis are reported as the signs of osteonecrosis. Thus, our results are coherent with the literature and indicated that we were able to effectively generate a trauma model for FHO in mice for the first time in literature.

EXPLORING A ROBOTIC ARM BIOREACTOR TO SCREEN THROUGH TENDON BIOMATERIALS

Muhammad Hanif Nadhif[1], Tania Choreño Machain[1], Sarah Snelling[1], Pierre-Alexis Mouthuy[1]

[1]Botnar Research Centre, Nuffield Department of Orthopaedics, Rheumatology, and Musculoskeletal Sciences (NDORMS), University of Oxford, Oxford, United Kingdom

Introduction: Various treatments are available for rotator cuff tears (RCTs), including the use of biomaterials. Unfortunately, treatments using biomaterials still lead to re-ruptures of RCTs in 20% to 54% of surgeries. This may arise from poor designs (i.e. mechanical mismatches). The current limitation is the lack of dynamic *in vitro* models that can assess biomaterial properties with physiological relevance. Evaluations are often limited to uniaxial mechanical testing. In recent years, our group has been exploring a robotic arm bioreactor, that can provide realistic shoulder motions and forces to cells and materials in the context of tendon tissue engineering. Here, we explore the platform to screen through tendon biomaterials.

Method: Two commercial biomaterials were selected: Poly-Tapes (synthetic non-degradable implant) and GraftJacket (biological patch). The two materials were multiaxially stimulated in the platform using rehabilitation exercises with gradually increased peak forces from 0 N to 25 N. This was carried out with continuous perfusion of saline solution at 37°C for 4 weeks. The robot was compared to a uniaxial stage with similar force regimes and static control (both with similar perfusion treatments).

Result: For Poly-Tapes, no significant differences were observed in deformations, remaining volume, and linear mass density in comparison to the other two treatments. Scanning electron microscopy (SEM) and micro-computed tomography (μCT) also presented no mechanical damage after the treatments. Oppositely, GraftJacket was torn: 1 out 6 in both uniaxial and multiaxial stimulations. The multiaxial samples experienced more length deformation. More structural damage was also discovered using SEM. Furthermore, abundant particle depositions were seen in the multiaxial samples compared to the uniaxial ones.

Conclusion: The robotic arm bioreactor demonstrated a potential as a more robust screening device for tendon biomaterials compared to the uniaxial counterpart. The mechanical impact of the bioreactor was more pronounced in the biological materials than in the synthetic non-degradable materials.

ASSESSING ROTATOR CUFF COMPENSATIONS: EFFECTS OF SUPERIOR CAPSULAR RECONSTRUCTION (SCR) AND LOWER TRAPEZIUS TRANSFER (LTT) ON TERES MINOR AND SUBSCAPULARIS FORCES IN CADAVERIC SHOULDER MODELS

Nirav Mungalpara[1], Sunjung Kim[2], Hayden Baker[3], Cody Lee[3], Ashish Shakya[1], Kevin Chen[3], Aravind Athiviraham[3], Jason Koh[4], Bassem Elhassan[5], Nicholas H. Maassen[6], Farid Amirouche[1]

[1]University of Illinois at Chicago, Chicago, United States, *[2]Hospital for Special Surgery, New York, United States*, *[3]University of Chicago, Chicago, United States*, *[4]Northshore Health System, Chicago, United States*, *[5]Massachusetts General Hospital, Boston, United States*, *[6]Department of Orthopaedic Surgery and Rehabilitation Medicine, The University of Chicago Medicine & Biological Sciences , United States*

Introduction: Supraspinatus and infraspinatus tears (Massive Rotator Cuff Tear- MRCT) cause compensatory activation of the teres minor (TM) and subscapularis (SubS) to maintain humeral head alignment. This study measures force changes in TM and SubS using a dynamic shoulder testing setup. We hypothesize that combining superior capsule reconstruction (SCR) and lower trapezius tendon (LTT) transfer will correct rotator cuff forces.

Methods: Eight fresh-frozen human shoulder specimens from donors aged 55-75 (mean = 63.75 years), balanced for gender, averaging 219.5 lbs, were used. Rotator cuff and deltoid tendons were connected to force sensors through a pulley system, with the deltoid linked to a servohydraulic motor for dynamic force measurement. The system allowed unrestricted humeral abduction from 0 to 90 degrees.

Results: *Teres Minor (TM):*

- Control: 7.43 N (SD = 1.66)
- SS tear: 5.46 N (SD = 1.45)
- MRCT: 3.94 N (SD = 1.43)
- LTT post-MRCT: 5.85 N (SD = 1.13)
- SCR post-MRCT: 4.68 N (SD = 0.71)
- Combined LTT+SCR: 6.43 N (SD = 1.24)
- TM force reduction: 26.51% post-SS tear, 46.97% from intact to MRCT, 63.20% increase with LTT+SCR.

Subscapularis (SubS):

- Control: -0.73 N (SD = 0.43)
- SS tear: -0.46 N (SD = 0.36), 36.99% increase
- MRCT: 0.96 N (SD = 0.47), 31.51% increase

- LTT post-MRCT: -0.32 N (SD = 0.47), 66.67% reduction

- SCR post-MRCT: -0.28 N (SD = 0.16), 70.83% reduction

- Combined LTT+SCR: -0.66 N (SD = 0.32), 31.25% reduction

Non-parametric Friedman's ANOVA showed overall statistical significance for TM ($P = 1.083\times10^{-6}$) and SubS ($P = 4.77\times10^{-4}$).

Conclusion: The cadaveric model assesses rotator cuff compensations, showing significant TM force reductions following rotator cuff tears and improvements with LTT and SCR, particularly when combined. SubS exhibited negative force during normal abduction but compensated during MRCT, returning to normal values post-LTT and SCR.

INVESTIGATING THE DIAGNOSTIC ACCURACY OF ULTRASONOGRAPHY IN DETECTION OF MEDICAL MENISCAL EXTRUSION IN KNEE OSTEOARTHRITIS PATIENTS, A SYSTEMATIC REVIEW AND META-ANALYSIS

Mohammad-Taha Pahlevan-Fallahy[1,1], Farhad Shaker[1], Fatemeh Ghanbari[1], Mohammad Amin Aslani[1], Sara Mohammadi[1], Sadra Behrouzieh[1]

[1]Students' Scientific Research Center, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran, Tehran, Iran

Introduction: Knee Osteoarthritis (KOA) is a prevalent joint disease requiring accurate diagnosis and prompt management. The condition occurs due to cartilage deterioration and bone remodeling. Ultrasonography has emerged as a promising modality for diagnosing KOA. Medial meniscus extrusion (MME), characterized by displacement of medial meniscus beyond the joint line has been recognized as a significant marker of KOA progression. This study aimed to explore potentials Ultrasound findings in timely detection of MME and compare it to magnetic resonance imaging (MRI) as a reference standard.

Method: A comprehensive literature search was performed in 4 databases from inception to May 1 2024. Two independent reviewers, initiated screening protocols and selected the articles based on inclusion and exclusion criteria and then extracted the data. Meta-analysis was conducted using R 4.3.2 packages mada and metafor.

Result: A total of 2500 articles from 4 databases was retrieved; however, following the application of inclusion and exclusion criteria 23 articles were finally extracted. These studies collectively encompassed a total of 777 patients with mean age of 53.2±7.4. The mean BMI calculated for patients was 28.31 ± 2.45. All patients underwent non-weight bearing knee ultrasonography in supine position with 0° flexion. The reported medial meniscus extrusion was 2.58 mm for articles using MRI and 2.65 mm for those using Ultrasound (MD: 0.05 ± 0.12, P= 0.65, I^2: 54%). Our meta-analysis revealed insignificant difference between US and MRI. (SMD: 0.03, 95% CI: -0.18 _0.23, P= 0.77, I^2: 56%) Meta analysis for diagnostic accuracy measures yielded a pooled sensitivity and specificity of 90.8% and 77% (95% CI: 84.2% - 94.8%, 35.5% - 95.3%, respectively, I^2: 44%).

Conclusion: Our results indicate a close alignment in the accuracy of measurements obtained using Ultrasound modality. The narrow range suggests a minimal discrepancy in MME values between MRI and ultrasound, highlighting their comparable precision in diagnostic assessments.

THE UTILITY OF EXTENDED BACTERIAL CULTURES AND NEXT-GENERATION SEQUENCING IN IDENTIFYING PATHOGENS IN 'CULTURE NEGATIVE' FRACTURE RELATED INFECTIONS

Jagdish Menon[1,1], Thiruselvam Murugan[1], Rakhi Biswas[1], Prashanth K[2]

[1]JIPMER (Jawaharlal institute of Postgraduate Medical Education and Reasearch), Pondicherry, India,
[2]Pondicherry Central university, Pondicherry, India

INTRODUCTION: Identification of the causative pathogen in musculoskeletal infection is critical as it directs further treatment. Fracture-related infection is often associated with 'no growth' in standard culture. We investigated the efficiency of two alternate methods to identify the causative pathogen, namely extended bacterial culture and 16Sr RNA gene sequence analysis with next generation sequencing (NGS) in 'culture negative' fracture related infections.

METHOD: Patients were diagnosed as having fracture related infection based on the MSIS criteria (n=120). All patients had samples taken for culture and sensitivity. All samples which were culture negative by standard culture methods formed the study group. These samples were subjected to further extended culture in both aerobic and anaerobic medium for 14 days to improve recovery of pathogens. Further, DNA isolated from implants from a sub-group of these culture negative patients were subjected to 16SrRNA gene amplification followed by Sanger sequencing. Subsequent sequencing analysis was performed using the Illumina NGS platform which identified and detected the most abundant genera/species present in those samples more precisely.

RESULT: 57 culture negative samples formed the study group. Eight samples (14%) converted to positivity after 14 days of culture. Bacteroides fragilis was the commonest yield. 14 samples underwent 16SrRNA gene amplification followed by Sanger sequencing. Acinetobacter baumannii, Enterococcus faecalis, Pseudomonas aeruginosa were identified as common pathogens. Next generation sequencing (n=12) not only identified common pathogens like as Staphylococcus, Acinetobacter baumannii, but also many uncultivable species.

CONCLUSION: Positive results from extended bacterial culture are about 15%. The delay in definite identification of pathogens in extended culture may be critical in certain clinical situations. Molecular methods are quicker and have additional yield in culture negative infections. The exact role of all microorganisms identified by molecular methods in the pathogenesis of infection is unknown.

COMPREHENSIVE ANALYSIS OF GENETICAL ETIOLOGY OF CONGENITAL SCOLIOSIS: FROM GENES TO PATHWAYS

Halil Bulut[1], Fatima Abasova[1], Tuncay Basaran[1], Pelin Balaban[1]

[1]*Istanbul University Cerrahpasa, Türkyie*

Introduction: Congenital scoliosis is a prevalent congenital spinal deformity, more frequently encountered than congenital lordosis or kyphosis. The prevailing belief is that most instances of congenital scoliosis are not hereditary but rather stem from issues in fetal spine development occurring between the 5th and 8th weeks of pregnancy. However, it has been linked to several genes in current literature. Our goal was to explore potential pathways through an exhaustive bioinformatics analysis of genes related to congenital scoliosis.

Method: The literature from the 1970s to February 2024 was surveyed for genes associated with CS, and 63 genes were found to be associated with AIS out of 1743 results. These genes were analyzed using DAVID Bioinformatics

Result: Our pathway analysis has unveiled several significant associations with congenital scoliosis. Notably, "Glycosaminoglycan biosynthesis - chondroitin sulfate / dermatan sulfate" (P-Value:8.8E-3, Fold Enrichment: 20.6), "Central carbon metabolism in cancer" (P-Value:1.3E-3, Fold Enrichment: 10.3), and "Lysine degradation" (P-Value: 9.0E-3, Fold Enrichment: 9.1) emerge as statistically significant pathways. Additionally, "Endocrine resistance" (P-Value:4.4E-3, Fold Enrichment:7.4) and"EGFR tyrosine kinase inhibitor resistance" (P-Value: 1.7E-2, Fold Enrichment:7.3) pathways are noteworthy. These findings suggest a potential involvement of these pathways in the biological processes underlying congenital scoliosis. Furthermore, "Signaling pathways regulating pluripotency of stem cells" (P-Value:4.0E-4, Fold Enrichment:7.1), "Notch signaling pathway" (P-Value:6.7E-2, Fold Enrichment: 7.0), and "TGF-beta signaling pathway" (P-Value:6.2E-3, Fold Enrichment: 6.7) exhibit a less pronounced yet intriguing association that may warrant further investigation.

Conclusion: In conclusion, our comprehensive analysis of the genetic etiology of congenital scoliosis has revealed significant associations with various pathways, shedding light on potential underlying biological mechanisms. While further research is needed to fully understand these associations and their implications, our findings provide a valuable starting point for future investigations into the management and treatment of congenital scoliosis.

BIOMECHANICAL ASSESSMENT OF NOVEL DYNAMIC VERSUS CONVENTIONAL HIGH-STRENGTH SUTURES IN DISTAL BICEPS TENDON REPAIR

Ivan Zderic[1], Moritz Kraus[1], Luke van Rossenberg[1], Boyko Gueorguiev[1], Geoff Richards[1], Hans Christoph Pape[2], Tatjana Pastor[3], Torsten Pastor[4]

[1]AO Research Institute Davos, Davos, Switzerland, *[2]University Hospital Zürich, Zürich, Switzerland*, *[3]Inselspital University Hospital Bern, Bern, Switzerland*, *[4]Cantonal Hospital Lucerne, Lucerne, Switzerland*

Introduction: Tendon ruptures are a common injury and often require surgical intervention to heal. A refixation is commonly performed with high-strength suture material. However, slipping of the thread is unavoidable even at 7 knots potentially leading to reduced compression of the sutured tendon at its footprint. This study aimed to evaluate the biomechanical properties and effectiveness of a novel dynamic high-strength suture, featuring self-tightening properties.

Method: Distal biceps tendon rupture tenotomies and subsequent repairs were performed in sixteen paired human forearms using either conventional or the novel dynamic high-strength sutures in a paired design. Each tendon repair utilized an intramedullary biceps button for radial fixation. Biomechanical testing aimed to simulate an aggressive postoperative rehabilitation protocol stressing the repaired constructs. For that purpose, each specimen underwent in nine sequential days a daily mobilization over 300 cycles under 0-50 N loading, followed by a final destructive test.

Result: After the ninth day of cyclic loading, specimens treated with the dynamic suture exhibited significantly less tendon elongation at both proximal and distal measurement sites (-0.569±2.734 mm and 0.681±1.871 mm) compared to the conventional suture group (4.506±2.169 mm and 3.575±1.716 mm), $p=0.003/p<0.002$. Gap formation at the bone-tendon interface was significantly lower following suturing using dynamic suture (2.0±1.6 mm) compared to conventional suture (4.5±2.2 mm), $p=0.04$. The maximum load at failure was similar in both treatment groups (dynamic suture: 374± 159 N; conventional suture: 379± 154 N), $p=0.925$. The predominant failure mechanism was breakout of the button from the bone (dynamic suture: 5/8; conventional suture: 6/8), followed by suture rupturing, suture unraveling and tendon cut-through.

Conclusion: From a biomechanical perspective, the novel dynamic high-strength suture demonstrated higher resistance against gap formation at the bone tendon interface compared to the conventional suture, which may contribute to better postoperative tendon integrity and potentially quicker functional recovery in the clinical setting.

ASSESSMENT OF A NOVEL DYNAMIC HIGH-STRENGTH SUTURE TAPE IN DISTAL TRICEPS TENDON REPAIR - A BIOMECHANICAL COMPARATIVE STUDY

Ivan Zderic[1], Moritz Kraus[1], Bogdan Axente[1], Mehar Dhillon[1], Luise Puls[1], Boyko Gueorguiev[1], Geoff Richards[1], Hans Christoph Pape[2], Tatjana Pastor[3], Torsten Pastor[4]

[1]AO Research Institute Davos, Davos, Switzerland, *[2]University Hospital Zürich, Zürich, Switzerland*, *[3]Bürgerspital Solothurn, Solothurn, Switzerland*, *[4]Cantonal Hospital Lucerne, Wolhusen, Switzerland*

Introduction: Distal triceps tendon rupture is related to high complication rates with up to 25% failures. Elbow stiffness is another severe complication, as the traditional approach considers prolonged immobilization to ensure tendon healing. Recently a dynamic high-strength suture tape was designed, implementing a silicone-infused core for braid shortening and preventing repair elongation during mobilization, thus maintaining constant tissue approximation. The aim of this study was to biomechanically compare the novel dynamic tape versus a conventional high-strength suture tape in a human cadaveric distal triceps tendon rupture repair model.

Method: Sixteen paired arms from eight donors were used. Distal triceps tendon rupture tenotomies and repairs were performed via the crossed transosseous locking Krackow stitch technique for anatomic footprint repair using either conventional suture tape (ST) or novel dynamic tape (DT). A postoperative protocol mimicking intense early rehabilitation was simulated, by a 9-day, 300-cycle daily mobilization under 120N pulling force followed by a final destructive test.

Result: Significant differences were identified between the groups regarding the temporal progression of the displacement in the distal, intermediate, and proximal tendon aspects, $p<0.001$. DT demonstrated significantly less displacement compared to ST (4.6±1.2mm versus 7.8±2.1mm) and higher load to failure (637±113N versus 341±230N), $p\leq0.037$. DT retracted 0.95±1.95mm after each 24-hour rest period and withstood the whole cyclic loading sequence without failure. In contrast, ST failed early in three specimens.

Conclusion: From a biomechanical perspective, DT revealed lower tendon displacement and greater resistance in load to failure over ST during simulated daily mobilization, suggesting its potential for earlier elbow mobilization and prevention of postoperative elbow stiffness.

NOVEL APPLICATION OF THE OXFORD KNEE SCORE TO ASSESS KNEE PAIN, FUNCTION, AND QUALITY OF LIFE AFTER WEIGHT LOSS SURGERY

Simon Federer[1,2], Madeleine Dunne[1,2], Chris Pring[2], Neal Smith[1], Penny Hudson[1]

[1]University of Chichester, Chichester, United Kingdom, *[2]St. Richard's Hospital, University Hospitals Sussex,, Chichester, United Kingdom*

Introduction: Many patients with obesity experience knee pain. Excess body weight is a modifiable risk factor for osteoarthritis (OA) and weight loss is encouraged in patients with OA. Bariatric surgery could improve or limit the progression of these conditions through significant weight loss. The Oxford Knee Score (OKS) is a validated tool in the assessment of knee replacement surgery for OA. We present a novel application of the OKS to assess knee pain & function after weight loss surgery. The primary aim of this study was to assess whether there was a significant difference in mean OKS before and 24 months after weight loss surgery.

Method: Eighteen female participants were included in this study. They underwent sleeve gastrectomy or Roux-en-Y gastric bypass. Patient demographics, body mass index (BMI) and OKS were collected pre- and 24 months post operatively.

Result: There was an increase in the mean OKS from 31.8 (SD 11.8) pre surgery to 36.6 (SD 12.3) at 24 months. This was statistically significant (95% CI 0.99-10.5, p=0.02). Mean BMI reduced from 46.6 kg/m^2 (SD 5.8) to 33.0 kg/m^2 (SD 3.5).

Conclusion: A significant improvement in mean OKS was seen after weight loss surgery. These findings demonstrate an improvement in knee pain & function with weight loss. This study contributes to a larger project evaluating the kinetic and kinematic changes to walking gait from weight loss.

BIOMECHANICAL EVALUATION OF DOUBLE-STRANDED KNOT CONFIGURATIONS IN HIGH-STRENGTH SUTURES AND TAPES. HOW MANY KNOTS ARE NECESSARY TO ACHIEVE KNOT SECURITY?

Mehar Dhillon[1,2], Tatjana Pastor[1], Ivan Zderic[1], Torsten Pastor[3], Boyko Gueorguiev[4]

[1]AO Research Institute Davos, Switzerland, *[2]Postgraduate Institute of Medical Education & Research (PGIMER), Chandigarh, India*, *[3]Department of Orthopaedic and Trauma Surgery, Lucerne Cantonal Hospital, Lucerne, Switzerland, Switzerland*, *[4]AO Research Institute, Davos, Switzerland*

Introduction: Recently, a new dynamic high-strength round suture dynacord (DC) was introduced featuring a salt-infused silicone core attracting water in a fluid environment to preserve tissue approximation which is also available in tape form (DT). Study aims: (1) assess the influence of securing knot number on knot security of two double-stranded knot configurations (Cow-hitch and Nice-knot) tied with either dynamic (DC and DT) or conventional round sutures fiberwire (FW) and conventional suture tapes (ST), (2) compare the ultimate force and knot slippage of (a) Cow-hitch and Nice-knot and (b) DC and DT versus FW and FT at their minimal number of needed securing knots.

Method: Seven specimens of each FW, ST, DC and DT were considered for tying with Cow-hitch or Nice-knots. The base of these Cow-hitch and Nice-knots were secured with surgeons' knots using 1-3 alternating throws. Tensile tests were conducted under physiologic conditions to evaluate knot slippage, ultimate force at rupture, and minimum number of knots ensuring 100% knot security

Result: 100% knot security for both Cow-hitch and Nice-knots was achieved with 2 securing knots for DC, DT, ST, and with 3 securing knots for FW. With these minimum number of securing knots ultimate force was significantly higher for Nice-knots versus Cow-hitch in DT ($p=0.001$) and slippage was significantly higher in Cow-hitch versus Nice-knot tied with DC ($p=0.019$).

Conclusion: The minimum number of securing knots required to achieve 100% knot security was 2 for DC, DT and ST both with Cow-hitch and Nice-knots. In contrast, 3 securing knots were needed in FW. With these minimum number of securing knots Nice-knots were associated with higher ultimate forces in DT and lower slippage in DC versus Cow-hitch knots. Furthermore, the novel self-tightening suture material (DT and DC) does not reduce slippage, which is unavoidable in all used sutures.

ESTABLISHING A HUMAN OSTEOCYTE-STAPHYLOCOCCUS EPIDERMIDIS INFECTION MODEL TO REVEAL MECHANISMS OF CHRONIC BONE AND JOINT INFECTIONS.

Claudia Siverino[1], Qi Sun[2], Dongqing Yang[2], Bogdan Solomon[2], Fintan Moriarty[1], Gerald Atkins[2]

[1]AO Research Institute, Davos, Switzerland, *[2]University of Adelaide, Adelaide, Australia*

Introduction: Bone and joint infection (BJI) is often characterized by severe inflammation and progressive bone destruction. Osteocytes are the most numerous and long-lived bone cell type, and therefore represent a potentially important long-term reservoir of bacterial infection. *Staphylococcus aureus* is known to establish stable intracellular osteocytic infections, however, little is known about the less virulent yet second most prevalent BJI pathogen, *S. epidermidis*, associated with late-diagnosed, chronic BJI. Thus, this study sought to establish an *in vitro* model to study the infection characteristics of *S. epidermidis* in human osteocyte-like cells.

Methods: SaOS2 cells (1 x10^4 cells/cm^2) were grown to confluence either without differentiation, representing an osteoblast-like (OB) state (SaOS2-OB) or differentiated to an osteocyte-like stage (SaOS2-OY), using established methods. Four *S. epidermidis* strains used (ATCC-12228, ATCC-14990, ATCC-35984 and a clinical osteomyelitis strain RAH-SE1) were tested to be Lysostaphin-resistant, necessitating antibiotic (Levofloxacin) control of extracellular bacteria. Infection of host cells (OB or OY) was tested at three multiplicities of infection (MOI: 10, 100 and 1000). Extracellular bacteria were controlled by overnight incubation at a 10X minimum inhibitory concentration (MIC) of Levofloxacin and thereafter at 1XMIC. At each time point (days 1, 3, 5) viable intra- and extracellular bacteria were quantified.

Result: All strains displayed similar intracellular infection and persistence capabilities in SaOS2-OB and SaOS2-OY. Independent of MOI, intracellular bacteria in SaOS2-OB decreased over time, becoming non-culturable by day 5. In contrast, SaOs2-OY displayed enhanced intracellular bacterial persistence at each time point. In the presence of increased Levofloxacin concentration (10XMIC), *S. epidermidis* could persist intracellularly for at least 14 days.

Conclusion: This study showed for the first time that *S. epidermidis* can infect human osteocytes and persist intracellularly. Additionally, even a 10xMIC antibiotic concentration failed to eradicate intracellular bacteria, suggesting that persistence within osteocytes could contribute to treatment failure and establishment of chronic BJI.

DYNAMIC UNLOADING OF HEALTHY BOVINE TAIL DISCS: BIOMECHANICS AND BIOLOGY SUGGEST FACILITATED WATER UPTAKE

Astrid Soubrier[1,2], Hermann Kasper[1], Mauro Alini[1], Ilse Jonkers[2], Sybille Grad[1]

[1]AO Research Institute Davos, Davos, Switzerland, *[2]KU Leuven, Leuven, Belgium*

Introduction: Intervertebral disc degeneration has been associated with low back pain (LBP) which is a major cause of long-term disability worldwide. Observed mechanical and biological modifications have been related to decreased water content.

Clinical traction protocols as part of LBP management have shown positive outcomes. However, the underlying mechanical and biological processes are still unknown.

The study purpose was to evaluate the impact of unloading through traction on the mechanobiology of healthy bovine tail discs in culture.

Method: We loaded bovine tail discs (n=3/group) 2h/day at 0.2Hz for 3 days, either in dynamic compression (-0.01MPa to -0.2MPa) or in dynamic traction (-0.01MPa to 0.024MPa). In between the dynamic loading sessions, we subjected the discs to static compression loading (-0.048MPa). We assessed biomechanical and biological parameters.

Result: Over the 3 days of loading, disc height decreased upon dynamic compression loading but increased upon unloading. The neutral zone was restored for all samples at the end of the dynamic unloading. Upon dynamic compression, the stiffness increased over time while the hysteresis decreased. Upon dynamic unloading, sulfated glycosaminoglycan (sGAG) release in the medium was lower at the endpoint. In the outer annulus fibrosus (AFo), we saw a higher water/sGAG of at least 30%. In the nucleus pulposus, COL2 mRNA was expressed more highly upon dynamic unloading while MMP3, iNOS and TRPV4 expression levels were lower. In the AFo of the unloading group, COL2 expression was higher but COL1 was lower.

Conclusion: The biomechanical and biological results consistently indicate that dynamic unloading of healthy bovine discs in culture facilitates water uptake and promotes an anti-catabolic response which reflects a function optimization of the disc.

This work combines biomechanical and biological results and opens the door to evidence-based improvement of regenerative protocols for degenerated discs and conservative LBP management.

This study is funded by AO Foundation and AO Spine.

COMPARISON OF POSTOPERATIVE CLINICAL OUTCOMES BETWEEN CRUCIATE RETAINING AND RESECTING TOTAL KNEE ARTHROPLASTY WITH A CRUCIATE SUBSTITUTING INSERT

Kei Kato[1], seiju hayashi[1]

[1]yawatahama hosp, yawatahama, Japan

Purpose: To compare postoperative clinical outcomes between posterior cruciate ligament (PCL) retaining and resecting total knee arthroplasty (TKA) using same cruciate-substituting (CS) inserts, and to elucidate the clinical relevance of the residual PCL in cruciate-retaining TKA, considering intraoperative influence factors, such as the posterior tibial slope, posterior condylar offset, joint gap, joint balance, and joint laxity.

Methods: A total of 64 consecutive knees (44 patients) were enrolled in this study and divided into following two groups: 39 knees underwent PCL-retaining TKA group (CR group), and 25 underwent PCL-resecting TKA group (CS group). Preoperative patients' demographic data and one-year postoperative clinical outcomes including range of motion, the Knee Injury and Osteoarthritis Outcome Score (KOOS), the Japanese Orthopaedic Association (JOA) score, and Forgotten Joint Score-12 (FJS-12) were compared between two groups.

Results: Regarding range of motion, the average preoperative ROM was -14.3/120.0 degrees in the CR group and improved to -2.4/118.9 degrees postoperatively. In the CS group, the average preoperative ROM was -7.5/130 degrees and changed to -2.2/122.4 degrees postoperatively. There was no significant difference in the postoperative ROM between the groups (P=0.16). The KOOS (from 47.1 to 69.5 in CR group; from 41.1 to 70.8 in CS group) and JOA scores (from 59.2 to 76.9 in CR group; from 55.6 to 80.8 in CS group) were significantly improved postoperatively in both groups ($P < 0.01$). However, there was no significance in these postoperative scores between two groups ($P = 0.09$). There was also no significance in FJS-12 between two groups (70.3 in CR group and 66.9 in CS group; P=0.53).

Conclusions: Residual PCL in TKA with a CS insert would not impact one-year postoperative clinical outcomes including KOOS, JOA, and FJS-12.

THE ROLE OF THE PLANTAR FASCIA IN SUPPORTING THE ARCH IN PROGRESSIVE COLLAPSING FOOT DEFORMITY

Hamed Malakoutikhah[1], Erdogan Madenci[1], Daniel Latt[1]

[1]*University of Arizona, Tucson, United States*

Introduction: The arch of the foot has been described as a truss where the plantar fascia (PF) acts as the tensile element. Its role in maintaining the arch has likely been underestimated because it only rarely torn in patients with progressive collapsing foot deformity (PCFD). We hypothesized that elongation of the plantar fascia would be a necessary and sufficient precursor of arch collapse.

Method: We used a validated finite element model of the foot reconstructed from CT scan of a female cadaver. Isolated and combined simulated ligament transection models were created for each combination of the ligaments. A collapsed foot model was created by simulated transection of all the arch supporting ligaments and unloading of the posterior tibial tendon. Foot alignment angles, changes in force and displacement within each of the ligaments were compared between the intact, isolated ligament transection, and complete collapse conditions.

Result: Isolated release of the PF did not cause deformity, but lead to increased force in the long (142%) and short plantar (156%), deltoid (45%), and spring ligaments (60%). The PF was the structure most able to prevent arch collapse and played a secondary role in preventing hindfoot valgus and forefoot abduction deformities. Arch collapse was associated with substantial attenuation of the spring (strain= 41%) and interosseous talocalcaneal ligaments (strain= 27%), but only a small amount in the plantar fascia (strain= 10%).

Conclusion: Isolated PF release did not cause arch collapse, but arch collapse could not occur without at least 10% elongation of the PF. Simulated transection of the PF led to substantial increase in the force in the other arch supporting ligaments, putting the foot at risk of arch collapse over time. Chronic degeneration of the PF leading to plantar fasciitis may be an early sign of impending PCFD.

REDUCED HEART RATE VARIABILITY AND INCREASED STRESS HORMONE LEVELS INDICATE AN AUTONOMIC DYSFUNCTION IN OSTEOARTHRITIS PATIENTS

Rebecca Sohn[1], Tina Assar[2], Isabelle Kaufhold[2], Marco Brenneis[1], Sebastian Braun[3], Marius Junker[4], Frank Zaucke[1], Georg Pongratz[5], Zsuzsa Jenei-Lanzl[1]

[1]Department of Trauma Surgery and Orthopedics, Goethe University Frankfurt, University Hospital, Frankfurt am Main, *[2]3Department of Trauma Surgery and Orthopedics, Goethe University Frankfurt, University Hospital, Frankfurt am Main*, *[3]Charité - Universitätsmedizin Berlin, Berlin, Germany*, *[4]Department of Orthopedics, Tabea Hospital Hamburg, Hamburg, Germany*, *[5]Medical Faculty of the University of Regensburg, Regensburg*

Introduction: Recent studies suggested that the progression of osteoarthritis (OA), a chronic degenerative joint disease, may be affected by the autonomic nervous system (ANS). Under healthy conditions, the sympathetic (SNS) and parasympathetic (PNS) branches of the ANS are well coordinated to maintain homeostasis. However, pathological conditions are frequently associated with a disturbance of this fine-tuned balance. Therefore, we analyzed whether an autonomic dysfunction occurs in OA patients.

Method: 225 participants with early- or late-stage knee OA as well as 40 healthy age-matched probands were included in this study. Autonomic activity was investigated by analyzing heart rate variability (HRV), which decreases under chronic sympathetic overactivity. Time- and frequency-domain HRV indices SDRR, RMSSD, pRR50 and LF were examined. Linear regression analysis was performed to adjust for clinical characteristics, such as age, sex, BMI, or medication. Moreover, perceived chronic stress (PSQ) and pain (WOMAC) were assessed via questionnaires. In addition, the serum stress hormones cortisol, DHEA-S and IL-6 were analyzed via ELISA.

Result: SDRR, RMSSD, and pRR50 were slightly reduced in the early stage of OA and showed significant decrease in the later stage of the disease. Also LF decreased significantly with OA progression. HRV was significantly influenced by the grade of OA, but not other patient characteristics. Moreover, late-stage OA patients demonstrated significantly higher PSQ and WOMAC levels compared to healthy controls. In addition, cortisol/DHEA-S ratio and IL-6 serum concentrations were significantly higher in late-stage than in early-stage OA patients and healthy controls.

Conclusion: Reduced HRV, increased cortisol/DHEA-S ratio and PSQ level as well as elevated systemic IL-6 concentration indicated an autonomic shift towards a more pronounced SNS activity due to PNS deficiency in OA patients, particularly in the late-stage of the disease. Therefore, modulation of the ANS, for example by vagus nerve stimulation, might be a potential treatment strategy for of knee OA patients.

PROGRESSIVE RESISTANCE TRAINING OR NEUROMUSCULAR EXERCISE FOR HIP OSTEOARTHRITIS. A MULTICENTER CLUSTER RANDOMIZED CONTROLLED TRIAL

Troels Kjeldsen[1,2,3], Søren Thorgaard Skou[3], Ulrik Dalgas[4], Lisa Tønning[1], Sara Birch[5], Thomas Frydendal[1], Claus Varnum[6], Mette Garval[7], Kim G Ingwersen[8], Inger Mechlenburg[6]

[1]Department of Orthopedic Surgery, Aarhus University Hospital, Aarhus, Denmark, Denmark, *[2]Department of Clinical Medicine, Aarhus University, Aarhus, Denmark, Denmark*, *[3]The Research and Implementation Unit PROgrez, Department of Physiotherapy and Occupational Therapy, Næstved-Slagelse-Ringsted Hospitals, Slagelse, Denmark, Denmark*, *[4]Exercise Biology, Department of Public Health, Aarhus University, Aarhus, Denmark, Denmark*, *[5]Department of Orthopedic Surgery, Gødstrup Regional Hospital, Herning, Denmark, Denmark*, *[6]Department of Orthopedic Surgery, Lillebaelt Hospital - Vejle, University Hospital of Southern Denmark, Denmark, Denmark*, *[7]Elective Surgery Centre, Regional Hospital Silkeborg, Silkeborg, Denmark, Denmark*, *[8]Department of Physio- and Occupational Therapy, Lillebaelt Hospital - Vejle, University Hospital of Southern Denmark, Denmark, Denmark*

Introduction: Exercise is recommended as first-line treatment for patients with hip osteoarthritis (OA). Interestingly, content and dose of exercise interventions seem to be important for the effect of exercise interventions, but the optimal content and dose is unknown. This warrants randomized controlled trials providing evidence for the optimal exercise program in Hip OA. The aim of this trial was to investigate whether progressive resistance training (PRT) is superior to neuromuscular exercise (NEMEX) for improving functional performance, hip pain and hip-related quality of life in patients with hip OA.

Method: This was a multicenter, cluster-randomized, controlled, parallel-group, assessor-blinded, superiority trial. 160 participants with clinically diagnosed hip OA were recruited from hospitals and physiotherapy clinics and randomly assigned to twelve weeks of PRT or NEMEX. The PRT intervention consisted of 5 high-intensity resistance training exercises targeting muscles at the hip and knee joints. The NEMEX intervention included 10 exercises and emphasized sensorimotor control and functional stability. The primary outcome was change in the 30-second chair stand test (30s-CST). Key secondary outcomes were changes in scores on the pain and hip-related quality of life (QoL) subscales of the Hip Disability and Osteoarthritis Outcome Score (HOOS).

Result: The mean changes from baseline to 12-week follow-up in the 30s-CST were 1.5 (95% CI, 0.9 to 2.1) chair stands with PRT and 1.5 (CI, 0.9 to 2.1) chair stands with NEMEX (difference, 0.0 [CI, 0.8 to 0.8] chair stands). For the HOOS pain subscale, mean changes were 8.6 (CI, 5.3 to 11.8) points with PRT and 9.3 (CI, 5.9 to 12.6) points with NEMEX. For the HOOS QoL subscale, mean changes were 8.0 (CI, 4.3 to 11.7) points with PRT and 5.7 (CI, 1.9 to 9.5) points with NEMEX.

Conclusion: In patients with hip OA, PRT is not superior to NEMEX for improving functional performance, hip pain, or hip-related QoL.

FUCOIDANS FROM LAMINARIA HYPERBOREA DEMONSTRATE BACTERICIDAL ACTIVITY AGAINST DIVERSE BACTERIA.

Luke Beagan[1,2], Line Lundegaard Bang[1,2], Jens Pettersen[1,2], Rasmus Birkholm Gronnemose[1], Sebastian Foertsch[3], Thomas Emil Andersen[1,2], Ming Ding[1,2]

[1]Odense University Hospital, Odense , Denmark, *[2]University of Southern Denmark, Odense , Denmark*, *[3]IFF N&H Germany GmbH & Co. KG, Walsrode, Germany*

Introduction: Fucoidans are a heterogenous class of fucose-rich sulfated carbohydrates which have attracted increasing attention in cancer and inflammation research due to their bioactive properties. There are reports that fucoidans may have direct antibacterial effects and synergy with antibiotics. However, the literature is conflicting, potentially due to the limited reporting of origin, characteristics, and extraction methods of the fucoidans tested. Here we report the results of 18 defined fucoidans screened for direct, indirect, and synergistic antibacterial effects.

Method: 15 distinct fucoidan fractions, isolated from *Laminaria hyperborea* using a solvent-free extraction process, were characterised for molecular weight, pH, viscosity, and sulfur content. These, together with three commercially available crude fractions, were assessed at concentrations from 0.03125-24mg mL^{-1} for minimum inhibitory concentration against *Staphylococcus aureus*, *Streptococcus mutans* and *Streptococcus sanguinis.* Furthermore, we tested a selection of fucoidans for antibacterial synergy with vancomycin and indirect antibacterial effects in whole blood survival assays. Reverse-transcription quantitative polymerase chain reaction (RT-qPCR) was performed to assess the stress response in fucoidan-treated *S. aureus* cultures.

Result: We have identified one fucoidan fraction with bactericidal activity against diverse bacteria. This effect is dose-, fucoidan fraction- and bacteria-specific, and furthermore, not related to osmotic stress. No synergistic effects were observed with fucoidan in combination vancomycin.

Conclusion: Fucoidans have exciting potential as antimicrobial agents. Further analysis is required to establish the precise molecular characteristics responsible for their potent bactericidal activity.

TAILOR-MADE NANOSWITCHES FOR TARGETED MODULATION OF PIEZO1 MECHANOSENSING INFLUENCE STEM CELL FATE

Simao P. B. Teixeira[1,2], Alberto Pardo[3], Pablo Taboada[3], Maja Wolleb[4,5], Jess Snedeker[4,5], Rui L. Reis[1,2], Maria Manuela Estima Gomes[1,2], Rui M. A. Domingues[1,2]

[1]3B's Research Group, I3Bs - Research Institute on Biomaterials, Biodegradables and Biomimetics, University of Minho, 4805-017 Barco, Guimaraes, Portugal, *[2]ICVS/3B's–PT Government Associate Laboratory, Braga/Guimaraes, Portugal*, *[3]Colloids and Polymers Physics Group, Department of Particle Physics and Health Research Institute, University of Santiago de Compostela, 15782 Santiago de Compostela, Spain*, *[4]Department of Orthopedics, Balgrist University Hospital, University of Zurich, 8008 Zurich, Switzerland*, *[5]Institute for Biomechanics, ETH Zurich, 8093 Zurich, Switzerland*

Introduction: PIEZO mechanoreceptors are increasingly recognized to play critical roles in fundamental physiological processes like proprioception, touch, or tendon biomechanics. However, their gating mechanisms and downstream signaling are still not completely understood, mainly due to the lack of effective tools to probe these processes. Here, we developed new tailor-made *nanoswitches* enabling wireless targeted actuation on PIEZO1 by combining molecular imprinting concepts with magnetic systems.

Method: Two epitopes from functionally relevant domains of PIEZO1 were rationally selected in silico and used as templates for synthesizing molecularly imprinted nanoparticles (MINPs). Highly-responsive superparamagnetic zinc-doped iron oxide nanoparticles were incorporated into MINPs to grant them magnetic responsiveness. Endothelial cells (ECs) and adipose tissue-derived stem cells (ASCs) incubated with each type of MINP were cultured under or without the application of cyclical magnetomechanical stimulation. Downstream effects of PIEZO1 actuation on cell mechanotransduction signaling and stem cell fate were screened by analyzing gene expression profiles.

Result: Nanoswitches showed sub-nanomolar affinity for their respective epitope, binding PIEZO1-expressing ECs similarly to antibodies. Expression of genes downstream of PIEZO1 activity significantly changed after magnetomechanical stimulation, demonstrating that nanoswitches can transduce this stimulus directly to PIEZO1 mechanoreceptors. Moreover, this wireless actuation system proved effective for modulating the expression of genes related to musculoskeletal differentiation pathways in ASCs, with RNA-sequencing showing pronounced shifts in extracellular matrix organization, signal transduction, or collagen biosynthesis and modification. Importantly, targeting each epitope led to different signaling effects, implying distinct roles for each domain in the sophisticated function of these channels.

Conclusion: This innovative wireless actuation technology provides a promising approach for dissecting PIEZO-mediated mechanobiology and suggests potential therapeutic applications targeting PIEZO1 in regenerative medicine for mechanosensitive tissues like tendon.

Acknowledgements: EU's Horizon 2020 ERC under grant No. 772817 and Horizon Europe under grant No. 101069302; FCT/MCTES for PD/BD/143039/2018, COVID/BD/153025/2022, 10.54499/2020.03410.CEECIND/CP1600/CT0013, 10.54499/2022.05526.PTDC, 10.54499/UIDB/50026/2020, 10.54499/UIDP/50026/2020, and 10.54499/LA/P/0050/2020.

IS ASSESSING HUMERAL HEAD MIGRATION IN A SUPINE POSITION ASSOCIATED WITH ITS ASSESSMENT IN FUNCTIONALLY-RELEVANT ARM POSITIONS?

Nazanin Daneshvarhashjin[1], Philippe Debeer[2], Michael Skipper Andersen[3], Filip Verhaegen[2], Lennart Scheys[1,2]

[1]KU Leuven University, Leuven, Belgium, *[2]UZ Leuven hospital, Leuven, Belgium*, *[3]Aalborg University, Denmark*

Introduction: Assessment of the humeral head translation with respect to the glenoid joint, termed humeral head migration (HHM), is crucial in total shoulder arthroplasty pre-operative planning. Its assessment informs current classification systems for shoulder osteoarthritis as well as the evaluation of surgical correction. In current clinical practice, HHM assessment relies on computed-tomography (CT) imaging. However, the associated supine position might undermine its functional relevance as it does not reflect the weight-bearing condition with active muscle engagement associated with the upright standing position of most daily activities. Therefore, we assessed to what extent HHM in a supine position is associated with HHM in a range of functional arm positions.

Method: 26 shoulder osteoarthritis patients and 12 healthy volunteers were recruited. 3D shapes of the humerus and scapula were reconstructed from their respective CT scans using an image processing software [3], and their CT-scan-based HHMs were measured. Furthermore, all subjects underwent low-dose biplanar radiography [4] in four quasi-static functional arm positions while standing: relaxed standing, followed by 45 degrees of shoulder extension, flexion, and abduction. Using a previously validated method implemented in the programming platforms[5], 3D shapes were registered to the pairs of biplanar images for each arm position and the corresponding functional HHM was measured. Bivariate correlations were assessed between the CT-based HHM and each functional arm position.

Result: HHM in 45 degrees of flexion and extension both showed significant and strong correlations ($r>0.66$ and $P<0.01$) with HHM assessed in the supine position. However, such a high correlation was not found for relaxed standing and 45 abduction.

Conclusion: Although HHM in a supine position correlates with HHM in 45-degree extension and flexion, it is poorly associated with the HHM in abduction and relaxed standing. These results may suggest the inclusion of more functionally-relevant patient positioning toward better-informed shoulder arthroplasty planning.

Acknowledgement: Funding from PRosPERos-II Project.

[3] Mimics (Materialise, Belgium)
[4] EOS system (EOS imaging, France)
[5] MATLAB (The Mathworks, USA) and 3-matic (Materialise, Belgium) scripting platform.

DEVIATION FROM PREOPERATIVE PLANNING AND ACCURACY OF TRANSPEDICULAR SCREW FIXATION USING INTRAOPERATIVE 3D NAVIGATION FOR LUMBAR SPONDYLOLISTHESIS

Gianluca Vadalà[1], Giuseppe Francesco Papalia[1], Fabrizio Russo[1], Niccolò Nardi[1], Luca Ambrosio[1], Rocco Papalia[1], Vincenzo Denaro[1]

[1]*Fondazione Policlinico Universitario Campus Bio-Medico, Rome, Italy*

Introduction: Intraoperative navigation systems for lumbar spine surgery allow to perform preoperative planning and visualize the real-time trajectory of pedicle screws. The aim of this study was to evaluate the deviation from preoperative planning and the correlations between screw deviation and accuracy.

Method: Patients affected by degenerative spondylolisthesis who underwent posterior lumbar interbody fusion using intraoperative 3D navigation since April 2022 were included. Intraoperative cone-beam computed tomography (CBCT) was performed before screw planning and following implantation. The deviation from planning was calculated as linear, angular, and 3D discrepancies between planned and implanted screws. Accuracy and facet joint violation (FJV) were evaluated using Gertzbein-Robbins system (GRS) and Yson classification, respectively. Statistical analysis was performed using SPSS version28. One-way ANOVA followed by Bonferroni post-hoc tests were performed to evaluate the association between GRS, screw deviation and vertebral level. Statistical significance was set at $p<0.05$.

Result: This study involved 34 patients, for a total of 154 pedicle screws. Mean age was 62.6±8.9 years. The mean two-dimensional screw tip deviation in mediolateral (ML), craniocaudal (CC), and anteroposterior (AP) was 2.6±2.45mm, 1.6±1.7mm, and 3.07±2.9mm, respectively. The mean screw tip 3D deviation was 5±3.3mm. The mean two-dimensional screw head deviation in ML, CC and AP was 1.83±1.8mm, 1.7±1.67mm and 3.6±3.1mm, respectively. The mean screw head 3D deviation was 4.94±3.2mm. 98% of screws were clinically acceptable (grade A+B), and grade 0 for FJV. Significant results were found between GRS and ML ($p=0.005$), AP ($p=0.01$) and 3D ($p=0.003$) tip deviations, and between GRS and AP and 3D head deviations (both $p=0$). Moreover, a significant correlation was found between GRS and vertebral level ($p=0$).

Conclusion: Our results showed a reasonable rate of discrepancy between planned and positioned screws. However, accuracy was clinically acceptable in almost all cases. Therefore, pedicle screw fixation using intraoperative CBCT, 3D navigation and screw planning is safe and accurate.

TRICARBOXYLIC ACID CYCLE INTERMEDIATE A-KETOGLUTARATE PRESERVES BONE FORMATION AND COUNTERACTS OSTEOPOROSIS DEVELOPMENT

Yu-Shan Chen[1], Wei-Shiung Lian[1], Yu-Han Lin[2], Feng-Sheng Wang[1]

[1]Core Laboratory for Phenomics and Diagnostic, Department of Medical Research, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung City, Taiwan, *[2]Center for Mitochondrial Research and Medicine, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung City, Taiwan*

Introduction: Promoting bone mass homeostasis keeps skeleton away from osteoporosis. a-Ketoglutarate (a-KG) is an indispensable intermediate of tricarboxylic acid cycle (TCA) process for cellular energy production. a-KG mitigates cellular senescence, tissue degeneration, and oxidative stress. We investigated whether a-KG affected osteoblast activity or osteoporosis development.

Method: Serum and bone specimens were biopsied from 26 patients with osteoporosis or 24 patients without osteoporosis who required spinal surgery. Ovariectomized or aged mice were fed 0.25% or 0.75% a-KG in drinking water for 8 - 12 weeks *ad libitum*. Bone mineral density, trabecular/cortical bone microarchitecture, mechanical strength, bone formation, and osteoclastic erosion were investigated using mCT, material testing device, in vivo calcein labelling, and TRAP histochemical staining. Serum a-KG, osteocalcin, and TRAP5b levels were quantified using ELISA kits. Bone-marrow mesenchymal cells and macrophages were incubated osteogenic and osteoclastogenic media. Histone H3K27me3 levels and enrichment were investigated using immunoblotting and chromatin precipitation-PCR.

Result: Serum a-KG levels in patients with osteoporosis were less than controls; and were correlated with T-scores of hips ($R2 = 0.6471$, $P < 0.0001$) and lumbar spine ($R2 = 0.7235$, $P < 0.001$) in osteoporosis (AUC = 0.9941, $P < 0.001$). a-KG supplement compromised a plethora of osteoporosis signs in ovariectomized or aged mice, including bone mass loss, trabecular bone microarchitecture deterioration, and mechanical strength loss. It elevated serum osteocalcin levels and decreased serum TRAP5b. a-KG preserved caclein-labelling bone formation and repressed osteoclast resorption. It reversed osteogenic differentiation of bone-marrow stromal cells and reduced osteoclast formation in ovariectomized mice. Mechanically, a-KG attenuated H3K27 hypermethylation and Runx2 transcription repression, improving mineralized matrix production in osteogenic cells.

Conclusion: Decreased serum a-KG is correlated with human and murine osteoporosis. a-KG reverses bone loss by repressing histone methylation in osteoblasts. This study highlighted a-KG supplement as a new biochemical option for protecting osteoporosis.

IMPLANT DETECTION AND CLASSIFICATION FROM A SMALL DATASET OF LOWER LIMB X-RAYS: PERFORMANCE OF DEEP LEARNING MODELS PRE-TRAINED ON LARGER DATASETS

Franz Birkholtz[1,2], Maaike Eken[2,3], Matthew Swanevelder[4], Andries Engelbrecht[4,5]

[1]Institute of Orthopaedics and Rheumatology, Mediclinic Winelands Orthopaedic Hospital, Stellenbosch, South Africa, *[2]Division of Orthopaedic Surgery, Department of Surgical Sciences, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa*, *[3]Division of Sport and Exercise Medicine, Department of Exercise, Sport and Lifestyle Medicine, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa*, *[4]Department of Industrial Engineering, and Computer Science Division, Stellenbosch University, Stellenbosch, South Africa*, *[5]Center for Applied Mathematics and Bioinformatics, Gulf University for Science and Technology, Mubarak Al-Abdullah, West Mishref, Kuwait*

Introduction: Inaccurate identification of implants on X-rays may lead to prolonged surgical duration as well as increased complexity and costs during implant removal. Deep learning models may help to address this problem, although they typically require large datasets to effectively train models in detecting and classifying objects, e.g. implants. This can limit applicability for instances when only smaller datasets are available. Transfer learning can be used to overcome this limitation by leveraging large, publicly available datasets to pre-train detection and classification models. The aim of this study was to assess the effectiveness of deep learning models in implant localisation and classification on a lower limb X-ray dataset.

Method: Firstly, detection models were evaluated on their ability to localise four categories of implants, e.g. plates, screws, pins, and intramedullary nails. Detection models (Faster R-CNN, YOLOv5, EfficientDet) were pre-trained on the large, freely available COCO dataset (330000 images). Secondly, classification models (DenseNet121, Inception V3, ResNet18, ResNet101) were evaluated on their ability to classify five types of intramedullary nails. Localisation and classification accuracy were evaluated on a smaller image dataset (204 images).

Result: The YOLOv5s model showed the best capacity to detect and distinguish between different types of implants (accuracy: plate=82.1%, screw=72.3%, intramedullary nail=86.9%, pin=79.9%). Screw implants were the most difficult implant to detect, likely due to overlapping screw implants visible in the image dataset. The DenseNet121 classification model showed the best performance in classifying different types of intramedullary nails (accuracy=73.7%). Therefore, a deep learning model pipeline with the YOLOv5s and DenseNet121 was proposed for the most optimal performance of automating implants localisation and classification for a relatively small dataset.

Conclusion: These findings support the potential of deep learning techniques in enhancing implant detection accuracy. With further development, AI-based implant identification may benefit patients, surgeons and hospitals through improved surgical planning and efficient use of theatre time.

BIOMECHANICAL ANALYSIS OF ADOLESCENT IDIOPATHIC SCOLIOSIS: INVESTIGATING MUSCLE ACTIVATION ASYMMETRY DURING GAIT USING A COMPREHENSIVE THORACIC MUSCULOSKELETAL MODEL

Hamed Shayestehpour[1], Mohammad Amin Shayestehpour[2], Christian Wong[3], Jesper Bencke[4], John Rasmussen[5]

[1]AnyBody Technology, former PhD student at Aalborg University, Denmark, *[2]Norwegian University of Science and Technology, Denmark*, *[3]University Hospital of Denmark, Rigshospitalet, Denmark*, *[4]Amager and Hvidovre Hospital, Department of Orthopedic Surgery, Denmark*, *[5]Aalborg University, Denmark*

Introduction: Adolescent Idiopathic Scoliosis (AIS) is a three-dimensional deformity of the spine with unclear etiology. Due to the asymmetry of lateral curves, there are differences in the muscle activation between the convex and concave sides. This study utilized a comprehensive thoracic spine and ribcage musculoskeletal model to improve the biomechanical understanding of the development of AIS deformity and approach an explanation of the condition.

Methods: In this study, we implemented a motion capture model using a generic rigid-body thoracic spine and ribcage model, which is kinematically determinate and controlled by spine posture obtained, for instance, from radiographs. This model is publicly accessible via a GitHub repository. We simulated gait and standing models of two AIS (averaging 15 years old, both with left lumbar curve and right thoracic curve averaging 25 degrees) and one control subject. The marker set included extra markers on the sternum and the thoracic and lumbar spine. The study was approved by the regional Research Ethics Committee (Journal number: H17034237).

Results: We investigated the difference between the muscle activation on the right and left sides including erector spinae (ES), psoas major (PS), and multifidus (MF). Results of the AIS simulations indicated that, on average throughout the gait cycle, the right ES, left PS and left MF had 46%, 44%, and 23% higher activities compared to the other side, respectively. In standing, the ratios were 28%, 40%, and 19%, respectively. However, for the control subject, the differences were under 7%, except ES throughout the gait, which was 17%.

Conclusion: The musculoskeletal model revealed distinct differences in force patterns of the right and left sides of the spine, indicating an instability phenomenon, where larger curves lead to higher muscle activations for stabilization.

Acknowledgement: The project is funded by the European Union's Horizon 2020 program through Marie Skłodowska-Curie grant No. [764644].

ENHANCING BIOMECHANICAL SPINE MODELS WITH NON-LINEAR RHYTHMS

Morten Lund[1], Hamed Shayestehpour[1]

[1]*AnyBody Technology, Aalborg, Denmark*

Introduction: This research aims to enhance the control of intricate musculoskeletal spine models, a critical tool for comprehending both healthy and pathological spinal conditions. State-of-the-art musculoskeletal spine models incorporate segments for all vertebra, each possessing 3 degrees-of-freedom (DOF). Manually defining the posture with this amount of DOFs presents a significant challenge. The prevalent method of equally distributing the spine's overall rotation among the vertebrae often proves to be an inadequate assumption, particularly when dealing with the entire spine.

Method: We have engineered a comprehensive non-linear spine rhythm and the requisite tools for its implementation in widely utilized musculoskeletal modelling software (1). The rhythm controls lateral bending, axial rotation, and flexion/extension. The mathematical and implementation details of the rhythm are beyond this abstract, but it's noteworthy that the implementation accommodates non-linear rhythms. This means, for example, that one set of rhythm coefficients is used for flexion and another for extension. The rhythm coefficients, which distinguish the movement along the spine, were derived from a review of spine literature. The values for spine and vertebra range-of-motion (ROM) vary significantly in published studies, and no complete dataset was found in any single study. Consequently, the rhythm presented here is a composite, designed to provide the most consistent and average set of rhythm coefficients.

Result: The novel spine rhythm simplifies the control of detailed spine models, accommodating varying amounts of input data. It allows for the specification of only the overall motion or the posture at a more detailed level (i.e., lumbar, thoracic, neck). The tools and rhythm coefficients are publicly available on GitHub.

Conclusion: The innovative spine rhythm enhances the usability of cutting-edge spine models. For flexion/extension of the spine, it introduces a non-linear rhythm, exhibiting distinct behaviour between flexion and extension - a feature not previously observed in musculoskeletal spine models.

1) The AnyBody Modeling System

CAN PIN SITE INFLAMMATION BE DETECTED WITH THERMOGRAPHIC IMAGING? A CROSS-SECTIONAL MULTICENTER STUDY OF PATIENTS TREATED WITH EXTERNAL FIXATORS.

Marie Fridberg[1], Ole Rahbek[1], Hans-Christen Husum[1], Anirejuoritse Bafor[2], Kirsten Duch[1], Christopher Iobst[2], Søren Kold[1]

[1]Interdisciplinary Orthopedics, Aalborg University Hospital, Aalborg, Denmark, *[2]Center for Limb Lengthening and Reconstruction, Nationwide Children's Hospital, Columbus, Ohio, United States*

Introduction: Patients with external fixators are at risk of pin site infection. A more objective assessment of possible pin site infection is warranted, particularly for future home-based monitoring of pin sites. The aim was to determine if thermography can detect signs of inflammation around pin sites by 1) Establishing a maximum temperature cut-off value 2) Investigating the correlation between local temperature and visual signs of inflammation 3) Adjust for anatomical location and ambient room temperature.

Method: This was a cross-sectional international multi-center study following STROBE guidelines. All patients with external ring-fixators scheduled for a visit in the out-patient clinic were eligible. Visual signs of inflammation were categorized using the Modified Gordon classification System (MGS, simplified sMGS). Thermographic imaging was done with an infrared camera (FLIR T540) and the maximum temperature within the ROI (MaxTp) was the primary outcome measure. Sample size and reliability were estimated. Cohen-Kappa, ROC-curve/AUC and Poisson regression were used for statistical analysis.

Result: Data from 1970 pin sites were included. Inter-rater reliability of MGS was Kappa=0.79 and for MaxTp ICC=0.99 (95%CI: 0.99;0.99). Overall, a tendency of rising temperature with increasing sMGS was seen. The difference between sMGS=0 and sMGS>0 was significant. The performance of MaxTp as a screening tool to detect inflammation was reasonable with an AUC of 0.71 (95% CI: 0.65-0.76). The empirically optimal cut-off value was 34.1°C (Sensitivity=65%, Specificity=72%, Positive predictive value=23%, Negative Predictive value=94%). A 1°C increase in MaxTp increased the RR of visual signs of inflammation by a factor 1.5 (95% CI: 1.3; 1.7).

Conclusion: We found a clinical positive association between the temperature at the pin site measured with thermography and visual signs of inflammation. The empirically optimal temperature cut-off value for inflammation screening was 34.1°C. Thermography may be a promising tool for a for a future point of care technology.

ROLE OF ALPHA-CGRP IN THE DEVELOPMENT OF POSTTRAUMATIC OA IN THE CONTEXT OF FORCED EXERCISE

Patrick Pann[1], Shahed Taheri[2], Arndt F. Schilling[2], Susanne Graessel[1]

[1]Department of Orthopedic Surgery, University of Regensburg, Regensburg, Germany, *[2]University Medicine Göttingen, Göttingen, Germany*

Introduction: Osteoarthritis (OA) causes pain, stiffness, and loss of function due to degenerative changes in joint cartilage and bone. In some forms of OA, exercise can alleviate symptoms by improving joint mobility and stability. However, excessive training after joint injury may have negative consequences for OA development. Sensory nerve fibers in joints release neuropeptides like alpha-calcitonin gene-related peptide (alpha-CGRP), potentially affecting OA progression. This study investigates the role of alpha-CGRP in OA pathogenesis under different exercise regimen in mice.

Method: OA was induced in C57Bl/6J WT mice and alpha-CGRP KO mice via surgical destabilization of the medial meniscus (DMM) at 12 weeks of age (N=6). Treadmill exercise began 2 weeks post-surgery and was performed for 30 minutes, 5 days a week, for 2 or 6 weeks at intense (16 m/min, 15° incline) or moderate (10 m/min, 5° incline) levels. Histomorphometric assessment of cartilage degradation (OARSI scoring), serum cytokine analysis, immunohistochemistry, and nanoCT analysis were conducted.

Result: OARSI scoring confirmed OA induction 4 weeks post-DMM surgery, with forced exercise exacerbating cartilage degradation regardless of intensity. No significant genotype-dependent differences were observed. Serum analysis revealed elevated cytokine levels associated with OA and inflammation in KO mice compared to WT mice 4 and 8 weeks post-surgery (VEGF-A, MCP-1, CXCL10, RANTES, MIP1-alpha, MIP1-beta, and RANKL). The observed effects were often exacerbated by intense exercise but rarely by DMM surgery. NanoCT analysis demonstrated increased sclerotic bone changes after 6 weeks of forced exercise in KO mice compared to WT mice.

Conclusion: Our results suggest an OA promoting effect of exercise in early disease stages of posttraumatic OA. Intense exercise induced inflammatory processes correlated to increased cytokine levels in the serum that might exacerbate OA pathogenesis in later stages. The neuropeptide alpha-CGRP might play a role in protecting against these adverse effects.

WEARABLE INERTIAL SENSORS AND DEEP LEARNING TO DETECT CLINICALLY MEANINGFUL REAL-WORLD WALKING SURFACE CHARACTERISTICS.

Gabby Vinco[1], Christophe Ley[1], Philippe Dixon[2], Bernd Grimm[3]

[1]University of Luxembourg; Department of Mathematics, Belval Esch-sur-Alzette, Luxembourg, *[2]McGill University, Department of Kinesiology and Physical Education, Montreal, Quebec, Canada*, *[3]Luxembourg Institute of Health; Department of Precision Health, Luxembourg, Luxembourg*

Introduction: The ability to walk over various surfaces such as cobblestones, slopes or stairs is a very patient centric and clinically meaningful mobility outcome. Current wearable sensors only measure step counts or walking speed regardless of such context relevant for assessing gait function. This study aims to improve deep learning (DL) models to classify surfaces of walking by altering and comparing model features and sensor configurations.

Method: Using a public dataset, signals from 6 IMUs (Movella DOT) worn on various body locations (trunk, wrist, right/left thigh, right/left shank) of 30 subjects walking on 9 surfaces were analyzed (flat ground, ramps (up/down), stairs (up/down), cobblestones (irregular), grass (soft), banked (left/right)). Two variations of a CNN Bi-directional LSTM model, with different Batch Normalization layer placement (beginning vs end) as well as data reduction to individual sensors (versus combined) were explored and model performance compared in-between and with previous models using F1 scores.

Result: The Bi-LSTM architecture improved performance over previous models, especially for subject-wise data splitting and when combining the 6 sensor locations (e.g. F1=0.94 versus 0.77). Placement of the Batch Normalization layer at the beginning, prior to the convolutional layer, enhanced model understanding of participant gait variations across surfaces. Single sensor performance was best on the right shank (F1=0.88).

Conclusion: Walking surface detection using wearable IMUs and DL models shows promise for clinically relevant real-world applications, achieving high F1 levels (>0.9) even for subject-wise data splitting enhancing the model applicability in real-world scenarios. Normalization techniques, such as Batch Normalization, seem crucial for optimizing model performance across diverse participant data. Also single-sensor set-ups can give acceptable performance, in particular for specific surface types of potentially high clinical relevance (e.g. stairs, ramps), offering practical and cost-effective solutions with high usability. Future research will focus on collecting ground-truth labeled data to investigate system performance in real-world settings.

IS HUMAN HEIGHT BASED ON A LUCAS SEQUENCE RELATIONSHIP BETWEEN THE FOOT HEIGHT, TIBIAL LENGTH, FEMUR LENGTH AND BODY LENGTH?

Craig Robbins[1], Dror Paley[1], Sahra Sutaria[1], Daelan Pinsky[1], Darin Roberts[1]

[1]Paley Orthopedic & Spine Institute, West Palm Beach, United States

Introduction: Research studies have established mathematical correlations between the lengths of bone segments and the possible biomechanical implications of these correlations. The Lucas sequence comprises a series of integers that adhere to the same recurrence relation as the Fibonacci sequence; it differs in that it can start with any two initial integers. The purpose of this study is to determine whether segmental lengths of the foot height, tibia, femur, and upper body follow a Lucas sequence pattern.

Method: This was a retrospective radiographic review of patients who underwent full-body EOS scans. The AP scan was used to measure standing foot height (Ft), tibial length (T), femoral length (Fe), upper body length (UB), and full body length. A linear regression test was performed to determine whether a Lucas sequence-based relationship exists between Ft + T and Fe, and between T + Fe and UB.

Result: The regression for the relationship between Ft + T and Fe for the entire cohort (R= 0.82, R2= 0.70), the female subset (R= 0.94, R2= 0.88) and the male subset (R= 0.75, R2= 0.57), all demonstrated a strong positive correlation between Ft + T and Fe and showed that Ft + T is a likely predictor of Fe. The regression test for the entire cohort demonstrated a moderately positive correlation between T + Fe and UB (R= 0.41, R2= 0.17, F(1, 145) = 29.42, p= 2.4E-07). A stronger correlation was found for the relationship between T + Fe and UB (R= 0.57, R2= 0.32, F(1, 35) = 16.64, p= 2.5E-05) for the female subset relative to the male subset (R= 0.20, R2= 0.038, F(1, 35) = 4.37, p= 0.04).

Conclusion: This study demonstrates that total height is made up of sequential segments whose lengths approximate a Lucas series. The Fibonacci sequence is therefore once again implicated in human body proportions.

FRACTURE DETECTION IN WRIST TRAUMA X-RAY: OPTIMISING ALGORITHM PERFORMANCE USING TRANSFER LEARNING

Franz Birkholtz[1,2], Maaike Eken[1,3], Andrew Boyes[4], Andries Engelbrecht[4,5]

[1]Institute of Orthopaedics and Rheumatology, Mediclinic Winelands Orthopaedic Hospital, Stellenbosch, Stellenbosch, South Africa, *[2]Division of Orthopaedic Surgery, Department of Surgical Sciences, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa*, *[3]Division of Sport and Exercise Medicine, Department of Exercise, Sport and Lifestyle Medicine, Faculty of Medicine and Health Sciences, Cape Town, South Africa*, *[4]Department of Industrial Engineering, and Computer Science Division, Stellenbosch University, Stellenbosch, South Africa*, *[5]Center for Applied Mathematics and Bioinformatics, Gulf University for Science and Technology, Mubarak Al-Abdullah, West Mishref, Kuwait*

Introduction: With advances in artificial intelligence, the use of computer-aided detection and diagnosis in clinical imaging is gaining traction. Typically, very large datasets are required to train machine-learning models, potentially limiting use of this technology when only small datasets are available. This study investigated whether pretraining of fracture detection models on large, existing datasets could improve the performance of the model when locating and classifying wrist fractures in a small X-ray image dataset. This concept is termed “transfer learning”.

Method: Firstly, three detection models, namely, the faster region-based convolutional neural network (faster R-CNN), you only look once version eight (YOLOv8), and RetinaNet, were pretrained using the large, freely available dataset, common objects in context (COCO) (330000 images). Secondly, these models were pretrained using an open-source wrist X-ray dataset called “Graz Paediatric Wrist Digital X-rays” (GRAZPEDWRI-DX) on a (1) fracture detection dataset (20327 images) and (2) fracture location and classification dataset (14390 images). An orthopaedic surgeon classified the small available dataset of 776 distal radius X-rays (*Arbeidsgmeischaft für Osteosynthesefragen* Foundation / Orthopaedic Trauma Association; AO/OTA), on which the models were tested.

Result: Detection models without pre-training on the large datasets were the least precise when tested on the small distal radius dataset. The model with the best accuracy to detect and classify wrist fractures was the YOLOv8 model pretrained on the GRAZPEDWRI-DX fracture detection dataset (mean average precision at intersection over union of 50=59.7%). This model showed up to 33.6% improved detection precision compared to the same models with no pre-training.

Conclusion: Optimisation of machine-learning models can be challenging when only relatively small datasets are available. The findings of this study support the potential of transfer learning from large datasets to improve model performance in smaller datasets. This is encouraging for wider application of machine-learning technology in medical imaging evaluation, including less common orthopaedic pathologies.

ENHANCED RECOVERY AFTER SURGERY (ERAS) DAY SURGERY FOR ROBOTIC-ARM ASSISTED TKA; BETTER OUTCOME FOR PATIENTS, IMPROVED EFFICIENCY FOR HOSPITALS.

Ee Chern Ng[1], Sheng Xu[2], Xuan Eric Liu[2], Jason Beng Teck Lim[2], Ming Han Lincoln Liow[2], Hee Nee Pang[2], Darren Keng Jin Tay[2], Seng Jin Yeo[2], Jerry Yongqiang Chen[2]

[1]Lee Kong Chian School of Medicine, Singapore, Singapore, [2]Department of Orthopaedic Surgery, Singapore General Hospital, Singapore, Singapore

Introduction: Robotic Total Knee Arthroplasty (TKA) was designed to improve implant position accuracy by providing surgeons with real-time intra-operative data to tailor surgeries to patients with the aim of improving outcomes. However, there are concerns that the longer surgical duration in robotic TKA may lead to longer length of stay (LOS). This study aims to investigate the effect of robotic TKA combined with Enhanced Recovery After Surgery (ERAS) Day Surgery protocols on LOS and short-term outcomes.

Method: All patients who had undergone unilateral ERAS robotic TKA from August 2020 to July 2021 were prospectively followed up for 6 months and matched via propensity score matching to patients who underwent ERAS conventional TKA in the same time period. Factors including surgical duration, LOS, immediate reduction in pain, 30-day complications, 6-month patient reported outcome measures (PROMs) and knee range of motion (ROM) were compared between the two groups.

Result: A total of 42 patients who underwent ERAS robotic TKA were matched to 42 patients who underwent ERAS conventional TKA.

Despite the longer surgical duration, LOS was comparable between both groups (1.1±0.9days in robotic TKA group vs 1.0±0.3days in the conventional TKA group, p=0.755) and 88.1% of patients who underwent robotic TKA were successfully discharged within 24 hours. 6 months post-operatively, patients in the robotic TKA group achieved significantly better correction of their fixed flexion deformity and overall ROM compared to patients in the conventional group (Mean ROM for flexion (113.6°±14.7 vs 106.6°±12.3, p=0.009), extension (2.7°±5.2 vs 5.0°±4.5, p=0.03) and total ROM (107.7°±24.7 vs 101.6°±15.3, p=0.021)). Post-operative PROMs were comparable between both groups.

Conclusion: ERAS protocols can effectively reduce the LOS in patients undergoing robotic TKA. In the authors' institution this translated to a 17% cost reduction for robotic TKA, improving patient accessibility to improved clinical outcomes while reducing healthcare resources used.

ANALYSIS OF REOPERATIONS FOLLOWING POSTERIOR PEDICLE FIXATION IN SPINAL SURGERY

Halil Bulut[1,2], Maria Maestre[1], Daniel Tomey[1]

[1]Houston Methodist Hospital, United States, *[2]Istanbul University Cerrahpasa, Türkyie*

Introduction: Unplanned reoperations (UROs) following corrective surgery for adult spinal deformity (ASD) present significant challenges for both patients and surgeons. Understanding the specific UROs types is crucial for improving patient outcomes and refining surgical strategies in ASD correction.

Method: This retrospective analysis utilized data from the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) database spanning from 2017 to 2021. Patient information was extracted using specific CPT codes related to posterior pedicle fixation.

Result: In a cohort of 1088 patients undergoing posterior spinal deformity corrections, we examined various preoperative factors to discern their correlation with reoperation prevalence. Our analysis revealed no statistically significant differences in reoperation prevalence concerning gender (male: 4.0%, p=0.131) or ethnicity (Hispanic: 4.2%, p=0.192). Similarly, no notable associations were identified for diabetes mellitus, smoking status, dyspnea, history of severe COPD, hypertension, ASA classification, or functional health status before surgery, with reoperation prevalences ranging from 3.2% to 8.8% and p-values spanning from 0.146 to 0.744. Overall, the reoperation prevalence within the entire cohort stood at 5.2% (55 cases). In terms of the types of reoperations investigated, spinal-related procedures emerged as the most prevalent, accounting for 43.7% (24 cases), followed closely by wound site revisions at 23.6% (13 cases). Additionally, gastrointestinal-related procedures and various other miscellaneous interventions, such as uroscopy, demonstrated reoperation prevalences of 7.2% (4 cases) and 25.5% (14 cases), respectively.

Conclusion: our findings highlight the diverse spectrum of reoperation procedures encountered following posterior spinal deformity corrections, with wound site revisions and spinal-related interventions being the most prevalent categories. These results emphasize the complexity of managing UROs in spinal surgery and the need for tailored approaches and infection/incision protocols to address the specific challenges associated with each type of reoperation.

METASTRA: COMPUTER-AIDED EFFECTIVE FRACTURE RISK STRATIFICATION OF PATIENTS WITH VERTEBRAL METASTASES FOR PERSONALISED TREATMENT THROUGH ROBUST COMPUTATIONAL MODELS VALIDATED IN CLINICAL SETTINGS

Luca Cristofolini[1], giovanni barbanti bròdano[2], E. Dall'Ara[3], Rudolf Ferenc[4], Stephen J Ferguson[5], José Manuel García-Aznar[6], Aron Lazary[7], Peter Vajkoczy[8], Jorrit-Jan Verlaan[9], Laszlo Vidacs[10]

[1]Alma Mater Studiorum - University of Bologna, Bologna, Italy, *[2]Istituto Ortopedico Rizzoli, Bologna, Italy*, *[3]University of Sheffield, United Kingdom*, *[4]Front End Art, Hungary*, *[5]Federal Institute of Technology ETH Zurich, Switzerland*, *[6]University of Zaragoza, Spain*, *[7]Buda Health Center, Hungary*, *[8]Charité – Universitätsmedizin Berlin, Germany*, *[9]University Medical Center Utrecht, Netherlands*, *[10]University of Szeged, Hungary*

Introduction: Patients (2.7M in EU) with positive cancer prognosis frequently develop metastases (≈1M) in their remaining lifetime. In 30-70% cases, metastases affect the spine, reducing the strength of the affected vertebrae. Fractures occur in ≈30% patients. Clinicians must choose between leaving the patient exposed to a high fracture risk (with dramatic consequences) and operating to stabilise the spine (exposing patients to unnecessary surgeries). Currently, surgeons rely on their sole experience. This often results in to under- or over-treatment. The standard-of-care are scoring systems (e.g. Spine Instability Neoplastic Score) based on medical images, with little consideration of the spine biomechanics, and of the structure of the vertebrae involved. Such scoring systems fail to provide clear indications in ≈60% patients.

Method: The HEU-funded METASTRA project is implemented by biomechanicians, modellers, clinicians, experts in verification, validation, uncertainty quantification and certification from 15 partners across Europe. METASTRA aims to improve the stratification of patients with vertebral metastases evaluating their risk of fracture by developing dedicated reliable computational models based on Explainable Artificial Intelligence (AI) and on personalised Physiology-based biomechanical (VPH) models.

Result: The METASTRA-AI model is expected to be able to stratify most patients with limited effort end cost, based on parameters extracted semi-automatically from the medical files and images. The cases which are not reliably stratified through the AI model, are examined through a more detailed and personalised biomechanical VPH model. These METASTRA numerical tools are trained through an unprecedentedly large multicentric retrospective study (2000 cases) and validated against biomechanical *ex vivo* experiments (120 specimens).

Conclusion: The METASTRA decision support system is tested in a multicentric prospective observational study (200 patients). The METASTRA approach is expected to cut down the indeterminate diagnoses from the current 60% down to 20% of cases.

METASTRA project funded by the European Union, HEU topic HLTH-2022-12-01, grant 101080135

ARTIFICIAL INTELLIGENCE-BASED MODELS EFFICACY FOR SHOULDER ARTHROPLASTY IMPLANTS DETECTION AND CLASSIFICATION USING UPPER-LIMB X-RAYS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Amir-Mohammad Asgari[1], Farhad Shaker[1], Mohammad-Taha Pahlevan-Fallahy[1], Mohammad Soleimani[1], Seyyed Hossein Shafiei[1], Yousef Fallah[1]

[1]Orthopaedic Department, Orthopaedic Subspecialty Research Center (OSRC), Sina University Hospital, Tehran University of Medical Sciences, Tehran, Iran

Introduction: Shoulder arthroplasty (SA) has been performed with different types of implants, each requiring different replacement systems. However, data on previously utilized implant types are not always available before revision surgery, which is paramount to determining the appropriate equipment and procedure. Therefore, this meta-analysis aimed to evaluate the accuracy of the AI models in classifying SA implant types.

Methods: This systematic review was conducted in Pubmed, Embase, SCOPUS, and Web of Science from inception to December 2023, according to PRISMA guidelines. Peer-reviewed research evaluating the accuracy of AI-based tools on upper-limb X-rays for recognizing and categorizing SA implants was included. In addition to the overall meta-analysis, subgroup analysis was performed according to the type of AI model applied (CNN (Convolutional neural network), non-CNN, or Combination of both) and the similarity of utilized datasets between studies.

Results: 13 articles were eligible for inclusion in this meta-analysis (including 138 different tests assessing models' efficacy). Our meta-analysis demonstrated an overall sensitivity and specificity of 0.891 (95% CI:0.866-0.912) and 0.549 (95% CI:0.532,0.566) for classifying implants in SA, respectively. The results of our subgroup analyses were as follows: CNN-subgroup: a sensitivity of 0.898 (95% CI:0.873-0.919) and a specificity of 0.554 (95% CI:0.537,0.570), Non-CNN subgroup: a sensitivity of 0.809 (95% CI:0.665-0.900) and specificity of 0.522 (95% CI:0.440,0.603), combined subgroup: a sensitivity of 0.891 (95% CI:0.752-0.957) and a specificity of 0.547 (95% CI:0.463,0.629).

Studies using the same dataset demonstrated an overall sensitivity and specificity of 0.881 (95% CI:0.856-0.903) and 0.542 (95% CI:0.53,0.554), respectively. Studies that used other datasets showed an overall sensitivity and specificity of 0.995 (95% CI:969,0.999) and 0.678 (95% CI:0.234, 0.936), respectively.

Conclusion: AI-based classification of shoulder implant types can be considered a sensitive method. Our study showed the potential role of using CNN-based models and different datasets to enhance accuracy, which could be investigated in future studies.

IS ASSESSING HUMERAL HEAD MIGRATION IN A SUPINE POSITION ASSOCIATED WITH ITS ASSESSMENT IN FUNCTIONALLY-RELEVANT ARM POSITIONS?

Nazanin Daneshvarhashjin[1], Philippe Debeer[2], Michael Skipper Andersen[3], Filip Verhaegen[2], Lennart Scheys[1,2]

[1]KU Leuven University, Leuven, Belgium, *[2]UZ Leuven hospital, Leuven, Belgium*, *[3]Aalborg University, Denmark*

Introduction: Assessment of the humeral head translation with respect to the glenoid joint, termed humeral head migration (HHM), is crucial in total shoulder arthroplasty pre-operative planning. Its assessment informs current classification systems for shoulder osteoarthritis as well as the evaluation of surgical correction. In current clinical practice, HHM assessment relies on computed-tomography (CT) imaging. However, the associated supine position might undermine its functional relevance as it does not reflect the weight-bearing condition with active muscle engagement associated with the upright standing position of most daily activities. Therefore, we assessed to what extent HHM in a supine position is associated with HHM in a range of functional arm positions.

Method: 26 shoulder osteoarthritis patients and 12 healthy volunteers were recruited. 3D shapes of the humerus and scapula were reconstructed from their respective CT scans using an image processing software [6], and their CT-scan-based HHMs were measured. Furthermore, all subjects underwent low-dose biplanar radiography [7] in four quasi-static functional arm positions while standing: relaxed standing, followed by 45 degrees of shoulder extension, flexion, and abduction. Using a previously validated method implemented in the programming platforms[8], 3D shapes were registered to the pairs of biplanar images for each arm position and the corresponding functional HHM was measured. Bivariate correlations were assessed between the CT-based HHM and each functional arm position.

Result: HHM in 45 degrees of flexion and extension both showed significant and strong correlations ($r>0.66$ and $P<0.01$) with HHM assessed in the supine position. However, such a high correlation was not found for relaxed standing and 45 abduction.

Conclusion: Although HHM in a supine position correlates with HHM in 45-degree extension and flexion, it is poorly associated with the HHM in abduction and relaxed standing. These results may suggest the inclusion of more functionally-relevant patient positioning toward better-informed shoulder arthroplasty planning.

Acknowledgement: Funding from PRosPERos-II Project.

[6] Mimics (Materialise, Belgium)
[7] EOS system (EOS imaging, France)
[8] MATLAB (The Mathworks, USA) and 3-matic (Materialise, Belgium) scripting platform.

CHATBOTS IN LIMB LENGTHENING AND RECONSTRUCTION SURGERY

Anirejuoritse Bafor[1], Christopher Iobst[1], Kirsten Tulchin-Francis[1], Daryn Strub[1], Søren Kold[2]

[1]Nationwide Children's Hospital, Columbus, United States, *[2]Aalborg University Hospital , Aalborg, Denmark*

Introduction: The recent introduction of Chatbots has provided an interactive medium to answer patient questions. The accuracy of responses with these programs in limb lengthening and reconstruction surgery has not previously been determined. Therefore, the purpose of this study was to assess the accuracy of answers from 3 free AI chatbot platforms to 23 common questions regarding treatment for limb lengthening and reconstruction.

Method: We generated a list of 23 common questions asked by parents before their child's limb lengthening and reconstruction surgery. Each question was posed to three different AI chatbots (ChatGPT 3.5 [OpenAI], Google Bard, and Microsoft Copilot [Bing!]) by three different answer retrievers on separate computers between November 17 and November 18, 2023. Responses were only asked one time to each chatbot by each answer retriever. Nine answers (3 answer retrievers x 3 chatbots) were randomized and platform-blinded prior to rating by three orthopedic surgeons. The 4-point rating system reported by Mika et al. was used to grade all responses.

Result: ChatGPT had the best response accuracy score (RAS) with a mean score of 1.73 ± 0.88 across all three raters (range of means for all three raters – 1.62 – 1.81) and a median score of 2. The mean response accuracy scores for Google Bard and Microsoft Copilot were 2.32 ± 0.97 and 3.14 ± 0.82, respectively. This ranged from 2.10 – 2.48 and 2.86 – 3.54 for Google Bard and Microsoft Copilot, respectively. The differences between the mean RAS scores were statistically significant ($p < 0.0001$). The median scores for Google Bard and Microsoft Copilot were 2 and 3, respectively.

Conclusion: Using the Response Accuracy Score, the responses from ChatGPT were determined to be satisfactory, requiring minimal clarification, while the responses from Microsoft Copilot were either satisfactory, requiring moderate clarification, or unsatisfactory, requiring substantial clarification.

FEASIBILITY OF VIRTUAL REALITY IMMERSION IN REDUCING PAIN AND ANXIETY DURING EXTERNAL FIXATOR CARE PROCEDURES

Anirejuoritse Bafor[1], Christopher Iobst[1]

[1]*Nationwide Children's Hospital, Columbus, United States*

Introduction: Previous studies have shown the potential for virtual reality (VR) immersion as a promising technique for pain and anxiety management. The aim of our study was to evaluate the feasibility of VR in the management of pain and anxiety during post-op external fixator care procedures.

Method: This study involved patients aged 5-21 years following limb lengthening/reconstruction surgery with an external fixator. Aqua VR application from the KindVR® was utilized for this study. Subjects were seen during the first four postoperative visits and assigned to a 'VR-first' or 'no-VR-first' group. Visits alternated between VR immersion and no VR immersion during care procedures. The study endpoints (pain and anxiety levels) were assessed before, during, and after procedures using the Wong-Baker Faces (FACES) and Children's Fear Scale, respectively. Proxy scores for pain and anxiety were also obtained from parents or legal guardians and providers.

Result: A total of 29 patients (16 male and 13 female) were evaluated. The mean age at enrollment was 14.4 ± 2.2 years for group 1 and 14.7 ± 4.0 years for group 2. The median number of pin sites was 7. Anxiety scores were consistently higher during the non-VR immersion experience compared to the VR immersion visits. The pain and anxiety scores were significantly lower in the 'VR-first' group during the non-VR immersion study visits compared to patients in the 'no-VR-first' group. This observation was also consistent with survey findings among the parent proxies and providers.

Conclusion: VR immersion is associated with lower anxiety scores for pin-site care procedures. VR immersion at the first post-operative visit following limb reconstruction surgery was also associated with lower pain and anxiety scores during subsequent non-VR immersion visits.

PATIENT SPECIFIC CALIBRATION OF PREOPERATIVE CT SCANS PROVIDE OBJECTIVE CLASSIFICATION OF BONE DENSITY SUBGROUPS FROM PATIENTS UNDERGOING REVERSE SHOULDER ARTHROPLASTY

Daniel Ritter[1,2], Samuel Bachmaier[1], Coen Wijdicks[3], Patric Raiss[4]

[1]Arthrex GmbH, Munich, Germany, *[2]Ludwig Maximilian University, Munich, Germany*, *[3]Arthrex Inc., Naples, United States*, *[4]OCM Clinic, Munich, Germany*

Introduction: The increased prevalence of osteoporosis in the patient population undergoing reverse shoulder arthroplasty (RSA) results in significantly increased complication rates. Mainly demographic and clinical predictors are currently taken into the preoperative assessment for risk stratification without quantification of preoperative computed tomography (CT) data (e.g. bone density). It was hypothesized that preoperative CT bone density measures would provide objective quantification with subsequent classification of the patients' humeral bone quality.

Methods: Thirteen bone density parameters from 345 preoperative CT scans of a clinical RSA cohort represented the data set in this study. The data set was divided into testing (30%) and training data (70%), latter included an 8-fold cross validation. Variable selection was performed by choosing the variables with the highest descriptive value for each correlation clustered variables. Machine learning models were used to improve the clustering (Hierarchical Ward) and classification (Support Vector Machine (SVM)) of bone densities at risk for complications and were compared to a conventional statistical model (Logistic Regression (LR)).

Results: Clustering partitioned this cohort (training data set) into a high bone density subgroup consisting of 96 patients and a low bone density subgroup consisting of 146 patients. The optimal number of clusters (n = 2) was determined based on optimization metrics. Discrimination of the cross validated classification model showed comparable performance for the training (accuracy=91.2%; AUC=0.967) and testing data (accuracy=90.5 %; AUC=0.958) while outperforming the conventional statistical model (Logistic Regression (LR)). Local interpretable model-agnostic explanations (LIME) were created for each patient to explain how the predicted output was achieved.

Conclusion: The trained and tested model provides preoperative information for surgeons treating patients with potentially poor bone quality. The use of machine learning and patient-specific calibration showed that multiple 3D bone density scores improved accuracy for objective preoperative bone quality assessment.

DOES WEIGHT LOSS THROUGH BARIATRIC SURGERY REDUCE BIOMECHANICAL RISK FACTORS OF OSTEOARTHRITIS?

Penny Hudson[1], Simon Federer[1,2], Madeleine Dunne[1,2], Chris Pring[2], Neal Smith[1]

[1]University of Chichester, Chichester, United Kingdom, *[2]St Richard's Hospital, University Hospitals Sussex, Chichester, United Kingdom*

Introduction: Weight is a modifiable risk factor for osteoarthritis (OA) progression. Despite the emphasis on weight loss, data quantifying the changes seen in joint biomechanics are limited. Bariatric surgery patients experience rapid weight loss. This provides a suitable population to study changes in joint forces and function as weight changes.

Method: 10 female patients undergoing gastric bypass or sleeve gastrectomy completed 3D walking gait analysis at a self-selected pace, pre- and 6 months post-surgery. Lower limb and torso kinematic data for 10 walking trials were collected using a Vicon motion capture system and kinetics using a Kistler force plate. An inverse kinematic model in Visual 3D allowed for no translation of the hip joint centre. 6 degrees of freedom were allowed at other joints. Data were analysed using JASP with a paired samples t-test.

Result: On average participants lost 28.8±7.60kg. No significant changes were observed in standing knee and hip joint angles. Walking velocity increased from 1.10±0.11 ms^{-1} to 1.23±0.17 ms^{-1} ($t(9)=-3.060$, $p = 0.014$) with no change in step time but a mean increase in stride length of 0.12m (SE: 0.026m; $t(9)=-4.476$, $p = 0.002$). A significant decrease of 21.5±4.2% in peak vertical ground reaction forces was observed ($t(9)=12.863$, $p <0.001$). Stride width significantly decreased by 0.04m (SE: 0.010m; $t(9)=4.316$, $p = 0.002$) along with a decrease in lateral impulse of 21.2Ns (SE: 6.977Ns; $t(7)$, $p = 0.019$), but no significant difference in knee joint angles were observed. Double limb support time also significantly reduced by 0.02s (SE: 0.006s; $t(9) = 3.639$, $p=0.005$)

Conclusion: The reduction in stance width and lateral impulse suggests a more sagittal compass-gait walk is being achieved. This would reduce valgus moments on the knee reducing loading in the medial compartment. The reduction in peak ground reaction force would reduce knee contact forces and again potentially slow OA progression.

PRE- AND POSTOPERATIVE RESIDUAL URINE IN 796 MEN >65 YEARS, UNDERGOING ELECTIVE ORTHOPEDIC SURGERY: A SINGLE-CENTER, PROSPECTIVE COHORT STUDY

Inger GRYET[1], Charlotte Graugaard-Jensen[2], Asger Roer Pedersen[1], Simon Skov[3]

[1]Silkeborg Regional Hospital, Silkeborg, Denmark, *[2]Aarhus University hospital, Aarhus, Denmark*, *[3]Aalborg University Hospital, Aalborg, Denmark*

Introduction: Postvoid residualurine (PVR) can be an unknown chronic disorder, but it can also occur after surgery. A pilot-study initiated in Elective Surgery Center, Silkeborg led to collaboration with a urologist to develop a flowchart regarding treatment of PVR. Depending on the severity, men with significant PVR volumes were either recommend follow up by general practitioner or referred to an urologist for further diagnose and/or treatment. Aim: to determine the prevalence of pre- and postoperative PVR in men >65 years undergoing orthopedic surgeries and associated risk factors.

Method: A single-center, prospective cohort study. Male patients were consecutively included during one year from April 2022. Data was extracted from the electronic patient files: age, lower urinary tract symptoms (LUTS), co-morbidity (e.g. diabetes), type of surgery and anesthesia, opioid use, pre- and postoperative PVR.

Result: 796 participants; 316 knee-, 276 hip-, 26 shoulder arthroplasties and 178 lower back spinal surgeries.

95% (755) were bladder scanned preoperatively.

12% (89) had PVR 150-300ml, and 3% (23) had PVR >300ml.

There was a higher risk of preoperative PVR ≥150ml in patients reporting LUTS, OR 1.97(1.28;3.03), having known neurological disease, OR 3.09(1.41;6.74), and the risk increased with higher age, OR 1.08 per year (1.04;1.12). Diabetes and the type of surgery was not associated with higher risk of PVR.

72% (569) had a postoperative bladder scan. 15% (95%CI: 12-19%) (70) patients without PVR preoperatively had PVR ≥150ml postoperatively.

Conclusion: Approximately 15% of the men had PVR ≥150ml preoperatively. Neurological disease was the most severe risk factor and secondary if reporting LUTS. As expected, the risk increased with age. Neither diabetes nor the type of surgery was associated with higher risk.

15% of men without preoperative PVR had PVR after surgery. It is not possible to conclude if it is transient or chronic but further studies are ongoing.

A SYSTEMATIC REVIEW OF STAPLES, TENSION-BAND PLATES AND PERCUTANEOUS EPIPHYSIODESIS SCREWS FOR LEG-LENGTH DISCREPANCY (LLD) TREATMENT.

Maria Tirta[1], Mette Holm Hjorth[2], Jette Frost Jepsen[3], Søren Kold[1], Ole Rahbek[1]

[1]Interdisciplinary Orthopaedics, Aalborg University Hospital, Aalborg, Denmark, *[2]Department of Orthopaedics Surgery, Aarhus University Hospital, Aarhus, Denmark*, *[3]Medical Library, Aalborg University Hospital, Aalborg, Denmark*

Introduction: Epiphysiodesis, defined as the process of closing the growth plate (physis), have been used for several years as a treatment option of cases where the predicted leg-length discrepancy (LLD) falls between 2 to 5 cm. The aim of this study was to systematically review the existing literature on the effectiveness of three different epiphysiodesis techniques with implant usage for the treatment of leg-length discrepancy in the pediatric population. The secondary aim was to address the reported complications of staples, tension-band plates (TBP) and percutaneous epiphysiodesis screws (PETS).

Method: This systematic review was performed according to PRISMA guidelines. We searched MEDLINE (PubMed), Embase, Cochrane Library, Web of Science and Scopus for studies on skeletally immature patients with LLD treated with epiphysiodesis with an implant. The extracted outcome categories were effectiveness of epiphysiodesis (LLD measurements pre/post-operatively, successful/unsuccessful) and complications that were graded on severity.

Result: Forty-four studies (2184 patients) were included, from whom 578 underwent TBP, 455 PETS and 1048 staples. From pooled analysis of the studies reporting success rate, 64% (150/234) successful TBP surgeries (10 studies), 78% (222/284) successful PETS (9 studies) and 52% (212/407) successful Blount staples (8 studies). Severe complications rate was 7% for PETS, 17% for TBP and 16% for Blount staples. TBP had 43 cases of angular deformity (10%), Blount staples 184 (17%) while PETS only 18 cases (4%).

Conclusion: Our results highlighted that PETS seems to be the most successful type of epiphysiodesis surgery with an implant, with higher success rate and lower severe complications than TBP or Blount staples.

AO SPINE GUIDELINE FOR THE USE OF OSTEOBIOLOGICS (AOGO) IN ANTERIOR CERVICAL DISCECTOMY AND FUSION FOR SPINAL DEGENERATIVE CASES

Hans Joerg Meisel[1,1], Amit Jain[2], Yabin Wu[3], Christopher Martin[4], Sathish Muthu[5], Waeel Hamouda[6], Ricardo Rodrigues-Pinto[7], Jakobus J Arts[8], Gianluca Vadalà[9], AO Spine Knowledge Forum Degenerative Knowledge Forum Degenerative[10], Luca Ambrosio[11]

[1]BG Klinikum Bergmannstrost- Klinik für Neurochirurgie, Halle/ Saale, Germany, *[2]Department of Orthopaedic Surgery, Johns Hopkins University, Baltimore, United States*, *[3]Research Department, AO Spine, AO Foundation, Davos, Switzerland*, *[4]Department of Orthopaedic Surgery, University of Minnesota, Minneapolis, United States*, *[5]Department of Orthopaedics, Government Medical College, Dindigul, , Dindigul, India*, *[6]Department of Neurosurgery, Kasr Alainy Faculty of Medicine, Research, and Teaching Hospitals, Cairo University, Cairo, Cairo, Egypt*, *[7]Spinal Unit (UVM), Department of Orthopaedics. Centro Hospitalar Universitário do Porto, , Porto, Portugal*, *[8]Orthopaedic Biomechanics, Department of Biomedical Engineering, Eindhoven University of Technology, , Eindhoven, Netherlands*, *[9]Operative Research Unit of Orthopaedic and Trauma Surgery, Fondazione Policlinico Universitario Campus Bio-Medico, Rome, Italy*, *[10]AO Spine Knowledge Forum Degenerative Knowledge Forum Degenerative, Davos, Switzerland*, *[11]Orthopaedic Resident & Research Fellow Campus Bio-Medico University of Rome Department of Orthopaedic and Trauma Surgery, Rome, Italy*

Introduction: To develop an international guideline (AOGO) about use of osteobiologics in Anterior Cervical Discectomy and Fusion (ACDF) for treating degenerative spine conditions.

Method: The guideline development process was guided by AO Spine Knowledge Forum Degenerative (KF Degen) and followed the Guideline International Network McMaster Guideline Development Checklist. The process involved 73 participants with expertise in degenerative spine diseases and surgery from 22 countries. Fifteen systematic reviews were conducted addressing respective key topics and evidence were collected. . The methodologist compiled the evidence into GRADE Evidence-to-Decision frameworks. Guideline panel members judged the outcomes and other criteria and made the final recommendations through consensus.

Result: Five conditional recommendations were created. A conditional recommendation is about the use of allograft, autograft or a cage with an osteobiologic in primary ACDF surgery. Other conditional recommendations are about use of osteobiologic for single or multi-level ACDF, and for hybrid construct surgery. It is suggested that surgeons use other osteobiologics rather than human bone morphogenetic protein-2 in common clinical situations. Surgeons are recommended to choose one graft over another or one osteobiologic over another primarily based on clinical situation, and the costs and availability of the materials.

Conclusion: This AOGO guideline is the first to provide recommendations for the use of osteobiologics in ACDF. Despite the comprehensive searches for evidence, there were few studies completed with small sample sizes and primarily as case series with inherent risks of bias. Therefore high quality clinical evidence is demanded to improve the guideline.

DEVIATION FROM PREOPERATIVE PLANNING AND ACCURACY OF TRANSPEDICULAR SCREW FIXATION USING INTRAOPERATIVE 3D NAVIGATION FOR LUMBAR SPONDYLOLISTHESIS

Gianluca Vadalà[1], Giuseppe Francesco Papalia[1], Fabrizio Russo[1], Niccolò Nardi[1], Luca Ambrosio[1], Rocco Papalia[1], Vincenzo Denaro[1]

[1]*Fondazione Policlinico Universitario Campus Bio-Medico, Rome, Italy*

Introduction: Intraoperative navigation systems for lumbar spine surgery allow to perform preoperative planning and visualize the real-time trajectory of pedicle screws. The aim of this study was to evaluate the deviation from preoperative planning and the correlations between screw deviation and accuracy.

Method: Patients affected by degenerative spondylolisthesis who underwent posterior lumbar interbody fusion using intraoperative 3D navigation since April 2022 were included. Intraoperative cone-beam computed tomography (CBCT) was performed before screw planning and following implantation. The deviation from planning was calculated as linear, angular, and 3D discrepancies between planned and implanted screws. Accuracy and facet joint violation (FJV) were evaluated using Gertzbein-Robbins system (GRS) and Yson classification, respectively. Statistical analysis was performed using SPSS version28. One-way ANOVA followed by Bonferroni post-hoc tests were performed to evaluate the association between GRS, screw deviation and vertebral level. Statistical significance was set at $p<0.05$.

Result: This study involved 34 patients, for a total of 154 pedicle screws. Mean age was 62.6±8.9 years. The mean two-dimensional screw tip deviation in mediolateral (ML), craniocaudal (CC), and anteroposterior (AP) was 2.6±2.45mm, 1.6±1.7mm, and 3.07±2.9mm, respectively. The mean screw tip 3D deviation was 5±3.3mm. The mean two-dimensional screw head deviation in ML, CC and AP was 1.83±1.8mm, 1.7±1.67mm and 3.6±3.1mm, respectively. The mean screw head 3D deviation was 4.94±3.2mm. 98% of screws were clinically acceptable (grade A+B), and grade 0 for FJV. Significant results were found between GRS and ML ($p=0.005$), AP ($p=0.01$) and 3D ($p=0.003$) tip deviations, and between GRS and AP and 3D head deviations (both $p=0$). Moreover, a significant correlation was found between GRS and vertebral level ($p=0$).

Conclusion: Our results showed a reasonable rate of discrepancy between planned and positioned screws. However, accuracy was clinically acceptable in almost all cases. Therefore, pedicle screw fixation using intraoperative CBCT, 3D navigation and screw planning is safe and accurate.

PATIENT'S EXPERIENCES OF SHARED DECISION-MAKING, WHEN CHOOSING TREATMENT FOR THEIR DISTAL RADIUS FRACTURE; A QUALITATIVE STUDY.

Louise Marie Nøhr[1,2], Ane Simony[2,2], Charlotte Abrahamsen[2]

[1]Regional Health Services, Odense, Denmark, *[2]Department of Orthopedics, KOLDING*

Introduction: Shared decision making (SDM) was introduced in hospital Lillebelt in 2019 and research reports that patients are more satisfied with their treatment, if they play an active role in choosing treatment. A Decision-Helper was constructed and introduced in the treatment for Colles fractures. This study aimed to understand how patients experience shared decision-making (SDM) for an acute illness, and how it affects them when making decisions about the treatment of their distal radius fracture.

Method: An exploratory, qualitative study design was performed to understand the patient's experience, during the choice of treatment with SDM. 12 were recruited when they came to their first follow-up 5 days after the injury, in the outpatient clinic. 10 were interviewed; 3 face to face and 7 by telephone. All women aged 57-87 years and all had a displaced Colles fracture, which had been reduced in the Emergency Room.

Result: Analyzing the interviews three themes emerged: 1) Acute situation. Patients was positive towards SDM, but found it demanding to participate in. Patients was still in crisis, 5 days after suffering from a fracture. Patients were unable to remember the information given in the ER, regarding the use of the Decision helper. Few had prepared themselves for the consult in the outpatient clinic. 2) Influence on treatment choice. It was unclear to the majority of patients, that cast or surgery, resulted in similar clinical outcomes. 3) The treatment decision was based on personal factors, more than the information received during the consult.

Conclusion: Patients wants to be included in the treatment decision. It is important to highlight that booth treatments are equal in clinical outcome, before introducing the Decision-Helper. The doctor´s demeanor is of great importance to the patient's experience. Introducing SDM in the clinical setting requires training and repeated observations, to succeed.

AUTOMATIC MULTI-CLASS SEGMENTATION OF HIP JOINT SPACE USING 3D DEEP LEARNING ALGORITHMS.

Shivani Sawant[1], Bhushan Borotikar[1], Varsha Raghu[1], Emmanuel Audenaert[2], Vikas Khanduja[3]

[1]Symbiosis International (Deemed University), Pune, India, *[2]Ghent University, Ghent, Belgium*, *[3]Cambridge University Hospital, Cambridge, United Kingdom*

Introduction: Three-dimensional (3D) morphological understanding of the hip joint, specifically the joint space and surrounding anatomy, including the proximal femur and the pelvis bone, is crucial for a range of orthopedic diagnoses and surgical planning. While deep learning algorithms can provide higher accuracy for segmenting bony structures, delineating hip joint space formed by cartilage layers is often left for subjective manual evaluation. This study compared the performance of two state-of-the-art 3D deep learning architectures (3D UNET and 3D UNETR) for automated segmentation of proximal femur bone, pelvis bone, and hip joint space with single and multi-class label segmentation strategies.

Method: A dataset of 56 3D CT images covering the hip joint was used for the study. Two bones and hip joint space were manually segmented for training and evaluation. Deep learning models were trained and evaluated for a single-class approach for each label (proximal femur, pelvis, and the joint space) separately, and for a multi-class approach to segment all three labels simultaneously. A consistent training configuration of hyperparameters was used across all models by implementing the AdamW optimizer and Dice Loss as the primary loss function. Dice score, Root Mean Squared Error, and Mean Absolute Error were utilized as evaluation metrics.

Results: Both the models performed at excellent levels for single-label segmentations in bones (dice > 0.95), but single-label joint space performance remained considerably lower (dice < 0.87). Multi-class segmentations remained at lower performance (dice < 0.88) for both models. Combining bone and joint space labels may have introduced a class imbalance problem in multi-class models, leading to lower performance.

Conclusion: It is not clear if 3D UNETR provides better performance as the selection of hyperparameters was the same across the models and was not optimized. Further evaluations will be needed with baseline UNET and nnUNET modeling architectures.

MESENDODERMAL PROGENITORS IN COMBINATION WITH A SYNTHETIC HYDROGEL (NPGEL) IN A SHEEP MODEL OF LOW BACK PAIN: A SAFETY STUDY

Claudia Cicione[1,2], Veronica Tilotta[1,2], Andrea Ascione[3], Giuseppina Di Giacomo[1,2], Fabrizio Russo[2], Marianna Tryfonidou[4], Daniele Noel[5], Anne Camus[6], Christine Le Maitre[7], Gianluca Vadalà[1,2]

[1]Lab. of Regenerative Orthopaedic, Università Campus Bio-Medico di Roma, Roma, Italy, *[2]Dept. of Orthopaedic and Trauma Surgery, Campus Bio-Medico University Hospital Foundation, Roma, Italy*, *[3]Dept. of Medical and Surgical Sciences and Biotechnology, Sapienza Università di Roma, Latina, Italy*, *[4]Faculty of Veterinary medicine – dept. Clinical Sciences, Utrecht University, Utrecht, Netherlands*, *[5]IRMB, University of Montpellier, INSERM, Montpellier, France*, *[6]Nantes Université, Oniris, CHU Nantes, INSERM, Regenerative Medicine and Skeleton, RMeS, UMR 1229, Nantes, France*, *[7]Division of Clinical Medicine, School of Medicine and Population Health, University of Sheffield, Sheffield, United Kingdom*

Introduction: Low back pain (LBP) is a worldwide leading cause of disability. This preclinical study evaluated the safety of a combined advanced therapy medicinal product developed during the European iPSpine project (#825925) consisting of mesendoderm progenitor cells (MEPC), derived from human induced pluripotent stem cells, in combination with a synthetic poly(N-isopropylacrylamide) hydrogel (NPgel) in an ovine intervertebral disc degeneration (IDD) model.

Method: IDD was induced through nucleotomy in 4 adult sheep, 5 lumbar discs each (n=20). After 5 weeks, 3 alternating discs were treated with NPgel (n=6) or NPgel+MEPC (n=6). Before sacrifice, animals were subjected to: MRI of lumbar spines (disc height and Pfirmann grading); blood sampling (hematological, biochemical, metabolic and lymphocyte/monocytes immunological). After 3 months the sheep were sacrificed. The spines were processed for: macroscopic morphology (Thompson grading), microscopic morphology (Histological grading), and glycosaminoglycan content (GAG, DMMB Assay). Furthermore, at sacrifice biodistribution of human MEPC was assessed by Alu-sequences quantification (qPCR) from three tissue samples of heart, liver, spleen, brain, lungs, and kidneys, and PBMCs collected to assess activation of systemic immune cells. To each evaluation, appropriate statistical analysis was applied.

Result: Flow cytometry showed no induction of systemic activation of T cells or monocytes. Alu quantification did not give detection of any cells in any organ. Disc height index was slightly increased in discs treated with NPgel+MEPC. Pfirmann's and Thompson's classification showed that treatment with NPgel or NPgel+MEPC gave no adverse reactions. Histological grading showed similar degeneration in vertebrae treated with NPgel+MEPC or with NPgel alone. The amount of GAG was significantly increased in the nucleus pulposus following treatment with NPgel+MEPC compared to NPgel alone, in which a decrease was observed compared to untreated discs in both nucleus pulposus and annulus fibrosus.

Conclusion: This study showed the safety of both NPgel+MEPC and NPgel treatments.

PERFORMANCE OF CONVERSION TOTAL HIP ARTHROPLASTY AFTER FIXATION FAILURE WITH CEPHALOMEDULLARY NAILING

Leevi Karjalainen[1], Antti Ylitalo[1], Miika Lähdesmäki[1], Aleksi Reito[2], Jussi Repo[1]

[1]Tampere University Hospital, Tampere, Finland, *[2]Coxa hospital of joint replacement , Tampere, Finland*

Introduction: Cephalomedullary nailing (CMN) is commonly used for unstable pertrochanteric fracture. CMN is relatively safe method although various complications can potentially occur needing revision surgery. Commonly used salvage procedures such as renailing, hemiarthroplasty, conservative treatment or total hip arthroplasty (THA) are viable alternatives. The aim was to investigate the rate of THA after CMN and evaluate the performance on conversion total hip arthroplasty (cTHA) after failure of CMN.

Method: Collected data included patients from two orthopedic centers. Data consisted of all cTHAs after CMN between 2014-2020 and primary cementless THA operations between 2013-2023. Primary THA operations were treated as a control group where Oxford Hip Score (OHS) was the main compared variable.

Result: From 2398 proximal femoral hip procedures 1667 CMN procedures were included. Altogether 46/1667 (2.8%) CMNs later received THA. Indications for THA after CMN failure were 13 (28.3%) cut-outs, nine (19.6%) cut-throughs, eight (17.4%) nail breakages, seven (15.2%) post traumatic arthrosis, seven (15.2%) nonunions, one (2.2%) malunion and one (2.2%) collum screw withdrawal. Mean (SD) time to complication after CMN operation is 5.9 (6.8) months. Mean (SD) time from nail procedure to THA was 10.4 (12.0) months. Total complication rate for cTHA after CMN was 17.4%. Reported complications were infection with seven (15.2%) cases and one (2.2%) nerve damage. Mean (SD) time to cTHA complication was 3.6 (6.1) months. One-sample T-test showed OHS to be significantly better ($P<.001$) for primary cementless THA compared to cTHA after one year.

Conclusion: Altogether 2.8% of CMN were converted to THA. Nearly half (47.8%) of the cTHA procedures were due to CMN cut-out or cut-through. OHS was significantly better in primary cementless THA compared to cTHA. Prosthetic joint infection was the most frequent complication related to cTHA.

SAME-DAY DISCHARGE TRENDS IN TOTAL HIP ARTHROPLASTY: A NATIONWIDE ANALYSIS OF 235,393 PATIENTS AND 25,388 SAME-DAY DISCHARGES

Halil Bulut[1,2], Daniel Tomey[1]

[1]Houston Methodist Hospital, United States, *[2]Istanbul University Cerrahpasa, Türkyie*

Introduction: The concept of same-day discharge has garnered increasing significance within orthopedic surgery, particularly in hip and knee procedures. Despite initial concerns surrounding the absence of prolonged hospital care, a burgeoning body of evidence highlights numerous advantages associated with same-day discharge, ranging from mitigating in-hospital infections to offering substantial financial and psychosocial benefits for both patients and healthcare providers. In this study, we aim to scrutinize the trends in same-day discharge specifically within the realm of total hip arthroplasties.

Method: This retrospective analysis delves into the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) database spanning from 2017 to 2021. Leveraging patient data sourced from the ACS NSQIP database, we sought to elucidate patterns and shifts in same-day discharge practices pertaining to total hip arthroplasties.

Result: The preoperative analysis illuminated several notable disparities between patients undergoing same-day hip arthroplasty and those necessitating hospitalization. Notably, same-day hip patients skewed younger, comprising 48.3%females compared to 55.6% in hospitalized hip patients. Furthermore, a lower prevalence of medical comorbidities such as diabetes mellitus (8.5% vs.12.9%), current smoking (9.3% vs. 12.2%), and severe COPD(1.9% vs. 4.1%) was observed among same-day hip group. Operatively, same-day hip surgeries boasted shorter durations, averaging 83.9 minutes, in contrast to the 92.3minutes for hospitalized hip procedures. Postoperatively, same-day hip patients exhibited significantly diminished rates of 30-day readmissions (1.7%vs. 3.5%), procedure-related readmissions (1.0%vs.2.1%), reoperations (1.1%vs.1.9%), and mortality (0.02% vs. 0.04%). Moreover, the prevalence of the same-day discharge concept experienced a remarkable ascent from 2016 to 2021, with rates escalating from 1.5% to 25.6% of all total hip arthroplasties over a span of just six years.

Conclusion: In conclusion, same-day discharge is a feasible and safe option for selected THA patients.

TAILOR-MADE NANOSWITCHES FOR TARGETED MODULATION OF PIEZO1 MECHANOSENSING INFLUENCE STEM CELL FATE

Simao P. B. Teixeira[1,2], Alberto Pardo[3], Pablo Taboada[3], Maja Wolleb[4,5], Jess Snedeker[4,5], Rui L. Reis[1,2], Maria Manuela Estima Gomes[1,2], Rui M. A. Domingues[1,2]

[1]3B's Research Group, I3Bs - Research Institute on Biomaterials, Biodegradables and Biomimetics, University of Minho, 4805-017 Barco, Guimaraes, Portugal, *[2]ICVS/3B's–PT Government Associate Laboratory, Braga/Guimaraes, Portugal*, *[3]Colloids and Polymers Physics Group, Department of Particle Physics and Health Research Institute, University of Santiago de Compostela, 15782 Santiago de Compostela, Spain*, *[4]Department of Orthopedics, Balgrist University Hospital, University of Zurich, 8008 Zurich, Switzerland*, *[5]Institute for Biomechanics, ETH Zurich, 8093 Zurich, Switzerland*

Introduction: PIEZO mechanoreceptors are increasingly recognized to play critical roles in fundamental physiological processes like proprioception, touch, or tendon biomechanics. However, their gating mechanisms and downstream signaling are still not completely understood, mainly due to the lack of effective tools to probe these processes. Here, we developed new tailor-made *nanoswitches* enabling wireless targeted actuation on PIEZO1 by combining molecular imprinting concepts with magnetic systems.

Method: Two epitopes from functionally relevant domains of PIEZO1 were rationally selected in silico and used as templates for synthesizing molecularly imprinted nanoparticles (MINPs). Highly-responsive superparamagnetic zinc-doped iron oxide nanoparticles were incorporated into MINPs to grant them magnetic responsiveness. Endothelial cells (ECs) and adipose tissue-derived stem cells (ASCs) incubated with each type of MINP were cultured under or without the application of cyclical magnetomechanical stimulation. Downstream effects of PIEZO1 actuation on cell mechanotransduction signaling and stem cell fate were screened by analyzing gene expression profiles.

Result: Nanoswitches showed sub-nanomolar affinity for their respective epitope, binding PIEZO1-expressing ECs similarly to antibodies. Expression of genes downstream of PIEZO1 activity significantly changed after magnetomechanical stimulation, demonstrating that nanoswitches can transduce this stimulus directly to PIEZO1 mechanoreceptors. Moreover, this wireless actuation system proved effective for modulating the expression of genes related to musculoskeletal differentiation pathways in ASCs, with RNA-sequencing showing pronounced shifts in extracellular matrix organization, signal transduction, or collagen biosynthesis and modification. Importantly, targeting each epitope led to different signaling effects, implying distinct roles for each domain in the sophisticated function of these channels.

Conclusion: This innovative wireless actuation technology provides a promising approach for dissecting PIEZO-mediated mechanobiology and suggests potential therapeutic applications targeting PIEZO1 in regenerative medicine for mechanosensitive tissues like tendon.

Acknowledgements: EU's Horizon 2020 ERC under grant No. 772817 and Horizon Europe under grant No. 101069302; FCT/MCTES for PD/BD/143039/2018, COVID/BD/153025/2022, 10.54499/2020.03410.CEECIND/CP1600/CT0013, 10.54499/2022.05526.PTDC, 10.54499/UIDB/50026/2020, 10.54499/UIDP/50026/2020, and 10.54499/LA/P/0050/2020.

INTEGRIN A10B1-SELECTED HUMAN MESENCHYMAL STEM CELLS CAN DIRECTLY PARTICIPATE IN CARTILAGE REGENERATION AND HAVE IMMUNOMODULATORY CAPACITIES

Kristina Uvebrant[1], Camilla Andersen[1], Hooi Ching Lim[1], Lucienne Vonk[1], Evy Lundgren-Åkerlund[1]

[1]*Xintela AB, Lund, Sweden*

Introduction: Homogenous and consistent preparations of mesenchymal stem cells (MSCs) can be acquired by selecting them for integrin α10β1 (integrin a10-MSCs). Safety and efficacy of intra-articular injection of allogeneic integrin a10-MSCs were shown in two post-traumatic osteoarthritis horse studies. The current study investigated immunomodulatory capacities of human integrin a10-MSCs in vitro and their cell fait after intra-articular injection in rabbits.

Method: The concentration of produced immunomodulatory factors was measured after licensing integrin a10-MSCs with pro-inflammatory cytokines. Suppression of T-cell proliferation was determined in co-cultures with carboxyfluorescein N-succinimidyl ester (CFSE) labelled human peripheral blood mononuclear cells (PBMCs) stimulated with anti-CD3/CD28 and measuring the CFSE intensity of CD4+ cells. Macrophage polarization was assessed in co-cultures with differentiated THP-1 cells stimulated with lipopolysaccharide and analysing the M2 macrophage cell surface markers CD163 and CD206. In vivo homing and regeneration were investigated by injecting superparamagnetic iron oxide nanoparticles conjugated with Rhodamine B-labeled human integrin a10-MSCs in rabbits with experimental osteochondral defects. MSC distribution in the joint was followed by MRI and fluorescence microscopy.

Result: The production of the immunomodulatory factors indoleamine 2,3-dioxygenase and prostaglandin E2 was increased after inflammatory licensing integrin a10-MSCs. Co-cultures with integrin a10-MSCs suppressed T-cell proliferation and increased the frequency of M2 macrophages. In vivo injected integrin a10-MSCs homed to osteochondral defects and were detected in the repair tissue of the defects up to 10 days after injection, colocalized with aggrecan and type II collagen.

Conclusion: This study showed that human integrin a10-MSCs have immunomodulatory capacities and in vivo can home to the site of osteochondral damage and directly participate in cartilage regeneration. This suggests that human integrin α10β1-selected MSCs may be a promising therapy for osteoarthritis with dual mechanisms of action consisting of immunomodulation and homing to damage followed by early engraftment and differentiation into chondrocyte-like cells that deposit hyaline cartilage matrix molecules.

THE INFLUENCE OF BEARING SURFACES ON IGFBP-1 SERUM LEVELS IN THA PATIENTS

Gema Vallés Pérez[1], Eduardo García-Rey[1], Laura Saldaña Quero[1], Nuria Vilaboa Díaz[1]

[1]Hospital Universitario La Paz-IdiPAZ; CIBER de Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN), Madrid

Introduction: The identification of biological markers associated to implant failure in THA (total hip arthroplasty) patients remains a challenge in orthopedic surgery. In this search, previous studies have been mainly focused on typical mediators associated to bone metabolism and inflammation. Our group has evaluated changes in serum levels of insulin-like growth factor binding protein-1 (IGFBP-1), a protein which is not directly related to bone homeostasis, in patients undergoing THA.

Method: We assessed IGFBP-1 levels in serum obtained from 131 patients (58% female, 42 % male; age: 68 ± 13 years) who underwent THA in the Orthopedic Surgery and Traumatology Department of our institution. In this cohort, 57% of patients had metal on polyethylene (MoP) as hip-bearing surface combination, 17 % had ceramic on ceramic (CoC) and 26% of them did not have any prosthesis. A test based on an enzyme-linked immunosorbent assay (ELISA) was used to determine IGFBP-1 levels in serum obtained from these patients.

Result: Our results showed a significant increase in IGFBP- 1 levels in MoP group as compared to CoC and control groups, in which no differences in quantified levels were detected. Further analysis revealed no significant differences in IGFBP-1 between cemented and non-cemented MoP bearings. We performed a ROC curve to evaluate the accuracy of serum IGFBP-1 in discriminating MoP from the rest of patients (area under the curve: 0.7; 95% confidence interval: 0,6-0.8; $p<0.05$) and established a cut-off value of 10.2 ng/ml, according to the Youden´s Index. Logistic regression analysis showed that patients with MoP bearing surfaces had a higher risk of increased IGFBP- 1 levels in serum ($p<0.05$, Odds Ratio: 6.7, 95% Confidence Interval 3.1 to 14.8).

Conclusion: IGFBP- 1 levels are significantly elevated in THA patients with MoP bearing surfaces, suggesting that this protein might be a reliable biomarker for the outcome of patients implanted with MoP.

MOLECULAR EVIDENCE FOR THE EFFECT OF DICLOFENAC ON HUMAN MESENCHYMAL STEM CELL SURVIVAL AND DIFFERENTIATION UNDER HYPOXIA

Maritha Kumlin[1], Huan Cai[2], Johanna Ungerstedt[1], Li Felländer-Tsai[1], Hong Qian[1]

[1]Karolinska Institutet, Stockholm, Sweden, *[2]Soochow University, Suzhou, China*

Introduction: Joint pain, either traumatic or degenerative, is a common cause of morbidity. Diclofenac (DF), a common non-steroid anti-inflammatory drug (NSAID), has been used as symptomatic treatment for joint pain for decades. However, DF may have potentially devastating effects by altering the normal healing process, disturbing the cellular entities that contribute to tissue regeneration of the synovial joint. Mesenchymal stem cells (MSCs) have been considered important for tissue regeneration due to their multipotency in regenerating osteoblasts, chondrocytes and adipocytes and their immunomodulatory properties. Thus, the effect of DF treatment on MSCs can not be ignored. So far, it remains largely unclear how DF treatment affects human MSC properties, particularly under hypoxia, a feature of an injured synovial joint.

Method: Healthy human bone marrow-derived MSCs were subjected to 1 µM-250 µM DF *in vitro* under hypoxic culture conditions for 24 h. Subsequently, the MSC proliferation and adipocytic differentiation were evaluated and transcriptomic profile of the cells was examined by RNA sequencing.

Result: *In vitro* DF treatment for 24 hours at concentrations of 25 µM and beyond, impaired MSC proliferation and was accompanied by downregulation of genes associated with E2F Targets, cell cycle and DNA replication. Diclofenac at 50 µM had no significant effect on osteogenesis while revealing an effect on Sox9, a key regulatory gene of chondrogenesis. In addition, DF promoted adipocyte differentiation but had no molecular impact on tenogenesis.

Conclusion: Our results demonstrate new molecular evidence for the profound impact of short time exposure of DF on healthy human MSCs *in vitro*. The risk of unintended drug-induced tissue failure including deteriorating MSC proliferation in parallel with adipogenic differentiation must not be neglected. The potential risk and benefit induced by DF treatment should be considered during clinical practice. Future studies should aim to elucidate the functional consequence of the altered signaling pathways.

DOES THE ADDITION OF FLUORIDE TO BIOACTIVE GLASS AFFECT THE OSTEOGENIC AND ANGIOGENIC PROPERTIES OF BONE PROGENITOR CELLS?

Alina Durach[1], Elke Kunisch[1], Tobias Renkawitz[1], Fabian Westhauser[1], Delia Brauer[2], Frederike Hohenbild[1]

[1]Research Centre for Molecular and Regenerative Orthopaedics, Department for Orthopaedics, Heidelberg University Hospital, Heidelberg, Germany, [2]Otto-Schott Institute of Materials Research, Friedrich-Schiller-University, Jena, Germany

Introduction: Bioactive glasses (BGs) promote osteogenic differentiation of bone progenitor cells by releasing therapeutically active ions. The well-described 45S5-BG (in mol%: SiO_2 46.13; P_2O_5 2.60; CaO 26.91; Na_2O 24.35) was supplemented with CaF_2 and NaF being added to the batch at nominal 5 (F5-BG) and 25 mol% (F25-BG), respectively. While the effect on physical and chemical properties has already been characterized, the biological properties require further studies. This study investigates the effects of fluoride-supplemented BGs on the osteogenic and angiogenic properties of human bone marrow mesenchymal stromal cells (BMSCs) in vitro.

Method: BMSCs were co-cultured with melt-derived 45S5-BG, F5-BG, or F25-BG in ascending concentrations (1, 2 and 3 mg/ml). At 7 days, cell number was determined by 4,6-diamidine-2-phenylindole (DAPI) staining and cell viability by fluorescein diacetate (FDA) assay. The osteogenic potential of the BGs was evaluated through alkaline phosphatase (ALP) gene expression and activity, along with bone morphogenetic protein-2 (BMP2) gene expression and protein concentration. Vascular endothelial growth factor (VEGF) gene expression and protein concentration assessed angiogenic potential. As control, BMSCs were cultured without BG exposure.

Result: All BGs significantly promoted cell number and viability, with F25-BG showing the highest count at 3 mg/ml. Osteogenic markers showed a significant decrease in ALP gene expression and activity, especially at higher concentrations. All BG groups demonstrated increased BMP2 protein concentration and gene expression compared to the control, with higher BG and fluoride concentrations correlating with greater increases in BMP2. VEGF gene expression increased in all analysed BGs. The fluoride-free BG group had the highest VEGF protein concentrations, while the F25 BG group showed the highest VEGF gene expression.

Conclusion: The fluoride-substituted BGs exhibit excellent cytocompatibility, enhance BMSC proliferation and positively affect BMP2 gene expression and levels, suggesting their potential for osteogenic differentiation. Further research is necessary to assess their proangiogenic effect and potential advantages over 45S5-BG.

PREHABILITATION FOR FRAIL PATIENTS UNDERGOING HIP AND KNEE REPLACEMENT: JOINT PREP FEASIBILITY STUDY FOR A RANDOMISED CONTROLLED TRIAL

Tanzeela Khalid[1], Yoav Ben-Shlomo[1], Wendy Bertram[1], Lucy Culliford[1], Emily Henderson[1], Marcus Jepson[1], Emma Johnson[1], Shea Palmer[2], Michael WHITEHOUSE[1], Vikki Wylde[1]

[1]University of Bristol, Bristol, United Kingdom, *[2]University of Cardiff, Cardiff, United Kingdom*

Introduction: Approximately 20-25% of patients having joint replacement in the UK have moderate-severe frailty. Frailty is associated with poorer outcomes after joint replacement. Targeting frailty pre-operatively with exercise and protein supplementation could improve post-operative outcomes. Prior to conducting a randomised controlled trial (RCT), a feasibility study was necessary to inform trial design and delivery.

Method: We conducted a randomised feasibility study with embedded qualitative work. Patients aged ≥65 years, frail and undergoing THR or TKR were recruited from three UK hospitals. Participants were randomly allocated on a 1:1 ratio to the intervention or usual care group. The intervention group had a 1:1 appointment with a physiotherapist and were provided with a home-based, tailored daily exercise programme and a daily protein supplement for 12 weeks before their operation, supported by six telephone calls from a physiotherapist. Questionnaires were administered at baseline and 12 weeks after randomisation. Interviews were conducted with 19 patients. Feasibility outcomes were eligibility and recruitment rates, intervention adherence, and acceptability of the trial and the intervention.

Result: 411 patients were sent a screening pack. Of the 168 patients who returned a screening questionnaire, 79 were eligible and consented to participate, and 64 were randomised. Of the 33 participants randomised to the intervention, 26 attended the intervention appointment. Eighteen participants (69%) received all six intervention follow-up telephone calls. Nineteen participants completed an intervention adherence log; 13 (68%) adhered to the exercise programme and 11 (58%) adhered to the protein supplementation. The overall retention rate was 86% at 12 weeks. The 12-week follow-up questionnaire was returned by 84% of participants who were sent a questionnaire. Interviews found that the trial and intervention were generally acceptable, but areas of potential improvements were identified.

Conclusion: This study demonstrated that a larger study is possible and has identified improvements to optimise the design of a RCT.

PREOPERATIVE PREDICTORS OF HIP ABDUCTOR FOR GAIT SPEED IMPROVEMENT AFTER TOTAL HIP ARTHROPLASTY FOR PATIENTS WITH OSTEOARTHRITIS

Tadashi Yasuda[1], Satoshi Ota[1], Sadaki Mitsuzawa[1], Shinnosuke Yamashita[1], Yoshihiro Tsukamoto[1], Hisataka Takeuchi[1], Eijiro Onishi[1]

[1]Kobe City Medical Center General Hospital, Kobe, Japan

Introduction: A recent study to identify clinically meaningful benchmarks for gait improvement after total hip replacement (THA) has shown that the minimum clinically important improvement (MCII) in gait speed after THA is 0.32 m/sec. Currently, it remains to be investigated what preoperative factors link to suboptimal recovery of gait function after THA. This study aimed to identify preoperative lower-limb muscle predictors for gait speed improvement after THA for hip osteoarthritis.

Method: This study enrolled 58 patients who underwent unilateral primary THA. Gait speed improvement was evaluated as the subtraction of preoperative speed from postoperative speed at 6 months after THA. Preoperative muscle composition of the glutei medius and minimus (Gmed+min) and the gluteus maximus (Gmax) was evaluated on a single axial computed tomography slice at the bottom end of the sacroiliac joint. Cross-sectional area ratio of individual composition to the total muscle was calculated.

Result: The females (n=45) showed smaller total cross-sectional areas of the gluteal muscles than the males (n=13). Gmax in the females showed lower lean muscle mass area (LMM) and higher ratios of the intramuscular fat area and the intramuscular adipose tissue area to the total muscle area (TM) than that in the males. Regression analysis revealed that LMM/TM of Gmed+min may correlate negatively with postoperative improvement in gait speed. Receiver operating characteristic curve analysis for prediction of MCII in gait speed at $\geq$ 0.32 m/sec resulted in the highest area under the curve for Gmax TM with negative correlation. The explanatory variables of hip abductor muscle composition predicted gait speed improvement after THA more precisely in the females compared with the total group of both sexes.

Conclusion: Preoperative Gmax TM could predict gait speed MCII after THA. Preoperative muscle composition should be evaluated separately based on sexes for achievement of clinically important improvement in gait speed after THA.

MULTIFACTORIAL BIOENGINEERING TO CONTROL CELL FATE

Dimitrios Zevgolis[1]

[1]*University College Dublin, Dublin, Ireland*

Introduction: Bereft of their optimal tissue context, cells lose their phenotype, function and therapeutic potential during *in vitro* culture. Despite the fact that *in vivo* cells are exposed simultaneously to multiple signals, traditional *ex vivo* cultures are monofactorial. With these in mind, herein we assessed the combined effect of surface topography, substrate rigidity, collagen type I coating and macromolecular crowding in human tenocyte, skin fibroblast and bone marrow mesenchymal stromal cell cultures.

Methods: Thermal imprinted was used to pattern (groove depth: 2,000 nm, groove width: 2,000 nm, line width: 2,000 nm) polydimethylsiloxane substrates of different rigidity (50 kPa, 130 kPa, 1,000 kPa). Grooved and planar substrates were subsequently coated with collagen type I and used to culture the aforementioned cell populations without and with macromolecular crowding (100 μg/ml carrageenan). After 3, 7 and 14 days in culture, cell morphology, viability, metabolic activity, proliferation, protein synthesis and deposition and gene expression analyses were conducted.

Results: None of the variables assessed affected cell viability, metabolic activity and proliferation. Surface topography was found to be a potent regulator of cell morphology. Macromolecular crowding significantly increased extracellular matrix deposition, albeit in globular manner independently on whether grooved or planar substrates were used, possibly due to the low dimensionality of the grooves. Gene expression analysis made apparent that the 130 kPa and the 1,000 kPa grooved substrates under macromolecular crowding conditions maintained human tenocyte phenotype and directed human bone marrow mesenchymal stromal cells towards tendon-like lineage, respectively. None of the conditions assessed dramatically affected human skin fibroblast fate.

Conclusions: Collectively, our data indicate that the physicochemical *in vitro* microenvironment modulators assessed herein are capable of maintaining human tenocyte phenotype and differentiating human bone marrow mesenchymal stromal cells towards tenogenic lineage, but not in trans-differentiating human skin fibroblasts.

DEVELOPMENT AND IMPLEMENTATION OF THE INFORM GUIDELINES FOR THE TREATMENT AND MANAGEMENT OF PROSTHETIC HIP INFECTION

Andrew Moore[1], Michael WHITEHOUSE[1], Vikki Wylde[1], Nicola Walsh[2], Andrew Beswick[1], Catherine Jameson[1], Ashley Blom[3]

[1]University of Bristol, Bristol, United Kingdom, *[2]University West of England, Bristol, United Kingdom*, *[3]University of Sheffield, Sheffield, United Kingdom*

Introduction: Hip prosthetic joint infection (PJI) is a debilitating complication following joint replacement surgery, with significant impact on patients and healthcare systems. The INFection ORthopaedic Management: Evidence into Practice (INFORM: EP) study, builds upon the 6-year INFORM programme by developing evidence-based guidelines for the identification and management of hip PJI.

Methods : A panel of 21 expert stakeholders collaborated to develop best practice guidelines based on evidence from the previous INFORM research programme. An expert consensus process was used to refine guidelines using RAND/UCLA criteria. The guidelines were then implemented over a 12-month period through a Learning Collaborative of 24 healthcare professionals from 12 orthopaedic centres in England. Qualitative interviews were conducted with 17 members of the collaborative and findings used to inform the development of an implementation support toolkit. Patient and public involvement contextualised the implementation of the guidelines. The study is registered with the ISCRTN (34710385).

Result: The INFORM guidelines, structured around the stages of PJI management, were largely supported by surgeons, although barriers included limited awareness among non-surgical team members, lack of job planning for multidisciplinary teams, and challenges in ensuring timely referrals from primary care. Psychological support for patients was identified as a critical gap. Advanced Nurse Practitioners and multidisciplinary team (MDT) coordinators were seen as potential bridges to address these knowledge gaps. The guidelines were also viewed as a useful tool for service development.

Conclusions: This study presents the first evidence-based guidelines for hip PJI management, offering a comprehensive approach to prevention, treatment, and postoperative care. Effective implementation is crucial, involving wider dissemination amongst primary and community care, as well as non-specialist treatment centres. Further resources are needed to ensure job planning for MDTs and psychological support for patients. Overall, this study lays the foundation for improved PJI management, benefiting patients and healthcare systems.

THE RELATIONSHIP BETWEEN ULNAR FIXATION AND SOCIODEMOGRAPHIC DIVERSITY IN POSTOPERATIVE SATISFACTION FOR DISTAL RADIUS FRACTURES ACCOMPANIED BY ULNA STYLOID FRACTURE

Cumhur Deniz Davulcu[1], Derya Akbaba[1]

[1]ISTANBUL UNIVERSITY-CERRAHPASA, CERRAHPASA MEDİCAL FACULTY, DEPARTMENT OF ORTHOPEDICS AND TRAUMATOLOGY, ISTANBUL

Introduction: This study aims to investigate the relationship between ulnar fixation and postoperative satisfaction among patients with distal radius fractures accompanied by ulna styloid fractures, with a particular focus on how sociodemographic factors influence outcomes.

Method: A retrospective cohort study was conducted involving 120 patients aged 26-53 who underwent surgical treatment for distal radius fractures with concomitant ulna styloid fractures between January 2018 and December 2022. Patients were divided into two groups based on whether ulnar fixation was performed. Sociodemographic data, including age, gender, socioeconomic status, education level, and occupation, were collected. All patients underwent similar physical therapy protocols in the postoperative period, and no complications were observed in any patient. Postoperative satisfaction was assessed using the Patient-Rated Wrist Evaluation (PRWE) and the Disabilities of the Arm, Shoulder, and Hand (DASH) scores at 6 and 12 months post-surgery. Statistical analysis was conducted to evaluate the influence of ulnar fixation and sociodemographic factors on patient satisfaction.

Result: Patients who underwent ulnar fixation (n=60) reported significantly higher satisfaction levels compared to those who did not (n=60), as evidenced by lower PRWE and DASH scores ($p < 0.05$). Age, gender, and socioeconomic status were significant predictors of postoperative satisfaction. Younger patients, females, and those with higher socioeconomic status exhibited greater improvements in functional outcomes and satisfaction. However, education level and occupation did not significantly influence satisfaction scores.

Conclusion: Ulnar fixation in the surgical treatment of distal radius fractures accompanied by ulna styloid fractures is associated with improved postoperative satisfaction. Sociodemographic factors, particularly age, gender, and socioeconomic status, play a crucial role in patient-reported outcomes. Tailoring postoperative care to address these sociodemographic differences may enhance overall patient satisfaction and recovery.

MINIMALLY INVASIVE SURGICAL TREATMENTS VERSUS NON-SURGICAL TREATMENTS FOR PLANTAR FASCIOPATHY:

Stefan Møller[1]

[1]*Kolding Hospital, Kolding, Denmark*

Introduction: Plantar heel pain, or plantar fasciopathy (PF), is a common musculoskeletal complaint, affecting 39% of lower-extremity tendinopathies in general practice. Conservative management is recommended as the first-line treatment, yet many patients continue to experience symptoms even after ten years. There is a significant lack of high-quality evidence for the effectiveness of various treatments, highlighting the need for more research.

Minimally invasive surgical options, such as endoscopic plantar fascia release and radiofrequency microtenotomy, have shown promise in reducing pain and improving outcomes. This systematic review aims to evaluate the effectiveness of these minimally invasive surgical treatments compared to non-surgical options in managing PF.

Method: The systematic review, registered on PROSPERO (CRD42024490498) and adhering to PRISMA guidelines, searched databases including PubMed, Embase, Cochrane, and others for studies from January 1991 to May 2024. Keywords included plantar fasciitis, plantar fasciopathy, and heel pain. Limited to human trials, the search strategy was refined with an information specialist and found no protocol duplicates.

Result: The systematic review identified eight studies involving 495 patients (56.2% women, average age 46.5 years). The studies compared various treatments, including endoscopic plantar fascia release (EPF), mini-scalpel needle (MSN) treatment, ultrasound-guided pulsed radiofrequency (UG-PRF), and needle electrolysis (NE), to non-surgical interventions and corticosteroid injections (CSI). Primary outcomes focused on pain reduction, with some needle treatments showing superior results (between-group diffence). No severe adverse events were reported.

Conclusion: In conclusion, plantar fasciopathy (PF) remains a prevalent and challenging condition, that can be resistant to conservative treatments. This systematic review highlights the potential of minimally invasive surgical options, such as endoscopic plantar fascia release and needle treatments, in reducing pain and improving functional outcomes. Despite some needle treatments showing superior results, the overall lack of high-quality evidence underscores the need for further research to establish the most effective management strategies for PF.

COMPARISON OF THE GLENOID INDEX BY COMPUTED TOMOGRAPHY WITH MAGNETIC RESONANCE IMAGING.

Nida Anjum Ahmed[1], kailash narendran[2], Nishath anjum Ahmed[3]

[1]Trauma and Orthopaedics, Barnsley Hospital NHS foundation Trust,, Barnsley, United Kingdom, *[2]Dept. of General Surgery, East Lancashire Hospital NHS trust, Blackburn, United Kingdom*, *[3]Dr. B.R. Ambedkar Medical College and Research Institute, Bangalore, India*

Introduction: Anterior shoulder instability results in labral and osseous glenoid injuries. With a large osseous defect, there is a risk of recurrent dislocation of the joint, and therefore the patient must undergo surgical correction. An MRI evaluation of the patient helps to assess the soft tissue injury. Currently, the volumetric three-dimensional (3D) reconstructed CT image is the standard for measuring glenoid bone loss and the glenoid index. However, it has the disadvantage of exposing the patient to radiation and additional expenses. This study aims to compare the values of the glenoid index using MRI and CT.

Method: The present study was a two-year cross-sectional study of patients with shoulder pain, trauma, and dislocation in a tertiary hospital in Karnataka. The sagittal proton density (PD) section of the glenoid and enface 3D reconstructed images of the scapula were used to calculate glenoid bone loss and the glenoid index. The baseline data were analyzed using descriptive statistics, and the Chi-square test was used to test the association of various complications with selected variables of interest.

Result: The glenoid index calculated in the current study using 3D volumetric CT images and MR sagittal PD images was 0.95±0.01 and 0.95±0.01, respectively. The CT and MRI glenoid bone loss was 5.41±0.65% and 5.38±0.65%, respectively. When compared, the glenoid index and bone loss calculated by MRI and CT revealed a high correlation and significance with a p-value of <0.001.

Conclusions: The study concluded that MRI is a reliable method for glenoid measurement. The sagittal PD sequence combined with an enface glenoid makes it possible to identify osseous defects linked to glenohumeral joint damage and dislocation. The values derived from 3D CT are identical to the glenoid index and bone loss determined using the sagittal PD sequence in MRI.

Keywords: radiography, ct, mri, glenoid bone loss, glenoid index

PATIENT-SPECIFIC TIBIA IMPLANTS: ALGORITHMIC DESIGN PROCESSES FOR CLINICAL CASES

Julie Kühl[1], Jannek Grocholl[2], Andreas Seekamp[1], Tim Klüter[1], Sabine Fuchs[1]

[1]Experimental Trauma Surgery, Department of Orthopedics and Trauma Surgery, University Medical Center Kiel, Kiel, Germany, *[2]Computational Design Freelancer, Kiel , Germany*

Introduction: The surgical treatment of critical-sized bone defects with complex three-dimensional (3D) geometries is a challenge for the treating surgeon. Additive manufacturing such as 3D printing enables the production of highly individualized bone implants meeting the shape of the patient's bone defect and including a tunable internal structure. In this study, we showcase the design process for patient-specific implants with critical-sized tibia defects.

Methods: Two clinical cases of patients with critical tibia defects (size 63x20x21 mm and 50x24x17 mm) were chosen. Brainlab software was used for segmentation of CT data generating 3D models of the defects. The implant construction involves multiple stages. Initially, the outer shell is precisely defined. Subsequently, the specified volume is populated with internal structures using Voronoi, Gyroid, and NaCl crystal structures. Variation in pore size (1.6 mm and 1.0 mm) was accomplished by adjusting scaffold size and material thickness.

Results: An algorithmic design process in Rhino and Grasshopper was successfully applied to generate model implants for the tibia from Ct data. By integrating a precise mesh into an outer shell, a scaffold with controlled porosity was designed. In terms of the internal design, both Voronoi and Gyroid form macroscopically homogeneous properties, while NaCl, exhibits irregularities in density and consequently, in the strength of the structure. Data implied that Voronoi and Gyroid structures adapt more precisely to complex and irregular outer shapes of the implants.

Conclusion: In proof-of-principle studies customized tibia implants were successfully generated and printed as model implants based on resin. Further studies will include more patient data sets to refine the workflows and digital tools for a broader spectrum of bone defects. The algorithm-based design might offer a tremendous potential in terms of an automated design process for 3D printed implants which is essential for clinical application.

DEVELOPMENT OF TISSUE-ENGINEERED SUBSTITUTES FOR THE REGENERATION OF TENDON TOTAL RUPTURES

Ane Llucia[1], Sandra Camarero-Espinosa[2]

[1]BioSmarTE lab, POLYMAT, University of the Basque Country UPV/EHU, Spain, [2]BioSmarTE lab, POLYMAT, University of the Basque Country UPV/EHU; IKERBASQUE, Basque Foundation for Science, Spain

Introduction: Tendon ruptures represent one of the most common acute tendon injuries in adults worldwide, affecting millions of people anually and becoming more prevalent due to longer life expectancies and sports activities. Current clinical treatments for full tears are unable to completely restore the torn tendons to their native composition, structure and mechanical properties.

To address this clinical challenge, tissue-engineered substitutes will be developed to serve as functional replacements for total tendon ruptures that closely resemble the original tissue, restoring functionality.

Method: Water borne polyurethanes (WBPU) containing acrylate groups, specifically polyethylene glycol methacrylate (PEGMA) or 2-hydroxyethyl methacrylate (HEMA), were combined with mouse mesenchymal stem cells (MoMSCs) and heparin sodium to formulate bioinks for the fabrication of scaffolds via extrusion-based 3D bioprinting.

Result: The biocompatibility of acrylated-WBPUs was confirmed in 2D with MoMSCs using lactate dehydrogenase assay, DNA assay and live/dead assays. Cell-laden scaffolds were 3D-bioprinted by encapsulating MoMSCs at varying cell densities within the acrylated WBPUs. The resulting 3D structures support cell viability and proliferation within the scaffolds, as confirmed by live/dead assay, lactate dehydrogenase assay and DNA assays. Differentiation studies in the 3D-bioprinted scaffolds demonstrated the phenotype transition of MoMSCs toward tenocytes through gene expression and protein deposition analysis. The inclusion of sodium heparin in the bioinks revealed increased synthesis of matrix assembly proteins within the 3D-bioprinted constructs.

Conclusion: The developed bioinks were biocompatible and printable, supporting cell viability within the 3D-bioprinted scaffold. The fabricated cell-laden constructs sustained cell proliferation, differentiation, and tissue formation. The addition of heparin sodium enhanced tissue formation and organization, showing promising results for the regeneration of tendon total ruptures.

This work was supported by the Spanish State Research Agency (AEI) under grant No CPP2021-008754. The authors would like to thank their partners in the project, which are in charge of the synthesis of heparin sodium and acrylated-WBPUs.

CONGRUENCY OF ULTRASOUND MEASURE CHANGE AGAINST PATIENT REPORTED OUTCOME MEASURE IN PATELLAR TENDINOPATHY: A SYSTEMATIC REVIEW WITH META-ANALYSIS

Cameron Parks[1]

[1]*Queen Mary's University of London, London, United Kingdom*

Introduction: Patellar tendinopathy is a highly prevalent clinical diagnosis supported by ultrasound changes. Numerous interventions are targeted at improving both symptoms and structure of dysfunctional tendons, however little is known of the diagnostic value in a changing ultrasound profile whilst patient reported outcome measures determine recovery. The aim of this study was to assess if change in ultrasound measure is congruent with change in Victorian Institute of Sport Assessment – Patella (VISA-P) score and therefore indicates the use of using ultrasound to assess patellar tendinopathy during symptom change.

Method: Four databases (PubMed, Web of Science, Embase, Cinahl) were search in January 2014. Studies selected contained ultrasound and VISA-P scores from ≥ 2 type points. All included studies were quality assessed depending on type and available data underwent meta-analysis.

Result: 10 papers of varying study type, of limited to high quality, were synthesised. Meta-analysis indicated that change in ultrasound measure was not congruent with change in VISA-P score.

Conclusion: The variation in study quality, along with significant heterogeneity of ultrasound measure outcomes and reporting may influence the congruency of the data, but the association between gradual structure change and varying vascularity with pain or function is questionable throughout tendinopathy literature.

BIOENGINNERED LIVING FIBERS AS 3D MODELS OF TENDON HEALTH AND DISEASE

Manuel Gómez-Florit[1,2,3], Ana L. Graça[4], Rui M. A. Domingues[4], Maria Manuela Estima Gomes[4]

[1]Health Research Institute of the Balearic Islands, Palma, Spain, [2]Research Unit, Son Espases University Hospital (HUSE), Palma, Spain, [3]Group of Cell Therapy and Tissue Engineering (TERCIT), Research Institute on Health Sciences (IUNICS), University of the Balearic Islands (UIB), , Palma, Spain, [4]University of Minho, Guimaraes, Portugal

Introduction: Healthy tendons are mainly composed of aligned collagen hierarchically organized from collagen fibrils to fiber bundles with a scarce cellular population mainly composed of tenocytes and tendon stem/progenitor cells. However, injured tendon acquires a fibrotic state characterized by a loss of ECM alignment and increased cellularization. The lack of reliable 3D models that recreate the organization and microenvironment of healthy and diseased tendons is one of the main obstacles faced by the scientific community.

Method: To recreate the architecture of healthy and diseased tendons, electrospun nanofiber scaffolds with anisotropic and isotropic nanotopography were developed. These scaffolds were coated with a shell consisting of cell-laden hydrogels encapsulating human adipose-derived stem cells (hASCs) to include the living component. To show the versatility of the system, extracellular vesicles (EVs) were encapsulated in the hydrogel as biological cues. The living fibers were characterized by microscopy and morphological analysis. The morphology and phenotype of cells was evaluated using microscopy, gene expression analysis and immunostainings for tendon markers.

Results: Scaffolds mimicked the native hierarchical structure of tendons and size of tendon fascicles. hASCs showed high elongation and cytoskeleton anisotropic organization, typical of tenocytes. Moreover, the bioengineered living fibers supported the tenogenic differentiation of stem cells over time, as indicated by the sustained expression of tenogenic and extracellular matrix markers. Finally, the hydrogel layer acted not only as a hydrated biomimetic environment adequate for cell encapsulation but also as a carrier and delivery system of EVs to cells, which improved their tenogenic commitment.

Conclusion: We bioengineered composite living fibers made of hierarchically organized electrospun fibers, coated with hydrogel encapsulating hASCs and biofunctional EVs. These provide an in vitro system to recreate tendon, allowing for the study of the effects of biophysical cues in tendon microenvironments and the influence of biologics on cells behavior.

Acknowledgments: CP21/00136, PI22/01686, CA22170, 10.54499/2020.03410.CEECIND/CP1600/CT0013, 10.54499/2022.05526.PTDC

MACROPHAGE-DERIVED EXTRACELLULAR VESICLES AS POTENTIAL MODULATORS OF TENDON INFLAMMATION

Sara Bagur-Cardona[1,2,3], Kristiyan Stiliyanov-Atanasov[1,2,3], Javier Calvo[2,4], Antoni Gayà[2,4], Manuel Gómez-Florit[1,2,3]

[1]Health Research Institute of the Balearic Islands (IdISBa), Palma, Balearic Islands, Spain, [2]Group of Cell Therapy and Tissue Engineering (TERCIT), Palma, Balearic Islands, Spain, [3]Research Unit, Son Espases University Hospital (HUSE), Palma, Balearic Islands, Spain, [4]Fundació Banc de Sang i Teixits de les Illes Balears (FBSTIB), Palma, Balearic Islands, Spain

Introduction: Tendinopathies represent a significant health burden, causing inflammation, pain, and reducing quality of life. The pivotal role of macrophages (Mϕ) characterized by their ability to differentiate into proinflammatory (M1) or anti-inflammatory (M2) phenotypes depending on the microenvironment, has gained significant interest in tissue inflammation research. Additionally, existing literature states that the interplay between tenocytes and immune cells during inflammation involves unidentified soluble factors (SF). This study aimed to investigate the effect of extracellular vesicles (EVs) and SF derived from polarized Mϕ on tendon cells to provide deeper insights of their potential therapeutic applications in the context of inflammation.

Method: Human monocytes were isolated from blood donor buffy coats and differentiated into M1, M2, and hybrid M1/M2 phenotypes. Subsequently, EVs were isolated from the conditioned media from polarized Mϕ and comprehensively characterized. In parallel, the elution media containing SF was collected. Furthermore, the EVs and SF were released independently onto tenocytes from human donors, previously induced with IL-1β to simulate an inflammatory environment. Finally, mRNA levels of tendon-related markers were evaluated by qPCR after the exposure to these EVs and SF.

Result: Notably, the study found that the viability of the cells was not affected by the exposure to EVs nor SF, indicating their potential safety for therapeutic use. Moreover, the mRNA content of tendon-derived cells was evaluated following exposure to Mϕ-EVs and SF revealing alterations in gene expression. Interestingly, a significant increase in the expression of tenomodulin was observed in tendon cells treated with Mϕ-EVs.

Conclusion: These results mark a significant advancement in understanding the interplay between Mϕ and tenocytes at a molecular level. To fully understand the underlying causes of Mϕ-EVs effects, and its potential clinical application in tendon inflammatory diseases, further comprehensive research is required.

Acknowledgments: Carlos III Health Institute and the European Social Fund for contract CP21/00136 and project PI22/01686.

USE OF BIOABSORBABLE NANOTECHNOLOGY IN ACHILLES TENDON RUPTURES

Serkan Savaş[1], Mehmet Konya[1], Bilge Kağan Yılmaz[1], Sadık Kağa[2], Elif Kağa[1], Hasan Hüseyin Demirel[2]

[1]Afyonkarahisar Health Sciences University, Afyonkarahisar, Türkyie, *[2]Afyon Kocatepe University, Afyonkarahisar, Türkyie*

Introduction:The Achilles tendon is the thickest and strongest tendon in the human body.Even though the tendon is so strong, it is one of the most frequently injured tendons.Treatment of patients after rupture is planned conservatively and surgically.Conservative treatment is generally applied to elderly patients with sedentary lives.If the treatment is surgical, it can be planned as open surgery or percutaneous surgery. In our study with rabbits, we wrapped a membrane made of plga (polylactic-co-glycolic acid) nanotubes impregnated with type 1 collagen around the tendon in rabbits that underwent open Achilles tendon repair surgery.After surgery, biomechanical and histological tests were performed on the tendons.

Method:In the study consisting of 24 rabbits, 2 groups were created by random distribution.In the study group, after the Achilles tendon rupture was created, a type 1 collagen-impregnated plga-based membrane was placed around the tendon after the repair of 1 modified Kesslerr suture.In the control group, after the Achilles tendon rupture was created, 1 modified Kessler suture and Tendon repair was performed with the application of 3 primary sutures.At the end of the 6th week of the study, the rabbits in 2 groups were randomly distributed and histological examination was performed.Additionally, biomechanical testing was performed.Bonar and Movın scoring were used in histological examinations.

Result:As a result of biomechanical tests, it was seen that the resistance of the tendon against rupture was higher in the study group than in the control group.In addition, it was observed that the tendon rupture time was longer in the study group than in the control group.Histological examinations gave supportive results from biomechanical tests.

Conclusion:We think that the use of collagen-impregnated plga-based nanotubes in the surgical treatment of Achilles tendon ruptures has a positive healing effect.Although we think that the return to normal life after surgery may be faster, we believe that more clinical studies are needed.

STRESS RESPONSE OF ACHILLES TENOCYTES FROM NON DIABETIC AND DIABETIC RATS EXPOSED TO NORMO- AND HYPERGLYCEMIA DIFFERS

Priv.-Doz. Dr. Clemens Leo Gögele[1], Nils Fleischmann[1], Sarah Hofman[1], Eva Frank[1], Christian Werner[1], Maria Kokozidou[1], Prof. Dr. Gundula Schulze-Tanzil[1,1]

[1]*Institute of Anatomy and Cell Biology, Nürnberg*

Introduction: Diabetes mellitus type 2 (DMT2) patients often develop Achilles tendon (AS) degeneration. The ZDF rat model is often used to study DMT2. Hence, this study investigated whether tenocytes isolated from diabetic and non diabetic ZDF rats respond differentially to normo- (NG) and hyperglycemic (HG) conditions in the presence of tumor necrosis (TNF)α.

Method: AS tenocytes isolated from adult diabetic (fa/fa) or lean (fa/+) Zucker Diabetic Fatty (ZDF) rats were treated with 10 ng/mL TNFα either under NG or HG conditions (1 g/L *versus* 4.5 g/L glucose). Tendons were characterized histopathologically using Movin score. Tenocyte survival, metabolic activity, gene and/or protein expression of the main tendon extracellular matrix (ECM) component *collagen type 1*, the myofibroblast marker alpha smooth muscle actin (αSMA, *Acta2*), complement regulatory factors, the antioxidant defense enzyme *heme oxygenase-1* (*Hmox1*), *suppressors of cytokine signaling* (*Socs*)*1* and *Soc3* were analyzed.

Result: Tendons of diabetic rats showed significantly higher Movin score values suggesting tendon degeneration. Tenocyte vitality remained high, but metabolic activity was impaired by HG conditions, irrespectively of tenocyte origin. Higher amounts of αSMA were visualized in tendons/cells of diabetic rats or those exposed to TNFα. *Collagen type 1* protein and gene expression was suppressed by TNFα (NG), but only in cells of non diabetic animals. The anaphylatoxin receptor C3aR was higher expressed in tenocytes from diabetic animals. CD46 was suppressed by TNFα (NG) in cells of diabetic rats. *Hmox1, Socs1* and *Socs3* were induced by HG, but only in tenocytes of diabetic rats (4 h).

Conclusion: The response of tenocytes to TNFα depends on glucose supply and cell origin suggesting their irreversible impairment in DMT2.

MICROSTRUCTURAL AND TRANSCRIPTOMIC ANALYSIS OF TRABECULAR BONE IN PATIENTS WITH IDIOPATHIC OSTEONECROSIS OF THE FEMORAL HEAD

Laura Saldaña Quero[1], Clara Escudero-Duch[2], Nuria Vilaboa Díaz[1,2], Eduardo García-Rey[1]

[1]Hospital Universitario La Paz-IdiPAZ, Madrid, *[2]Centro de Investigación Biomédica en Red de Bioingeniería, Biomateriales y Nanomedicina, CIBER-BBN, Spain*

Introduction: The most frequent diagnosis in young adults undergoing total hip arthroplasty (THA) is osteonecrosis of the femoral head (ONFH), an evolving and disabling condition with an increasing prevalence worldwide. Treatment of ONFH remains a challenge mainly because of a lack of understanding of the disease's pathophysiological basis. This study investigated the biological processes that could be affected by ONFH by comparing the microstructure, histological characteristics and transcriptomic profile of trabecular bone from the femoral head (FH) and the intertrochanteric region (IT) of patients suffering from this condition.

Method: A total of 18 patients with idiopathic ONFH undergoing THA in our institution were included. Trabecular bone explants were taken intraoperatively from the FH and the IT of patients. Bone microstructure was examined by micro-computed tomography (micro-CT). After bone sectioning, histological features were studied by hematoxylin and eosin staining. Differential gene expression was investigated using a microarray platform.

Result: Micro-CT imaging showed higher trabecular separation and lower trabecular thickness and bone volume in trabecular bone from the FH than from the IT. Histological staining revealed that the number of osteoblasts on the bone surface and the percentage of empty lacunae were higher in trabecular bone from the FH. Transcriptome analysis identified a differential signature in trabecular bone from the FH compared to the IT. The gene ontology analyses of the genes overexpressed in trabecular bone from the FH revealed a range of enriched biological processes related to cell division and immune response. In contrast, most downregulated transcripts were involved in bone formation.

Conclusion: This study identified changes in the microarchitecture, histological features and transcriptomic signature of trabecular bone from the FH of patients with idiopathic ONFH, which might underlie the pathophysiology of this condition. This work was supported by PI22/00939 grant from ISCIII-FEDER-MICINN-AES and Luis Alvarez grant from IdiPAZ.

TIE2-ENHANCED NUCLEUS PULPOSUS CELL-DERIVED EXTRACELLULAR VESICLES ENHANCE DEGENERATIVE DISC CELL VIABILITY IN VITRO

Luca Ambrosio[1,2], Jordy Schol[2], Clara Ruiz-Fernández[2], Rocco Papalia[1], Gianluca Vadalà[1], Vincenzo Denaro[1], Daisuke Sakai[2]

[1]Campus Bio-Medico University of Rome, Italy, *[2]Tokai University School of Medicine, Japan*

Introduction: Intervertebral disc degeneration (IDD) is a progressive process affecting all disc tissues, namely the nucleus pulposus (NP), annulus fibrosus (AF), and cartilaginous endplates (CEPs). Several cell-based therapies have been proposed to replenish the disc cell population and promote tissue regeneration. However, cell-free therapeutics have been increasingly explored due to potentially higher advantages and cost-effectiveness compared to cell transplantation. Recently, extracellular vesicles (EVs) isolated from healthy $Tie2^{+}$-NP cells (NPCs) have shown promising regenerative outcomes on degenerative NPCs (dNPCs). The aim of this study was to assess the effect of such EVs on all disc cell types, including AF cells (AFCs) and CEP cells (CEPCs), compared to EVs isolated from bone-marrow derived mesenchymal stromal cells (BM-MSCs).

Method: NPCs harvested from young donors underwent an optimized culture protocol to maximize Tie2 expression ($NPCs^{Tie2+}$). BM-MSCs were retrieved from a commercial cell line or harvested during spine surgery procedures. EV characterization was performed via particle size analysis (qNano), expression of EV markers (Western blot), and transmission electron microscopy. dNPCs, AFCs, and CEPCs were isolated from surgical specimens of patients affected by IDD, culture-expanded, and treated with $NPCs^{Tie2+}$-EVs or BM-MSC-EVs ± 10 ng/mL IL-1b. EV uptake was assessed with PKH26 staining of EVs under confocal microscopy. Cell proliferation and viability were assessed with the CCK-8 assay.

Result: Upon characterization, isolated EVs exhibited the typical exosomal characteristics. $NPCs^{Tie2+}$-EVs and BM-MSC-EVs uptake was successfully observed in all dNPCs, AFCs, and CEPCs. Both EV products significantly increased dNPC, AFC, and CEPC viability, especially in samples treated with $NPCs^{Tie2+}$-EVs.

Conclusion: $NPCs^{Tie2+}$-EVs demonstrated to significantly stimulate the proliferation and viability of degenerative cells isolated from all disc tissues. Rather than the sole NP, EVs isolated by committed progenitors physiologically residing within the disc may exert their regenerative effects on the whole organ, thus possibly constituting the basis for a new therapy for IDD.

IMPACT OF TRANSFORAMINAL LUMBAR INTERBODY FUSION ON ROD LOAD: A COMPARATIVE BIOMECHANICAL ANALYSIS BETWEEN A CADAVERIC INSTRUMENTATION AND SIMULATED BONE FUSION

Maximilian Heumann[1], Chencheng Feng[1], Lorin Benneker[2], Maarten Spruit[3], Christian Mazel[4], Jan Buschbaum[1], Boyko Gueorguiev[1], Manuela Ernst[1]

[1]AO Research Institute Davos, Davos, Switzerland, *[2]Sonnenhof Spital, Spine Unit, University of Bern, Bern, Switzerland*, *[3]Sint Maartenskliniek, Orthopedics Center, Spine Unit, Nijmegen, Netherlands*, *[4]Institute Mutualiste Montsouris, Paris, France*

Introduction: In daily clinical practice, progression of spinal fusion is typically monitored during clinical follow-up using conventional radiography and Computed Tomography scans. However, recent research has demonstrated the potential of implant load monitoring to assess posterolateral spinal fusion in an in-vivo sheep model. The question arises to whether such a strain sensing system could be used to monitor bone fusion following lumbar interbody fusion surgery, where the intervertebral space is supported by a cage. Therefore, the aim of this study was to test human cadaveric lumbar spines in two states: after a transforaminal lumbar interbody fusion (TLIF) procedure combined with a pedicle-screw-rod-construct (PSR) and subsequently after simulating bone fusion. The study hypothesized that the load on the posterior instrumentation decreases as the segment stiffens due to simulated fusion.

Method: A TLIF procedure with PSR was performed on eight human cadaveric spines at level L4-L5. Strain sensors were attached bilaterally to the rods to derive implant load changes during unconstrained flexion-extension (FE), lateral bending (LB) and axial rotation (AR) loads up to ±7.5Nm. The specimens were retested after simulating bone fusion between vertebrae L4-L5. In addition, the range of motion (ROM) was measured during each loading mode.

Result: The ROM decreased in the simulated bone fusion state in all loading directions ($p \leq 0.002$). In both states, the measured strain on the posterior instrumentation was highest during LB motion. Furthermore, the sensors detected a significant decrease in the load induced rod strain ($p \leq 0.002$) between TLIF+PSR and simulated bone fusion state in LB.

Conclusion: Implant load measured via rod strain sensors can be used to monitor the progression of fusion after a TLIF procedure when measured during LB of the lumbar spine. However, further research is needed to investigate the influence of daily loading scenarios expected in-vivo on the overall change in implant load.

A NOVEL PLATE DESIGN FOR ROTATIONAL GUIDED GROWTH. AN EXPERIMENTAL STUDY IN IMMATURE PORCINE FEMURS.

Ahmed Halloum[1], Ole Rahbek[1], Shima Gholinezhad[1,2], Søren Kold[1], John Rasmussen[2], Jan D. Rölfing[3], Maria Tirta[1], Ahmed A. Abood[1,3]

[1]Interdisciplinary Orthopaedics, Aalborg University Hospital, Aalborg, Denmark, *[2]Department of Materials and Production, Aalborg University, Aalborg, Denmark*, *[3]3. Department of Orthopaedics, Aarhus University Hospital, Aarhus, Denmark*

Introduction: Current treatments of rotational deformities of long bones in children are osteotomies and fixations.
In recent years, the use of guided growth for correction of rotational deformities has been reported in several pre-clinical and clinical studies. Various techniques have been used, and different adverse effects, like growth retardation and articular deformities, have been reported. We tested a novel plate concept intended for correction of rotational deformities of long bones by guided growth, with sliding screw holes to allow for longitudinal growth, in a porcine model.

Method: Twelve, 12-week-old female porcines were included in the study.
Surgery was performed on the left femur. The right femur was used as control. Plates were placed distally to induce external rotation, as longitudinal growth occurred.
CT-scans of the femurs were processed to 3-D models and used for measuring rotation.

Result: The plates rotated as intended in all 12 porcines. One porcine was excluded due to congenital deformity of the proximal part of the femurs. Two porcines had cut-out of the proximal screw on the lateral side, observed at the end of the intervention. These two porcines were included in the results.
We observed a Δrotation of 5.7° ± 2° in external direction (CI: 3.7°- 7.7°).
ΔFemur length was -0.4 cm [-0.7 cm – 0 cm] equal to 1.5% shortening of the operated femur.
No significant difference was observed in coronal or sagittal plane.

Conclusion: Significant external rotation was achieved with minimal effect on longitudinal growth.
While the use of guided growth for correction of rotational deformities is already being used clinically, it is still to be considered an experimental procedure with sparse evidence.
This study shows promising results for the feasibility of the method in a large animal model and is an important first step in validating the technique and detecting possible adverse effects, before future clinical studies.

MINIMAL IMPORTANT CHANGE OF THE WESTERN ONTARIO OSTEOARTHRITIS OF THE SHOULDER (WOOS) INDEX IN PATIENTS WITH GLENOHUMERAL OSTEOARTHRITIS AND ROTATOR CUFF TEAR ARTHROPATHY

Josefine Beck Larsen[1,2], Theis Muncholm Thillemann[1,2], Antti P. Launonen[3], Helle Kvistgaard Østergaard[4], Thomas Falstie-Jensen[2], Bakir Sumrein[3], Srdjan Zivanovic[1,4], Steen Lund Jensen[5,6], Inger Mechlenburg[1,2], Ville Ponkilainen[3]

[1]Department of Clinical Medicine Aarhus University, Aarhus, *[2]Department of Orthopaedic Surgery, Aarhus University Hospital, Aarhus N*, *[3]Department of Orthopaedic Surgery, Tampere University Hospital, Tampere, Finland*, *[4]Department of Orthopaedic Surgery, Viborg Regional Hospital, Viborg, Denmark*, *[5]Department of Orthopaedics, Aalborg University Hospital, Aalborg, Denmark*, *[6]Department of Clinical Medicine, Aalborg University, Aalborg, Denmark*

Introduction: The Minimal Important Change (MIC) for patient-reported outcome measures is the value that describes the smallest improvement considered worthwhile by patients. To the best of our knowledge, no MIC of the Western Ontario Osteoarthritis of the Shoulder Index (WOOS) score or the Disabilities of the Arm Shoulder and Hand (DASH) has been reported using the anchor-based predictive modeling approach based on patients with glenohumeral osteoarthritis or rotator cuff tear arthropathy.

The aim of this study was to determine the MIC for WOOS and DASH in a cohort of patients with glenohumeral osteoarthritis or rotator cuff tear arthropathy treated with a total shoulder arthroplasty.

Method: Data on 231 patients were collected at four hospitals. Data were collected at baseline and 12 weeks after surgery. At 12 weeks, the patients were asked about their perceived overall improvement after surgery measured by the Patient Global Impression of Change (PGI-C). The MIC was estimated for the WOOS and DASH using the adjusted predictive modeling approach with the PGI-C as an anchor.

Result: Of the 231 included patients, 104 were included in the MIC analysis. Patients had a mean age of 71 years and 56% were women. The estimated adjusted MIC for the WOOS score was 13.3 (-6.2; 23.3) and 7.2 (12.8; 1.7) for DASH.

Conclusion: For patients with glenohumeral osteoarthritis or rotator cuff tear arthropathy treated with a total shoulder arthroplasty, the estimated MIC for was 13.3 for WOOS and 7.2 for DASH. The estimates show wide confidence intervals, which could be due to the low sample size but could also indicate a large heterogeneity within the patient group.

COAXIAL ELECTROHYDRODYNAMIC PRINTINGOFCORE-SHELL MICROFIBROUS SCAFFOLDS WITH LAYER-SPECIFIC GROWTH FACTORS RELEASEFOR ENTHESIS REGENERATION

Lang Bai[1,2], Zhanhai Yin[1]

[1]The first affiliated hospital of Xi'an jiaotong university, Xi'an, [2]State Key Laboratory for Manufacturing Systems Engineering, Xi'an

Introduction: Herein, a tri-layered core-shell microfibrous scaffold with layer-specific growth factors (GFs) release is developed using coaxial electrohydrodynamic (EHD) printing for in situ cell recruitment and differentiation to facilitate gradient enthesis tissue repair. Our findings suggest that the microfibrous scaffolds with layer-specific GFs release may offer a promising clinical solution for enthesis regeneration.

Method: Utilizing coaxial electrohydrodynamic (EHD) printing, we engineered tri-layered core-shell microfibrous scaffolds, each layer tailored with specific growth factors (GFs) for targeted enthesis tissue repair. This configuration aims to sequentially guide cell migration and differentiation, mirroring the natural enthesis' gradient structure. SDF-1 was strategically loaded into the shell, while bFGF, TGF-β, and BMP-2 were encapsulated in the core, each selected for their roles in stimulating the regeneration of corresponding enthesis tissue layers.

Result: The coaxial EHD-printed microfibrous scaffolds demonstrated a core-shell fiber width of 24.3 ± 6.3 μm, supporting distinct tenogenic, chondrogenic, and osteogenic layers with pore sizes of 81.5 ± 4.6 μm, 173.3 ± 6.9 μm, and 388.9 ± 6.9 μm, respectively. This structure facilitated a targeted and effective release of growth factors, optimizing stem cell recruitment and differentiation. In vivo assessments demonstrated that the scaffolds significantly enhanced biomechanical properties and facilitated the formation of gradient enthesis structures, with improved biomechanical strength approximately 2-3 times that of control groups. These results highlight the scaffold's capability to mimic the native enthesis structure, encouraging a conducive environment for cell-mediated repair and regeneration.

Conclusion: The integration of layer-specific growth factors not only fostered a conducive environment for tissue regeneration but also exemplified a leap in the design of scaffolds that closely mimic the native tendon-to-bone interface. The findings illuminate the scaffold's capacity to direct cellular behavior and tissue formation, heralding a new era in regenerative strategies and offering a promising avenue for clinical translation in the treatment of rotator cuff injuries.

BIOPRINTED LIVING TISSUE CONSTRUCTS WITH LAYER-SPECIFIC, GROWTH FACTOR-LOADED MICROSPHERES FOR IMPROVED ENTHESIS HEALING OF A ROTATOR CUFF ABSTRACT

Lang Bai[1], Zhanhai Yin[1]

[1]*The first affiliated hospital of Xi'an jiaotong university, Xi'an, China*

Introduction: The healing of rotator cuff injuries poses significant challenges, primarily due to the complexity of recreating the native tendon-to-bone interface, characterized by highly organized structural and compositional gradients. Addressing this, our innovative approach leverages bioprinted living tissue constructs, incorporating layer-specific growth factors (GFs) to facilitate enthesis regeneration. This method aims to guide in situ zonal differentiation of stem cells, closely mirroring the natural enthesis tissue architecture.

Method: Our strategy involves the utilization of advanced bioprinting technology to fabricate living tissue constructs. These constructs are meticulously designed with embedded microsphere-based delivery carriers, ensuring the sustained release of tenogenic, chondrogenic, and osteogenic growth factors. This layer-specific release mechanism is tailored to promote the precise differentiation of stem cells across different regions of the construct, aligning with the gradient nature of enthesis tissues.

Result: In vitro studies demonstrated that our layer-specific tissue constructs significantly outperformed basal constructs without GFs, achieving region-specific differentiation of stem cells. More critically, in a rabbit model of rotator cuff tear, these bioprinted living tissue constructs expedited enthesis regeneration. Key outcomes included improved biomechanical properties, enhanced collagen deposition and alignment, and the formation of a gradient fibrocartilage interface with aligned collagen fibrils. After 12 weeks, the constructs achieved an ultimate load failure of 154.3 ± 9.5 N resembling that of native enthesis tissues, marking a notable achievement in tissue engineering.

Conclusion: Our exploration introduces a viable and innovative strategy for engineering living tissue constructs that exhibit region-specific differentiation capabilities. This approach holds significant promise for the functional repair of gradient enthesis tissues, potentially revolutionizing the treatment of rotator cuff injuries by closely replicating the natural tendon-to-bone interface, thus offering a promising avenue for future clinical applications.

RETURN TO SPORT AMONG 1926 PATIENTS WITH HIP DYSPLASIA AFTER UNDERGOING PERIACETABULAR OSTEOTOMY

Lisa Tønning[1,2], Stig Storgaard Jakobsen[1], Joanne Kemp[3], Michael O'Brien[3], Ulrik Dalgas[4], Inger Mechlenburg[1,2,4]

[1]Department of Orthopedic Surgery, Aarhus University Hospital, Aarhus, Denmark, *[2]Department of Clinical Medicine, Aarhus University, Aarhus, Denmark*, *[3]La Trobe Sport and Exercise Medicine Research Centre, La Trobe University, Melbourne, Australia*, *[4]Department of Public Health, Sports, Aarhus University, Aarhus, Denmark*

Introduction: Symptomatic hip dysplasia is often treated with periacetabular osteotomy (PAO). Studies investigating the effect of PAO have primarily focused on radiographic measurements, pain-related outcomes, and hip survival whereas evidence related to sport participation is limited.

Methods: All patients in our institutional database were deemed eligible for this cohort study if they underwent PAO and had answered at least one question related to sport participation. Patients were asked if they were playing sport preoperatively, 6 months after PAO as well as 2, 5, 10, 15 and 20 years after. In addition, patients were asked if they were able to play their preferred sport, what type and at what level they were playing sport, and if surgery had improved their sport performance.

Results: Among 2398 patients surveyed, 1926 (80%) were included and 56% were playing sport 6 months after PAO. This number was 61% two years after PAO, and remained around that for the following years, before dropping 15 years after PAO. Between 56% and 71% of patients felt that their sporting performance improved following PAO at the different time points. Between 39% (6 months after PAO) and 63% (15 years after PAO) were able to participate in their preferred sport.

Conclusion: The majority of patients undergoing PAO due to hip dysplasia will return to, and maintain, sport after PAO. More than half of patients undergoing PAO believe that the surgery improved their sports performance, and long after the surgery more than half of patients undergoing PAO are able to play their preferred sport.

ADOLESCENT PORCINE STIFLE JOINT AS A MODEL FOR ACL BIOMECHANICS: EFFECTS OF AXIAL AND TORSIONAL LOADS

Jason Koh[1], Nirav Mungalpara[2], Nicole Chang[2], Ilakiya Murugesan Praba Devi[2], Mark Hutchinson[2], Farid Amirouche[1,2]

[1]Northshore Health System, Chicago, United States, *[2]University of Illinois at Chicago, Chicago, United States*

Introduction: Understanding knee joint biomechanics is crucial, but studying Anterior cruciate ligament (ACL) biomechanics in human adolescents is challenging due to limited availability cadaveric specimens. This study aims to validate the adolescent porcine stifle joint as a model for ACL studies by examining the ACL's behavior under axial and torsion loads and assessing its deformation rate, stiffness, and load-to-failure.

Methods: Human knee load during high-intensity sports can reach 5-6 times body weight. Based on these benchmarks, the study applied a force equivalent to 5-times body weight of juvenile porcine samples (90 pounds), estimating a force of 520N. Experiments involved 30 fresh porcine stifle joints (Yorkshire breed, Avg 90 lbs, 2-4 months old) stored at -22°C, then thawed and prepared. Joints were divided into three groups: control (load-to-failure test), axially loaded, and 30-degree torsion loaded. Using a servo-hydraulic material testing machine, the tibia's longitudinal axis was aligned with the load sensor, and specimens underwent unidirectional tensile loading at 1 mm/sec until rupture. Data on load and displacement were captured at 100 Hz.

Results: One-way ANOVA showed statistically significant differences in maximum failure force among loading conditions ($p = 0.0039$). Post hoc analysis indicated significant differences between the control and 500N (non-twisted) groups ($p = 0.014$) and between the control and 500N (twisted) groups ($p = 0.003$). However, no significant difference was found between 500N (non-twisted) and 500N (twisted) groups ($p = 0.2645$). Two samples broke from the distal femur growth plates, indicating potential growth plate vulnerability in adolescent porcines.

Conclusions: The study validates the adolescent porcine stifle joint as a suitable model for ACL biomechanical research, demonstrating that torsional loads are as damaging to the ACL's integrity as equivalent axial loads. It also highlights the potential vulnerability of growth plates in younger populations, reflected in the porcine model.

IMPROVED HUMAN TENOCYTE VIABILITY BY APPLYING PHYSIOLOGICALLY RELEVANT MECHANICAL LOADS IN A PERFUSION BIOREACTOR SYSTEM.

Tania Choreño Machain[1], Alona Kharchenko[2], Rafael Hostettler[2], Jürgen Lippl[2], Pierre-Alexis Mouthuy[1]

[1]University of Oxford, Oxford, United Kingdom, *[2]Devanthro GmbH, Munich, Germany*

Introduction: Supraspinatus tears comprise most rotator cuff injuries, the leading cause of shoulder pain and an increasing problem with ageing populations. Surgical repair of considerable or persistent damages is customary, although not invariably successful. Tissue engineering presents a promising alternative to generate functional tissue constructs with improved healing capacities. This study explores tendon tissue constructs' culture in a platform providing physiological mechanical stimulation and reports on the effect of different loading regimes on the viability of human tendon cells.

Method: Porcine decellularized tendon scaffolds were fixed into flexible, self-contained bioreactor chambers, seeded with human tenocytes, allocated in triplicates to either static control, low (15±0.8Newtons [N]), medium (26±0.5N), or high (49±2.1N)-force-regime groups, connected to a perfusion system and cultured under standard conditions. A humanoid robotic arm provided 30-minute adduction/abduction stimulation to chambers daily over a week. A metabolic activity assay served to assess cell viability at four time points. Statistical significance = $p<0.05$.

Result: One day after beginning mechanical stimulation, chambers in the medium and high-force regimes displayed a rise in metabolic activity by 3% and 5%, respectively. By the last experimental day, all mechanical stimulation regimes had induced an augment in cell viability (15%, 57% and 39% with low, medium, and high loads, respectively) matched against the static controls. Compared to all other conditions, the medium-force regime prompted an increased relative change in metabolic activity for every time point set against day one ($p<0.05$).

Conclusion: Human tenocytes' viability reflected by metabolic activity in a physiologically relevant bioreactor system is enhanced by loading forces around 25N when mechanically stimulating using adduction/abduction motions. Knowing the most favourable load regime to stimulate tenocyte growth has informed the ongoing exploration of the distinctive effect of different motions on tendon regeneration towards engineering tissue grafts.

This work was supported by the Engineering and Physical Sciences Research Council EP/S003509/1.

CHARACTERIZING THE SURFACE DEGRADATION OF OSTEOARTHRITIC CARTILAGE BASED ON RAMAN SPECTROSCOPY AND INVESTIGATING ITS MECHANO-TRIBOLOGICAL PROPERTIES.

Manoj Rajankunte Mahadeshwara[1], Hemant Pandit[2], Richard M Hall[3], Maisoon Al-Jawad[4], Michael Bryant[3], Reem El-Gendy[4,5]

[1]Institute of Functional Surfaces, Mechanical Engineering, Department of Oral Biology, Faculty of Dentistry, University of Leeds, Leeds, United Kingdom, *[2]Leeds Institute of Rheumatic and Musculoskeletal Medicine (LIRMM), University of Leeds, Chapel Allerton Hospital, Leeds, United Kingdom*, *[3]School of Engineering, College of Engineering and Physical Sciences, University of Birmingham, Birming-ham, B152TT, West Midlands, Birmingham, United Kingdom*, *[4]Department of Oral Biology, Faculty of Dentistry, University of Leeds, Leeds, United Kingdom*, *[5]Department of oral pathology, Faculty of Dentistry, Suez Canal university, Ismailia, Egypt*

Introduction: Osteoarthritis (OA) occurs due to a multi-scale degradation of articular cartilage (AC) surface which aggravates the disease condition. Investigating the micro-scale structural alterations and mechano-tribological properties facilitates comprehension of disease-mechanisms to improve future injectable-therapies. This study aims to analyze these properties using various experimental and analytical methods to establish correlations between their morpho-physiological features.

Method: In this study, Raman-spectroscopy was used to investigate microscale changes in AC constituents and categorize OA damage regions in knee-joint samples from joint replacement patients (Samples = 5 and Regions = 40). Following, microscale indentation and sliding tests were performed on these regions to evaluate variations in aggregate-modulus (AM) and elastic-modulus (EM), with coefficient of friction (COF). Finally, scanning electron microscopy (SEM) was employed to analyze these morphological variations.

Result: Raman spectroscopy revealed degree of collagen-damage (Amide-3 α-helix to random-coil ratio I-1250/I-1280), proteoglycan-damage (Sulphated bonds SO^{3-} to CH_2 twist ratio I-1065/I-1206), amount of bone exposure (Phosphated-hydroxyapatite PO_4^{3-} to Amide-1 ratio I-959/I-1669) and increased crystallinity (Carbonated hydroxyapatite CO_3^{2-} to Amide-1 ratio I-1075/I-959) in ECM. Subsequently, these regions were categorized into different groups (G) based on these damages; G1 (Proteoglycan); G2 (Collagen + Proteoglycan); G3 (Collagen + Proteoglycan + Carbonated crystallinity) G4 (Collagen or Proteoglycan + bone exposure); and G5 (Collagen + Proteoglycan + Bone exposure). Further experimentation revealed the differences in mechano-tribological properties (AM, EM, and COF) between the different groups. G5 displayed the highest values of AM (1.5 ± 0.2MPa), EM (0.3 ± 0.01MPa) and COF (0.39 ± 0.08), compared to other groups. These altered properties were confirmed via SEM that revealed micro-asperity junctions, superficial fronding, fibrillations and bone exposure at these damaged regions.

Conclusion: This study demonstrated micro-scale changes in AC among OA patients commensurate to the degree of tissue damage, which correlates with disease progression altering joint structure and function particularly in regions with high COF.

TIE2-ENHANCED NUCLEUS PULPOSUS CELL-DERIVED EXTRACELLULAR VESICLES ENHANCE DEGENERATIVE DISC CELL VIABILITY IN VITRO

Luca Ambrosio[1,2], Jordy Schol[2], Clara Ruiz-Fernández[2], Rocco Papalia[1], Gianluca Vadalà[1], Vincenzo Denaro[1], Daisuke Sakai[2]

[1]Campus Bio-Medico University of Rome, Italy, *[2]Tokai University School of Medicine, Japan*

Introduction: Intervertebral disc degeneration (IDD) is a progressive process affecting all disc tissues, namely the nucleus pulposus (NP), annulus fibrosus (AF), and cartilaginous endplates (CEPs). Several cell-based therapies have been proposed to replenish the disc cell population and promote tissue regeneration. However, cell-free therapeutics have been increasingly explored due to potentially higher advantages and cost-effectiveness compared to cell transplantation. Recently, extracellular vesicles (EVs) isolated from healthy $Tie2^{+}$-NP cells (NPCs) have shown promising regenerative outcomes on degenerative NPCs (dNPCs). The aim of this study was to assess the effect of such EVs on all disc cell types, including AF cells (AFCs) and CEP cells (CEPCs), compared to EVs isolated from bone-marrow derived mesenchymal stromal cells (BM-MSCs).

Method: NPCs harvested from young donors underwent an optimized culture protocol to maximize Tie2 expression ($NPCs^{Tie2+}$). BM-MSCs were retrieved from a commercial cell line or harvested during spine surgery procedures. EV characterization was performed via particle size analysis (qNano), expression of EV markers (Western blot), and transmission electron microscopy. dNPCs, AFCs, and CEPCs were isolated from surgical specimens of patients affected by IDD, culture-expanded, and treated with $NPCs^{Tie2+}$-EVs or BM-MSC-EVs ± 10 ng/mL IL-1b. EV uptake was assessed with PKH26 staining of EVs under confocal microscopy. Cell proliferation and viability were assessed with the CCK-8 assay.

Result: Upon characterization, isolated EVs exhibited the typical exosomal characteristics. $NPCs^{Tie2+}$-EVs and BM-MSC-EVs uptake was successfully observed in all dNPCs, AFCs, and CEPCs. Both EV products significantly increased dNPC, AFC, and CEPC viability, especially in samples treated with $NPCs^{Tie2+}$-EVs.

Conclusion: $NPCs^{Tie2+}$-EVs demonstrated to significantly stimulate the proliferation and viability of degenerative cells isolated from all disc tissues. Rather than the sole NP, EVs isolated by committed progenitors physiologically residing within the disc may exert their regenerative effects on the whole organ, thus possibly constituting the basis for a new therapy for IDD.

IN VITRO CO-CULTURE OF TISSUE-ENGINEERED MINERALISED CARTILAGE AND VESSEL NETWORKS TO MODEL ENDOCHONDRAL OSSIFICATION

Encheng Ji[1], Lieke Leijsten[1], Janneke Witte-Bouma[1], Adelin Rouchon[2], Nunzia Di Maggio[2], Andrea Banfi[2], Gerjo van Osch[3,4], Eric Farrell[1], Andrea Iolli[1]

[1]Department of Oral and Maxillofacial Surgery, Erasmus MC University Medical Center, Rotterdam, Netherlands, *[2]Department of Biomedicine, Basel University Hospital, Basel, Swaziland*, *[3]Department of Orthopaedics & Sports Medicine and Department of Otorhinolaryngology, Erasmus MC University Medical Center, Rotterdam, Netherlands*, *[4]Department of Biomechanical Engineering, University of Technology, Delft, Netherlands*

Introduction: Endochondral ossification (EO) is the process of bone development via a cartilage template. It involves multiple stages, including chondrogenesis, mineralisation and angiogenesis. Importantly, how cartilage mineralisation affects angiogenesis during EO is not fully understood. Here we aimed to develop a new in vitro co-culture model to recapitulate and study the interaction between mineralised cartilage generated from human mesenchymal stromal cells (hMSCs) and microvascular networks.

Method: Chondrogenic hMSC pellets were generated by culture with transforming growth factor (TGF)-β3. For mineralised pellets, β-glycerophosphate (BGP) was added from day 7 and TGF-β3 was withdrawn on day 14. Conditioned medium (CM) from the pellets was used to evaluate the effect on human umbilical vein endothelial cells (HUVECs) in migration, proliferation and tube formation assays. To perform direct co-cultures, pellets were embedded in fibrin hydrogels containing vessel-forming cells (HUVECs, adipose stromal cells) for 10 days with BGP to induce mineralisation. The pellets and hydrogels were characterised by immunohistochemistry and confocal imaging.

Result: The CM from d14 chondrogenic or mineralised pellets significantly stimulated HUVEC migration and proliferation, as well as in vitro vascular network formation. When CM from pellets subjected to prolonged mineralisation (d28) was used, these effects were strongly reduced. When chondrogenic and mineralised pellets were directly co-cultured with vessel-forming cells in fibrin hydrogels, the cartilage matrix (collagen type II /X stainings) and the mineral deposition (von Kossa staining) were well preserved. Confocal imaging analyses demonstrated the formation of microvascular networks with well-formed lumina. Importantly, more microvascular structures were formed in the proximity of chondrogenic pellets than mineralized pellets.

Conclusion: The angiogenic properties of tissue engineered cartilage are significantly reduced upon prolonged mineralisation. We developed a 3D co-culture model to study the role of angiogenesis in endochondral bone formation, which can have applications in disease modelling studies.

CHANGES IN STIFFNESS OF THE EXTRACELLULAR AND PERICELLULAR MATRIX IN THE ANULUS FIBROSUS OF LUMBAR INTERVERTEBRAL DISCS OVER THE COURSE OF DEGENERATION

Sebastian Gerke-Höflsauer[1], Florian Bonnaire[2], Marina Danalache[3,4], Martina Feierabend[5], Ulf Hofmann[6]

[1]Universitätsmedizin Göttingen, Göttingen, Germany, *[2]Kreiskliniken Reutlingen GmbH, Reutlingen, Germany*, *[3]Eberhard Karls Universität Tübingen, Tübingen, Germany*, *[4]Laboratory of Cell Biology, Department of Orthopaedic Surgery, University Hospital of Tübingen,, Tübingen , Germany*, *[5]Institute for Plant Sciences at the Cologne Biocenter, Cologne, Germany*, *[6]Clinic for Orthopaedics, Trauma and Reconstructive Surgery, University Hospital, RWTH Aachen, Aachen, Germany*

Introduction: Analogous to articular cartilage, changes in spatial chondrocyte organisation have been proposed to be a strong indicator for local tissue degeneration and destruction in the intervertebral disc (IVD). While a progressive structural and functional degradation of the extracellular (ECM) and pericellular (PCM) matrix occurs in osteoarthritic cartilage, these processes have not yet been biomechanically elucidated in the IVD. We aimed to evaluate the local stiffness of the ECM and PCM in the anulus fibrosus of the IVD on the basis of local cellular spatial organisation.

Method: Using atomic force microscopy, we measured the elastic modulus of the local ECM and PCM in human disc samples using the spatial chondrocyte patterns as an image-based biomarker.

Result: By measuring tissue from 30 patients, we found a significant difference in the elastic moduli of the PCM in clusters when compared to the healthy patterns single cells ($p=0.029$), pairs ($p=0.016$), and string formations ($p=0.010$) whereas the values of the elastic moduli of the ECM only reached statistical significance when clusters were compared with string formations. The ECM/PCM ratio ranged from 0.62 to 0.89. Overall, the reduced elastic moduli in clusters demonstrates that cluster formation is not only a morphological phenomenon describing disc degeneration, but it marks a compromised biomechanical functioning.

Conclusion: This study is the first to describe and quantify the differences in the elastic moduli of the ECM in relation to the PCM in the anulus fibrosus of the IVD by means of atomic force microscopy on the basis of spatial chondrocyte organisation. Advanced disc degeneration is accompanied by a biomechanically compromised tissue functioning.

TRIAMCINOLONE: A MODULATOR OF CHONDROCYTE ELASTICITY AND MECHANOSENSITIVITY

Felix Umrath[1,2], Chen Liang[1], Sina Jud[1], Dorothea Alexander[2], Marina Danalache[1]

[1]Clinic for Orthopaedic Surgery, University Hospital Tübingen, Tübingen, Germany, *[2]Clinic for Oral and Maxillofacial Surgery, University Hospital Tübingen, Tübingen, Germany*

Introduction: Osteoarthritis (OA) often results from joint misloading, which affects chondrocyte calcium signaling through mechano-sensitive receptors such as Piezo1, -2, and TRPV4. Activation of Piezo1, especially under inflammatory conditions, can trigger premature chondrocyte apoptosis. Intra-articular glucocorticoid therapy, while beneficial against inflammation and pain in osteoarthritis, may induce oxidative stress and chondrotoxicity at higher doses. This study aims to assess the effects of glucocorticoids, particularly triamcinolone, on chondrocyte elasticity and mechanosignaling.

Method: Chondrocytes isolated from articular condyles obtained from patients undergoing knee replacement surgery (n= 5) were cultured for 7 days in triamcinolone acetonide (TA) at different concentrations (0.2µM – 2mM). Cytoskeletal changes were assessed by F-actin labeling. Cell elasticity was measured using atomic force microscopy (AFM). Labeling cells (n=6 patients) with the calcium-sensitive dye (Fluo-4) enabled monitoring changes in intracellular calcium fluorescence intensity during guided single-cell mechanical indentation (500 nN) by AFM.

Result: Cell exposure to 2 mM TA led to cell death and crystallization of TA in the cell culture media. However, the concentration of TA for intra-articular application is 46 times higher at 92.1 mM (40 mg/ml). The maximal pharmacological effect on viable cells was observed at 0.2 mM. AFM results showed a significant decrease of elasticity ($p<0.001$), alongside significantly higher calcium intensities both prior to and during mechanical stimulation in the TA-treated samples ($p<0.05$).

Conclusion: Administration of TA significantly impacts the mechanical properties of chondrocytes, reducing cellular elasticity while simultaneously enhancing calcium-dependent mechanosensitivity. This data suggests a correlation between glucocorticoid-induced changes in cell elasticity and cell mechanosensitivity. Finding ways to minimize the effect of glucocorticoids on cell mechanosensitivity could help to make future therapies safer and reduce side effects.

PIEZO1 AS A MEDIATOR OF CHONDROCYTE NUCLEAR MECHANICS AND CHROMATIN METHYLATION STATE

Jaquelin Garcia-Castorena[1,2,3,4], Rosa Riester[5], Miranda Gamino-Ornelas[1], Farshid Guilak[1,2,4], Marina Danalache[5]

[1]Department of Orthopaedic Surgery, Washington University in Saint Louis, Saint Louis, United States, *[2]Shriners Hospitals for Children – St. Louis, Saint Louis, United States*, *[3]Division of Biology and Biomedical Sciences, Washington University in Saint Louis, Saint Louis, United States*, *[4]Center of Regenerative Medicine, Washington University in Saint Louis, Saint Louis, United States*, *[5]Department of Orthopedic Surgery, University Hospital of Tübingen, Tübingen, Germany*

Introduction: Piezo1 is a mechanosensitive Ca^{2+} ion channel that has been shown to transduce hyper-physiologic mechanical loads in chondrocytes. In osteoarthritic cartilage, Piezo1 expression was shown to be upregulated by interleukin-1 alpha (IL-1α) and resulted in altered calcium dynamics and actin cytoskeleton rarefication. Together these studies highlight the importance of Piezo1 channels during joint injury. However, the mechanism by which Piezo1 regulates chondrocyte physiology and mechanotransduction during homeostasis is still largely unknown. In this study, we investigate the impact of Piezo1 activation on nuclear mechanics and chromatin methylation state.

Methods: Porcine chondrocytes (n=3-5 pigs) were treated with Yoda1, a Piezo1-specific agonist, for either 2, 5, 15 or 180 minutes. To characterize chromatin state, we monitored the abundance of a chromatin methylation marker (H3K9Me3) using immunofluorescence (IF). Atomic force microscopy (AFM, 25 nm cantilever) was employed to quantify the nuclear elastic modulus (NEM) of individual cell nuclei. To explore the interplay between cytoskeletal dynamics and nuclear mechanics, chondrocytes were treated with Latrunculin A (LatA), an actin polymerization inhibitor.

Result: IF experiments showed chromatin methylation was the lowest 2 minutes post Yoda1 activation of Piezo1 ($p=0.027$). Additionally, we found that 2 or 5 minutes post-Piezo1 activation resulted in a significantly lower NEM when compared to the control ($p<0.00001$). The observed decrease in NEM at 2 and 5 minutes post-Piezo1 activation was not observed after knocking down Piezo1 ($p>0.99$). In LatA treated cells, the elevated NEM persisted even after Piezo1 activation with Yoda1 ($p>0.75$).

Conclusion: These findings illuminate the mechanism by which Piezo1 activation and actin remodeling regulate transient mechanotransduction during homeostasis. Further research into the transient decrease in nuclear stiffness and chromatin methylation observed during the initial 5 minutes of Piezo1-induced Ca2+ signaling, may contribute to a better understanding of the role of Piezo1 channels in joint injury and development of therapeutic interventions for osteoarthritis.

ANISOTROPIC COLLAGEN/HYALURONAN 3D PRINTED HYDROGELS AS NOVEL IN VITRO MODEL OF ANNULUS FIBROSUS

Stephanie De Oliveira[1], Gregor Miklosic[2], Jérôme Guicheux[3], Catherine Le Visage[3], Matteo D'este[2], Christophe Helary[1]

[1]Chemistry of Condensed Matter Laboratory (LCMCP), Sorbonne University, Paris, France, *[2]AO Research Institute Davos (ARI), AO Foundation, Davos, Switzerland*, *[3]RMES - University of Nantes, Nantes, France*

INTRODUCTION: Intervertebral disc (IVD) degeneration is not completely understood because of the lack of relevant models. In vivo models are inappropriate because animals are quadrupeds. IVD is composed of the Nucleus Pulposus (NP) and the Annulus Fibrosus (AF), an elastic tissue that surrounds NP. AF consists of concentric lamellae made of collagen I and glycosaminoglycans with fibroblast-like cells located between layers. In this study, we aimed to develop a novel 3D in vitro model of Annulus Fibrosus to study its degeneration. For this purpose, we reproduced the microenvironment of AF cells using 3D printing.

METHOD: An ink consisting of dense collagen (30 $mg.mL^{-1}$) and tyramine-functionalized hyaluronic acid (THA) at 7.5 $mg.mL^{-1}$ was first designed by modulating pH and [NaCl] in order to inhibit the formation of polyionic complexes between collagen and THA. Then, composite inks were printed in different gelling baths to form collagen hydrogels. Last, THA photocrosslinking using eosin and green light was performed to strengthen hydrogels. Selected 3D printed constructs were then cellularized with fibroblasts.

RESULTS: The physicochemical study revealed that collagen/THA solutions (4:1 ratio) used at pH 5 with 200 mM NaCl were homogenous. In addition, collagen fibrils were observed in these solutions. The dense composite collagen/THA inks printed in a 2X PBS bath rapidly gelled and the photo-crosslinking increased the mechanical properties by 2 to reach 25 kPa (Young's modulus). Then, 3D printing parameters were optimized (85 kPa, extrusion, 4.5 mm/s speed and 80% fill-in percentage) to generate flat and anisotropic lamellae observed by polarized light microscopy. For the in vitro study, several anisotropic layers were printed and fibroblasts seeded between them. Cells adhered to layers, spread, proliferate and aligned along the axis of printed layers.

CONCLUSION: Taken together, these results show it is possible to reproduce in vitro the main AF's biochemical and physical properties.

IMPACT OF ANNULUS FIBROSUS STIFFNESS ON THE FRACTURE LOAD OF FUNCTIONAL SPINE UNITS

Daniel Strack[1], Moustafa Mesbah[2,3], Nithin Manohar Rayudu[4], Thomas Baum[5,6], Jan Kirschke[6], Karupppasamy Subburaj[1]

[1]Department of Mechanical and Production Engineering, Aarhus University, Aarhus, Denmark, *[2]Materials and Production Department. Aalborg University. Denmark, Aalborg, Denmark*, *[3]Department of Mechanical Engineering. Faculty of Sciences and Technology. University of Mostaganem. Algeria, Mostaganem, Algeria*, *[4]Department of Ophthalmic Research, Lerner research institute, Cleveland Clinic, Cleveland, United States*, *[5]TUM-Neuroimaging Center, Klinikum rechts der Isar, Technical University of Munich, Munich, Germany*, *[6]Department of Diagnostic and Interventional Neuroradiology, School of Medicine and Health, Klinikum rechts der Isar, Technical University of Munich, Munich, Germany*

Introduction: Functional Spine Units (FSUs) play a vital role in understanding biomechanical characteristics of the spine, particularly bone fracture risk assessment. While established models focus on simulating axial compression of individual bones to assess fracture load, recent models underscore the importance of understanding fracture load within FSUs, offering a better representation of physiological conditions. Despite the limited number of FSU fracture studies, they predominantly rely on a linear material model with an annulus fibrosus Young's modulus set at 500 MPa, significantly higher than stiffness values (ca. 4 MPa) utilized in other FSU and spine section biomechanical models. Thus, this study aims to study the effect of varying annulus fibrosus stiffness on FSU fracture load, aiming to identify physiologically relevant biomechanical parameters.

Method: Subject-specific geometry and material properties of bones were derived from computed tomography (CT) image data of five human cadaveric FSU specimens. The annulus fibrosus and nucleus pulposus were manually recreated and assigned linear elastic material properties. By subjecting the model to axial compression, the fracture load of the FSU was deduced from the peak of the force-displacement graph. To explore the effect of stiffness of the annulus fibrosus on simulated fracture load, we conducted a parameter study, varying stiffness values from the high 500 MPa to a more physiologically relevant 25 MPa, aiming to approximate values applied in FSU kinematic models while achieving bone fracture.

Result: Significant reductions in fracture load were observed, ranging from 23% to 46%, as annulus stiffness decreased from 500MPa to 25MPa. Additionally, a discernible, gradual decline in fracture load was observed with a decrease in stiffness values.

Conclusion: The stiffness of the annulus fibrosus significantly influences the simulated fracture load of an FSU. Future investigations should prioritize biomechanically accurate modeling of the intervertebral disc, ensuring alignment with experimental findings regarding FSU fracture load while maintaining biomechanical fidelity.

HOW SHOULD FEMORAL ANATOMY FOR SURGICAL CORRECTION BE MEASURED?

Jasmin Dhaliwal[1], Simon Harris[1], Kartik Logishetty[1], Miloš Brkljač[1], Justin Cobb[2]

[1]Imperial College London, London, United Kingdom, *[2]Imperial College , London, United Kingdom*

Introduction: The current methods for measuring femoral torsion have limitations, including variability and inaccuracies. Existing 3D methods are not reliable for abnormal femoral anteversion measurement. A new 3D method is needed for accurate measurement and planning of proximal femoral osteotomies. Currently available software for viewing and modelling CT data lacks measurement capabilities. The MSK Hip planner aims to address these limitations by combining measurement, planning, and analysis functionalities into one tool. We aim to answer 5 key questions: Is there a difference between 2D measurement methods? Is there a difference between 3D measurement methods? Is there a difference between 2D and 3D measurement methods? Are any of the measurement methods affected by the presence of osteoarthritis or a CAM deformity?

Method: After segmentation was carried out on 42 femoral CT scans using Osirix, 3D bone models were landmarked in the MSK lab hip planning software. Murphy's, Reikeras', McBryde, and the novel MSK lab method were used to measure femoral anteversion.

Result: Murphy's method had the lowest mean femoral neck anteversion (FNA) at 24.98°, while the MSK method had the highest at 28.55°. Bland-Altman plots showed systematic errors between 2D (1.201°) and 3D (1.074°) methods. All methods demonstrated good intra- and inter-user reliability. Significant differences were found between measurement methods and between patient groups.

Conclusion: The MSK Hip Planner software proved useful and convenient to measure FNA. Statistically significant differences in FNA were observed between the measurement methods, as well as between patient groups when split by presence of osteoarthritis and cam deformity. Complex joint pathology and altered femoral morphology should be considered by clinicians when deciding which method to use when measuring FNA.

FUNCTIONAL, RADIOLOGICAL, AND MORTALITY ANALYSIS OF LOCKING PLATE AND INTRAMEDULLARY NAIL TREATMENTS FOR PERIPROSTHETIC FRACTURES OF THE DISTAL FEMUR FOLLOWING TOTAL KNEE ARTHROPLASTY

MUHAMMED YUSUF AFACAN[1], CUMHUR DENİZ DAVULCU[1]

[1]Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine, Department of Orthopaedics and Traumatology, ISTANBUL

Introduction: The evaluation of treatment modalities for distal femur periprosthetic fractures (DFPF) post-total knee arthroplasty (TKA) has predominantly focused on functional and radiological outcomes in existing literature. This study aimed to comprehensively compare the functional and radiological efficacy of locking plate (LP) and retrograde intramedullary nail (IMN) treatments, while incorporating mortality rates.

Method: Twenty patients (15 female, 5 male) with a minimum 24-month follow-up period, experiencing Lewis-Rorabeck type-2 DFPF after TKA were included. These patients underwent either LP (n=10) or IMN (n=10). The average follow-up duration was 48 months (range: 24-192). Treatment outcomes, including functional scores, alignment, union time, complications, and mortality rates, were assessed and compared between LP and IMN groups. Clinical examination findings pre-treatment and at final follow-up, along with two-way plain radiographs, were utilized. Statistical analyses comprised Student's t-test and Kaplan-Meier survival analysis with a 95% confidence interval.

Result: At final follow-up, the LP group demonstrated a mean Knee Society score of 67.2 ± 16.1, while the IMN group exhibited a score of 72.8 ± 9.4($P = 0.58$). No statistically significant differences were observed in alignment between the groups[aLDFA (anatomical lateral distal femoral angle), $P = 0.31$; aPDFA (anatomical posterior distal femoral angle), $P = 0.73$]. The mean time to union was 3.7 ± 0.8 months for LP and 3.9 ± 0.6 months for IMN ($P = 0.62$). Complications such as infection occurred in 1 LP patient, and non-union was observed in 2 LP patients, while no complications were noted in IMN group($P < 0.01$). Mortality rates were notably lower in the IMN group compared to the LP group across various time intervals.

Conclusion: Both LP and IMN treatments yielded similar functional scores, alignment, and union time for DFPF post-TKA. However, the lower incidence of complications and mortality rates associated with IMN treatment suggest its superiority in managing DFPF following TKA.

DECIPHERING WRIST DYNAMICS: EXPLORING THE IMPACT OF SCAPHOLUNATE LIGAMENT INJURIES ON WRIST STABILITY, KINETICS, AND CARTILAGE STRESS IN ORTHOPAEDIC PRACTICE

Farid Amirouche[1,2], Sunjung Kim[3], Majd Mzeihem[1], Wedam Nyaaba[1], Nirav Mungalpara[1], Alfonso Mejia[1], Mark Gonzalez[1]

[1]University of Illinois at Chicago, Chicago, United States, *[2]Northshore Health System, Chicago, United States*, *[3]Hospital for Special Surgery, New York, United States*

Introduction: The human wrist is a highly complex joint, offering extensive motion across various planes. This study investigates scapholunate ligament (SLL) injuries' impact on wrist stability and arthritis risks using cadaveric experiments and the finite element (FE) method. It aims to validate experimental findings with FE analysis results.

Method: The study utilized eight wrist specimens on a custom rig to investigate Scapho-Lunate dissociation. Contact pressure and flexion were measured using sensors. A CT-based 3D geometry reconstruction approach was used to create the geometries needed for the FE analysis. The study used the Friedman test with pairwise comparisons to assess if differences between testing conditions were statistically significant.

Result: The study found significant variations in scaphoid and lunate bone movement based on ligament condition. Full tears increased scapholunate distance in the distal-proximal direction and decreased in the medial-lateral direction. Lunate angles shifted from flexion to extension with fully torn ligaments. Conversely, the scaphoid shifted significantly from extension to flexion with full tears. A proximal movement was observed in the distal-proximal direction in all groups, with significant differences in the partial tear group. Lateral deviation of the scaphoid and lunate occurred with ligament damage, being more pronounced in the partial tear group. All groups exhibited statistically significant movement in the volar direction, with the full tear group showing the least movement. Also, radiocarpal joint and finger contact pressure and contact area were studied. Whereas the differences in contact area were not significant, scapholunate ligament tears resulted in significantly decreased finger contact pressures. FEA confirmed these findings, showing notable peak radiocarpal contact pressure differences between intact and fully torn ligaments.

Conclusion: Our study found that SLL damage alters wrist stability, potentially leading to early arthritis. The FEA model confirmed these findings, indicating the potential for the clinical use of computer models from CT scans for treatment planning.

TOWARDS ROUTINE, LOW-COST CLINICAL MOVEMENT ANALYSIS TO ASSESS SHOULDER FUNCTION USING COMPUTER VISION AND CONSUMER CAMERAS: A SCOPING REVIEW.

Sebastian Spoo[1], Frederic Garcia[2,3], Benedikt Braun[4], Jan Cabri[5], Bernd Grimm[3]

[1]University of Trier, Dept. Nursing Science, Diagnostics in Health Care & E-Health, Trier, Germany, *[2]Luxembourg Institute of Health; Department of Precision Health, Luxembourg, Luxembourg*, *[3]Luxembourg Institute of Health (LIH), Department of Precision Health, Luxembourg, Luxembourg*, *[4]University Hospital Tuebingen, Eberhard-Karls-University Tuebingen, BG Unfallklinik, Tuebingen, Germany*, *[5]Luxembourg Institute of Research in Orthopedics, Sports Medicine and Science (LIROMS), Luxembourg, Luxembourg*

Introduction: The objective assessment of shoulder function is important for personalized diagnosis, therapies and evidence-based practice but has been limited by specialized equipment and dedicated movement laboratories. Advances in AI-driven computer vision (CV) using consumer RGB cameras (red-blue-green) and open-source CV models offer the potential for routine clinical use. However, key concepts, evidence, and research gaps have not yet been synthesized to drive clinical translation. This scoping review aims to map related literature.

Method: Following the JBI Manual for Evidence Synthesis, a scoping review was conducted on PubMed and Scholar using search terms including "shoulder," "pose estimation," "camera", and others. From 146 initial results, 27 papers focusing on clinical applicability and using consumer cameras were included. Analysis employed a Grounded Theory approach guided iterative refinement.

Result: Studies primarily used Microsoft Kinect (infrared-based depth sensing, RGB camera; discontinued) or monocular consumer cameras with open-source CV-models, sometimes supplemented by LiDAR (laser-based depth sensing), wearables or markers. Technical validation studies against gold standards were scarce and too inconsistent for comparison. Larger range of motion (RoM) movements were accurately recorded, but smaller movements, rotations and scapula tracking remained challenging. For instance, one larger validation study comparing shoulder angles during arm raises to a marker-based gold-standard reported Pearson's R = 0.98 and a standard error of 2.4deg. OpenPose and Mediapipe were the most used CV-models. Recent efforts try to improve model performance by training with shoulder specific movements.

Conclusion: Low-cost, routine clinical movement analysis to assess shoulder function using consumer cameras and CV seems feasible. It can provide acceptable accuracy for certain movement tasks and larger RoM. Capturing small, hidden or the entirety of shoulder movement requires improvements such as via training models with shoulder specific data or using dual cameras. Technical validation studies require methodological standardization, and clinical validation against established constructs is needed for translation into practice.

POLYACRYLAMIDE HYDROGEL FOR KNEE OSTEOARTHRITIS: 4-YEAR RESULTS FROM A PROSPECTIVE STUDY

Henning Bliddal[1], Jannie Beier[2], Andreas Hartkopp[3], Philip Conaghan[4], Marius Henriksen[5]

[1]The Parker Institute, Bispebjerg-Frederiksberg Hospital, University of Copenhagen, Copenhagen, Denmark, *[2]Rheumatology Odense, Odense, Denmark*, *[3]A2 Rheumatology and Sports Medicine, Holte, Denmark*, *[4]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds & NIHR Leeds Biomedical Research Centre, Leeds, United Kingdom*, *[5]The Parker Institute, Bispebjerg-Frederiksberg Hospital, University of Copenhagen, Copenhagen, Copenhagen, Denmark*

Introduction: Polyacrylamide hydrogel (iPAAG[1]), is CE marked for treating symptomatic knee osteoarthritis (OA), meeting the need for an effective, long-lasting, and safe non-surgical option. This study evaluates the efficacy and safety of a single 6 ml intra-articular injection of iPAAG in participants with moderate to severe knee OA over a 5-year post-treatment period, presenting data from the 4-year follow up.

Method: This prospective multicentre study (3 sites in Denmark) involved 49 participants (31 females) with an average age of 70 (range 44 – 86 years). They received a single 6 mL iPAAG injection. All participants provided informed consent and re-consented to continue after 1 year. The study followed GCP principles and was approved by Danish health authorities and local Health Research Ethics committees. Twenty-seven participants completed the 4-year follow-up.

The study evaluated WOMAC pain, stiffness, function, and Patient Global Assessment (PGA) of disease impact. Changes from baseline were analysed using a mixed model for repeated measurement (MMRM). Sensitivity analyses were applied on the extension data, where the MMRM analysis was repeated only including patients in the extension phase and an ANCOVA model was used, replacing missing values at 4-years with baseline values (BOCF).

Results: The planned MMRM analysis (n=49) revealed a statistically significant decrease in WOMAC pain subscale scores (-22.0; 95%CI: -29.5; -14.4) from baseline to 4-years. Analysis of the extension phase (n=27) showed similar results (-21.8; 95%CI: -29.0; -14.6) compared to the initial analysis. Furthermore, BOCF analysis indicated a statistically significant reduction in WOMAC pain subscale scores from baseline (-13.0 units). Four new adverse events were reported between the 3-year and 4-year visits; none were related to treatment.

Conclusions: This study shows that single injections of 6 ml intra-articular iPAAG were well tolerated and continued to provide clinically important effectiveness at 4-years after treatment.

Acknowledgements: The study was sponsored by Contura International A/S.

SEMAPHORIN3A COUPLES OSTEOGENESIS AND ANGIOGENESIS DOWNSTREAM OF VEGF IN TISSUE-ENGINEERED OSTEOGENIC GRAFTS

Andrea Grosso[1], Priscilla Briquez[2], Dirk Schaefer[3], Jeffrey A. Hubbell[4], Maximilian G. Burger[1,3], Nunzia Di Maggio[1], Andrea Banfi[1,3]

[1]Department of Biomedicine, Basel University Hospital , Basel, Switzerland, *[2]Department of General and Visceral Surgery, University of Freiburg, Freiburg, Germany*, *[3]Department of Plastic, Reconstructive, Aesthetic and Hand Surgery, Basel University Hospital, Basel, Switzerland*, *[4]Pritzker School of Molecular Engineering, University of Chicago, Chicago, United States*

Introduction: Coupling of angiogenesis and osteogenesis is crucial to efficiently generate bone grafts. Semaphorin 3a (Sema3a) regulates osteoblasts and osteoclasts to promote bone synthesis through Neuropilin-1 receptor (NP1). We previously found that: 1) delivery of Vascular Endothelial Growth Factor (VEGF) in osteogenic grafts dose-dependently decreases bone formation by increasing resorption and impairing progenitor differentiation; 2) in skeletal muscle VEGF dose-dependently inhibits endothelial Sema3a, impairing recruitment of NP1-expressing monocytes and TGF-b1 signaling. Here we investigated whether: a) endogenous Sema3a loss is the mechanism by which VEGF impairs bone formation; b) Sema3a treatment couples bone formation and vascularization in engineered grafts.

Method: Fibrin matrices were decorated with recombinant VEGF or Sema3a proteins engineered with a transglutaminase substrate sequence (TG-VEGF and TG-Sema3a) to allow cross-linking into fibrin hydrogels. Osteogenic grafts were prepared with human bone marrow mesenchymal cells and hydroxyapatite granules in fibrin hydrogels containing TG-VEGF, TG-Sema3a or both at 1:1 ratio and implanted in nude mice. Sema3a blockade was achieved with a specific NP1 antibody (anti-$NP1^{A}$).

Result: 100 mg/ml of TG-VEGF (high) caused severe bone loss and downregulation of endogenous Sema3a. 0.1 µg/ml of TG-VEGF (low) instead preserved both bone formation and Sema3A expression. Blocking Sema3a signaling significantly impaired bone formation, increased osteoclasts recruitment and interestingly also decreased vascular invasion. Further, Sema3a blockade significantly reduced both endogenous Sema3a expression and TGF-b1 activation, confirming the positive feed-back loop we previously described in skeletal muscle. Conversely, TG-Sema3a co-delivery was able to prevent bone loss induced by high TG-VEGF, while preserving efficient vascular growth. Notably, TG-Sema3a alone could increase both the amount of mineralized matrix and vascular invasion also in the absence of any TG-VEGF.

Conclusion: These data suggest that Sema3a provides a key molecular link coupling angiogenesis and bone formation and identify Sema3a as a promising target to generate vascularized bone grafts in a clinical setting.

CAN 3D PLANNING HELP OPTIMISE FEMORAL HEAD COVERAGE IN PERIACETABULAR OSTEOTOMY?

Anshini Thakur[1], Simon Harris[1], Miloš Brkljač[1], Justin Cobb[1], Kartik Logishetty[1]

[1]*Imperial College London, United Kingdom*

Introduction: Bernese periacetabular osteotomy (PAO) repositions the acetabulum to increase femoral head coverage (FHC) in hip dysplasia. Currently, there is a paucity of objective peri-operative metrics to plan for optimal acetabular fragment repositioning. The MSk Lab Hip 3D Planner (MSkL-HP) measures acetabular morphology and simulates PAO cuts to achieve optimal FHC. We evaluated how adjusting location and orientation of cutting planes can alter FHC.

Method: MSkL-HP simulated 274 feasible PAOs on four dysplastic hips. Femoroacetabular anatomy was landmarked to simulate cutting planes. Posterior column and ischial cuts were standardised, whilst iliac and pubic cut combinations varied. The slope of the iliac cut was either neutral (aligned to pelvis), exit point 5mm above the entry point (+5), or 5mm below (-5). The slope of the pubic cut was either 90°, 50°, or 70° (medial-to-lateral). Iliac and pubic cuts were simulated 0, 5 and 15mm - distal and medial – to a classic cut. Outcome measures were achieved LCEA, Tönnis, FHC and % bone overlap at the pubic cut. Targets were LCEA >30°, Tönnis angle <10°, and FHC >70% and minimum bone overlap ≥10%.

Results: All feasible PAOs resulted in improvement from pre-operative metrics. Personalised cutting planes provided greater benefit than standard planes. Kruskal Wallis tests showed that the iliac cut at 5mm or 15mm resulted in a greater LCEA and lower Tönnis compared to the classic cut ($p<0.05$). Changing location of the pubic cut, and slope of the iliac and pubic cuts did not significantly affect LCEA and Tönnis in all hips ($p<0.05$). Cut combinations optimising metrics were associated with a lower % pubic cut overlap.

Conclusion: MSkL-HP feasibly and reliably planned personalised PAO, measuring pre-operative and simulated post-operative objective metrics. Patient-specific pubic and iliac cuts enable greater correction whilst maintaining bone overlap. Further simulations on patients with varying morphology may improve standard techniques.

COMPREHENSIVE EVALUATION OF MUSCULOSKELETAL SOFT TISSUES BY CONTRAST ENHANCED MICROCT AND HISTOLOGY: PERSPECTIVE AND LIMITS

Gregorio Marchiori[1], Stefano Zaffagnini[1], Luca Cavazza[1], Giacomo Dal Fabbro[1], Alberto Grassi[1], Nicola Francesco Lopomo[2], Gianluca Giavaresi[1], Melania Maglio[1]

[1]IRCCS Istituto Ortopedico Rizzoli, Bologna, Italy, *[2]Politecnico di Milano, Milano, Italy*

Introduction: Histology is still considered the gold standard method for the evaluation of soft tissues in the musculoskeletal field, thanks to the possibility of studying structures using different staining and high magnification microscopy. To overcome the intrinsic limits of this method, contrast enhanced microtomographic (CE- microCT) protocols are constantly evolving to allow 3D study of soft tissues. However, no standardized approaches are available, and many concerns exist about the alterations induced to the samples.

Method: microCT/histology protocols were explored on human tendons and menisci. To enhance contrast tissues for microCT scanning 1) examethyldisilazane drying 2) 2% phosphotungstic acid (PTA) in alcoholic solution exposition and 3) 2% PTA in aqueous solution exposition were performed; to observe PTA contrast progression, three exposition and scanning times were selected. microCT images were compared to histological slices obtained from the same samples, after rehydration protocols, or from adjacent tissues portion, stained with Picrosirius red to highlight the peculiar collagenic structures.

Result: Exposition times influence PTA diffusion and tissue contrast; its specificity for collagenic structure allow a clearer contrast of the tissues. Histological processing on the same samples is possible: PTA removal requires careful washing in basic solution to reduce the hardening of the sample, while drying can be reverted applying inverse protocol. Comparison with microCT images is really accurate if histology is performed on the same sample, although all protocols induce tissue shrinkage with relative packing of collagen fibers.

Conclusion: The contrast approaches tested proved effective in highlighting the structures of both tendons and menisci, but the structural effects induced by tissue shrinkage do not allow a completely real microCT visualization of native tissue. Histology can be the reference method to monitor the efficacy of the contrast methods and the alterations induced to define the possibility of improvement of the technique.

Acknowledgement: PR23-PAS-P4 “ADJOINT 2”- INAIL

SAFETY AND PERFORMANCE OF DEXTRAN-TYRAMINE HYDROGEL IMPLANT FOR FOCAL ARTICULAR CARTILAGE LESIONS OF THE KNEE (ACTIVE): PRELIMINARY DATA OF THE SAFETY COHORT.

Goran van der Weiden[1], Nienke van Egmond[1], Marcel Karperien[2], Sanne Both[2], Simon Mastbergen[1], Peter Emans[3], Jacob Caron[4], Roel Custers[1]

[1]UMC Utrecht, Utrecht, Netherlands, *[2]University of Twente, Enschede, Netherlands*, *[3]Maastricht UMC, Maastricht, Netherlands*, *[4]Elisabeth-TweeSteden hospital, Tilburg, Netherlands*

Introduction: The ACTIVE(Advanced Cartilage Treatment with Injectable-hydrogel Validation of the Effect) study investigates safety and performance of a novel dextran-tyramine hydrogel implant for treatment of small cartilage defects in the knee (0.5-2.0cm2). The hydrogel is composed of a mixture of natural polymer conjugates that are mixed intra-operatively and which cross-link in situ through a mild enzymatic reaction, providing a cell-free scaffold for cartilage repair.

Method: The ACTIVE study is split into a safety (n=10) and a performance cohort (n=36). The Knee Injury and Osteoarthritis Outcome Score (KOOS), pain (numeric rating scale, NRS), Short-Form Health Survey (SF-36) were compared at baseline and 3, 6, and 12 months after surgery. The primary performance hypothesis is an average change in the KOOS from baseline to 12 months (ΔKOOS) greater than a minimal clinically important change (MIC) of 10. No statistical tests were performed as these are preliminary data on a smaller portion of the total study.

Result: All patients of the safety cohort (n=10, mean age±SD, 30±9 years) were treated with the hydrogel for a symptomatic (NRS≥4) cartilage defect on the femoral condyle or trochlear groove (mean size±SD, 1.2±0.4cm2). No signs of an adverse foreign tissue reaction or serious adverse events were recorded within the safety cohort. At final follow-up mean KOOS±SD was 66.9±23.5, mean NRS resting±SD was 1.3±1.9, NRS activity±SD was 3.8±2.9 and mean SF-36±SD was 72.0±10.9. ΔKOOS was 21. One patient sustained new knee trauma prior to final follow-up, affecting final scores considerably. When excluded, ΔKOOS was 24(n=9).

Conclusion: These promising initial findings provide a solid basis for continuation and expansion of this unique cartilage treatment. The MIC of 10 was surpassed. Though, results should be interpreted cautiously as they are based solely on preliminary data of the first 10 patients.

Acknowledgements: Study is sponsored by Hy2Care, producer of the CartRevive®(dextran-tyramine) Hydrogel implant.

MICROCRYSTALS IN THE SYNOVIAL FLUID OF PATIENTS WITH FEMOROACETABULAR IMPINGEMENT IMPACT ON CLINICAL OUTCOMES

Enrico Tassinari[1], Marta Favero[2], Michela Battistelli[3], Francesco Castagnini[1], Laura Valentini[3], Francesca Oliviero[2], Roberta Ramonda[2], Stefano Zaffagnini[1], Brunella Grigolo[1], Eleonora Olivotto[1]

[1]IRCCS Istituto Ortopedico Rizzoli, Bologna, *[2]University-Hospital of Padova, Bologna*, *[3]Urbino University "Carlo Bo", , Bologna*

Introduction: Femoroacetabular impingement (FAI) has a prominent role in early osteoarthritis (OA) development. As calcium crystal deposition is common in OA, also labral calcifications are present in FAI patients. Calcium crystals can activate proinflammatory pathways and release nociceptor stimulating substances. Thus, calcium crystal deposition may be involved in generating joint pain. The aim of the study was to investigate the associations among preoperative symptoms, outcomes after arthroscopy for FAI and presence of crystal in synovial fluids (SFs).

Method: Patients scheduled for hip arthroscopy for FAI treatment were enrolled and SFs collected. OA severity was assessed with Kellgren and Lawrence score. Physical examination, joint pathology and clinical assessment using Hip disability & Osteoarthritis Outcome Score (HOOS) were performed at the time of surgery. HOOS was also evaluated after 6 months. Crystals identification was performed by compensated polarized light microscopy, spectrophotometric analysis, and Environmental scanning electron microscope (ESEM). SFs were also collected from OA patients as control.

Result: 49 FAI patients were enrolled (median age 35 years) and 35 SFs were avaliable for the analysis. 12 SFs samples were also analyzed from OA patients. All FAI samples showed the presence of cartilage damage markers as glycosaminoglycan (GAGs) and matrix metalloproteinase-13. Calcium crystals were detected by Alizarin Red staining with optical microscopy in both groups and the level, measured by spectrophotometric analysis, was different in SFs of FAI and OA patients. The ESEM analysis showed the same crystal composition, in both groups and the presence of microcrystals in FAI patients. Moreover, calcium crystal level in SFs from FAI patients was associated with labral lesions and OA signs.

Conclusion: Our study showed that calcium crystals level in SFs of FAI patients are correlated with worst post-operative outcome, and it might be used as a potential new biomarker for early diagnosis, prognosis and monitoring of therapeutic responses.

VASCULAR NETWORK INVESTIGATION AFTER TISSUE ENGINEERING PROCEDURE ON SOFT TISSUE.

Julia Vettese[1], Manon Julie[1], Robin Evrard[1], Lies Fieve[2], Benoît Lengelé[3], Olivier Cornu[4]

[1]Université Catholique de Louvain (UCLouvain), Institut de Recherche Expérimentale et Clinique (IREC), Neuro musckulo Skeletal lab (NMSK) , Brussels, Belgium, *[2]Université Catholique de Louvain (UCLouvain), Institut de Recherche Expérimentale et Clinique (IREC), Pole of Morphology (MORF) , Brussels, Belgium*, *[3]Université Catholique de Louvain (UCLouvain), Institut de Recherche Expérimentale et Clinique (IREC), Pole of Morphology (MORF). Department of Plastic and Reconstructive Surgery, Cliniques Universitaires Saint-Luc , Brussels, Belgium*, *[4]Université Catholique de Louvain (UCLouvain), Neuro musckulo Skeletal lab (NMSK), Centre de Thérapie Cellulaire et Tissulaire Locomoteur, Department of Orthopaedic and Trauma Surgery (Cliniques Universitaires Saint-Luc) , Brussels, Belgium*

Introduction: In tissue engineering, the establishment of sufficient vascularization is essential for tissue viability and functionality. Inadequate vascularization disrupts nutrients and oxygen supply. Nonetheless, regenerating intricate vascular networks represents a significant challenge. Consequently, research efforts devoted to preserving and regenerating functional vascular networks in engineered tissues are of paramount importance. The present work aims to validate a decellularisation process with preservation of the vascular network and extracellular matrix (ECM) components in fasciocutaneous flaps.

Method: Five vascularized fasciocutaneous flaps from cadaveric donors were carefully harvested from the anterolateral thigh (ALT), preserving the main perforator of the fascia lata. The entire ALT flap underwent decellularization by perfusion using a clinically validated chemical protocol. Fluoroscopy and computed tomography (CT) were used to analyze the persistence of the vascular network within the flap, pre- and post-decellularization. Histological analysis, including hematoxylin and eosin staining, and quantitative DNA assessment evaluated decellularization efficacy. Further qualitative (immunohistochemistry, IHC) and quantitative analyses were conducted to assess the preservation of ECM components, such as collagen, glycosaminoglycans, and elastin.

Result: On average, the ALT flap maintains 82% of the perfusion area ($p = 0.094$) post-treatment. Histological analysis confirmed decellularization efficacy and revealed structural rearrangement. Paired analysis revealed a significant decrease in DNA levels (<14.8 ng/mg of dry weight, $p^{****} < 0.0001$) and well-maintained ECM. IHC indicated the persistence of elastine, collagen IV and laminin. Quantitative analysis confirmed elastin ($p = 0.44$) and collagen persistence (+74%, $p^{***} = 0.001$, albeit with a decrease in matrix glycosaminoglycans (-41%, $p^{***} = 0.01$)

Conclusion: Decellularization effectively removed cells, while preserving the ECM overall and maintaining some vascular network integrity. Yet, further study is needed to validate these findings, involving microCT examination of the vascular network and its ability to support cell colonization and viability.

COMPARATIVE EFFECTIVENESS OF SILVER-COATED IMPLANTS IN PERIPROSTHETIC INFECTION PREVENTION: A SYSTEMATIC REVIEW AND META-ANALYSIS

Halil Bulut[1], Sefa Giray Batibay[2], Enes Kanay[3], Korhan Özkan[3]

[1]Istanbul University Cerrahpasa, Türkyie, *[2]umraniye training and research hospital, Türkyie*, *[3]Acibadem Atasehir Hospital, Türkyie*

Comparative Effectiveness of Silver-Coated Implants in Periprosthetic Infection Prevention: A Systematic Review and Meta-Analysis

Introduction: Despite the implementation of numerous preventive measures in recent years, the persistent challenge of periprosthetic infections remains. Among the various strategies, metallic modification of implants, particularly with silver, has emerged as a promising avenue. Silver's antimicrobial properties, coupled with its low human toxicity, render it an appealing option. However, ongoing debate surrounds its comparative efficacy in infection prevention when contrasted with titanium-coated prostheses.

Methods: The PubMed database was systematically searched up to March 2024. Studies in English that met predetermined inclusion/exclusion criteria and utilized "Megaprosthesis AND infection" and " silver-coated AND infection " as key terms were included. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses(PRISMA) statement guided the article selection process.

Results: From a pool of 1892 potential papers after literature screening, 11 studies with a total of 1419 patients were meticulously selected for analysis. Among these patients, 638 were treated with silver-coated implants, while 781 received titanium-coated implants, resulting in 166 recorded cases of infection. Remarkably, the infection rate stood at 9.2% for the silver-coated group, contrasting with 13.4% for the titanium-coated group. The subsequent analysis unveiled a notable discrepancy in proportions (P difference = -0.0473, 95%CI: -0.088 to -0.006), signaling a statistically significant decrease in infections within the silver-coated cohort. Furthermore, the I2 statistic, denoting heterogeneity in effect sizes, stood at 21.8% (95%CI: 0.0-66.9), indicating a modest degree of variability among the studies.

Conclusion: In conclusion, our systematic review and meta-analysis shed light on the potential of silver-coated implants in mitigating periprosthetic infections. Despite the persistent challenge posed by such infections, our findings suggest a statistically significant decrease in infection rates among patients treated with silver-coated implants compared to those with titanium-coated ones.

A NEUROANGIOGENIC SCAFFOLD WITH SPATIOTEMPORAL CONTROL FOR TISSUE REGENERATION IN MEDICATION-RELATED OSTEONECROSIS OF THE JAW, EMPLOYING BIOACTIVE ELASTIN-LIKE RECOMBINAMERS (ELRS)

Israel Gonzalez de Torre[1,2], Luis Miguel Redondo[1], Claudia García Sierra[1], José Carlos Rodríguez Cabello[1,2], Angel José Alvarez Bsarcia[1]

[1]BIOFORGE, Valladolid, Spain, *[2]CIBER-BBN, Valladolid, Spain*

Introduction: The objective of the work is construction of a multi-bioactive scaffold based on that allows a space/time control over the regeneration of damaged bones by Medication-Related Osteonecrosis of the Jaw using a minimal invasive approach based on the injection of the fast-degrading pro neuro and angiogenic ELR (Elastin-Like Recombinamers) based hydrogels.

Method: Chemical crosslinking facilitated the creation of multi-bioactive scaffolds using ELRs with reactive groups. Cell-loaded multi-bioactive scaffolds, prepared and incubated, underwent evaluation for adhesion, proliferation, angiogenic, and neurogenic potential. In vitro assessments utilized immunofluorescence staining and ELISA assays, while live-recorded monitoring and live-dead analysis ensured cytocompatibility. In rat and rabbit models, preformed scaffolds were subcutaneously implanted, and the regenerative process was evaluated over time. Rabbit models with MRONJ underwent traditional or percutaneous implantation, with histological evaluation following established bone histological techniques.

Result: A 3D scaffold using ELR that combines various peptides with different degradation rates to guide both angiogenesis and neurogenesis has been developed. Notably, scaffolds with different degradation rates promoted distinct patterns of vascularization and innervation, facilitating integration with host tissue. This work demonstrates the potential for tailored tissue engineering, where the scaffold's bioactivities and degradation rates can control angiogenesis and neurogenesis. In an animal model of medication-related osteonecrosis of the jaw (MRONJ), the scaffold showed promising results in promoting bone regeneration in a necrotic environment, as confirmed by histological and imaging analyses. This study opens avenues for novel tissue-engineering strategies where precise control over vascularization and nerve growth is crucial.

Conclusion: A groundbreaking dual approach, simultaneously targeting angiogenesis and innervation, addresses the necrotic bone in MRONJ syndrome. Vascularization and nerve formation play pivotal roles in driving reparative elements for bone regeneration. The scaffold achieves effective time/space control over necrotic bone regeneration.

The authors are grateful for funding from the Spanish Government (PID2020-118669RA-I00)

WALKING AND RUNNING OF CHILDREN WITH DECREASED FEMORAL TORSION

Christos Tsagkaris[1], Marry Everdina Hamberg[2], Christina Villefort[2], Thomas Dreher[2], Britta K Krautwurst[2]

[1]University Childrens Hospital of Zurich, Zurich, Switzerland, [2]1. Pediatric Orthopedic and Trauma Surgery, Children's University Hospital Zürich, 8032 Zürich, Switzerland 2. Pediatric Orthopedics, Balgrist University Hospital, University of Zurich, 8008 Zürich, Switzerland , Switzerland

Introduction: Understanding the implications of decreased femoral torsion on gait and running in children and adolescents might help orthopaedic surgeons to optimize treatment decisions. To date, there is limited evidence regarding the kinematic gait deviations between children with decreased femoral torsion and typically developing children as well as regarding the implications of the same on the adaptation of walking to running.

Method: A three dimensional gait analysis study was undertaken to compare gait deviations during running and walking among patients with decreased femoral torsion (n=15) and typically developing children (n=11). Linear mixed models were utilized to establish comparisons within and between the two groups and investigate the relation between clinical examination, spatial parameters and the difference in hip rotation between running and walking.

Result: Patients exhibited increased external hip rotation during walking in comparison to controls accompanied by higher peaks for the same as well as for, knee valgus and external foot progression angle. A similar kinematic gait pattern was observed during running with significant differences noted in peak knee valgus. In terms of variations from running to walking, patients internally rotated their initially external rotated hip by 4°, whereas controls maintained the same internal hip rotation. Patients and controls displayed comparable kinematic gait deviations during running compared to walking. The passive hip range of motion, torsions and velocity did not notably influence the variation between mean hip rotation from running to walking.

Conclusion: This study underlines the potential of 3D gait kinematics to elucidate the functional implications of decreased FT and hence may contribute to clinical decision making.

SPATIAL TRANSCRIPTOMICS WORKFLOW ENABLES DISTINCT TISSUE-SPECIFIC MOLECULAR CHARACTERIZATION OF NON-UNION AND UNION BONE FRACTURES IN MICE

Nico Giger[1], Maria Schröder[1], Daniel Arens[1], Lena Gens[1], Stephan Zeiter[1], Martin Stoddart[1], Esther Wehrle[1]

[1]*AO Research Institute Davos, Davos Platz, Switzerland*

Background: The molecular mechanisms underlying non-union bone fractures largely remain elusive. Recently, spatial transcriptomics approaches for musculoskeletal tissue samples have been developed requiring direct placement of histology sections on barcoded slides. However, Formalin-Fixed-Paraffin-Embedded (FFPE) bone sections have been associated with limited RNA quality and read depth compared to soft tissue. Here, we test spatial transcriptomics workflows based on transcriptomic probe transfer to characterize molecular features discriminating non-union and union bone fractures in mice.

Method: Histological sections (n=8) used for spatial transcriptomics (Visium CytAssist FFPE; 10x Genomics, n=4 on glass slides, n=4 on hydrogel-coated slides) were obtained from a fracture healing study in female 20-week-old C57BL/6J mice receiving either a femur osteotomy (0.7mm) or a segmental defect (2.4mm) (license 22/2022, Grisons CH). Sequence alignment and manual segmentation of different tissues (bone, defect region/callus, bone marrow, muscle) were performed using SpaceRanger and LoupeBrowser (10x Genomics). Differential gene expression was performed using DESeq2 (Seurat) followed by Gene-Set-Enrichment-Analysis (GSEA) of Gene Ontology (ClusterProfiler). Group comparison of quality measures was done using a Welch's t-test. Results are given as mean±standard deviation.

Result: The quality measures, mean counts, and genes per spot, were significantly ~10x higher for sections on hydrogel slides (counts: 4700±1796, genes: 2389±1170) compared to glass slides (counts: 463±415, genes: 250±223). In challenging tissues like cortical bone, we reached high counts+genes in comparison to published data.

Direct comparison of a non-union and union section showed a total of 432 differentially regulated genes, 538 in the defect region/callus. GSEA revealed differential regulation of pathways involved in muscle organ morphogenesis, cartilage development and endochondral ossification.

Conclusions: Optimized spatial transcriptomics workflows based on transcriptomic probe transfer enable for improved read depth in musculoskeletal tissue enabling the characterization of molecular features discriminating non-union and union bone fractures.

Acknowledgements: AO Foundation (AOTRAUMA), SNSF (PhD salary)

A SCOPING REVIEW TO INFORM CORE OUTCOME SET DEVELOPMENT: WHAT OUTCOMES HAVE BEEN REPORTED IN LITERATURE ON PATIENTS UNDERGOING LOWER-LIMB LENGTHENING SURGERY, AND HOW HAVE THEY BEEN MEASURED?

Ali Yalcinkaya[1,2], Maria Tirta[1,2], Michael Skovdal Rathleff[3,4], Christopher Iobst[5], Ole Rahbek[1,2], Søren Kold[1,2]

[1]Interdisciplinary Orthopaedics, Aalborg University Hospital, Aalborg, Denmark, *[2]Department of Orthopaedic Surgery, Aalborg University Hospital, Aalborg, Denmark*, *[3]Center for General Practice at Aalborg University, Aalborg, Denmark*, *[4]Department of Health Science and Technology, Faculty of Medicine, Aalborg University, Aalborg, Denmark*, *[5]Center for Limb Lengthening and Reconstruction, Nationwide Children's Hospital, Columbus, Ohio, United States*

Introduction: The heterogeneity of outcomes used in the field of lower limb lengthening surgery (LLLS) affects our ability to synthesize evidence. This hampers robust systematic reviews and treatment recommendations for clinical practice. Ultimately this reduces the impact of research for both patients and healthcare professionals. This scoping review aimed to describe the outcomes and outcome measurement instruments (OMIs) used within the field of LLLS.

Method: A systematic literature search of WOS, Scopus, Embase, MEDLINE, and the Cochrane Library identified all studies reporting outcomes in children and adults after LLLS. All outcomes and OMIs were extracted verbatim. An iterative process was used to group outcome terms under standardized outcome headings categorized using the COMET Taxonomy of Outcomes.

Result: Data saturation was achieved in 2020. A total of 142 studies were included between 2024-2020, reporting 2964 verbatim outcomes with 663 standardized outcome terms collapsed into 119 outcome headings (subdomains). A total of 29 patient-reported and 26 clinician-reported outcome instruments were identified. The most commonly reported outcome was "Lengthening amount", reported in over 72% of the included studies, while "health-related quality of life" was measured in 16% and all life impact outcomes were reported in 19% of the included studies.

Conclusion: A large number of peer-reviewed publications are available, demonstrating that significant resources are being devoted to research on LLLS. However, reported outcomes for people with LLLS are heterogeneous, subject to reporting bias, and vary widely in the definitions and measurement tools used to collect them. Outcomes likely to be important to patients, such as quality of life and measures of physical function, have been neglected. This scoping review identifies a need to standardize outcomes and outcome measures reported on patients recovering from lower limb lengthening surgery; this can be addressed by creating a core set of outcomes.

PATHOLOGIC FRACTURE OF LONG BONES AS A COMPLICATION OF ACUTE OSTEOMYELITIS IN PEDIATRICS: A CHALLENGING TASK FOR ORTHOPEDIC SURGEONS

Ramin Zargarbashi[1], Fardis Vosoughi[2], Farhad Shaker[2], Mona Mirbeyk[3], Mozhgan Seifi[1], Amir R Vafaee[1]

[1]Department of Pediatric Orthopedy, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran, [2]Department of Orthopaedic and Trauma Surgery, Shariati Hospital and School of Medicine, Tehran University of Medical Sciences, Tehran, Iran, [3]Department of Immunology, Children's Medical Center and School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

Introduction:The management of pathologic fractures (PF) following osteomyelitis (especially acute subtype) has not been widely investigated. This is challenging due to the infection-induced destructive process causing bone architecture defects. Therefore, this study aims to assess a stepwise treatment plan for the acute incidence of PF in long bone following pediatric acute Hematogenous osteomyelitis(AHO) (the most common mechanism in children).

Method: This case series was conducted in a tertiary pediatric center. Patients with fracture incidence within the first 10 days after AHO diagnosis were included. Patients' characteristics were retrospectively reviewed.

Result: Nine patients (7 boys, involved bone: the femur(4), tibia(3), Radius(1), and Ulna(1)) were included, with a mean age of 52.56±66.18 months (7-216) and a follow-up time of 11.62±3.61 years (6.5-16 years). The etiology in all patients was hematological(Methicillin-resistant Staphylococcus aureus).

Our stepwise treatment plan was as follows:

1. Intravenous antibiotics until ESR<20, then oral to ESR<5
2. Debridemnt surgery was performed if abscesses were detected.
3. Fracture type determined initial fixation: external fixation (4 patients, 2 unions) or casting (2 patients, both unions).
4. If the union was not obtained, internal fixation (with (2 patients) or without (2 patients) bone graft) was applied (all obtained union).
5. Circular external fixation was applied if the union was not obtained or leg length discrepancy occurred (1 case).

A mean of 3.2 surgical procedures (1-6) was required to control the infection, and 1.4 surgical procedures (0-4) were required to obtain union.

Except for one patient who died of septic shock, all other patients (88.8%) reached complete recovery (average length of hospital stay of 19.2 days (5-35).), and the union was obtained (the average union time of 17.25 months(4-36)) without long-term sequelae of osteomyelitis.

Conclusion: The outcome of the stepwise plan in this study suggests that acute PF following AHO in pediatrics can be managed efficiently.

FATIGUE STRENGTH ASSESSMENT OF A NOVEL LIGHT-CURABLE BONE FIXATION TECHNIQUE

Peter Varga[1], Paula Cameron[1], Daniel Hutchinson[2], Micheal Malkoch[2], Peter Schwarzenberg[1]

[1]AO Research Institute Davos, Davos, Switzerland, *[2]KTH Royal Institute of Technology, Stockholm, Sweden*

Introduction: When designing a new osteosynthesis device, the biomechanical competence must be evaluated with respect to the acting loads. In a previous study, the loads on the proximal phalanx during rehabilitation exercises were calculated. This study aimed to assess the safety of a novel customizable osteosynthesis device compared to those loads to determine when failure would occur.

Method: Forty proximal phalanges were dissected from skeletally mature female sheep and divided into four testing groups. A custom 3D printed cutting and drilling guide was used to create a reduced osteotomy and pilot holes to insert four 1.5 mm cortical screws. A novel light-curable polymer composite was used to fixate the bones with an in situ fixation patch. The constructs were tested in cyclic four-point bending in a bioreactor with ringer solution at 37°C with a valley load of 2 N. Four groups (N = 10) had increasing peak loads based on varying safety factors relative to the physiological loading (G1:100x, G2:150x, G3:175x, G4:250x). Each specimen was tested for 12,600 cycles (6 weeks of rehabilitation) or until failure occurred. After the test the thickness of the patch was measured with digital calipers and data analysis was performed in Python and R.

Result: All samples survived in G1, and all failed in G4. G2 and G3 had 1 and 8 failures, respectively. There was no significant difference in patch thickness in all survivor samples against failures ($p = 0.131$), however, there was a significant difference in the displacement amplitude in the final cycle (0.072 mm vs. 0.15 mm; $p < 0.001$).

Conclusion: This study found the survival and failure limits of a novel osteosynthesis device as a function of physiological loading. These results indicate that such fixations could withstand 100x the loading for typical non-weightbearing rehabilitation. Further studies are needed to confirm the safety for other conditions.

RISK FACTORS FOR DEVELOPMENTAL DYSPLASIA OF THE HIP AT 3 MONTHS OF AGE – A SYSTEMATIC REVIEW AND META-ANALYSIS.

Maria Tirta[1], Ole Rahbek[1], Søren Kold[1], Hans-Christen Husum[1]

[1]*Interdisciplinary Orthopaedics, Aalborg University Hospital, Aalborg, Denmark*

Introduction: Selective screening of children at risk for developmental dysplasia of the hip (DDH) is based on clinical examination and risk factor identification. Two meta-analyses published in 2012 found breech presentation, family history of DDH, female sex and primiparity to increase the risk of DDH. However, the DDH definition, reference tests and age of the examined children vary considerably, complicating the translation of those findings to current screening guidelines. The aim of this meta-analysis was to evaluate the association of previously proposed risk factors to the risk of sonographically verified DDH.

Method: We searched PubMed, EMBASE and Cochrane library to identify cohort, RCTs, case-control and cross-sectional studies from 1980 to 2023 in English language. Eligible studies included participants under three months of age, where the diagnosis of DDH was made by hip ultrasound using the gold standard Graf method and reported information on one or more of the proposed risk factors and final diagnosis was available.

Result: Of 5363 studies screened, 20 studies (n=64543 children) were included. Breech presentation (OR: 4.2, 95%CI 2.6-6.6), family history (3.8, 95%CI 2.1-7.2), female sex (2.5, 95%CI 1.7-3.6), oligohydramnios (3.8, 95%CI 1.7-8.5) and high birthweight (2.0, 95%CI 1.6-2.5) significantly increased the risk of DDH. C-section, primiparity, multiple births, low birthweight and prematurity were not found to increase the risk for DDH, and there was only one study about clubfoot as a risk factor. Heterogeneity was high (I^2>75%) in all the tested factors except high birthweight (I^2=0%). Subgroup analysis was performed to investigate these heterogeneities.

Conclusion: Family history of DDH and breech presentation are associated with significant increase of the risk of sonographic DDH in children aged three months. A similar risk increase was detected for oligohydramnios, which was not detected in previous meta-analyses. Additionally, the DDH risk increase of female sex was found to be lower than previously reported.

RISKS FOR REOPERATION TO PROMOTE UNION IN PERIPROSTHETIC DISTAL FEMUR FRACTURES

Adam Schlauch[1], Ishan Shah[1], Benjamin Crawford[1], Anna Martin[1], Anton Denisov[2], Pierre Tamer[1], Brian Farrell[3]

[1]San Francisco Orthopaedic Residency Program, San Francisco, United States, *[2]Traumatologia Elgeadi/Hospital, Madrid, Spain*, *[3]Kaiser Permanente Oakland Medical Center, Oakland, United States*

Introduction: Distal femur fractures around a total knee arthroplasty (TKA) are a growing problem for orthopaedic surgeons. The purpose of this study was to identify risks of reoperation for nonunion following open reduction and internal fixation of TKA periprosthetic distal femur fractures (PDFF).

Method: Patients with PDFF (AO 33A-C[VB1, C1, D1], Su types 1-3) managed operatively with open reduction and internal fixation (ORIF) were retrospectively reviewed. Exclusion criteria were acute management with a distal femur replacement, less than 6 months of follow-up, and lack of injury or follow-up radiographs. The primary outcome measure was reoperation to achieve bony union. Comparisons were made between cases that did and did not require a reoperation to achieve union. Univariate analysis was used to identify factors to be analyzed in multivariate analysis to determine independent risk factors for the primary outcome.

Result: A total of 77 patients met inclusion criteria. Union rate was 69/77 (89.6%). There were no differences between the groups for age, sex, BMI, comorbidities, Su classification, open injury, or mechanism of injury. Multivariate analysis identified risks for nonunion including post-operative malalignment (OR 1.41; CI 1.20-1.64; p<0.001), notching pre-operatively (OR 1.22; CI 1.04-1.42; p=0.012), presence of screws through fracture line (OR 1.28; CI 1.17-1.39; p<0.001), plate length <12 holes (OR 1.16; CI 1.02-1.33; p=0.024) and screw density greater than 0.4 (OR 2.18; CI 1.25-3.78; p=0.006)

Conclusion: The reoperation rate to promote union was 10.4%. The study identified post-operative malalignment, notching pre-operatively, presence of screws through fracture line, plate length <12 holes, and proximal screw density greater than 40% as independent risk factors for nonunion.

EXPLORING THE LINK BETWEEN CHRONIC STRESS AND OSTEOARTHRITIS IN A MURINE MODEL

Gundula Rösch[1], Anna E. Rapp[1], Pei-Ling Tsai[2], Helena Kohler[1], Shahed Taheri[3], Arndt F. Schilling[3], Frank Zaucke[1], David Slattery[2], Zsuzsa Jenei-Lanzl[1]

[1]Dr. Rolf M. Schwiete Research Unit for Osteoarthritis, Department of Trauma Surgery and Orthopedics, Goethe University Frankfurt, University Hospital Frankfurt, Frankfurt, Germany, *[2]Department of Psychiatry, Psychosomatic Medicine and Psychotherapy, Goethe University Frankfurt, University Hospital Frankfurt, Frankfurt, Germany*, *[3]Department of Trauma Surgery, Orthopedic Surgery and Plastic Surgery, University Medical Center Göttingen, Göttingen, Germany*

Introduction: Osteoarthritis (OA) is a chronic degenerative disease of the entire joint leading to joint stiffness and pain (PMID:33571663). Recent evidence suggests that the sympathetic nervous system (SNS) plays a role in the pathogenesis of OA (PMID:34864169). A typical cause for long-term hyperactivity of the SNS is chronic stress. To study the contribution of increased sympathetic activity, we analyzed the progression of OA in chronically stressed mice.

Method: We induced OA in male C57BL/6J mice by destabilizing the medial meniscus (DMM)(PMID:17470400) and exposed half of these mice to chronic unpredictable mild stress (CUMS)(PMID:28808696). Control groups consisted of sham-operated mice with and without CUMS exposure. After 12 weeks, CUMS efficacy was determined by assessing changes in body weight gain and activity of mice, measuring splenic norepinephrine and serum corticosterone levels. OA progression was studied by histological analysis of cartilage degeneration and synovitis, and by µCT to evaluate changes in calcified cartilage and subchondral bone microarchitecture. A dynamic weight-bearing system was used to assess OA-related pain.

Result: CUMS resulted in significantly decreased body weight gain and activity, as well as increased splenic norepinephrine and serum corticosterone concentrations compared to the respective controls. Surprisingly, already DMM alone resulted in elevated stress hormone levels. CUMS significantly exacerbated cartilage degeneration and synovial inflammation and increased OA pain in DMM mice. The underlying cellular and molecular mechanisms are currently being analyzed using FACS, single cell RNAseq, and spatial proteomics.

Conclusion: Overall, chronic stress exacerbates OA severity and pain. Moreover, increased levels of stress hormones were observed in OA mice without CUMS induction, suggesting a complex bi-directional interaction between the SNS and OA. Targeting the autonomic nervous system, such as attenuating the SNS but also stimulating the activity of the parasympathetic nervous system, as a counterpart of the SNS, may therefore be promising for novel preventive or causal treatments of OA.

PALMITOYLATION OF SHP2 PROMOTES OSTEOCLASTOGENESIS AND OSTEOLYTIC DISEASES

KUO-YANG SUN[1]

[1]*The First Affiliated Hospital of Nanchang University, Nanchang, China*

Introduction: Understanding osteoclastogenesis is key to treat osteolytic diseases such as periprosthetic osteolysis and osteoporosis. SHP2 has been reported to promote osteoclast differentiation and fusion, but the exact mechanism is poorly understood. Our research aims to illustrate the specific role of SHP2 in upregulating osteoclastogenesis.

Method: Molecular and cell biology experiments like western blot, qPCR, gene knockout, TRAP staining and fluorescence imaging are used to verify the function of SHP2 in osteoclastogenesis. Then, acly-biotin exchange and site-mutated plasmids transfection are conducted to explain the role of SHP2 palmitoylation. Finally, micro-computed tomography and histological analysis are included in particle-induced osteolysis and osteoporosis mouse models.

Result: Firstly, our results show that phosphorylation of SHP2 (a sign of SHP2 activation) is elevated during osteoclastogenesis. Both SHP2 inhibitor and macrophage-conditional deletion of SHP2 decrease osteoclast differentiation and fusion in vitro. Secondly, we identify SHP2 can be palmitoylated and its palmitoylation is positively associated with osteoclastogenesis. Palmitoylated SHP2 not only enhances its activation or phosphorylation, but also promotes itself to translocate onto cell membrane for binding the important receptor——RANK. Thirdly, the specific amino acid site to be palmitoylated is further confirmed. Site-mutated SHP2 impairs its activation and cell membrane recruitment, which emphasizes the significance of SHP2 palmitoylation once again. Lastly, knockout of SHP2 as well as pharmacological inhibiting its palmitoylation can alleviate particle-induced osteolysis and osteoporosis in mouse models.

Conclusion: Our study elucidates the molecular mechanism of SHP2 in facilitating osteoclastogenesis through a unique posttranslational modification——palmitoylation, and provides a potential therapeutic strategy for osteolytic diseases.

Acknowledgments：This work is supported by National Key R&D Program of China (2018YFC1105904), Key Program of NSFC (81730067), National Science Foundation of China (81772335, 81941009, 81802196, 82202717).

INITIAL CONSTRUCT STABILITY OF LONG CEPHALOMEDULLARY NAILS WITH CONVENTIONAL DISTAL LOCKING COMPARED TO SIMILAR NAILS WITH SUPERIOR LOCKING FOR COMPLEX TROCHANTERIC FRACTURES AO31-A2.2 - A BIOMECHANICAL STUDY

Arndt Peter Schulz[1,2,3], Matthias Münch[1], Tobias Barth[1], Jasper Frese[1,3], Nico Hinz[1,4], Maximilian Hartel[1,4]

[1]BG Klinikum Hamburg, Hamburg, Germany, *[2]Fraunhofer IMTE, Lübeck, Germany*, *[3]Universität zu Lübeck, Lübeck, Germany*, *[4]Universitätsklinikum Eppendorf, Hamburg, Germany*

Introduction: A long nail is often recommended for treatment of complex trochanteric fractures but requires longer surgical and fluoroscopy times. A possible solution could be a nail with an appropriate length which can be locked in a minimally invasive manner by the main aiming device. We aimed to determine if such a nail model* offers similar structural stability on biomechanical testing on artificial bone as a standard long nail when used to treat complex trochanteric fractures.

Method: An artificial osteoporotic bone model was chosen. As osteosynthesis material two cephalomedullary nails (CMN) were chosen: a superior locking nail (SL-Nail) which can be implanted with a singular targeting device, and a long nail (long-nail) with distal locking using free-hand technique. AO31-A2.2 fractures were simulated in a standardized manner. The insertion of the nail was strictly in accordance with the IFU and surgical manual of the manufacturer. The nail was locked dynamically proximally and statically distally. Axial height of the construct, varus collapse, and rotational deformity directly after nail insertion were simulated. A Universal Testing Machine was used. Measurements were made with a stereo-optic tracking system. Reactive movements were recorded and evaluated in all six degrees of freedom. A comparative analysis provided information about the stability and deformation of the assemblies to be compared.

Result: There was a detectable difference in the axial fracture movement resulting in narrowing of the fracture gap. The load displacement was 1.7mm higher for the SL-Nail. There was no difference in varus collapse or rotational deformity between the nail variants.

Conclusion: We conclude that there are small differences which are clinically insignificant and that a superior locking nail can safely be used to manage complex trochanteric fractures.

*DCN SL nail, SWEMAC, Linköping, Sweden

Funding: no funding