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Conference Abstract Booklet

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Session 1: Clinical Biomechanics

In-vivo kinematics of the ankle complex during level gait

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Objectives: The ankle complex is a highly intricate structure made up of a complex arrangement of joints, bones, ligaments, tendons, and muscles. Its anatomical complexity poses challenges for accurately measuring the internal joints of the ankle (including the tibiotalar, subtalar, and talonavicular joints). Understanding the kinematics of level gait in healthy individuals provides a crucial baseline for comparing the gait patterns of patients with injuries and musculoskeletal diseases. Biplane Videoradiography (BVR) combined with Magnetic Resonance Imaging (MRI) overcomes this challenge and allows direct measurement of the bones. The primary objective of this study was to measure the in-vivo kinematics of the ankle complex during level gait for a healthy population. *Methods*: A custom raised walkway was manufactured to position the foot and ankle inside the BVR field of view. Healthy participants performed level gait while capturing BVR (125Hz, 1.25ms pulse width, 80kVp and 160mA) and simultaneous marker-based motion capture. Ethical approval for the study was obtained from the Wales Research and Ethics Committee. Written informed consent was received from all participants (N=7, 5F/2M, Age 28±11.4Y). Participants underwent MRI (Magnetom 3T Prisma, Siemens) where the tibia, talus, calcaneus and navicular were manually segmented into 3D bone models (Simpleware Scan IP, Synopsys). Anatomical coordinate systems were applied to each bone automatically using an open-source toolbox[1]. Bone position and orientation for each bone were calculated by scientific rotoscoping of the 3D models to the biplane X-Ray images (DSX Suite, HAS-Motion, Inc.). Bone positions were filtered using an adaptive low pass Butterworth filter[2] (Frequency range: 10-30Hz). Kinematics were calculated and defined as changes from a neutral position (static trial of participant standing) with each trial normalised to percentage of stance phase as determined by the ground reaction forces from the motion capture. All kinematic processing was carried out using MATLAB (MathWorks, Inc). Averages and standard deviation kinematic waveforms were calculated from all of the participants. *Results:* Euler rotations for the tibiotalar, subtalar, and talonavicular joints were calculated for the stance phase of level gait. The talonavicular joint had the largest ROM for dorsi-plantarflexion (27.0°), followed by the tibiotalar (10.4°) and subtalar (9.0°) joints. Inversion-eversion ROM was highest for the tibiotalar (20.2°), with the talonavicular (11.7°) and subtalar (5.2°) joints with reduced ROM. For internal-external rotation, the talonavicular joint had the largest ROM (25.5°), while the Tibiotalar (6.9°) and Subtalar (6.4°) joints had similar ROMs. These findings align with expected joint functions[3,4] and provide baseline kinematic data for healthy gait, essential for comparing with pathological patterns to improve understanding and treatment of ankle disorders. *Conclusions*: In-vivo kinematics of the ankle complex are crucial for understanding its function and role and these results provide an important comparator for future studies for patients with ankle injuries or diseases to aid in improving diagnosis and treatment.
References:[1]Peterson et al. Front Bioeng Biotechnol. 2023. [2]Erer, K. S. J. Biomech. 2007 [3]Yang et al. J.

Biomech 116 (2021) [4]Wang, S. et al. J Bionic Eng 2023 *Acknowledgments*: Funding received from the EPSRC Impact Accelerator Account.

Exploring long-term effects: dynamic stability and gait variability in adults with previous lower limb injury

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Objectives Lower limb injuries are extremely prevalent among the general population, particularly among athletes and active young adults. Much has been done to study the biomechanics of developing osteoarthritis (OA), but there has been limited research on the effects of untreated injuries. Dynamic stability and spatiotemporal gait parameters have been observed to vary dramatically in patients with OA, and other similar conditions, leading to the question of whether such values vary in untreated cases. The objective of this study is to observe long-term differences in gait patterns and dynamic stability of people who have previously suffered lower limb injuries. By examining these effects, the aim is to equip ourselves with a better understanding and knowledge of such injuries, providing scope to improve treatment through physiotherapy. *Methods* A biomechanical analysis of 5 young adults (21.2 ± 1 year old) with a history of an ankle injury and 4 young adults (21.5 ± 1 year old) with a history of a knee injury was carried out under two different conditions: a 'standard walk' and a walk along an adverse camber. This was compared with data obtained from 11 young adults (22.3 ± 1 year old) under the same conditions. All participants were equipped with the PlugIn Gait Lower Limb reflective marker model and were given time to become familiar with the feel of the markers before data was recorded. Anthropometric data was also collected from the participants to provide a depth and understanding required during the analysis of the results. All results were obtained at the University of Sheffield Motion Capture Laboratory in March 2024. From the data collected, MATLAB was used to process the kinematic data to calculate variables such as margin of stability, joint range of motion and various spatiotemporal parameters. *Results* Injured participants underwent longer double stance compared to the control group on the standard walk (21.1%, 19.9% and 18.3% respectively) and on the camber walk (24.3%, 25.1% and 22.6% respectively). There were also differences in margin of stability between the participant groups, showing greater maximum stability in the injured participants, but lower minimum and average stability also. It was also seen that range of motion was impacted in the injured participants with a decrease in knee flexion of approximately 6° when compared to the control group. *Conclusion* The results show that previously injured participants prolong their double stance in order to have more control over their CoM and hence stability. Other gait parameters, such as range of motion, are seen to change within the injured groups, showing that as a result of injury, humans can adopt altered gait patterns for years after injury. Furthermore, this study shows that walking speed and stride length do not vary and therefore are not the impacting factor on dynamic stability, contrary to some previous studies. The exact reasons for the differences in stability are unclear and require further research.

Experimental simulation of the natural shoulder joint.

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Objectives The rotator cuff muscles surround the glenohumeral joint to prevent dislocation and allow movement. Tears of the rotator cuff tendons are common and surgical treatments often lead to unsatisfactory results. Development of surgical repair techniques are limited by a lack of appropriate functional pre-clinical testing, especially over extended motion cycles [1]. The objectives of this study were to: - Develop a novel human shoulder simulator capable of producing repeatable controlled movements over extended motion cycles. - Assess changes in muscle forces between an intact rotator cuff, a supraspinatus tear and a double row repair of the supraspinatus tendon. *Methods* A shoulder simulator was developed which applied controlled movements/displacements to tendons of a cadaveric human shoulder to produce cyclic abduction and flexion motions representative of normal shoulder function (consent for research under HTA license 12279). The resultant force applied to each tendon during the cycles was measured. Braided polyethylene thread was secured to tendon ends (supraspinatus, infraspinatus, subscapularis, teres minor, anterior and middle deltoid) using a modified finger trap suture. Eyelet screws were attached to the scapula to act as pulleys and maintain the line of action of the muscles. Forces applied by the stepper motors were measured using a custom load measurement platform and a compression load cell. Three cadaveric samples, treated with the saturated salt solution method were used and tested in an intact state, 50% tear of the supraspinatus tendon, 100% tear and a double row tendon repair performed by a consultant surgeon. At each state the shoulder underwent motion cycles of 0-50° abduction and 0-45° flexion in the simulator and the force required in each muscle was recorded. *Results and Discussion* The force was recorded in each muscle throughout the cyclic motion for each condition. For all conditions, force magnitude in all muscles decreased during the initial six cycles to plateau, force in each muscle then remained similar throughout the remaining cycles. Three human cadaveric samples were available for the study, upon dissection, one sample was found to have a large degenerative tear of the supraspinatus tendon. Consequently two samples were suitable for use in the second objective. The supraspinatus muscle initiated the abduction motion followed by the deltoid muscles as supported by literature [2]. When the supraspinatus tendon was torn, force in the supraspinatus tendon decreased and this was compensated by additional force in the anterior deltoid muscle. The total magnitude of force within all the muscles increased when the supraspinatus was torn suggesting a higher level of joint instability. After a double row repair of the supraspinatus tendon, the force in the supraspinatus tendon increased and surpassed the magnitude observed during intact condition tests. *Conclusions* The study indicated that successful cyclic testing of cadaveric samples could be achieved using the novel shoulder simulator to obtain repeatable force data through abduction and flexion motions. The difference in muscle forces and contributions during sequential injury and repair states was studied in two cadaveric samples, and observations were similar to those seen clinically.

Minimal consideration of rehabilitation in randomised trials of stem cell interventions for tendon injuries could affect clinical outcomes: a systematic review using the TIDieR framework

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BACKGROUND. Mesenchymal Stem Cell (MSC) interventions are a new frontier in the clinical management of tendon injury. In terms of tissue repair and regeneration, both tendon cells and stem cells are mechanotransductive, i.e. they require mechanical stimulus, it therefore follows that well-structured post-intervention rehabilitation is needed to support MSC interventions and should be well considered in MSC clinical trials. This review evaluates the completeness of reporting of rehabilitation following MSC interventions or tendon pathology in clinical trials. *METHODS*. A systematic review of randomised controlled trials was conducted in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and using the Template for Intervention Description and Replication (TIDieR) framework. We applied a PICO framework to inform our search strategy to find clinical trials that used either bone marrow or adipose-derived MSCs as an intervention on human tendons. Electronic searches were conducted in Medline, PubMed, CINAHL and SPORTDiscus, from inception to 12th May 2024 with additional manual citation searching of included studies. MeSH terms and Boolean operators were employed, with English language the only additional filter. Two investigators independently screened by title and abstract and reviewed full texts. Data was extracted to complete the TIDieR checklist separately by three researchers and cross checked by a third to ensure consistency. The Cochrane risk of bias tool was employed to review trial internal validity. *RESULTS.* The search returned 142 articles. Following removal of duplicates, 118 papers were evaluated against the inclusion criteria. Eight RCTs were included, comprising five in rotator cuff pathology and individual trials in Achilles, gluteal and patellar tendinopathies. Various MSC preparations were utilised and reported, however the accompanying rehabilitation framework was poorly described with a mean TIDieR score of 2.375 ± 2.56 points (of a maximum of 12). The maximum score was 6/12 for a single trial, while 3 scored 0/12. There was large variability in rehabilitation reporting, however 'why', and 'where' domains were reported in only 1 study, with 'tailoring', 'modifications', 'adherence' and 'fidelity' TIDieR domains not reported in any trial. The included studies demonstrate a high risk of bias. Concerns regarding participant randomisation, participant blinding and group allocation were common across the included studies. CONCLUSIONS. Current randomised controlled trials demonstrate a poor standard of reporting of physical rehabilitation following MSC interventions for tendon pathologies, and highlight the lack of consideration given to post intervention loading. This highlights an opportunity for a reviewed approach to clinical trial intervention design in this area, incorporating loading parameters and rehabilitation.

Early versus delayed weight-bearing following operatively treated ankle fracture (WAX). A randomised controlled trial and health economic evaluation

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Objectives: After surgery for a broken ankle, patients are usually instructed to avoid walking for six weeks (delayed weight-bearing). Walking two weeks after surgery (early weight-bearing) may be a safe and preferable rehabilitation strategy. This study aimed to determine the clinical and cost-effectiveness of an early weight-bearing strategy compared to a delayed weight-bearing strategy. Methods:A pragmatic, multicenter, randomised non-inferiority trial including 561 participants (aged ≥18 years) who received acute surgery for an unstable ankle fracture in 23 UK NHS hospitals assigned to either a delayed weight-bearing (n=280) or an early weight-bearing rehabilitation strategy (n=281). The primary outcome was ankle function measured using the Olerud and Molander Ankle Score (OMAS) at 4 months post-randomisation. Secondary outcomes included health-related quality of life, complications, and cost-effectiveness. Results: Primary outcome data were collected from 86% (n=480) of participants. At 4 months post-randomisation, the mean OMAS score was 65·9 in the early weight-bearing and 61·2 in the delayed weight-bearing group; adjusted mean difference 4·47 95% confidence interval (CI) 0·58, 8·37; p=0·024 in favour of early weight bearing. Complications were similar between groups. The mean costs from the NHS and personal social services perspective in the early and delayed weight-bearing groups were £725 and £785 respectively (mean difference £-60 (95% CI -£342 to £232)). The probability that early weight-bearing is cost-effective exceeded 80%. Conclusions: An early weight-bearing strategy was found to be clinically non-inferior and highly likely to be cost-effective compared to the current standard of care (delayed weight-bearing).

Session 2: Mechanobiology

The effects of decellularisation process optimisation on the structure-function relationship of tendon comparing 4-day and 26-day processes.

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Objectives: Rupture of the anterior cruciate ligament has an annual incidence of approximately 80 per 100,000 in the general population [1]. Natural ACL healing is difficult to achieve and surgery is usually required with substitutes such as autografts or allografts. A biomaterial developed at the University of Leeds is a decellularised porcine tendon, where animal cells are removed to produce an immunologically compatible biological scaffold [1]. This decellularisation process is currently lengthy at 26 days and previous research studies have indicated it can alter the structure and mechanical properties of the tendon [1].The aim of this study was to determine if a shorter 4-day process reduces or eliminates any decellularisation mediated biomechanical changes compared to the more established 26-day process. Three groups of tendons (native unprocessed, 4-day and 26-day processed) were mechanically tested to determine their biomechanical properties. *Methods:* Porcine flexor tendons were harvested from 3-6 month old pigs (J. Pennys, Leeds), 1-3 days following sacrifice. The 26-day decellularised group were produced following a well-established process in our lab [1]. The 4-day process in brief, consists of shorter washes and replaces the acetone, antibiotic and peracetic acid treatment, with isopropanol. Decellularisation was validated using histological techniques (H&E and DAPI). Tendon groups (n=6) were subjected to stress relaxation and failure testing in tensile conditions using previous protocols [1]. A second order Maxwell-Weichert viscoelastic model was fitted to stress relaxation data to determine a time independent elastic modulus (E_0), time-dependant moduli (E_1, E_2) and relaxation times (τ_1, τ_2). The loading to failure determined the maximum force (P_{FAIL}), ultimate tensile stress (UTS), strain at maximum tensile (ε_{FAIL}) and displacement at fail (δ_{FAIL}). Fitting this data to a custom written Matlab programme [2], the toe and linear region modulus (E_{toe}, E_{linear}), and transition strain and stress (ε_T, σ_T) were also found. Data was analysed by one-way ANOVA using the Tukey method to determine significant difference ($p<0.05$). *Results:* H&E and DAPI found the 26-day group had no indication of remaining cellular material. The 4-day group were predominantly clear with some evidence of residual material around the perimeter of the tissue. The mechanical properties found to significantly differ between the 26-day group and native group were E_0, E_1, E_2 and τ_2 for stress relaxation testing and P_{FAIL}, UTS, E_{linear} and ε_T for failure testing. Between 4-day and native group, significant differences were determined for E_1 and E_2 under stress relaxation and E_{linear} for failure testing. Between 4-day and 26-day group, significant differences were determined for E_0 and τ_2 during stress relaxation, whereas no differences during failure testing. *Conclusions:* A 4-day decellularisation process better maintains the tensile and viscoelastic properties of the native tissue indicating a reduction in alterations to the extracellular matrix. Future work includes DNA quantification to confirm sufficient nuclear material has been removed from the 4-day group and atomic force microscopy to confirm the reduction in structural alterations. [1] Solis-Cordova, J. et al. J Mech Behav Biomed Mater. 2023, 139(105671), [2] Herbert, A. et al. J. Biomech. 2016, 49(1607-1612)

Effects of Mechanical Loading on Lacunae Morphology across Enthesis Calcified Fibrocartilage

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Introduction: The calcified fibrocartilage (CFC) of the enthesis is considered as a transitional zone where tendon collagen fibres merge with the mineralised tissue. Understanding the morphometry of CFC lacunae is crucial for elucidating its biomechanical properties, response to mechanical stimuli, and insights into underlying reasons for degeneration and inflammation progression at the tendon-bone interface. Existing research suggests that mechanical loading influences the structure of entheseal tissue [1-2]. However, the specific effects of mechanical load on CFC lacunae morphology is not understood. *Objectives:* This study aims to investigate the full field lacunae size, shape, and angle within CFC and how these change under in-situ uniaxial tensile testing. *Methods:* Achilles tendon attached to the calcaneus were dissected from euthanised 8 months old male mice (ethical approval 2022-104588). *In-situ* µCT (Versa 610, Zeiss) tensile testing was performed with 4X optical magnification, 1.3 µm pixel size, and 1601 projection number. The tendon's tensile axis was aligned to the calcaneus axis. Samples were scanned once in unloaded condition and then at 4.5N uniaxial load corresponding to physiological range (Deben CT500, Deben Ltd, UK). Images were rigidly registered (Avizo, USA). Tomograms before and after load were scaled using HA phantom to match the intensity histograms and the lacunae network was extracted using interactive thresholding. Morphometry parameters including Lacunae Volume (Lc.V), number (Lc.N), Stretch (Lc.St), and angle (Lc.θ) were calculated (XamFlow, Lucid AG, Switzerland). *Results:* µCT 3D tomograms showed the distribution of lacunae volume ranging between 50 and 1000 μm^3, with higher volumes predominantly concentrated in the central areas of the CFC. Before applying the tensile load, lacunae below 300 μm^3 were round with value between 0 to 0.5, and as the volume increased, the lacunae became more oval and stretched (value between 0.5 to 1). After loading, larger lacunae were mostly between 0.4 to 0.6. The angle of lacunae with respect to the coronal plane had the highest frequency between 45 and 75 degrees, which increased after loading to 55 and 90 degrees. *Conclusion:* µCT tomograms, combined with morphometry analysis, were employed to capture lacunae characteristics under both unloaded and loaded conditions. The study revealed that larger lacunae within CFC undergo shape and angle alterations, highlighting the adaptation process in response to physiological loading conditions. Lacunae morphology transitioned from predominantly circular to increasingly elongated shapes as their size increased. However, after loading, the larger lacunae exhibited a transition from elongated towards spherical Furthermore, alterations in lacunae orientation after loading were observed, with a notable shift towards higher angles with respect to the coronal plane. However this is dependent on the angle of loading. *Acknowledgement:* This research has been funded by Faculty of Technology University of Portsmouth and Carl Zeiss Microscopy. *References:* 1- Benjamin et al., J of Anatomy, V. 208 (2006) 2- Sang et al., J Mech Behavior of Biomedical Materials, V.135 (2022)

Metaphyseal trabecular bone separation is bimodal

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Introduction/Objectives Micro-computed tomography with morphometric analysis is the gold standard methodology for skeletal phenotyping of small animal models of bone disease. Metaphyseal trabecular bone is the most common site of assessment. The 2010 guidelines for the assessment of bone microstructure recommend a minimal set of parameters to be reported: bone volume fraction (BV/TV), trabecular number (Tb.N), thickness and separation (Tb.Sp). We use three osteoporosis models (rat spinal cord injury, mouse ovariectomy and mouse ageing) to demonstrate metaphyseal Tb.Sp is bimodal both in the femur of the tibia. We propose that metaphyseal Tb.Sp should be reported as two distinct values, preliminarily named $Tb.Sp_1$ (representing thickening/thinning of trabeculae) and $Tb.Sp_2$ (representing loss of centrally located trabeculae).MethodsBV/TV, Tb.N and Tb.Sp analyses were performed on metaphyseal trabecular bone VOIs. The outputs from Tb.Sp analysis are the volume-weighted average Tb.Sp, Tb.Sp histogram, and Tb.Sp dataset. Metaphyseal Tb,Sp histograms appeared bimodal (or multimodal), which is particularly clear in osteoporotic datasets. A global threshold (350µm) was applied, separating the two peaks in the distribution, enabling the acquisition of $Tb.Sp_1$ and $Tb.Sp_2$ VOIs. The $Tb.Sp_1$ (or Tb.Sp2) VOI was applied to the original dataset and the Tb.Sp analysis was rerun, generating results for $Tb.Sp_1$ (or $Tb.Sp_2$) . Results For the age-induced osteoporosis datasets (14-, 36- and 62-weeks-old), a monotonic decrease in BV/TV and Tb.N, and increase in Tb.Sp was observed ($p < 0.01$) confirming age-induced osteoporosis. Tb.Sp histograms were multimodal. Segmenting the Tb.Sp dataset based on sphere diameter enabled the distinction of effects due to intra-trabecular thinning (first peak) captured by $Tb.Sp_1$, from those due to complete resorption of centrally-located trabeculae, which widens the metaphyseal marrow cavity, captured by $Tb.Sp_2$. All 3 types of Tb.Sp were different ($p<0.01$), indicating that both trabecular thinning/thickening and marrow cavity expansion contribute to Tb.Sp. In the 62-weeks-old dataset $Tb.Sp_2$ became dominant. Similar results were observed for ovariectomy and spinal cord injury models. Conclusions We envision that this methodological update will enable a more sensitive distinction of skeletal phenotypes.

Mechanisms of Relaxation and Creep in a Bovine Intervertebral Disc – An Experimental and Computational Study

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Objectives - Degeneration of the intervertebral discs (IVDs) is one of the major causes of back pain. The viscoelastic properties of the IVDs are critical to their biomechanical function. While experimental and computational studies have examined the relaxation and creep behaviour separately, comparison of viscous responses remains unexplored. This study aims to compare the viscous response of IVDs subjected to relaxation and cyclic loading experiments and to determine if one loading protocol can capture both behaviours. Methods - Eight bovine caudal bone-disc-bone (BDB) units obtained from the agrifood industry were dissected and imaged using computed tomography. Axial compressive relaxation followed by cyclic loading experiments were conducted in a PBS fluid bath after the BDBs were held under a load of 40 N for 12 hours. For relaxation, a 10% axial compressive strain was held for 60 minutes. The BDBs were then subjected to cyclic axial compression for 1,000 cycles at 1 Hz, with load limits based on applied pressures of 0.75 MPa and 0.5 MPa and the stiffness over the loading part of each cycle was extracted. Generalized Maxwell and Voigt models were fitted onto respectively the stress-relaxation data, and the cyclic stiffness data, each capturing the viscous behaviour with two time constants. The short and long time constants of each rheological model were compared with either a paired t-test or a Wilcoxon signed-rank test ($\alpha = 0.05$) depending on normality (Shapiro-Wilk test). Hyper-viscoelastic IVD-only FE models were developed using Abaqus (v. 2022, Dassault Systèmes, France), with simplified specimen-specific geometries and boundary conditions replicating the in-vitro protocol. The material parameters of the annulus (anisotropic hyperelasticity coupled to a viscous model with two time constants) were calibrated against the relaxation force data and then used to model the rest of the in-vitro protocol, to evaluate the difference between computational and experimental cyclic response. Results - No significant differences were present between the short time constant of the Maxwell and Voigt models (p-value = 0.4235, t-test), with a short response time of 70 ± 13s. However, differences were present in the long time constants (p-value: 0.0078, Wilcoxon test), with the cyclic behaviour exhibiting a faster viscous response (1067 ± 152s vs 4542 ± 1728s). Following calibration from the relaxation data (resulting in error of 4 ± 3%), the FE models were not able to capture the cyclic behaviour (difference in cyclic stiffness of 46 ± 10%). Conclusions - The short time constant of both loading cases relates to the rapid viscoelastic response of the IVD, which exists regardless of loading protocol. The long time constant however captures different mechanisms during different loading conditions, likely representative of the differences in fluid flow within the tissue: continuous outwards flow in relaxation and alternating flow in cyclic loading with gradual variation in the flow with cycles. The differences were also evident in the FE simulations, where relaxation-calibrated parameters could not accurately capture cyclic behaviour. This indicates that material properties of the IVD depend on the loading type and constitutive properties calibrated or validated for different contexts respectively are not interchangeable.

Session 3 – Clinical studies

TLICS: Reliable In the hands of Pre-registrar clinicians?

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Objectives The Pre-registrar tier in the Trauma & Orthopaedic department is often the first point of contact for patients with thoracolumbar fractures. Fracture classification systems aim to standardise decision-making and optimise clinical care, particularly benefiting clinicians with infrequent exposure to such pathology in a non-specialist centre. This study aims to assess the inter-rater reliability and usability of the Thoracolumbar Injury Classification and Severity Score (TLICS) by non-experts.

Methods

Twenty clinicians working in the pre-registrar tier in South Yorkshire trauma and orthopaedic departments were recruited. Participants were asked to retrospectively review anonymised imaging of 25 trauma patients and score the fractures using the TLICS system. The TLICS scores were categorized into three groups: <4 (non-operative), 4 (indeterminate), and >4 (operative). Inter-observer reliability was calculated using the Fleiss-Kappa statistic and assessed against the Landis and Koch criteria.

Results

The overall TLICS scoring demonstrated an inter-rater reliability coefficient of 0.49 - moderate reliability according to the Landis and Koch criteria (P<0.001; 95% CI 0.47 to 0.51). Morphology, 0.36 (P<0.001; 95% CI 0.34 to 0.38) and posterior ligamentous complex (PLC) disruption 0.39 (P<0.001; 95% CI 0.37 to 0.41) had the lowest reliability with neurology, 0.92 (P<0.001; 95% CI 0.90 to 0.94) the highest.

Conclusion

The TLICS classification demonstrates moderate reliability when used by pre-registrar clinicians. Neurology status subcategory showed almost perfect agreement, with morphology having the lowest inter-rater reliability.These findings suggest the use of this scoring system is of some benefit, however moderate reliability is not appropriate when deciding management plans for such patients. Based on a previous study demonstrating improved reliability with senior clinician input, we advocate for early involvement of senior non-specialist clinicians.

A Transgluteal Approach to the Hip Which Preserves Abductor Function and Maintains a Low Dislocation Rate - A Retrospective Study of Short and Mid-term Outcomes

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Objectives: A modified Transgluteal Approach (TGA) in Total Hip Arthroplasty (THA) can be utilised to preserve abductor muscle function and reduce dislocation rate. We present a study evaluating outcomes for modified TGA using a validated patient reported outcome measure (PROM) tool, the Oxford Hip Score (OHS). Methods: This was a retrospective single centre study over a four-year period. Short term data was collected including intra-operative and post-operative complications, length of stay (LOS) in hospital and time from operation to mobilising independently. One year data was collected including plain radiograph findings and Trendelenburg gait. Patients were contacted at a mean time of 2.7 years post-operatively to conduct an OHS. Results: A total of 100 patients were identified within the inclusion criteria. Mean LOS for all patients was 2.8 days. Mean time from operation to mobilising independently without walking aids was 4.9 weeks. At one year follow-up there was satisfactory radiographic assessment in 100% of patients. The mean OHS was 45.5 at 2.7 years, indicating satisfactory joint function in all patients. Conclusion: This study supports the use of the modified TGA in THA, with favourable outcomes of time from operation to cessation in use of walking aids, LOS and OHS. We report zero cases of Trendelenburg gait at one year follow-up and no dislocations at three year follow up. Further studies are required comparing outcomes of TGA to other approaches in THA.

Joint awareness, function, and pain measures characterise 70% of the variance in 29 knee arthroplasty outcome measures: A principal component analysis

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Objectives: To identify and categorise a reduced set of meaningful outcome measures, by examining and attributing the total variance within the multiplicity of questions in patient reported outcome measures (PROMs) through principal component analysis. *Methods:* A dataset comprising 841 unilateral TKAs performed between 2021 and 2022 at the Golden Jubilee National Hospital with complete six-week and one-year post-operative patient-reported outcome measures (PROMs) was collected retrospectively. Principal component analysis was used to identify the components necessary to explain 60-70% of variance within the 29 variables of the Forgotten Joint Score (FJS), Oxford Knee Score (OKS) and EuroQoL five-dimension health questionnaire (EQ5D-5L). A variable was considered to meaningfully contribute to a component if the magnitude of its load was at least 0.5. *Results:* In the cohort, 431 (51. 2%) of the patients were female and 391 (46.5%) of patients were less than 70 years old. The cohort mean (SD) age was 69.8 (8.7) and mean (SD) BMI was 31.4 (4.8). The BMI distribution was: normal weight - 76 (9%), over-weight - 270 (32.1%), obese class I - 292 (34.7%), obese class II - 168 (20%) and obese class III-35(4.2%). Three principal components explained 61.6% of the variance in the six-weeks' data while two

components explained 67.5% of variance in the one-year data. However, for further comparative analysis, three components accounting for 70.5% of variance were extracted for the one-year data. The first principal component was categorised as a construct for "joint awareness" having all the subscales of the FJS loading saliently on it. Consequently, it can be considered equivalent to the FJS and it explained 48% and 58% of variance in six-weeks and one-year data respectively. The second and third principal components can be categorised as "function" and "pain" components accounting for 9% and 4% of variance for six-weeks data and 9% and 3% for one-year data, respectively. Cross-loadings were observed on the function and pain components particularly from OKS subscales indicating some overlap between pain and function. OKS-2 (washing) and OKS-3 (transport) loaded saliently on the function component in both 6-weeks and one-year data and only OKS-8 (night pain) loaded saliently on the pain component. The remaining OKS subscales cross-loaded on function and pain components. Moreover, OKS-7 (kneeling) showed inconsistency in its cross-loading at the different time-points (on pain and function at 6 weeks, on function and joint awareness at one-year). Also, the communality values of OKS-7 (kneeling) were particularly low in both six-weeks (0.269) and one-year (0.397) data. All EQ5D-5L subscales loaded saliently on the function component (2nd principal component) in the six-weeks data (except EQ-5D pain/discomfort which loaded on the pain component) and one-year data. *Conclusion:* Three principal components can explain up to 70% of the variance in 29 PROM scores and were categorised as "joint awareness", "function" and "pain" components. The FJS has clearly provided additional value in the assessment of patient outcomes, its contribution has been validated by this analysis and supports ongoing collection.

Identifying effective interventions to maintain bone health in lower limb amputees

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OBJECTIVES Bone mineral density (BMD) loss was identified in a cohort of highly active veteran lower limb amputees [1], with above-knee amputees more severely affected. It was also observed that BMD decreases were not systemic but occurred predominately on the amputated-side proximal femur, with minimal changes in the spine. We hypothesise this occurs due to reduced mechanical stimulus to the amputated femur. To explore this, a combined musculoskeletal (MSK) and finite element (FE) modelling framework, with an iterative strain-driven bone adaptation algorithm [2], was utilised to predict bone remodelling of an above-knee amputee (AKA) and a through-knee amputee (TKA) compared to an able-bodied (control) subject. METHODS OpenSim MSK models of each subject were adapted from the London Lumbar Spine Model (LLSM) [3] and used to simulate five common daily activities (walking, stand-to-sit, sit-to-stand, stair-ascending, and stair-descending). The muscle forces and joint forces being exerted onto the intact and amputated femurs were calculated and exported into Abaqus FE models for bone adaptation simulations. A strain-based bone adaptation algorithm [2] was

used to predict changes in cortical bone thickness and trabecular bone Young's modulus (related to BMD) in response to the altered mechanical stimulus created by the loading envelope produced by daily activities of control, TKA and AKA subjects. RESULTS The amputated-side hip joint contact forces and muscle forces of AKA were lower than those of the control subject for all five activities. However, the amputated-side hip joint contact force of TKA was found to be higher than the control subject for stair descent with higher gluteus and re-attached bicep femoris muscle forces. TKA also generated hip joint forces closer to the control during walking activity, though for sit-to-stand and stand-to-sit activities, the amputated side leg was unfavoured, like the AKA subject. In agreement with clinical studies [1, 4], the FE models predicted BMD loss, with reduced cortical thickness in the diaphysis and reduced Young's modulus in regions of trabecular bone in the proximal femur for both AKA and TKA, though to a lesser extent for TKA. CONCLUSIONS The altered and asymmetric loading supports the hypothesis in our previous study [1] that localized BMD reduction in lower limb amputees is associated with reduced mechanical stimulus. AKA was more susceptible to disuse osteopenia due to the lack of end loading on the femur. TKA, despite preservation of end loading, indicated BMD loss due to reduced mechanical stimulation caused by the loss of muscles crossing the knee joint. The developed modelling framework will underpin future work investigating possible effective interventions such as socket design modifications such as the introduction of controlled end loading and reduction of ischial containment for AKA, as well as direct fixation, and tailored activity regimes to prevent and mitigate localised bone degradation in amputee populations. REFERENCES 1. McMenemy L et al., J Bone Miner Res, 38:1227-1233, 2023. 2. Phillips et al., IntBiomech, 2:43-61, 2015. 3. Favier et al., Comput. Methods Biomech. Biomed. Engin., 24: 1310-1325, 2021. 4. Sherk et al., Bone Miner Res 2008;23:1449–1457.

Lifetime Cost-per-QALY of Primary and Revision Total Knee Arthroplasty: A Markov Model and Empirical Analysis

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BACKGROUND. Revision knee arthroplasty is generally considered a costly and complex intervention that requires considerably more resources than the index surgery, however the cost-effectiveness is largely unknown as few studies have detailed change in health-related quality of life following revision TKA, and scant data exists for QALY gain or cost-per-QALY following revision TKA. There is no cost-per-QALY data available as to cost-effectiveness of primary and revision procedures from the same institution with consistent populations and cost bases. *METHODS.* Local ethical approvals were obtained and data were retrieved for all primary and revision TKA procedures performed at a tertiary Swiss hospital between 2006 and 2019. Patients were identified as primary or revision total knee replacement with the revision group further sub-divided based on 1 or 2-stage procedures. EQ-5D questionnaire data were available at pre-operative and 1-year post-operative timepoints. A Markov model was created to evaluate revision risk and we calculated lifetime QALY gain and lifetime procedure costs through

individual EQ-5D scores (based on the German reference value set), individual hospital costs, national life expectancy tables and standard discounting processes with 3% rates. Cost-per-QALY gain (reported in Euro) was calculated for primary and revision procedures, based on the means of QALYs gained and lifetime cost. All hypotheses were tested on a 0.05 significance level *RESULTS.* 1-year post-operative EQ-5D data were available for 1.343 primary and 103 revision procedures. Mean age was 69.36 ± 9.70 for primary TKA and 67.97 ± 10.29 for revision TKA. Mean BMI was 29.24 ± 5.66 for primary TKA and 29.31 ± 6.16 for revision TKA. 60.8% of the primary TKA group and 61.3% of the revision TKA group were female. Clinically and statistically significant increases in EQ-5D utility value were observed following surgery in both primary and revision groups ($p<0.001$) and also in both revision subgroups ($p=0.001$). The improvement in EQ-5D following primary TKA was greater than following revision TKA ($p=0.007$). No difference was found between the increase in EQ-5D scores between the two revision subgroups ($p>0.05$). Lifetime cost differences between primary and revision TKA, as well as between the revision subgroups were significant ($p<0.0001$). Significant QALY gains were seen following surgery in all cases. Similar, but significantly more QALYs were gained following primary TKA (5.67 ± 3.98) than following revision TKA (4.67 ± 4.20), $p=0.014$. Cost-per-QALY was €4686 for primary TKA and €10,364 for revision TKA. The highest average cost-per-QALY was seen in two-stage revision TKA (€12,292), followed by one-stage revision TKA (€8,982). *CONCLUSIONS.* Primary and revision TKA are highly effective for the patient in terms of improved HRQoL, and highly cost-effective for the healthcare system in terms of cost-per-QALY gained. The €4,686 cost-per-QALY estimate for TKA, which incorporates future revision costs, highlights the value of this procedure. The cost of achieving the HRQoL gain in revision knee arthroplasty was 2-3 times that of primary knee arthroplasty. The €10,364 cost-per-QALY estimate for revision TKA is 121% more than that of primary TKA, however substantially below international cost per-QALY threshold values

Revision For Dislocation and All-causes Following Primary Total Hip Replacement Using 36-mm Versus 32-mm Femoral Heads on Polyethylene Liners: A Systematic Review and Meta-Analysis

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Background: Use of a 36mm femoral head in primary total hip replacement (THR) theoretically offers a wider impingement-free range of motion and reduces the risk of dislocation. However, concerns exist regarding its potentially greater impact on polyethylene wear and associated aseptic loosening, liner fracture, and head-neck taper corrosion. This systematic review and meta-analysis aims to compare the risk of revision for dislocation and all-causes when using 36mm versus 32mm metal or ceramic femoral heads with polyethylene liners for primary THR. Methods: Medline, Embase, Web of Science, and Cochrane Library were searched for relevant studies. Random effects meta-analysis was performed. Sensitivity analysis was conducted, limiting to THR performed for osteoarthritis and using cross-linked polyethylene liners, or statistically adjusting for this factor. Results: Four observational studies and two registry reports were identified. Median follow-up ranged from 2.1±4.7 years (inter-quartile range values 0.9±7.7 years). The primary analysis demonstrated that 36mm heads were associated with a reduced risk of revision for dislocation (HR 0.78, 95%CI 0.68±0.90, p< 0.001; n=241,136) but an increased risk of all-cause revision (HR 1.10, 95%CI 1.03±1.17; p=0.004; n=942,617). However, the sensitivity analysis demonstrated no significant differences in all-cause revision (HR 1.02, 95%CI 0.91±1.15, p=0.74; n=284,591) and found similar results for revision for dislocation (HR 0.78, 95%CI 0.67±0.90, p< 0.001; n=236,106). Conclusions: Compared to 32mm heads, 36mm heads resulted in fewer revisions for dislocation. However, this did not lead to a reduced risk of all-cause revision. In the main analysis, this discrepancy may be due to confounding factors. In the sensitivity analysis, this may be due to an insufficient protective effect to influence a change, given that revision for dislocation constitutes a small proportion of revision indications. Alternatively, there may have been a greater proportion of revisions performed for other indications in the patient group with 36mm heads.

Session 4 – Biomechanical Modelling

Intra-rater Repeatability and the Confidence of True Change for Spinal Measurements Taken From 3D EOS Models

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Background: EOS bi-planar x-ray imaging allows 3D reconstructions of the spine and pelvis, providing 3 planes of segmental vertebral measurements from a postural neutral pelvis. This study assesses the repeatability of measures and the confidence in defining true measurement changes. Methods: 20 patients were included. Patients were retrospectively identified from 4 clinical backgrounds (surgical threshold, bracing threshold, micro-dose and in-brace). Bi-planar spinal EOS scans were modelled using the "full spine" protocol and then re-modelled after a minimum of 4 weeks by the same researcher. All 3D measurements were recorded and compared. Results: Time between modelling averaged 6.7 weeks. Paired measures showed low risk of bias for all parameters ($p>0.05$) apart from the thoracic (Spearman's=0.67; $p<0.05$) and lumbar (Spearman's=0.40; $p>0.05$) plane of maximal curvature (PMC). Interclass correlation coefficients (ICCs) showed excellent agreement. Thoracic and lumbar Cobb angles averaged 0.989. Sagittal measurements ranged from 0.926 (L1/S1 Lordosis) to 0.962 (T1/T12 Kyphosis). Pelvic parameters ranged from 0.875 (obliquity) to 0.994 (tilt). The transverse profile ranged from 0.817 (apical thoracic rotation) to 0.977 (average lumbar rotation). The technical error of measurement (TEM, 1SD measurement error) for both Cobb angles was ± 4.4 degrees. The sagittal profile averaged ± 7.7 degrees. Pelvic parameters averaged ± 5.0 degrees. The transverse profile had a TEM of ± 4.8 degrees whilst the automated thoracic and lumbar PMC averaged ± 100.4 degrees. Discussion: Spinal 3D EOS measurements show excellent intra-rater repeatability with a considerable "true" measurement error. Repeatable measurements of the segmental and global vertebral rotation, from a neutral pelvis, are historically often difficult on plain x-ray. Furthermore, semi-automated modelling provides quick measurements of the 3D spinal alignment. Furthermore, this is the first paper to report the TEM for 3D EOS models. The TEM should be used to build future definitions and compare confidence in true changes once modelling has occurred. The PMC shows unacceptable levels of disagreement warranting further discussion and research.

Impingement in Dual Mobility Hip Joint Replacement according to ASTM F2582:2020

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Objectives: The aim of this study is to evaluate the consequences of impingement in dual mobility (DM) hip replacement systems using the guidelines established in ASTM F2582:2020. Impingement between the femoral neck stem and acetabular liner and/or shell can occur in total hip replacement due to various factors such as patient anatomy, surgical positioning, or implant design. The study also focuses on understanding the damage mechanism that occurs due to impingement in a scenario where the polyethylene mobile bearing becomes fixed. Methods: Dual mobility bearings, consisting of CoCr head tapered locked on a titanium femoral stem and articulating against polyethylene mobile bearing, and in turn articulating against modular CoCr liner taper-locked in a titanium acetabular shell or a monobloc stainless steel acetabular cup, were used in this study. The multi-station electromechanical ProSim simulator was used to simulate a scenario where the mobile polyethylene bearing gets restricted and impingement between the femoral stem neck and the polyethylene bearing occurs (Figure 1a). Two designs with three different sizes were use (n=6 each). The multi-station AMTI VIVO simulator was used to simulate another scenario where the femoral stem makes contact of the acetabular cup rim and/or shell. Two designs with various combinations of stem materials and acetabular cup size was used (n=3 each). The standard requires test stations to be subjected to flexion / extension of 0°/ 10°, adduction / abduction of 0°/ 5° (from initial contact) and internal / external rotation of 5°/ 5° applied in a sinusoidal waveform about the centre of rotation of the machine and the articular bearing. A load of 600N was applied vertically through the acetabular cup at a frequency of 1Hz. The lubricant used was bovine serum (protein concentration of 30g/L). The temperature was maintained at 37℃ ± 2℃. Each test ran for a total of 1 million cycles undertaking qualitative assessment of the damage every 0.2 million cycles. Results: Crack initiation or fracture was observed on all aged conventional moderately cross-linked samples at the impingement site at 0.2 Mc, whereas there was no damage in the form of fracture or crack observed after 1.0 Mc for antioxidant polyethylene samples. All polyethylene components showed signs of wear and plastic deformation. The polyethylene MB samples had an increased lever-out torque after impingement compared to non-impingement baseline. For impingement between the femoral stem neck and the acetabular cup, the location and severity of damage on the femoral stem, metal liner, and metal shell was dependent on the acetabular cup size, femoral head offset and the design of the metal liner rim and the acetabular shell. The contact profiles of the acetabular portion of the test construct determined the damage profile on the femoral neck. The damage patterns observed where the acetabular liners were lipped cobalt-chrome alloy liners were observed to be deep, smoothed grooves into the femoral neck. Conclusion: Impingement in hip replacement can hold significant clinical consequences and this study present the different damage mechanisms that occurred on different design Dual Mobility components under these adverse conditions.

Wear of Antioxidant and moderately cross-linked Polyethylene in a Dual Mobility Hip bearings with addition of Third Body Particles

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Objectives: Previous retrieval analyses have indicated that the presence of third body particles can cause damage to the bearing surfaces in hip replacements. These particles can originate from various sources such as surrounding bone, bone cement, metal particles, or coating materials. In vitro studies have demonstrated that the addition of third body particles can lead to increased wear of the articulating surfaces and potentially compromise the integrity of the bearing surfaces. Therefore, this study aimed to compare the performance of the two materials, antioxidant and moderately cross-linked polyethylene, in the presence of adverse third body particle conditions. Methods: Two dual mobility systems (Johnson and Johnson MedTech, UK) were used: DM bearings consisting of CoCr head (28mm) articulating against antioxidant polyethylene mobile bearing (38/28 mm) and in turn articulating against modular CoCr liner, DM bearings consisting of CoCr head (36mm) articulating against antioxidant polyethylene mobile bearing (46/36 mm) and in turn articulating against modular CoCr liner, BI-MENTUM™ DM bearings consisting of CoCr head (28mm) articulating against moderately cross-linked gamma barrier polyethylene mobile bearing (40.5/28 mm) and in turn articulating against a monobloc stainless-steel shell. Al_2O_3 particles (50/50 weight % mixture of 60 and 80 grit) were embedded onto the inner and outer surfaces of the polyethylene mobile bearings. The size range of the particles (50-500µm) was representative of the third body particles found embedded in explanted polyethylene liners. the VIVO single station simulator (AMTI, USA) was used to embed the particles (2mg) applying a 1000N constant axial load and ±30° IE rotation to the intended bearing surface for 20 cycles at 1Hz. The same femoral heads and acetabular cups used during the particle embedment were used during the wear simulation. The components were tested under standard gait (n=5, equivalent to ISO14242-1) in 25% bovine serum for six million cycles. The wear of the polyethylene bearing was assessed gravimetrically, and the mean wear rate determined (ISO14242-2). One way ANOVA was carried out with significance at $p<0.05$. RESULTS: The third body particles remained embedded for the duration of the wear test. The mean wear rates (±95% confidence interval) after six million cycles of test were as follows; antioxidant polyethylene mobile bearing (38/28 mm): 4.4 ± 1.6 mg/million cycles, antioxidant polyethylene mobile bearing (46/36 mm): 10 ± 3.2 mg/million cycles and, moderately cross-linked gamma barrier polyethylene mobile bearing (40.5/28 mm): 25 ± 10.5 mg/million cycles. The wear of antioxidant polyethylene material (for both sizes) was significantly lower ($p=0.001$) than the wear of moderately cross-linked polyethylene material under this adverse in vitro condition. Significant scratching was observed on the metal head and acetabular cups for both Dual mobility systems. There was no sign of cracking, fracture or delamination of either polyethylene materials. The serum lubricant turned black due to release of significant quantities of metal particles from the metal bearing surfaces. Conclusion: The antioxidant polyethylene material has shown superior wear performance in vitro compared to moderately cross-linked polyethylene under adverse third body particle conditions in a Dual Mobility system.

A cautionary tale in using inertial measurement unit-based wearables for the assessment of 3D pelvic orientation: An objective comparison against an optoelectrical motion capture system.

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Objectives: Inertial measurement unit (IMU) wearables are increasingly being used as a cost-effective practical method to measure patient biomechanics to inform preoperative planning of total hip replacement surgery. Tracking pelvic motion can provide information on patient-specific, dynamic orientation of the acetabular cup, affecting risk of implant edge loading, impingement, and dislocation. Pelvic tilt influences acetabular cup version angle [1] and has been quantified as a change of 2.5° to 5° of version for every 5° of pelvic tilt [2]. This study assesses the output of an IMU based wearable versus an optoelectrical motion capture system (MOCAP) when measuring 3D pelvic orientation during level walking in healthy participants. Methods: Three-dimensional pelvic orientation was tracked in six participants whilst they performed 10 repetitions of self-selected speed along a 7-meter level walkway, using two measurement methods simultaneously. A wearable sensor (G-Walk, BTS Bioengineering, MI, Italy) was positioned at the sacrum (top-edge of sensor aligned with line between left and right posterior superior iliac spines) as per manufacturers recommendations. The G-Walk recorded an aggregate estimate of pelvic orientation over the 7-meter walk. Thirty-six reflective markers were positioned on bony landmarks of the participants (in the CAST marker set) and 10 Vicon (Oxford, UK) MX cameras were used to track their motion. Pelvic orientation was calculated over a complete gait cycle (after 4th heel strike representing steady state gait). Two AMTI (MA, US) force plates were used to define heel strike. The protocol was performed again with three walk repetitions with the sensor repositioned approximately 2cm below, 2cm above and 4cm above the recommended position. Tape with marked horizontal lines, was positioned on the participants skin/clothing underneath the G-Walk to align it to the alternate positions and monitor movement between repetitions. Results: Agreement was shown between the Gait lab and G-Walk values for pelvic obliquity and rotation with mean RMSE (range) across all conditions being 3.04° (5.72°) and 2.45° (4.59°) respectively. Changing sensor height had little impact on pelvic obliquity and rotation estimation, range of mean RMSE of the 4 sensor position conditions was 0.87° and 1.47° respectively. Greater variability was seen in absolute pelvic tilt values with mean RMSE (range) being 6.40° (12.09°) and mean RMSE when the G-Walk was positioned at the recommended location, 2cm below, 2cm above and 4cm above, was 5.64°, 4.40°, 8.22° and 7.33° respectively. For two participants the mean RMSE when the G-Walk was positioned at the recommended location was 1.51° and 1.58°. Conclusions: Large variation in absolute pelvic tilt values may be caused by difficulty in associating the IMU to the pelvic segment as the sensor orientation in the sagittal plane is impacted by its position inferiorly and superiorly on the sacrum. The G-Walk is a convenient tool that when positioned correctly can measure absolute pelvic tilt to a satisfactory level of error when compared to MOCAP and so may aid in pre-surgical hip replacement planning. However, large errors in absolute pelvic tilt can occur and incorrect positioning can introduce bias. [1] doi.org/10.3390/bioengineering11020151 [2] doi.org/10.5301/HIP.2013.10715 Ethics: UoL.EPS.FREC.2024-1147.

Assessment of Fluid Ingress into the Graft-Host Interface of Osteochondral Autografts under Cyclic Loading in the Knee using a Porcine Model

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Objectives: Osteochondral grafts are used clinically to treat cartilage lesions, restoring surface congruency, with the aim of delaying the progression of osteoarthritis. One of the failure mechanisms of these grafts is the development of cysts in the graft-host interface. Ingress of synovial fluid into the graft-host interface has been theorized as contributing to the development of these cysts. The aim of this study was to develop an in vitro method to evaluate fluid ingress and graft subsidence using a porcine tibio-femoral model. *Methods:* Six porcine knees were used to develop a method. Specimens were prepared for testing by potting the femoral and tibial shafts in PMMA at full extension with the joint fully intact. Following dissection, two osteochondral autografts (10 mm long and 6.5 mm diameter), harvested from an unloaded part of the same femur, were implanted with an Acufex™ Mosaicplasty surgical toolkit (Smith and Nephew, MA, USA). One graft was implanted axially with the loading direction at the point of initial contact of the two bones ("test graft"); the other on an unloaded portion of the opposite condyle ("control graft"). Specimens were tested under a uniaxial cyclic loading regime replicating the axial load during normal walking (37° degrees, peak load of 1000N) to different numbers of cycles (2500, 5000 and 10000), using an ElectroPuls® E10000 (10 kN load cell, Instron, USA). The specimen was housed in a gaiter containing a contrast medium (0.8 mol solution of NaI in PBS). Fluid ingress was quantified by comparing the greyscale distribution across line profiles between CT scans collected before and following testing, using Simpleware ScanIP (2018.12, Synopsis, USA). Sensitivity tests were performed to determine the optimum number and location of line profiles to capture the ingress variation at six sites – two at each graft site ("graft-host interface" and "graft centre"), one through loaded bone ("loaded site"), and one through unloaded bone ("unloaded site"). *Results:* The results of the sensitivity tests indicated that 4 locations with 3 measurements at each site were necessary to determine ingress, and 5000 cycles was sufficient to see differences between sites. For two specimens tested to 5000 cycles, ingress was greater at the test graft sites (12.7 ± 1.8 mm for the test graft centre; 10.9 ± 1.9 mm test graft-host interface), than the control graft sites (7.8 ± 1.1 mm for the control graft centre; 8.4 ± 2.0 mm control graft-host interface), loaded site (9.0 ± 1.6 mm), and unloaded site (9.3 ± 1.6 mm). In some specimens, graft subsidence and micro-cracking was also detectable from the µCT images. The presence of osteochondral grafts lead to greater variation in measured fluid ingress. *Conclusions:* A new method was developed to evaluate osteochondral grafting in vitro, enabling subsidence and fluid ingress to be measured over multiple loading cycles. The method captures differences in fluid ingress at graft-host interfaces and through bone, and between loaded and unloaded sites, and can now be applied to examine the effect of clinically relevant variables such as graft oversizing, dilation, and drilling approaches.

Session 5 – Disease Pathobiology

Application of spatial transcriptomics to human osteochondral explants and intervertebral disc tissue to identify molecular pathways during disease.

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Objectives: Spatial transcriptomics holds potential to unravel the complex pathophysiology of diseases including osteoarthritis, and intervertebral disc degeneration. However, to date its application to these tissues has been limited to mouse and early human embryonic tissues. Application in the non-foetal human has been hampered by low metabolic activity of cells resulting in low transcriptional reads. The presence of calcified tissues necessitates the application of decalcification procedures which can further decrease RNA quality. Finally, such tissues are notoriously difficult to retain tissue attachment due to high proteoglycan content and tissue swelling during the procedures. These limitations have hampered the application of this technique to human cartilage, bone and intervertebral disc samples. Here, we describe an optimised and validated methodology to apply spatial transcriptomics to human bone, cartilage, and intervertebral disc samples. Methods: Osteochondral samples were collected from patients undergoing knee replacement, osteolytic bone samples from those undergoing revision hip surgery, and intervertebral disc samples from those undergoing discectomy for nerve root compression. Tissue samples were fixed in 10% neutral buffered formalin, and where bone was present decalcified in 20% EDTA in DEPC treated water until clear on µCT prior to embedding in paraffin wax using DEPC treated solutions. To confirm RNA integrity and quantity, RNA was isolated from 20µm sections using Qiagen RNA extraction kit for paraffin sections, and DV200 determined using an Agilent bioanalyzer. Tissue samples were selected based on DV200 and RNA quantity for spatial transcriptomic analysis. Adhesion of sections for spatial transcriptomics was optimised testing slide types, drying method and downstream transcriptomics protocol. Spatial transcriptomics was performed using 10x genomics Cytassit Visium v2 platform, and libraries sequenced by Novogene. The analysis pipeline was optimised using Spaceranger, Loupe Browser, and Seurat in R, a brain sample was analysed in parallel as a validated tissue. Results: Optimal methodology involved mounting 7µm paraffin sections using DEPC treated water onto Suprafrost Plus slides, drying at 37◦C for 48hrs, prior to room temperature silica gel container for 2 weeks. Spatial transcriptomics methodology was adjusted to decrease agitation during staining steps and careful application of all solutions to retain tissue adhesion. Analysis pipelines required manual tissue alignment using the 10x Loupe browser and manual spot selection to avoid folded or lifted tissue regions. Whist mean reads per spot within osteochondral, osteolytic membrane and disc samples were lower than brain tissues (Osteochondral samples: ~25; Osteolytic membrane: ~1000, Disc: ~150; Brain: 2,500), the total number of genes identified were similar (17,500-18,000 genes in all tissue types). The method was able to resolve genes that were spatially differentially expressed across all tissues, identifying between 3 and 7 differential cell clusters dependant on tissue type, with key differential genes identified between clusters (Figure 1). Conclusions: To the authors knowledge, this is the first report of the successful adaptation of 10x spatial transcriptomics to low transcriptomic and high extracellular matrix rich tissues including human bone, cartilage, and intervertebral disc samples.

Analysis is ongoing to investigate differential expression across pathophysiological status, and the network and pathways involved.

The lncRNA CASC20 influences differential gene expression during osteogenic differentiation

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Objectives/Background: CASC20 is a human-only long noncoding RNA hypothesised to play a role as a regulator of bone formation. CASC20 is expressed in human bone and is upregulated in BMP2-induced osteogenic differentiation, where it has been shown to increase the efficiency of differentiation into osteoblasts. A murine knock-in model of CASC20 was created to study its effects on gene expression during osteogenesis. Methods: Murine mesenchymal stem cells (MSCs) were transduced with either a CASC20-expressing lentivirus or a control GFP-expressing lentivirus. Cells were cultured for 0, 10 or 20 days in osteogenic media, plus BMP2, to induce osteogenic differentiation. After that RNA-sequencing was conducted, with biological replicates for each condition and time point. Transcriptomic analysis was performed on the sequencing output, using R. Differentially expressed genes (DEGs) were identified using DESeq2 and filtering for those with a p-adjusted value <0.05 and absolute log2 fold change of >0.5 or < -0.5. Gene ontology (GO) enrichment was performed to identify biological processes impacted in CASC20 overexpression versus control. Results: Differential expression analysis showed that the greatest differences occurred between timepoints, i.e. genes upregulated at day 10 or 20, compared to day 0. Additionally, separate clustering was observed between the control and CASC20-expressing samples. We identified 10, 379 and 11 DEGs for CASC20 overexpression versus control on day 0, 10 and 20, respectively. On day 10, the GO analysis suggested a role for CASC20 in splicing. The GO categories 'U2 snRNP', 'U2-type spliceosomal complex' and 'spliceosomal complex' were among the top 10 most significant, with p-adjusted values of 1.3 x10-4, 5.7x10-6 and 5.7 x10-6, respectively. The percentage of hits in these categories were 33.3%, 31.0% and 10.8%, indicating these categories were the most upregulated with CASC20 expression. Conclusions: As expected, day 10 showed the highest number of differentially expressed genes, due to the enhanced rate of osteogenic differentiation caused by CASC20. By day 20, it would be expected that cells under both conditions would have undergone osteogenic differentiation, and consistent with this, there were fewer genes showing differential expression. Further studies will include RNA-sequencing of human MSCs to determine whether a similar differential effect occurs with CASC20 over-expression. Also, the interactions of the transcriptome with microRNAs will be studied, to help identify the potential mechanisms for the observed effect of CASC20 on osteogenesis. The hypothesis of a role for CASC20 in splicing during osteogenic differentiation will also be tested.

Using nanopore sequencing to diagnose prosthetic joint infections: a comparison of two methods

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Objectives: Infection is a serious complication following joint replacement surgery, and if not treated effectively can have serious consequences. The diagnosis of prosthetic joint infection is difficult. Current techniques include blood biochemical markers, histopathology and microbiological cultures to identify the species of bacteria. However, cultures take time (~14 days) and frequently results in the delay of correct antibiotic treatment. They also may produce false-negative results as some species of bacteria can be challenging to culture successfully. This study compares two different methods of nanopore sequencing, as a quicker alternative to identify bacteria species causing prosthetic joint infection.

Methods: Samples of joint fluid were obtained during surgical intervention for prosthetic joint infection. DNA was extracted and prepared for nanopore sequencing using the MinION device (Oxford Nanopore Technologies). DNA from 12 fluid samples was prepared for sequencing using both the 'Rapid Sequencing' and '16S Barcoding' library preparation kits (genomic sequencing of the 16S ribosomal DNA region being a commonly accepted method of bacterial identification). In the rapid sequencing method, DNA was sequenced for 15 minutes without further preparation. Following sequencing, the adapter sequences that were added during DNA library preparation were removed using porechop. Human DNA was removed using Bowtie2 and the remaining reads classified using Basic Local Alignment Tool (BLAST). Using the 16S method, samples were barcoded using adapter sequences and the 16S ribosomal DNA is amplified before pooled sequencing of up to 24 samples was performed. Pooled samples were identified using their individual barcodes added during library preparation. Genomic sequencing of the 16S ribosomal DNA region is a commonly accepted method of bacterial identification. Adapter sequences were removed using porechop and sequence classification was performed using BLAST.

Results: Samples from 7 infected and 5 non infected patients were analysed using both sequencing methods and compared to microbiological culture results as the current 'gold standard'.Both methods were equally sensitive in diagnosing prosthetic joint infection (86%). However, the 16S method was more specific when identifying the bacterial species causative of the infection (83% vs 58%).

Conclusions: 16S nanopore sequencing is more sensitive than rapid sequencing in diagnosis of prosthetic joint infection. However, this method takes longer and does not have the potential to identify antibiotic resistance. With further improvements, it is likely rapid sequencing can be used to diagnose prosthetic joint infection and potentially be used to investigate antibiotic resistance genes.

Optimising Synovial Fluid Preparation for Gas Chromatography- Mass Spectrometry Metabolomics Analysis for Orthopaedic Research

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Objective: Metabolomics assesses all the metabolites (e.g. lipids, sugars, organic and amino acids) in a sample and its application for understanding the consequences of genetic and environmental interactions of tissue/disease phenotypes in orthopaedic research continues to grow. Metabolite instability is introduced in biological samples as they are subjected to a range of pre-analytical procedures including sample collection, transportation, storage and preparation for analysis. Synovial fluid (SF) has additional pre-analytical challenges due to its high viscosity, the occurrence of blood contamination and sample dilution, when collected via joint washout; all of which may interfere with downstream analysis. This study aimed to optimise sample processing by determining the effects of pre-analytical variables (freeze-thaw cycles, dilution, viscosity and blood contamination) on SF metabolite stability and on the number of metabolites that could be detected using Gas Chromatography-Mass Spectrometry (GC-MS), a common tool for metabolomic analysis.

Method: SF human samples aspirated from the knee during total knee replacement surgeries, immediately centrifuged and stored at -80°C were used for this study (n = 5 per test group). The effect of freeze-thaw cycles was assessed by exposing samples to either one, two or three freeze-thaw cycles. The effect of dilution was assessed via the mixing of samples with 0.85% physiological saline solution at either a 1:5, 1:10 or 1:20 ratio. To assess viscosity effects, samples were enzymatically pre-treated using hyaluronidase and blood contamination was tested by the addition of patient-matched whole non-haemolyzed blood to the samples. Metabolic profiling of the samples was carried out using an untargeted GC-MS approach, and the resulting spectra were processed using MSDIAL v4.93 software.

Results: Preliminary results revealed a total of 334 metabolic features (i.e., unique peaks that are yet to be annotated) that were detected in the control group (undiluted and no-freeze thaws) including 124 metabolites that had been reference matched to an external database (Level 2 identification of MSI) and 210 unknown metabolites. The group that underwent two freeze-thaws exhibited a total of 350 metabolites (128 reference matched and 222 unknown) whilst the samples that had undergone three freeze-thaws had a total of 331 metabolites. Dilution of samples in a 1:20 ratio, resulted in only 161 metabolites being detected. Both hyaluronidase treated and blood contamination groups demonstrated an increase in metabolite numbers detected (401 and 369 total metabolites respectively) in comparison to the control group.

Conclusion: These initial findings suggest that freeze-thawing of SF samples does not greatly affect the number of detectable metabolites. Further hyaluronidase pre-treatment may be beneficial in allowing

detection of metabolites and blood stained samples will introduce non-SF metabolites. Further investigation to determine the effects of these procedures on individual metabolites is ongoing. The optimisation of SF preparation for GC-MS is essential to ensure accurate and reproducible data is generated in metabolomics studies for orthopaedic research.

C. acnes is present in non-herniated human intervertebral discs; what is its influence?

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Objectives: Cutibacterium acnes (C. acnes) and other microorganisms have been identified in humanintervertebral disc (IVD) tissue through Metabolomics and microbial cultures. This studyinvestigated the presence of C. acnes and other microbes in IVD tissue to determine whetherthey are true in-vivo disc bacteria or result from perioperative contamination.Immunohistochemistry (IHC) was performed to detect Gram-positive bacteria, C. acnes andStaphylococcus aureus (S. aureus), in non-herniated human IVDs. The study also examinedthe expression of pattern recognition receptors (TLR2, TLR4, NOD 1 & 2, NLRP3) and thepyroptosis marker Gasdermin D. Additionally, co-culture experiments were conducted withwhole bovine IVDs and S. aureus under static and dynamic loading conditions to assessbacterial infiltration, its interaction with the disc environment, and its influence on discphenotype. Methods:IHC was performed on 95 human IVD samples to detect Gram-positive bacteria, S. aureus,C. acnes, TLR2, TLR4, and NOD 2. Cell detection and classification were carried out usingQuPath. Nucleus pulposus (NP) cells were treated with Lipopolysaccharide (LPS) (5-50µg/ml) and Peptidoglycan (PGN) (5-50µg/ml) in monolayer and alginate beads for up to 72hours, followed by secretome analysis using Luminex. Bovine IVDs were cultured understatic and dynamic loads in the presence of S. aureus. Post-culture, discs were fixed,embedded in wax, and analysed using IHC to determine the presence of bacteria and NP cellphenotype, consistent with human IVD testing. Statistical analysis included Kruskal-Wallis,Dunn’s multiple comparison test, and Pearson correlation. Results:IHC on human samples revealed Gram-positive bacteria exclusively within cells, with C.acnes positivity ranging from 5% to 99%, correlating with the degenerative state (p= 0.048)of the tissue, and the positivity rate of the NOD 2 (p =0.009). The positivity rate of NOD 2further showed a correlation with the positivity rate of both TLR2 (p=8.232e-7) and TLR4(p=2.395e-7). A strong correlation was detected between the positivity rate of TLR2 andTLR4 (p= 1.25e-8). The quantification for catabolic factors is ongoing. Examination ofbovine samples showed C. acnes is present in all the samples. Its positivity rate issignificantly higher (p= 0.0024) in the inner annulus fibrosus compared to the outer.Treatment of NP cells with bacterial components led to an increase in several catabolicccytokines, including IL-1, TNF, IL-6, and IFN-γ, along with increased production ofchemokines, neurotrophic, and angiogenic factors associated with IVD degeneration.Conclusion:This study confirms the presence of Gram-positive bacteria in non-herniated human discsamples and highlights their potential role in triggering a catabolic response in disc cells.

Understanding the physiological behaviour of disc cells in an in vitro imitation of the healthy and degenerated disc niche

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Objectives: The natural physiological environment within the intervertebral disc is hypoxic, acidic, low in nutrition and exerts a high osmotic pressure. This is due to the location of IVDs within the spine, their avascularity and reliance on nutrient diffusion, and an extracellular matrix (ECM) that is hydrophilic and cation-retaining. Therefore, native IVD cells have adapted, and their functions are finely tuned to any alterations within their local environment. Once cells have been isolated from their native tissue and cultured in vitro within off-the-shelf media compositions and conditions that do not physiologically represent the IVD, cells un-differentiate and their behaviour may be substantially altered when compared to in vivo. Hence, we aimed to formulate media that more closely mimics the conditions of the native IVD, with regards to pH, osmolality, and glucose content, alongside culture at low oxygen concentration, to investigate their effects upon IVD cells. Methods: To mimic the IVD environment in vitro, non-degenerate media osmolality was altered to 425mOsm/kg using a cell membrane-impermeant cation, N-methyl-D-glucosamine-HCL, to prevent any permeable solute-specific effects. Degenerate media osmolality was retained at 325mOsm/kg. To mimic the low nutrition environment, low glucose DMEM (1g/L glucose) in powdered, non-buffered form, was utilised. Media pH was altered (non-degenerate pH7.2, degenerate pH6.8) with the addition of sodium bicarbonate calculated using the Henderson-Hasselbalch equation, to reach the correct pH under culture at 5% CO2. Basal culture media exchanged FBS for Albumax, ITS and L-Proline. Media was supplemented with ascorbic acid to support collagen synthesis. Degenerate media was further supplemented with a physiological concentration of IL-1β (100pg/ml) to mimic the catabolic environment of the degenerate disc. IVD cells and tissue were cultured in these media compositions to determine functional effects on viability, gene expression and cytokine production. Results: Media composition (pH, osmolality) remained stable for 5d at 37°C, 5% CO2, 5% O2. IVD cell viability was not significantly altered by any media compositions compared to control media. Mitochondrial activity, expression of genes (col II) and the secretion of cytokines (IL-1β, IL-6, LIF) was significantly altered by culture within degenerate media + IL-1β ($p<0.05$). Conclusions: Here, the development and validation of media compositions to mimic the healthy and degenerate IVD have been developed. Human NP cells, bovine and human NP tissue explants were successfully cultured within these media without any detectable loss of viability and minimal phenotypic expression changes. The only differential effects observed within cultures were seen with the addition of physiological concentrations of IL-1β. These conditions provide appropriate environmental conditions in vitro which mimic more closely the intra-discal conditions observed during healthy and degenerate physiology. These media can be utilised to test potential therapeutic approaches and gain a further understanding of the pathophysiology of IVD degeneration using in vitro and ex vivo models.

Session 6 – New Investigator Awards

Using in-vivo biplane videoradiography to validate tibiofemoral kinematics derived from musculoskeletal models.

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Objectives: Investigate the accuracy of the tibiofemoral (TF) kinematics calculated by a musculoskeletal (MSK) modelling pipeline's optimisation routine by comparing with accurate TF kinematics from Biplane Videoradiography (BVR) data[1]. By comparing subject-specific MSK model kinematics with in-vivo BVR data, the model's predictive capabilities were assessed to understand its strengths and limitations for future research on joint function changes due to injury or disease. Methods: Ethical approval for the study was obtained from the Wales Research and Ethics Committee. 5 healthy volunteers (3M/2F, mean age 47.8 years) were recruited and provided written informed consent. BVR (60 FPS, 1.25ms pulse width) with simultaneous marker-based motion capture was recorded whilst each participant performed a stair ascent on an instrumented staircase. The marker trajectories were tracked (Qualysis Track Manager). A static trial was used to scale a generic MSK model[2]. TF flexion was calculated using an inverse kinematics routine, and a concurrent optimisation algorithm calculated the other 5 degrees of freedom (DOF) simultaneously with the muscle activations and forces[3]. For each participant, 3D models of the femur and tibia were segmented (Simpleware Scan IP, Synopsis) from an MRI scan (Magnetom 3T Prisma, Siemens). Anatomical Coordinate Systems (ACS) were applied to the femur models using an automated algorithm[4]. The tibia ACS was set coincident to the femur ACS (to match the relationship of the MSK model bones). Each bone's ACS position in relation to the global coordinate system was determined at each frame through image registration (DSX Suite, HAS-Motion Inc.). TF kinematics were calculated from the BVR data using the Joint Coordinate System approach[5] and filtered using a digital adaptive low-pass Butterworth filter (cut-off frequency range 5-10 Hz). A Bland-Altman analysis[6] was used to compare the mean and distribution of the differences between the MSK model and BVR kinematics across all frames. Results: The MSK modelling pipeline generally overestimated flexion and abduction, while underestimating external rotation. Flexion showed the largest absolute mean difference due to its greater range of motion (ROM). Internal-external rotation had significant differences relative to its ROM, indicating challenges in predicting this DOF from motion-capture data. Translational difference ranges were ~10-20 mm, comparable to the calculated translational ROMs. Small inaccuracies in translational calculations lead to large percentage errors, affecting joint contact pressure maps since the contact region depends on the relative bone motion. Conclusion: Differences were found in kinematic outputs between the MSK modelling pipeline and in-vivo BVR-derived kinematics across all 6 DOF. Investigating these differences is crucial to understand their impact on other model outputs, like joint contact pressure, and to determine the models' suitability for clinically-driven research questions.
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Sex differences in osteocyte expression responses to pathological mechanical load may be responsible for the higher burden of osteoarthritic pain in females.

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OBJECTIVES: Osteoarthritic (OA) pain affects 18% of females and 9.6% of males over 60 worldwide, with 62% of all OA patients being women. Female OA patients use more health care, suffer more from debilitating pain, and have more rapid disease progression. However, the molecular drivers of the differences between males and females in osteoarthritis is unknown. Bone is intricately coupled with sensory nerves and one ofthe only joint tissues to show changes that correlate with patient pain in OA.Profound neuroplasticity occurs in OAsubchondral bone and is associatedwith pain. Bone osteocytes are mechanically sensitiveand orchestratorsof bone responses. There are fundamental sex differences inpain sensation and bone biology which may be intrinsic to OA diseaseprogression, however these differences are vastly under researched. Hypothesis:Mimicking osteoarthritic pathology by pathologicalmechanical stimulation of osteocytes regulatessignalling factors associated with osteoarthritis progressionand pain that are differentiallyexpressed in males and females. METHODS:Human Y201 mesenchymal stem cells were embedded in 3D type-I collagen (0.05 x 106 cell/gel) anddifferentiated into osteocytes and subjected to mechanical loading (4300µstrain, 10Hz, 3000 cycles) or left unloaded(n=5/group).RNA extracted 1-hr post load wasquantified by RNAseq whole transcriptome analysis (NovaSeqS1 flow cell 2 x 100bp PE reads).Differentially expression was identified using DEseq2 analysis on normalisedcount data (>2-foldchange and FDR $p<0.05$).RNAseq data was integrated with publishedsexually differential expression data in human bone tissue4,5 and mouseosteocytes6 and combinedwith OA risk loci data from Genome Wide Association Studies (GWAS)7. RESULTS:Pathological mechanical loading induceddifferential expression of 7564 osteocyte genes, with 3861 showing sex-specificdifferences in human long bone. Gene ontology analysis revealed enrichment The co-regulatedgenes included numerousneuronal associatedgenes: 155genes associated with the synapse including TENM4, fourgenes associated with the sensory perception of pain: PTGES,EDNRB, 8members of the MAPK signalling pathwayand UCHL1, and 44 genes associated with axon guidance including, SEMA3A andSEMA7A. In mice at 16 and 26 weeks, 5 and 77 differentially expressed osteocyte mechanosome genes were found between males and females, respectively, including TENM4 and SEMA7A, with GO-term enrichment associated with positive regulation of axon extension. 32 GWAS OA effector genes showed mechanical regulation in the osteocyte mechanosome, including CTSK, RUNX2, NOS3, and members of the TGF-β pathway. CONCLUSIONS:We have shown that pathological loadingin osteocytesas shown in osteoarthritiselicits cellular responses that are differentiallyregulated in males andfemales. Many of these genes are associated with regulationof the outgrowth and development of the peripheral nervous system withlinks to neural plasticity and invasion. REFERENCES: 1.Steinmetz, et al. Lancet Rheumatol. 5, e508–e522 (2023). 2.Tschon, et al. J. Clin. Med. 10, 3178 (2021). 3.Hunter, et al. 21, 1170–1178 (2013). 4.Rojas-Peña, et al. J. Genomics 2, 121–130 (2014). 5.Shi, M.-W. et al. Nucleic Acids Res. 47, D835–D840 (2019). 6.Youlten. et al. Nat. Commun. 12, 2444 (2021). 7.Boer, C. G. et al. Cell 184, 4784-4818.e17 (2021).

Whole-Organ Computed Tomography Score (WOCT) of the Knee

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Objectives: To present a semi-quantitative, multi-feature scoring system developed to assess the health status of the complete knee: the Whole-Organ assessment using CT in the knee (WOCT score). We aimed to determine the inter-observer agreement for this scoring method, particularly of the mineralised tissues within the knee joint, and to compare strengths and weaknesses with the well-known Whole-Organ Magnetic Resonance Imaging Score (WORMS) which is optimal for soft tissues and inflammation. Methods: This retrospective study included 64 patients (41.8 ± 9.6 years) undergoing autologous cell implantation (ACI) for chondral/osteochondral defects in the knee, as part of a randomised controlled trial of cell therapy (11/WM/0175; ISRCTN98997175), with full ethical consent. Patients' knees were imaged using conventional 3-T MRI (operated leg only) and CT (both legs) scanning techniques pre-operatively (6.0±3.0 weeks prior to cell implantation) and post-operatively (13.0±3.1 months post cell implantation). Images were independently scored by two musculoskeletal radiologists using the WORMS (MRI) and WOCT (CT) scores. The following features were assessed: cartilage (swelling and chondrocalcinosis), subarticular bone marrow abnormality, subarticular bone attrition, subarticular cysts, central and marginal osteophytes, medial and lateral meniscal integrity, joint effusion, loose bodies, synovial cysts/bursae and the following ligaments: anterior and posterior cruciates (ACL and PCL) and medial and lateral collaterals (MCL and LCL), as well as the patella alignment and integrity of the extensor apparatus (TT-TG distance). Intraclass correlation coefficients (ICCs) were determined for each feature and CT results compared with MRI Scores using a Spearman correlation analysis. Results: All knees undergoing ACI showed structural abnormalities with both MRI and CT scores. The most prevalent degenerative changes were cartilage alterations and osteophyte formations. The ICC of the total WOCT scoring system (summing all parameters for each joint) on both legs pre- and 13 months post-operatively was excellent (ICC 0.99), similar to that for the patellar alignment measurement (0.96). The reliability of each individual parameter was also excellent (ICC values >0.88) for all items except synovial cysts/bursal collections, which had a good reliability (ICC 0.64). The Spearman rank correlation coefficient between the total MRI and CT scores was high (0.81), as was the patellar alignment measurement (0.80) between the two imaging modalities. Conclusion: The WOCT score provides a multi-feature, whole-organ assessment of the knee using CT scans, showing high inter-observer agreement between readers. This score may be useful in epidemiological studies and clinical trials involving knee pathologies when MRI is not feasible. Furthermore, it provides additional information on the bone and cartilage unit, which is particularly prudent in the case of osteochondral defects, which make up a significant proportion of patients undergoing cartilage repair.

Mechanobiological model of bone adaption in vertebrae of individual multiple myeloma patients

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Objectives: Vertebral lytic lesions are a common complication of multiple myeloma (MM), a cancer of the plasma cells. Patients with MM are most affected by spinal involvement (80-90%) [1]. The standard care is invasive surgical intervention when patients present with spinal instability. However, the surgery is associated with increased morbidity and high infection risk [2]. A non-surgical strategy has been adopted by externally bracing the spine; bone apposition in the affected region has subsequently been observed [3,4]. However, it is unclear if this change is mainly mechanobiologically driven or due to other biological mechanisms. Methods: We developed a mechanobiological model using data from non-cancer volunteers (control group, n=10) and MM patients (braced, n=10). Three-dimensional finite element (FE) models of vertebrae were generated from baseline and follow-up computed tomography (CT) scans. CT images were densitometrically calibrated with a phantomless approach. Bone was modelled as heterogenous (based on bone mineral density, BMD), isotropic, and elastic-plastic. Uniaxial compression (0.15% strain, ANSYS) was simulated, and failure load (FL) was defined as the load at 1.9% strain [5]. The organ-level FE was coupled with a cell-level model, which adjusts material properties based on biological pathways described by differential equations [6,7]. Remodelling parameters were optimised for each patient where the algorithm was run continuously until convergence with different combinations of parameters, until the standard error in the average BMD was minimised. Results: The mechanobiological model can predict average BMD well in both the control and MM group with no significant difference between follow-up and predicted. However, for failure load, there was a significant difference between the follow up and predicted follow up ($p<0.01$). Nonetheless, when subgrouping the MM cohort, the algorithm performed similar to the controls in the patients with no/small lesions, whilst for the subgroup with large lesions, there was larger discrepancies between follow up and predicted. Conclusions: The mechanobiological model effectively predicted average BMD and FL in the control group of healthy patients, however, for patients with vertebra with large lesions post-MM treatment through bracing the prediction is not as effective. This is the first time this has been identified and implies that changes in mineralisation and bone strength are not driven by mechanical stimulation alone, suggesting an unknown biological mechanism inherent in MM-affected bone tissue driving anabolic bone formation. Changes in serum biomarkers carboxy-terminal collagen crosslinks (CTX), Procollagen 1 N-Terminal Propeptide (P1NP), and sclerostin, which offer insights into bone turnover dynamics, will be used to scale the bone formation and resorption parameters. This has the potential to incorporate patient-specific biological data, improving accuracy for vertebrae with large lesions. References: [1] Bird et al., Br. J. Haematol., 2011; [2] Nucci and Anaissie, Clin. Infect. Dis., 2009; [3] Malhotra, et al., Spine J., 2016; [4] Malhotra et al., BMC Cancer, 2016; [5] Keaveny et al., J Bone Miner Res 29(1) 2014 [6] Hambli, Frontiers in Bioeng and Biotech, 2014; [7] Komarova, et al., Bone, 2003

Association Between Surgeon Grade and Radiographic Implant Alignment in Unicompartmental Knee Replacement

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Objectives: Unicompartmental knee replacement (UKR) is a technically challenging operation. When deemed competent, attendings permit their residents to perform UKRs. This study aimed to investigate implant alignment and all cause re-operation following UKR performed by attendings compared to residents. Methods: 100 consecutive UKRs performed by residents and attendings were analysed. Two blinded individuals independently assessed post-operative knee radiographs on four parameters: flexion/extension of femoral component, posteroinferior slope of tibial component, and varus/valgus of femoral and tibial components. All-cause reoperation was assessed using Cox proportional hazards model. Primary outcome was implant alignment and secondary outcome was all-cause re-operation. Sample size calculation determined 14 patients were needed for primary outcome. Results: Median varus/valgus angles for femoral components were -3.3 degrees(IQR -5.75 to -1.3) among residents and-3.5 degrees (IQR -7.05 to -0.15) among attendings (p=0.916), while for tibial components, they were -3.3 degrees(IQR -5.8 to -1.7) for residents and -3.8 degrees (IQR -5.85 to -2.2) for attendings (p=0.432). Median values for posteroinferior tibial slope were7.08 degrees (IQR 5.2 to 9.30) and 5.35 degrees (IQR 2.65 to 7.05) by residents and attendings (p=0.004). Median flexion/extension angle for femoral components by residents and attendings were -14.45 degrees (IQR -19.2 to -9.85) and -10.2 degrees (IQR -13.55 to-6.95) (p=0.004). For this parameter, a relatively greater proportion of implants positioned by residents were outliers (46% versus 20%; p=0.006). However, there were no differences in outliers for this parameter when residents were directly supervised by attendings (25% versus 20%; p=0.730). There were no differences in all-cause reoperation between groups (p=0.137).Conclusions: Residents are more likely to misposition the femoral component in excessive flexion. This difference was present only when residents were indirectly supervised by attendings. There were no differences in the proportion of mispositioned implants that were outliers between residents and attendings for other parameters. Resident surgical training should include greater emphasis on achieving accurate positioning of the femoral component.

Session 7 Therapeutics

The effect of denosumab on osteoclast precursor cells in postmenopausal women with osteoporosis.

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Objectives: Upon discontinuation of denosumab, a “rebound” phenomenon in bone turnover has been observed, potentially leading to a reduction in bone mineral density and an increased risk of vertebral fractures. One proposed explanation for this phenomenon is the accumulation of osteoclast precursors during treatment. Our study aimed to investigate the effects of denosumab on osteoclast precursors in postmenopausal women with osteoporosis. Methods: We recruited 15 osteoporotic postmenopausal women on denosumab and 15 age-matched controls. The inclusion criteria for the control group were postmenopausal women over 65 years with osteoporosis or osteopenia. Exclusion criteria included recent fractures (within the past year), bisphosphonate use, steroid use and bone diseases such as Paget’s disease. Additionally, we included a historical cohort of 69 postmenopausal women from the TRIO study, which examined the effect of bisphosphonate treatment on osteoclast precursor cells. Both concurrent and historical controls had similar inclusion criteria. Blood samples were collected from all participants. Peripheral blood mononuclear cells (PBMCs) were isolated from whole blood and stained for CD14, MCSFR, CD11b, and TNFRII. Osteoclast precursors (CD14+/MCSFR+, CD14+/CD11b+, or CD14+/TNFRII+) were identified using fluorescence-activated cell sorting (FACS). The proportion of osteoclasts was determined by calculating their percentage of the total cell population in each whole blood sample. Results: The median duration of denosumab treatment was 4 years (range 0.5 to 9 years). There were no statistically significant differences between the denosumab and control groups in terms of age and T-scores for the hip and spine.When comparing the number of osteoclast precursors between the control and treatment groups, denosumab-treated patients exhibited a higher count of CD14+/CD11b+ osteoclast precursors compared to both the concurrent controls and the historical cohort (TRIO controls) (median 4% vs 0.75%, p=0.011 and 4% vs 2.76%, p=0.004). Conclusions: Denosumab administration resulted in an increase in the number of CD14+/CD11b+ cells, potentially indicating a blockade in the differentiation of osteoclast precursors to mature osteoclasts during denosumab therapy. This accumulation of osteoclast precursors could explain the rebound increase in bone turnover observed upon treatment discontinuation.

Development of a Robust Isolation and Culturing Pipeline of Knee Fat Pad-Derived Mesenchymal Stem Cells

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Background: Cell-based therapies have shown promise as a disease-modifying strategy for osteoarthritis (OA). However, standardised methods for the isolation and culturing of adipose derived mesenchymal stem cells (MSC) for clinical application are not well-established. Here, we aimed to establish a robust and scalable human primary vascular stromal fraction (SVF) derived -MSC isolation pipeline from donated surgical waste (knee fat pad).Methods: Human primary SVF derived MSCs were harvested from infrapatellar fat pads of patients with OA undergoing elective knee replacement. SVF were isolated from fat pad tissue using an enzymatic-digestion method to reproducibly produce a high yield of adhering MSCs with maintained viability during culture. Fat pad tissues ranging from 3g to 43g were homogenised to smaller pieces prior to enzymatic digestion. Homogenised fat pads were digested using 0.015% collagenase I for 1 hour. Digested tissue was further homogenised with a cell dissociator and cells were filtered through a cell strainer to achieve a single cell suspension. Characterisation of isolated MSCs' included proliferative ability, analysis of isolates' population doubling level (PDL) and time (PDT). Tri-lineage differentiation of isolated MSCs into osteoblasts, adipocytes, and chondrocytes was conducted to characterise the isolated MSCs pluripotency. Oil Red O stain, Alizarin Red stain, and Glycosaminoglycan (GAG) assays were performed as a surrogate readout for the differentiation of MSCs. Results: The optimised protocol was successful in achieving 87% success rate (>20k viable MSC/g tissue) in (n=37) isolations of SVF-derived MSCs. MSC yield ranged between 20k - 201k cell/g fat tissue. PDL analysis demonstrated a steady increase in the PDL in (n=5) samples (3, 2.7, 2.5, 4.3, 4.1, and 4.2). Analysis of the effect of age on PDT showed no statistically significant difference ($p=0.6$, $r2=0.5774$) between age and PDT in (n=7). Comparing the rate of growth of isolated MSCs between passage 0 and passage 3 in (n=10) indicated no change in growth rate during this culture period ($p=0.04$, $r= 0.42$). Tri-lineage differentiation of (n=3) samples showed lipid deposition at day 7 and 14; chondrocytes' release of (GAG) into media was significant at day 3 ($p=0.03$) and day 7 ($p=0.05$) and bone nodules and calcium deposition was observed by D14 and D21.Conclusion: Reproducible isolation of viable MSCs was achieved using a standardised protocol, with characterisation of the isolated MSCs by population doubling analysis to assess their proliferative potential and pluripotency characterised by tri-lineage differentiation. Further characterisation of isolates is underway through in depth transcriptomic and functional analysis to identify MSC derived proteins with cartilage regenerative potential.

Osteochondral cell isolation for single-cell RNA sequencing

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Objectives: Single-cell RNA sequencing (scRNA-seq) enables the functional clustering of cells within a tissue by their gene expression. This tool will help disentangle the biological complexity of osteochondral tissue in osteoarthritis (OA). However, the application of scRNA-seq workflows to osteochondral tissues has been limited by low cell density and their entrapment within proteoglycan rich matrix of cartilage and mineralised bone, requiring extraction protocols that limit the quality and integrity of the chondrocyte, osteoblast and osteocyte cell isolates achieved. By optimising tissue extraction, the quality of downstream scRNA-seq can be improved. We describe an optimised extraction protocol for chondrocytes, osteoblasts and osteocytes from human knee tissue that is suitable for downstream scRNA-seq analyses. Methods: Osteochondral joint tissue was obtained from patients undergoing total knee replacement surgery under NRES ethics approval 20/SC/0144. Osteochondral tissue explants were graded by macroscopic appearance using the International Cartilage Repair Society grading system as 0-1 (healthy to superficial wear) or 3-4 (multiple lesions, crevices over half the cartilage thickness to full thickness cartilage loss). Patient matched grade 0-1 (n=24) and 3-4 (n=21) cartilage was removed, diced, and washed in PBS prior to digestion in 10mg/mL collagenase type II at 37°C to isolate chondrocytes. Subchondral bone pieces from each grade were harvested using a tissue biopsy punch and washed in PBS. Osteoblasts were isolated by digestions in 2mg/mL collagenase type II, followed by 5mM EDTA digestions to isolate osteocytes from the same samples, all at 37°C. Subsequently, the effects of digestion length, cryopreservation, and sample clean-up methods, including filtering and density gradient centrifugation, on cell number, viability and nuclei quality were investigated prior to downstream applications. Results: The total number of chondrocytes isolated were substantially increased when cartilage was digested for 4hr (≥3x106) compared to 2hr (≥1x106), with no decrease in viability (both >80%). The number of osteoblasts and osteocytes isolated after a total digestion time of 4hr was not significantly altered compared to a digestion for 2hr (1-2x106), with no adverse effects on viability (≥75% for each cell type). Cryopreservation of cells had no adverse effects on cell number or viability. Density gradient centrifugation using an OptiPrep barrier enabled removal of dead cells and tissue debris from bone cell isolates, and enabled the collection of good quality, single nuclei following lysis (Figure 1). Combining optimised steps during sample collection, isolation and clean-up substantially improved the overall quality of samples for scRNA-seq. Conclusions: The extraction and processing of chondrocytes, osteoblasts and osteocytes from the dense osteochondral matrix is complex. Here we show that sample processing by sharp maceration followed by collagenase then EDTA digest, filtering and density gradient centrifugation yields intact cells of sufficient number that are suitable for downstream scRNA-seq applications. However, the digest time varies with the matrix being processed, with cartilage optimised for 4-hour digest whilst bone digest generated better cell yields with a total 2-hour digest.

Factors Associated With Increased Opioid Consumption Following Total Hip Arthroplasty

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Objectives: Effective postoperative pain management is imperative in Total Hip Arthroplasty (THA) to enable early mobilization and accelerate recovery pathways. This study investigated the patterns of in-hospital opioid consumption following THA and identified the factors associated with increased opioid usage. Methods: In this large-scale, single-institution study, we analyzed data from 2,048 primary THAs between May 2019 and July 2023. We collected data on demographics, length of stay (LOS), type of anaesthesia, Post Anaesthesia Care Unit (PACU) admissions, 30-day readmissions, total opioid consumption (morphine equivalents), implant fixation techniques, surgical characteristics and pre- and post-operative haemoglobin (Hgb) levels. Factors associated with increased opioid consumption (patients above the third quartile in opioid consumption distribution) were identified through univariate and multivariate logistic regression models. Results: The cohort included 1,260 (61.5%) female and 788 (38.5%) male patients. The median in-hospital opioid consumption was 88 mg (Q1, Q3: 39 mg, 211 mg). In the univariate model, significant predictors included age, ASA score, conventional surgical technique, general anaesthesia, pre- and post-operative Hb levels and the need for PACU admission. After adjusting for baseline demographics in the hierarchical multivariate logistic regression model, significant predictors of higher opioid utilization were ASA score (OR 1.492, 95% CI [1.193 – 1.866], p<0.001), post-operative Hb levels (OR 0.981, 95% CI [0.970 – 0.992], p<0.001), age (OR 0.989, 95% CI [0.981– 0.997], p=0.010), general anaesthesia (OR 2.386, 95% CI [1.865 - 3.054], p<0.001), and the need for PACU admission (OR 2.098, 95% CI [1.310 – 3.358], p<0.001).Conclusions: The most significant correlations with higher opioid consumption were ASA score, younger age, lower levels of post-operative hemoglobin, the necessity for PACU admission and general anesthesia. It is essential to consider potential confounding factors related to opioid use, such as individual pain thresholds and daily variations in pain scores. Furthermore, larger-scale prospective studies and randomized controlled trials are required to expand on these findings.

Abstracts: Posters with 2- minute pitch

Effectiveness of neural mobilization for cervical radiculopathy: A systematic review of randomized controlled trials

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Objectives: To assess the analgesic effect of neural mobilization (NM) in people with cervical radiculopathy. Methods: We searched through Medline via PubMed, Cochrane Central Register of Clinical Trials (CENTRAL), Web of Science (WOS), and Scopus databases from 2019 to January 2024, as well as the reference lists of included articles. We only included randomized controlled trials (RCTs) published in English that examined the effect of neural mobilization in people with cervical radiculopathy. Our critical outcome was pain. Two reviewers independently screened, extracted data, assessed the trial quality (ROB2), and certainty of evidence of key outcome using GRADE. Results: We included 5 trials involving 261 people. The studies were conducted in adults with a variety of symptoms and used different NM techniques. Overall, the studies showed some concerning evidence of bias due to missed protocol information. Most of the studies showed relieved pain and a superior effect of NM compared to other groups ($P < 0.001$) in a short time with clinical importance; however, no study reported any adverse effects. Conclusions: Neural mobilization relieves pain significantly. There is moderate-quality evidence that neural mobilization reduces the symptoms of pain in people with cervical radiculopathy, and the decision to use it should integrate the patient's values and preferences. There is a need for more randomized controlled trials with a large number of patients.

PyCT2S: An Automated Pythonic Approach to CT2S

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Objectives: Use of quantitative CT based finite element (QCT-SSFE) models in the analysis of bone strength is a potential method to provide additional information to the current dual X-ray absorptiometry scans that utilise areal bone mineral density (DXA-aBMD) to assess strength. aBMD, while useful for other elements of clinical prediction, is limited as a predictor of strength; Viceconti et al. (2018) found CT-based models have proven to achieve higher accuracy in bone strength prediction. However, the process is time-consuming and requires a trained professional to run through the pipeline providing human input during several steps. CT2S (Computed Tomography to Strength) developed by the University of Sheffield is one of these pipelines. The aim of this work is to automate the FE analysis processes of CT2S so that more users can use the pipeline with minimal training and a user-friendly frontend. *Methods*: The CT2S workflow is comprised of sequential steps that produce a result of bone strength. The meshing and finite element step for which an operator is required is the area of improvement that this work focuses on. In addition, landmarking in the original pipeline involved eye identification of landmarks on the model. This is time-consuming and introduces variation, the process was changed to complete automatically in the background using principal directions to identify landmarks. ANSYS ICEM steps were replicated through CLI TCL code injection, while ANSYS APDL steps were tied together with pyMAPDL. Result stages were translated through python analysis libraries to allow for the generation of graphs and CSV data reports without user interaction. ANSYS simulation results were plotted through the pyDPF. Overall, these provide an automatic, repeatable, and consistent pipeline called PyCT2S. *Results:* Performance of the different approaches was measured from initialisation to completion. This includes the time to set up the ANSYS environment appropriately. The PyCT2S performance results showed improvement of 19% overhead reduction on laptop hardware and a 9.5% overhead increase on standard PC hardware. However, overall pipeline performance was cut by 49-61% from 25 minutes down to 12 minutes for experienced and 35 minutes down to 14 minutes for inexperienced user. Results further improved to a 61-70% time reduction with a dynamic multi-threading approach. These show that in the scope of the finite element analysis pipeline step, a pythonic method is both user-friendly and faster due to its ability to complete many steps outside of the ANSYS environment. *Conclusions:* A pythonic approach is a consistent method of running the CT2S pipeline while still allowing interaction; but significantly limiting the chance of human error. Additionally, steps where the use of ANSYS can be removed or minimised are also improved, particularly in the meshing and result plotting steps where the pythonic approach is substantially faster. Overall, the pythonic approach provides simpler operation and time efficiencies. This is particularly apparent in the meshing, material, and result steps. With the additional benefit of providing a consistent and friendly environment with minimal engineering knowledge required.

Introducing a new pathway for early management of the paediatric forearm fracture -guided by BOAST- in the emergency department of a trauma unit

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Paediatric Forearm fractures are a common injury with closed reduction indicated for cases exceeding remodelling potential. Practice is variable with some units refusing procedural analgesia and manipulation in the emergency department (ED) due to either staff shortages, lack of competencies or concerns about children distress. In the absence of clear pathways & guidance, manipulation of paediatric forearm fractures under anaesthesia (MUA) in theatres exposes the patient to unnecessary risks of general anaesthesia (GA) and incurs significant cost to the NHS due to unnecessary admission and theatre time. The T&O, ED & Anaesthetics teams concurred that there was a need to change this practice. A retrospective analysis, spanning a year, identified 354 patients with potential paediatric forearm fractures. 32 of these were identified as having forearm fractures amenable to manipulation in the ED. 12 out of 32 of the forearm fractures were manipulated in the ED. 1 of the 12 manipulated cases required admission for manipulation in theatre. Approximately 65% (21 out of 32) of the eligible children in our study were admitted and underwent MUA in theatres. Variability in practice was noted when compared to BOAST guidance . E.g. fracture clinic appointment within a week. Incomplete documentation was noted for the consenting process, pain scores & analgesia on discharge. Lack of local guidance leads to variation in practice & inequality of care. A simplified pathway and local guidance were created to address this, facilitating fast tracking of our patients to have procedural analgesia and manipulation in the ED. This reduces the risk of GA on the patient as well as cost burden. A minimum level of competencies is recommended for the specialist doing the manipulation to ensure safe practice. A leaflet was designed, giving red flag symptom advice, to educate the patients of complications as well as a proforma to ensure a standardised documentation.

Developing a novel low-cost orthotic intervention to improve functional lower limb biomechanics in people with haemophilia in the global south

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Objectives: Low income, and lower-middle income populations make up around 70% of the global haemophilia population. However, account for less than 10% of the pharmaceutical treatments for haemophilia. Over 80% of bleeds occur in the musculoskeletal system, leading to poor joint health outcomes in these patients. Based on the model in NHS England, of podiatry, orthotic, and/or physiotherapy services being offered to service users, this research aimed to design a novel low-cost orthotic intervention for use in developing countries, and test this in a healthy control group. Methods: Eight orthotic device designs were developed based on sandals being the preferred footwear of choice in much of the global south. This footwear style is typically not recommended for people with haemophilia (PwH), due to the lack of stability. Combinations of components that have proven valuable in podiatric care in PwH, such as forefoot rockers and SACH heels were included. Four of the designs have integrated the orthotic components into a footwear, and four have been designed as an attachment to a standard flip-flop. Testing was carried out on samples of regions of the design, to assess for mechanical strength, attachment method, and functionality – to assert potential failure mechanisms – of both the attachment style orthotic, and integrated footwear. As a result of this, prototypes of the four integrated designs (forefoot rocker only, SACH heel only, forefoot rocker and SACH heel, and forefoot rocker and SACH heel, with ankle strap) were 3D printed using thermoplastic polyurethane (TPU), for testing on a healthy control population. N=12 healthy adult males were recruited to participate in motion capture assessment under local ethical approval (FHS 23-24.58). Biomechanical assessment considered the difference in joint ROM of motions at the hip, knee, and ankle; peak plantar flexion moments; and ground reaction force (GRF) centre of progression width and length, from a baseline standard flip-flop, and barefoot walking. The IOR multi-segment foot model was utilised, to be able to draw further conclusions on foot biomechanics utilising the device in future. Results: Mechanical testing highlighted that the attachment style orthotic would be ineffective if a forefoot rocker component was required for improved functional biomechanics, as the shape of the designed rocker was deformed by the Ethylene-vinyl acetate (EVA) flip-flop it was attached to. This led to the decision to only test the fully integrated device on the control population. Trialling the four designs against the standard flipflop, and barefoot walking, generated a breadth of information on the biomechanical influence of each component of the design, and their potential efficacy in reinstating “normal” biomechanics in PwH. The most effective combination was both the forefoot rocker and SACH heel. Conclusions: Healthy populations provide good evidence that biomechanics can be influenced using a flip-flop style design. Therefore, two prototypes will be taken forward for testing in haemophilia populations. Testing in PwH is necessary as proprioception is reduced in PwH, therefore, results may differ. However, the relative safety demonstrated improves confidence in concept to move to testing on a patient population.

Verification Of Magnetic Resonance Image Based Finite Element Models Of The Ankle

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Objectives: The gold standard imaging technique for generation of segmentation specific finite element models is CT scans. However, this imaging modality does not allow for modelling of early stages of disease, due to the inability to visualise cartilage changes. Therefore, the aim of this research is to verify whether MRI produces equivalent results to CT scans, using a validated loading profile. The objectives included qualifying and quantifying the morphological differences between MRI based segmentations, and CT based segmentations; and quantifying the consequent differences between FE model outcomes. Methods: N = 4 cadaveric ankles were scanned under local ethical approval, to acquire both MRI and CT scans. Three of the four ankles were fresh frozen and then thawed for 48hrs ahead of scanning, so as not to impact MRI scan quality. The fourth was fresh, and not required to go through a freeze thaw cycle ahead of scanning. Finite element models were constructed from both MRI and CT of the same ankle samples in Simpleware ScanIP (U-2022.12), using sagittal plane images. Image specific segmentations were generated where visualisation of tissues was possible. Where cartilage was not visible in the CT scans, a uniform cartilage thickness was extruded from the bone surface, and a separate mask of cartilage only produced. Volumes were measured for the tibia, talus, and tibial and talar cartilage components, before producing a FE model from the segmentations. The FE models produced used a 1 mm target edge length for the cartilage, and a 3 mm target edge length for the bone. These models were imported into Abaqus (2023) for finite element analysis; homogenous linear elastic material properties were assumed for both MRI and CT models (E = 7300 MPa, ν = 0.3). In future work, further assessment could be made between the heterogenous bone properties achievable in CT. Models were loaded axially with a 600 N force, to allow comparisons to a previously validated study. Results: Qualitative and quantitative differences were seen in the morphology between MRI and CT, with different bone volumes in scan types. 15% differences in bone volume were seen in the tibia, which related to the larger field of view in the CT scans, while the talus only saw a maximum of 1.2% volume difference. Cartilage saw gross over-estimations in CT scans, with almost every cartilage component being over 30% greater in volume in CT than MRI. It was also noted that 2D MRI was not suitable for modelling purposes in this assessment, due to large stepping artefacts in both bone and cartilage. The large volumetric differences in the cartilage, led to differences in contact pressure and area in these regions. Conclusions: MRI, once validated, will provide more detailed finite element models of the ankle complex, providing the opportunity to model – and consequently gain insight into – earlier stages of diseases such as osteoarthritis.

Shall we not pressurise it? Effects of bone cement pressurisation on mortality and revision following hip hemiarthroplasty for neck of femur fracture patients: A comparative cohort study

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Objectives: Pressurisation of bone cement in arthroplasty aims to improve the quality of the bone-cement interface and reduce the risk of aseptic loosening. This technique is performed by some surgeons during hip hemiarthroplasty for hip fracture patients. However, some surgeons avoid this practice due to the theoretical increased risk of bone cement implantation syndrome including cardiovascular compromise. Aims: To compare 30-day post-operative mortality and revision for aseptic femoral component loosening and all-causes following hip hemiarthroplasty performed with or without pressurisation of the bone cement in hip fracture patients. Methods: Hip fracture patients over 60 years of age who underwent cemented hemiarthroplasty between 2007–2023 were identified using our hospital database. Patients were grouped by whether or not cement was pressurised using an interference plug sealing the proximal femoral canal opening. Revision outcomes were assessed using an adjusted Cox proportional hazards model. Results: 406 and 722 procedures were performed with and without cement pressurisation respectively. There were no differences in 30-day post-operative mortality (7.15% versus 8.18%; hazard ratio 0.89, 95%CI 0.46–1.73, p=0.727). There were no differences in all-cause revision (hazard ratio 1.04, 95% CI 0.27–4.04, p=0.953) and no revisions were performed for aseptic loosening. Survival at 10 years post-operatively was 15.29% (95%CI 11.46–19.64) and 12.61% (95%CI 7.67–18.82) among patients who underwent hemiarthroplasty with and without bone cement pressurisation respectively. Incidence of intraoperative periprosthetic fracture was 0.80%.Conclusions: There were no differences in 30-day post-operative mortality rates among patients who underwent hemiarthroplasty with and without bone cement pressurisation. Pressurisation of bone cement did not confer any advantages for revision outcomes. This could be due to these patients' low functional demands and ten year survival rate which reduces their risk of experiencing a revision procedure. Surgeons' preferences for uncemented hemiarthroplasty as a means of avoiding the perceived need for bone cement pressurisation is unsupported.

Biomarkers of sarcopenia in patients with hip fracture: A systematic review

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Objectives: Despite the growing recognition of sarcopenia as a significant factor contributing to high morbidity and mortality in hip fracture patients, there remains a lack of consensus regarding reliable biomarkers for its assessment. This systematic review aims to identify peri-operative diagnostic and predictive sarcopenia biomarkers related to patients admitted with hip fractures found within existing literature. Methods: A systematic search was conducted in MEDLINE, EMBASE and Google Scholar databases according to the PRISMA guidelines. Studies involving the assessment of sarcopenia biomarkers in patients that underwent surgery for primary proximal femoral fractures were included. Biomarker study quality was assessed using the BIOCROSS score. Results: A total of 19 studies were identified and screened, 11 publications were included in the review and in total 7 studies met the inclusion criteria. In total there were 515 patients, of which 402 (78%) were female and 113 (22%) were male. Mean age of the participants was 83.1yrs (SD: 5.9). All patients underwent surgery for primary proximal femoral fractures. The gold standard three sarcopenia parameters were measured in 14% (1/7) of studies, two parameters were measured in the remaining studies 86% (6/7) studies, where both low muscle mass and low muscle strength parameters had to be present to diagnose sarcopenia. Skeletal muscle biopsies were used for biomarker assessment in 14% (1/7) of studies, the remaining 86% (6/7) studies assessed biomarkers from venous blood samples. Two studies (28%) showed the pathogenetic role of insulin-like growth factor IGF-I in sarcopenia, which mediates cell proliferation, apoptosis and differentiation. IGF-I was associated with muscle denervation in sarcopenia leading to subsequent muscle decline. Systemic inflammatory pathway biomarkers were assessed in 28% (2/7) studies, showing that tumour necrosis factor-α was lower in sarcopenic than in non-sarcopenic participants and IL-6 at baseline were significantly higher in the group of participants who died in the year after the hip fracture. In the remainder of the studies, serum myostatin levels were significantly decreased in sarcopenic patients compared to non-sarcopenic patients undergoing postoperative rehabilitation. Similarly, serum bioavailable vitamin D levels were significantly decreased in the sarcopenia group compared with the non-sarcopenia group. Overall, the BIOCROSS score was satisfactory for all included articles, with 4 studies ascertaining a score of 14 and remaining 3 studies a score of 13. Conclusions: The orthoapedic literature is limited and few molecular biomarkers of sarcopenia have been assessed in hip fracture patients. However, existing data in molecular studies confirms that sarcopenia increases postoperative morbidity and mortality. Sarcopenic patients are more likely to have higher expression of systemic pro-inflammatory biomarkers at baseline and during the recovery period from surgery. In studies, assessing specifically muscle biopsies, IGF-I and muscle denervation is associated with increased sarcopenia presence and poorer post operative outcomes. Further muscle tissue specific studies are required to identify therapeutic molecular targets, however if identified, sarcopenic patients stand to benefit from targeted peri-operative interventions that aim to improve outcomes.

A computational study of the effects of obesity on the inflammatory process in osteoarthritis

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Objectives: Obesity is a predominant risk of osteoarthritis (OA), and adipokines mediate the OA inflammation by signalling the release of other inflammatory mediators. As an effective method of prevention and intervention, exercise can alter the level of adiposity in addition to strengthening muscle to reduce the risk of OA, but the regulatory mechanism of inflammation remains unclear at the molecular scale. Therefore, this study aims to analyse the obesity-associated inflammatory process where body mass index (BMI), physical activity level (PAL) and nutrition are studied for the variations of adipokines, using a 5D computational model. Methods: The inflammatory activities are simulated through a computational model of adipokine-mediated inflammation developed from a four-dimensional cartilage model (Baker et al., 2017). Five mediators, the pro- and anti-inflammatory cytokines (PICs and AICs), matrix metalloproteinases (MMPs), fibronectin fragments (Fn-fs) and adipokines, are included to describe the level of inflammation, damage and obesity. The model was verified and nondimensionalised to analyse the inflammation dynamics through bifurcation diagrams. This study focuses on the application of the model with dimensional parameter estimation. Parameters are estimated according to the decay rates of those five mediators determined by their half-life. The sensitivity of minimum cartilage injury measured by a parameter of damage (C_{22}) is analysed when varying BMI. Over the inflammation system with BMI = 30, eight strategies of PAL intervention altering the adiposity are applied to the evolution of the inflammatory process where a certain damage (C_{22} = 1) is introduced at month 12. Results: The minimum damage inducing inflammation decreases to zero as BMI gradually reaches a threshold that results in a state of persistent inflammation. The normalised risk of inflammation onset exponentially rises, which qualitatively matches the report that each additional BMI unit can lead to a 15% increase in OA risk when the threshold is exceeded (Berenbaum and Sellam, 2008). In addition, PAL intervention reduces the adipokine level so that the risk of OA inflammation can be reduced within a window period of 4 months. However, it is found that high PAL can only prevent OA inflammation instead of returning to a healthy state of the system. The inflammatory responses are inhibited and postponed during the period of PAL intervention, and inflammation persistently exists after its activation if PAL intervention is outside the 4-month window period. Conclusions: This computational study simulated obesity-associated inflammation during OA and analysed the effects of BMI and PAL on the regulation of inflammation. Obesity significantly increases the inflammation risk through the reduction of the minimum damage level activating inflammatory process. The increase of PAL can reduce adiposity to regulate the inflammatory process before its onset within a 4-month window period after damage.

Waste Not Want Not: An Assessment of the Environmental Impact of Hip Hemiarthroplasties

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Introduction:With the UK leading the initiative to be net zero carbon emissions by 2040, it is imperative that change is made wherever possible to reduce the NHS carbon footprint. Establishing greener operating theatres is an integral part of sustainable healthcare.RCS England's "Green Surgery Checklist" provides trusts with an evidence-based checklist to reduce the environmental impact of operating theatres. One of which is to "recycle waste into the lowest carbon waste stream possible".Fragility hip fractures are a significant healthcare burden with an annual incidence of more than 76,000 cases/year. Of this, approximately 50% are intracapsular fractures. Due to an ageing population, the majority of patients are not medically suitable for a THR, hence hemiarthroplasties are the commonest operation recorded by the NHFD. This surgery is therefore a key starting point for research aiming for environmental change.Orthopaedics, as one of the largest surgical specialties, needs to consider how it can reduce its carbon footprint through the "reduce, reuse & recycle" mantra. Sustained behavioural change can only occur when supported by robust evidence.Aims:This study aims to assess the waste generation and associated carbon emissions from a cemented hip hemiarthroplasty.Methods:A prospective study of 15 hip hemiarthroplasties was performed at a high-volume hip fracture unit. Waste generated after each case was sorted and quantified. Disposal streams were defined as hazardous, dry non-hazardous and recycling.Hazardous waste was assumed to have been incinerated, which is known to generate 1.074KgeCO2/Kg.Results:A mean of 9.63 Kg (8.50-10.47) of waste was generated for each case. Only 11% of the waste was recycled, with the remaining waste incinerated. This equates to 9KgeCO2 emissions/case, and nearly ¼ million tonnes/year for the NHS as a whole. This is 1% of the NHS' total annual carbon emissions.The majority of the waste generated had the potential to be recyclable, but was not recycled due to unnecessary cross contamination with bodily fluids, poor waste management and a lack of information on the packaging itself.Conclusion:The current climate emergency presents a threat to the ongoing health of humanity. Any small meaningful change in our behaviour has the potential to be magnified into much greater global health benefits, and that change should start with our easily modifiable behaviours in theatres.

Time and Consent – The Effect of Extended Waiting Lists on the Consent Process

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Objectives: As the NHS grapples with extended wait lists for lower limb arthroplasty, the risk of reduced recall of critical information obtained during consenting increases. Consent forms are often used as documentation of the consent process rather than as the consent itself. Post Montgomery ruling, clinicians are charged with using a diverse range of consent aids to help identify material risk for patients. We set out to investigate how effectively patients awaiting lower limb arthroplasty retained procedural information and the potential costs of repeated consent sessions. Methods: We identified 59 patients were from the waiting lists for lower limb arthroplasty in a DGH. Each patient was interviewed via phone to assess recall of potential surgical risks, the sources from which they primarily received their information, and the number of return visits to consent clinics they had. Results: The average number of risks recalled negatively correlated with time since consent . No correlation with age was identified. Patients in their 40s and 50s sourced significantly more information from online sites, while patients over 60 obtained a larger proportion of information from consultants during clinic appointments. For patients of all ages, procedural leaflets continue to be a valuable information resource. Our findings reflect the current evidence base of generally poor patient recall of surgical risks. At National Tariff the cost of an orthopaedic follow up appointment is £99, highlighting a potential financial impact and the need to co-ordinate waiting list pathways. Conclusion: Extended time on waiting lists reduces the retention of procedural information. Further, there is an increased expense of healthcare since more consent sessions are required. Our results emphasise the necessity of co-ordinating waiting list pathways and implementing age-specific consent aids to streamline the consent process.

Cauda Equina Syndrome- Can we get it right first time? An audit of Orthopaedic and Emergency Departments in St Marys Hospital, Isle of Wight

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Background: The cauda equina is a collection of nerves and nerve roots distal to the terminal end of the spinal cord, the conus medullaris, typically stemming from L1 to L5. Cauda Equina Syndrome (CES) often occurs due to compression of these nerve roots. It is rare but potentially devastating, and can cause severe symptoms, such as bilateral sensory and motor deficits, and urinary, bowel and sexual dysfunction. A detailed history is essential to identify red flag symptoms in patients suspected of having cauda equina syndrome, and should include back pain, bowel or bladder changes and bilateral sciatica. Decreased anal tone, saddle anaesthesia, and bilateral weakness and sensory deficit to the lower limbs. The Getting It Right First Time (GIRFT) team created a national CES pathway (February 23) to support teams making diagnosis and treating the condition without delay as per best practice guidelines for referral, imaging, surgical techniques, pain control and post-operative support. Methods: We are presenting an audit of 40 patients presenting to St Marys Isle of Wight Hospital orthopaedic and emergency departments since September 2023. We are retrospectively looking at clerking booklets and notes to assess whether their history, examination and documentation adhered to the GIRFT pathway. Results: Of 40 patients audited identified from the orthopaedic take list- 13 had no available data. 18 patients were asked about sudden onset bilateral radicular pain or unilateral radicular leg pain that has progressed to bilateral. 22 patients were asked about severe lower back pain. 15 patients were asked about altered perianal, perineal or genital sensation S2-S5 dermatomes. 24 patients were asked about difficulty initiating micturition or impaired sensation of urinary flow (urinary incontinence). 12 patients were asked regarding severe or progressive neurological deficit of both legs, such as major motor weakness with knee extension, ankle eversion, or foot dorsiflexion. No patients asked about sexual dysfunction. Only 5 out of 25 patients had documentation of post-void bladder scan, and only 1 patient had a documented catheter tug. Only 17/25 patients had sensory examinations documented, with minimal dermatomal distribution. Conclusion: We conclude that the documentation of patients referred with CES is poor. Key areas identified for improvement are the sensory examination and bladder scan. We have designed a proforma to aid documentation of history taking and examination. We plan to reaudit this once the proforma enters circulation at St Marys Hospital, Isle of Wight.

Mechanical axis image quality of the EOS imaging system compared to digital radiography

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Objective. To compare the image quality of the mechanical axis performed on the (low-dose) EOS imaging system to that of digital radiographs (DR). Methods. Retrospectively, this study included a total of 100 patients who had undergone both EOS and DR mechanical axis imaging. Images (analysed over six months) were randomly selected from a picture archiving and communication system in the Radiology Department at (BLINDED). Three observers (a paediatric musculoskeletal radiologist with 22 years of experience, a paediatric radiographer with 10 years of experience, and a radiographer with 5 years of experience) independently scored the DR and EOS images according to modified European guidelines on quality criteria for diagnostic radiographic images in paediatrics. They assessed the following criteria: resolution (visibility of trabecular pattern/bony outline), coverage of the area of interest (pelvis to ankles), positioning (level hips, patellae facing forward), contrast (a noticeable difference between muscle and fat), and motion. A paired t-test was used to test for a statistical difference between the quality scores for each modality, and the Kappa coefficient was used to evaluate the agreement between the observers. Results. The most frequently met criterion for EOS was "resolution" (exceptionally high, with an agreement coefficient (AC) of 0.993); for DR, it was "motion" (agreement coefficient of 0.958, indicating almost perfect concordance). The least frequently met criterion for EOS was "level hips" (moderate agreement, with an AC of 0.684); for DR, it was "patellae facing forward" (substantial agreement, with an AC of 0.644). All p-values are less than 0.001, indicating that these results are statistically significant. Conclusion. The mechanical axis image quality of the EOS imaging system is as good as that of DR, so EOS can be used instead of DR in this context and has the advantage of simultaneous capture of anteroposterior (AP) and lateral images and 3-dimensional reconstruction using a sterEOS workstation.

Evidence of fretting corrosion at the modular shell interface of retrieved ceramic-on-metal bearings for total hip replacement

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Objectives: Ceramic-on-metal (CoM) total hip replacements (THRs) were introduced as an alternative hard-on-hard bearing option. Theoretically these implants could reduce wear due to the differential hardness of the articulating components whilst eliminating risks associated with metal-on-metal or ceramic-on-ceramic implants such as edge loading of a metallic femoral head or malseating/fracture of a ceramic liner. In reality, CoM THRs were not widely adopted and have been associated with poor outcomes [1] and increased blood metal ions [2]. The source of these excess ions has not yet been identified but this remains a relevant issue despite their largely abandoned use as they share a modular shell concept with dual mobility (DM) THRs whose use continues to rise in both primary and revision settings. The modular shell interface includes a metal liner seated within a metal shell and may act as a potential source of ion release through a corrosive mechanism. Therefore, the aim of this study was to assess the modular shell interface of retrieved CoM implants for evidence of fretting corrosion. Methods: The backside of 19 modular metal liner inserts from retrieved CoM implants (study references: 09/H1307/60, 18/NW/1707, 24/PR/0385) were visually inspected for signs of fretting corrosion and graded using a modified Goldberg scoring system [3]. Each liner was assigned a score of 1 (none), 2 (mild), 3 (moderate) and 4 (severe) based on the extent and severity of fretting corrosion identified within the taper region. Results: No evidence of fretting corrosion was identified on four (21%) implants. A total of six (32%) implants were identified with mild grade 2 fretting corrosion, six (32%) with moderate grade 3 fretting corrosion and three (16%) with severe grade 4 fretting corrosion. There was no discernible trend between the Goldberg scores and implant time in-vivo. Conclusions: This is the first study, to the authors' knowledge, which investigates fretting corrosion at the modular shell interface of CoM bearings. Evidence of fretting corrosion was identified on the majority (80%) of samples, and approximately half of the implants presented with moderate to severe fretting corrosion which included black debris surface deposits. These results align well to those previously reported for both metal-on-metal [4, 5] and DM [6] modular shell interfaces, although few studies have investigated this design feature in any bearing type. This suggests that the modular shell interface may be a potential source of metal ion release, although further investigations are needed to compare this data against liner backside, head trunnion and bearing surface wear and patient blood ion levels which are planned in a future study. References: [1] National Joint Registry, Annual Report 2022.[2] Mehta et al. J. Orthop. 2021, 24, 131-4.[3] Goldberg et al. Clin. Orthop. Relat. Res. 2002, 401, 149-61. [4] Higgs et al. J. Arthroplasty. 2013, 28 (Suppl. 1), 2-6.[5] Hothi et al. J. Arthroplasty. 2015, 30 (9), 1652-6.[6] Kolz et al. J. Arthroplasty. 2020, 35, 3326-9.

Preventing periprosthetic joint infection: a novel drug-release sol-gel device coating

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Introduction

Arthroplasty surgeries and their subsequent complications are increasing, including devastating periprosthetic joint infections which follow 1-3% of primary surgeries[1] and approximately 15% revision procedures. The biofilm nature of these infections results in treatment resistance and a significant challenge, requiring invasive revision surgery and high dose, prolonged antibiotic treatment .Current prevention strategies include antibiotic-loaded bone cement; however, cementless applications have increased in recent years thus there is an urgent need for alternative, local antimicrobial delivery methods[2]. A novel, ultrathin silica-based sol-gel technology [3] is evaluated in this research as a localised antibiotic delivery method to prevent infection following surgery, including its biofilm growth inhibition, antibiotic elution and osteocompatibilty. This includes development of an *ex vivo* bone infection model which will reduce the need for *in vivo* animal bone healing experimentation in future research.

Methods

Reduction in clinically relevant microbial activity and biofilm reduction by the antimicrobial sol-gel coating, containing a selection of antibiotics, were assessed via disc diffusion and microdilution culture assays using the Calgary biofilm device[4].Proliferation, morphology, collagen, and calcium production by explanted primary bovine osteoblasts and bone marrow derived human mesenchymal stromal cells cultured upon antimicrobial sol-gel surfaces were examined. Cytotoxicity was evaluated using Alamar blue staining and lactate dehydrogenase assays. Concentrations of silica, calcium and phosphorus compounds within the cell layer cultured on sol-gel coatings and eluted into media, were quantified using ICP-OES. Cell viability was monitored via Hoechst and calcein staining over a two week culture period in addition to immunocytochemical staining for apoptosis and osteocalcin to assess cellular phenotype.

Results

Low antibiotic concentrations within sol-gel had an inhibitory effect on biofilm growth, for example 0.8 mg ml^{-1} tobramycin inhibited clinically isolated *S. aureus* (MRSA) growth with an 8-log reduction in colony forming units. There was no significant difference in metabolic activity between untreated and sol-gel exposed primary bovine osteoblasts in elution-based assays. In direct contact assays, there was no significant difference in viability of these cells. A reduction (32-57%) in metabolic activity in these direct contact assays following exposure to sol-gel over 14 days was likely to be due to increased osteoinduction, whereas no impact upon cell proliferation were observed ($p=0.92$ at 14 days culture). The morphology of primary osteoblasts was unaffected by culture on sol-gel coatings and collagen production was maintained, whilst calcium containing nodule production within bovine osteoblastic cells was increased 16-fold after 14 days culture upon solgel.

Conclusion

The ultrathin sol-gel coating showed low cytotoxicity, strong biofilm reducing activity and antimicrobial activity, demonstrating that sol-gel delivery of antibiotics could provide local antimicrobial effects to inhibit periprosthetic joint infection without the need for bone cement. Future work will develop and evaluate sol-gel performance in an *ex vivo* explant bone infection model which will reduce the need for animal experimentation.

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Micro-CT evaluation of thermally transitioned 3D bio-printed bone models

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Objectives: *In vitro* 3D bio-printed bone models typically do not encompass the complex micro-architecture of bone, including both cortical and trabecular morphology to achieve bio-mimicry and structural integrity. This study primarily aimed to utilise micro-CT as a high-resolution imaging method to generate computer assisted design (CAD) models from *ex-vivo* murine bone. Thermally transitioned polymer-based Laponite®, encapsulating hydroxyapatite nanoparticles (HAnp), known as B-gel[1], and pre-osteoblasts (MC3T3-E1) was optimised to achieve high fidelity and shape retention via extrusion-based bioprinting, and investigation of composition over time was achieved by micro-CT. Methods: *Ex-vivo* murine tibia, femur and vertebrae were imaged using Micro-CT with a voxel size of 9 µm and reconstructed to determine the morphometry of Tb and Cb. A volume of interest of Tb and Cb was processed and exported as a binary STL file. Utilising Autodesk® CAD software, Meshmixer and Fusion 360, the STL model was rendered *in-silico* to a translatable printable resolution in the mm range, for *in-vitro* bio-printing. Alongside this, a control STL model with known dimensions was developed as a simplified lattice (10W X 10L X 4.13H mm). Extrusion based bioprinting (BioX, Cellink) using B-gel (0.5mg/ml HAnp)[1] encapsulating fluorescently tagged - MC3T3-E1, was achieved using a thermo-reversible microparticle support slurry to achieve high structural stability during bioprinting of 3D structures. A variety of printing parameters was used to determine optimal printing fidelity, followed by culturing models for 21-days in +/- ascorbic acid, to allow differentiation. Models were compositionally analysed via Micro-CT, and for cellular population by fluorescent microscopy on Day 0, 7, 14 and 21 prior to fixation and decalcification for histological and immunohistochemical analysis. Results: Multi-species analysis of Cb and Tb highlighted significant differences in the morphometric outputs for both mouse and rat (N=3), including Tb. Thickness (mm) of the femur being 0.06 mm and 0.09 mm, respectively. Extrusion based bio-printing has limited resolution capability due to nozzle width inner diameter of 0.403 mm and

mechanical pressure impact on cells, therefore the morphometric outputs simply inform the ratios of possible creation of the 3D model. Optimisation of printing parameters were completed on a control lattice structure, with an average printing pressure of 65 kPa and speed of 7 mm/s to allow a representative structure to be produced (N=3). Due to the thermo-responsive nature of the B-gel, structural fidelity was not representative in micro-CT, however tissue mineral density showed an increase over a 21-day differentiation, 1.09 to 1.14 g/cm^3, demonstrating increased calcium deposition in culture (Figure 1). Microscopy reveals a stable population of viable osteoblasts. Conclusions: *In vitro* 3D bone models typically do not encompass the complex micro-architecture of bone, including both cortical and trabecular morphology. Using micro-CT as a method of 3-dimensional quantification allows for *ex-vivo* bone models to be rendered and translated for 3D bio-printing. This study represents the optimisation stages of developing a high-fidelity bone model, with the ability to retain cellular viability and calcification of the 3D bio-printed structure. References: 1A.A. Thorpe., S. Creasey., C. Sammon., and C. Le Maitre (2016). Doi: 10.22203/eCM.v032a01

Relationship between the mouse cortical thickness and its failure load evaluated along different loading directions

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Objectives: The tibia midshaft cortical thickness (Ct.Th) is a good predictor of the failure load (FL_FE) estimated by previously validated finite element (FE) models when the tibiae of treated or untreated ovariectomised C57BL/6 mice are compressed along the axial direction (R^2: 84.5%; $p<0.001$) [1]. In the same group of mice, validated micro-computed tomography (micro-CT) based finite element (micro-FE) models have shown that the loading direction affects the computed FL_FE [2]. The aim of this study was to investigate if the midshaft Ct.Th is a good predictor of the FL_FE even if calculated for different loading directions. Methods: Longitudinal micro-CT images were taken of the tibiae of eleven ovariectomised mice at ages 18 and 20 weeks [3]. Six of the mice underwent external controlled mechanical loading to stimulate bone apposition at age 19 weeks. The Ct.Th was measured in the bone midshaft (1mm thick region) [3]. Micro-FE models were generated, based on the segmented micro-CT images. Three models using unitary loads were linearly combined to simulate a range of loading directions, generated as a function of the angle from the inferior-superior axis (θ, 0°–30° range, 5° steps) and the angle from the anterior-posterior axis (φ, 0°: anterior axis, positive anticlockwise, 0°–355° range, 5° steps). θ=0° and φ=0° corresponded to the nominal axial case. The minimum principal strain was calculated and used to estimate the FL_FE, by linearly scaling the resultant strain until 10% of the nodes reached the critical strain level of −14,420 με [4]. Linear regression analyses were carried out to evaluate the correlation between the Ct.Th and the FL_FE at each loading direction. Results: The midshaft Ct.Th was a modest to good predictor of the FL_FE across all tested loading directions (R^2-range: 67.8-87.9%, all $p<0.001$). For

the loading conditions θ = 5°, φ = 215-280° and θ = 10°, φ = 225-290°, the R^2 values were all greater than that of the nominal axial case, with the maximum occurring at θ = 5°, φ = 240°. Above θ = 10°, the R^2 values were generally smaller than that of the axial case. Conclusion: These results suggest that the midshaft Ct.Th is a good surrogate measurement of FL_FE for a range of loading directions within 10° from the axial one. Above this, the midshaft Ct.Th loses its predictive ability. Acknowledgments: This work was supported by the EPSRC (grants X/013991-12, EP/K03877X/1 and EP/S032940/1) and the NC3Rs (NC/R001073/1). References: [1] Roberts B.C. et al. J. Orthop. Res. 2023, doi: 10.1002/JOR.25777; [2] Farage-O'Reilly S.M. et al. Front. Bioeng. Biotechnol. 2024, doi: 10.3389/fbioe.2024.1335955; [3] Roberts B.C. et al. Sci. Rep. 2020, doi: 1038/s41598-020-65921-1; [4] Oliviero S. et al. JMBBM. 2021, doi: 10.1016/j.jmbbm.2020.104190.

Development of a Primary Human Chondrocyte Culture Method for the Bioassay of Mesenchymal Stem Cell Secretome

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Background: Recent pilot studies in the field of regenerative medicine have demonstrated the feasibility of transplanting allogeneic mesenchymal stem cells (MSCs) to stimulate cartilage regeneration in osteoarthritis (OA). Nevertheless, little is known about the contributing factors of MSCs that facilitate cartilage regeneration. The overall goal of the work presented here is to optimise in vitro culture models of primary chondrocytes (PC) as a biological readout for a subsequent application to assess the cartilage regenerative potential of MSC derived factors. Aims: 1) To characterise the expression levels of anabolic and catabolic markers for human primary chondrocytes between freshly processed and frozen isolates. 2) Determine the influence of monolayer (2D) v.s 3D in vitro culture methods on anabolic and catabolic marker expression profiles of these cells and thus 3) create a reproducible model to study the effect of the MSC secretome on chondrocyte health.Methods: Comparison between freshly isolated versus frozen primary chondrocytes was performed on (n=3) isolates from relatively healthy explanted human cartilage obtained during knee replacement surgery (ICRS grade 0-1). 2D and 3D culture models were compared for the same isolates. qPCR was used to analyse the expression of anabolic, extracellular matrix (ECM) markers COL2A1 and ACAN, vs. catabolic markers of MMP13, GADD45β, and C/EBPβ. Statistical analysis was performed using paired t-test. Results: We found that the primary chondrocyte phenotype of (n=3) does not change when cultured after frozen at the end of isolation, with no differences in expression for COL2A1 (p-value: 0.76) and ACAN (p-value: 0.67), MMP13 (p-value: 0.33), GADD45β (p-value: 0.27), and C/EBPβ (p-value: 0.25). Additionally, fold change of gene expression analysis for COL2A1, ACAN, MMP13, GADD45β, and C/EBPβ (p- value: 0.43, 0.76, 0.77, 0.54, and 0.93, respectively) at day 3 culture were similar to those at day 0, indicating that cellular phenotype does not significantly alter during short term culture after freezing and thawing. Comparison between monolayer and 3D pellet culture models also demonstrated no differences in COL2A1, MMP13, GADD45β, and C/EBPβ (p- value: 0.34, 0.35, 0.72, and 0.63, respectively) gene expression. However, a trend towards difference in the level of gene expression of ACAN (p-value=0.08) between monolayer and 3D model was observed, with increased expression in 3D culture. Similarly, all analysed genes show no

increase in relative expression (day 0 vs day 3) in all of tested markers COL2A1, ACAN, MMP13, GADD45β, and C/EBPβ (p- value: 0.40, 0.41, 0.22, 0.43, and 0.48, respectively). Conclusion: Characterisation of (n=3) primary chondrocyte isolates demonstrated a hypertrophic phenotype where catabolic genes had higher expression than anabolic genes in both monolayer and 3D culture models , as well as fresh and frozen cultures. Our data show that there is no difference between fresh and frozen cultures. Similarly, the difference between monolayer and 3D culture model is not significant. Testing of the impact of MSC-conditioned media and putative MSC-secreted proteins on chondrocyte hypertrophy is currently underway.

It is time we started treating arthroplasty as a life-saving intervention: what have wearables, machine learning, and epidemiology taught us? (The UK Biobank)

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Objectives: Epidemiological studies suggest that people with arthritis die younger than non-arthritic aged-matched comparators. However, the causal mechanism underpinning this association has yet to be conclusively demonstrated. One possible explanation is a lack of physical activity (PA) in those with end-stage lower limb arthritis. Given emerging evidence from large cohort studies using wearables and machine learning to estimate PA, is it time we considered arthroplasty a life-saving intervention? Methods: We conducted a harmonisation review, drawing upon recently published literature on PA and all-cause mortality (Strain et al., 2020) and PA and arthritis (Small et al., 2024) in the UK Biobank. The UK Biobank is a large population cohort study with 96,476 participants with wrist-worn accelerometry data, 3506 of whom have been studied independently as arthritis patients. We harmonised the literature to explore the potential mortality risk reduction conferred by arthroplasty in end-stage arthritis patients. Results: Small et al. demonstrate patients with an ipsilateral hip replacement have equivalent PA levels to their non-arthritic peers at more than 1-year post-surgery. Further, end-stage arthritis patients have significantly lower moderate-vigorous activity than non-arthritic peers. Strain et al. show that low PA and lower-intensity PA are strongly associated with all-cause mortality. Harmonisation of these two studies suggests that arthroplasty confers a significant all-cause mortality hazard ratio risk reduction of approximately 0.2, based on volume alone. If intensity is also considered, the all-cause mortality risk reduction is closer to 0.5. Conclusion: Extrapolation of recently published epidemiological studies using wearables and machine learning suggests that arthroplasty reduces all-cause mortality through the restoration of PA. The magnitude of this all-cause risk reduction is not small, at roughly double the risk reduction conferred by statins based on volume of activity alone. This finding challenges the dogma that no harm – other than duration of pain – is done to end-stage arthritis patients facing lengthy waits for arthroplasty surgery. Further studies are needed to evaluate the risk/benefit of early intervention vs. traditional orthopaedic considerations, such as revision risk, patient selection and prioritisation for surgery.

Optimizing EDTA Decalcification Protocol for Osteochondral Explants to Maximise Transcriptomic Potential

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Objectives: Spatial transcriptomics is a new technology that could help unravel the molecular biology of osteoarthritis (OA), but to-date there is no evidence of successful application due to RNA degradation during processing of osteochondral tissue. In this study, the decalcification methodology was optimised to maximise preservation of RNA integrity for spatial transcriptomics analysis. Methods: Low- and high-grade OA osteochondral explants (7mm diameter) were harvested from surgical tissue of patients undergoing total knee arthroplasty surgery (REC reference: 20/SC/0144). To investigate the effect of temperature and time on RNA quality, explants from 5 patients were each decalcified in 15% EDTA at varying temperatures (4°C, room temperature and 37°C) for 1 week, 2 weeks or 4 weeks. Tissue was either snap frozen for immediate RNA extraction using TRIzol or embedded to paraffin blocks. Following embedding, RNA was extracted from sections using Qiagen RNeasy FFPE extraction kit. RNA yield and fragmentation rate was assessed with a bioanalyzer. Less explants were decalcified for 4 weeks due to tissue availability and thus were not included in statistical analysis. Furthermore, the timeframe for complete decalcification using μCT and impact of temperature was assessed in explants from 3 patients. Results: DV200 was slightly higher in samples decalcified for 1 week than those decalcified for 2 weeks for each temperature condition (Low grade 1week vs. 2weeks median: 4°C= 42.0% vs. 40.0%, Room Temp= 30.0% vs. 27.0%, 37°C= 27.0% vs. 21.0%; High grade 1week vs. 2weeks median: 4°C= 41.0% vs. 35.0%, Room Temp= 33.0% vs. 30.0%, 37°C= 17.0% vs. 24.0%), although this failed to reach significance (Kruskal-Wallis test, $p > 0.05$). Temperature also negatively affected RNA quality, with highest DV200 values in 4°C followed by Room Temperature and lastly 37°C, but also failed to reach significance (Kruskal-Wallis test, $p > 0.05$). Explants decalcified in higher temperatures resulted in complete decalcification faster (Low- and High grade combined median: 4°C= 20.5 days, Room Temp= 12.5 days, 37°C= 9.5 days), which reached significance in 4°C compared to 37°C (Dunn's multiple comparison test: 4°C vs. 37°C, $p= 0.007$). Even though explants took longer to decalcify in lower temperatures, DV200 was higher (Low- and High-grade combined median: 4°C= 19.0%, Room Temp= 11.5%, 37°C= 5.5%), with statistical significance reached in 4°C compared to 37°C (Dunn's multiple comparison test: 4°C vs. 37°C, $p= 0.037$). Conclusions: This study demonstrated longer time and higher temperature decreased RNA quality. Whilst lower temperatures resulted in a longer decalcification period, this did not result in more RNA degradation compared to decalcifying at higher temperatures, with the highest DV200 at 4°C. Thus, we recommend decalcification at 4°C to retain RNA integrity. The findings from this study will help guide successful spatial transcriptomics of osteochondral tissue.

Activation of the Interleukin-6 Signalling Pathway in Human Osteocytes through the Mechanosensitive Ion Channel, Piezo1

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OBJECTIVES: Using our physiological human 3D model of osteocytes, we found load increased the mechanosensitive ion channel, Piezo1 16-fold. In addition, treatment of osteocytes with the mechanical load mimic, Yoda1 increased expression and release of interleukin-6 (IL6), a proinflammatory cytokine that drives bone resorption and is implicated in the pathogenesis of post-traumatic osteoarthritis (PTOA). This study investigated the effect of IL6 and Yoda1 in our 3D osteocyte model to reveal mechanisms underlying interactions between load and inflammation, major risk factors for the development of OA.

METHODS: Human Y201 MSCs were embedded in type I collagen gels and differentiated to osteocytes in osteogenic media for 13-days. Cells were treated with IL6 (5ng/ml)/sIL6r (40ng/ml), Yoda1 (5mM) or IL6/sIL6r+Yoda1 for 2-24-hours (n=6-10); vehicle treated cells served as controls (n=4-6). cDNA was analysed by RT-qPCR and relative quantification (DDCt method) and an IL6/STAT3 PCR Array (Qiagen; regulated >1.5-fold); validation of 7 genes was performed from duplicate cultures. Proinflammatory cytokine release into the media was analysed using a multiplex ELISA (MSD). Data was compared using ANOVA (Minitab).

RESULTS: RT-qPCR: IL6 mRNA was increased following 2-hrs of Yoda1 treatment (103-fold; $p<0.001$ vs control), IL6/sIL6r treatment (7-fold; $p=0.009$), or Yoda1+IL6/sIL6r (5.5-fold, $p=0.019$ vs control, $p=0.001$ vs Yoda1). IL6/STAT3 PCR array: 19 genes were up regulated and 13 genes down regulated ($p<0.05$) by IL6/sIL6r + Yoda1 treatment. PCR array validation by RT-qPCR: 7 of the upregulated genes were chosen for validation; upregulation of 5/7 by Yoda1+IL6 were confirmed which included IL6, PIM1, IL1B, IL11, and MA2K1. However, Yoda1 alone increased MAP2K1 (8.9-fold, $p<0.001$), IL11 (7.5-fold $p<0.001$), EGFR (13.9-fold, $p<0.001$), and CEBPD (28.4-fold, $p<0.001$). Multiplex ELISA: 2-hrs of Yoda1 treatment resulted in an increased release into the media of IL6 protein (6.3-fold; $p=0.005$) whereas 24-hrs treatment resulted in an increased release of IFN-g (1.5-fold, $p<0.001$), IL12p70 (2.1-fold, $p<0.001$), IL6 (1.4-fold, $p=0.001$), and IL4 (7-fold, $p<0.001$) and an increase in the mean level of IL10 (1.3-fold, $p=0.09$) and TNFα (1.3-fold, $p=0.147$). IL6/sIL6r treatment for 2-hrs caused an increase in the release of IFN-g (4.5-fold; $p<0.001$), IL2 (3.8-fold, $p<0.001$), IL1β (2.6-fold, $p<0.001$), IL13 (2.4-fold, $p=0.009$), IL12p70 (3.4-fold, $p=0.001$), TNF-α (2.8-fold, $p=0.001$), IL10 (3.8-fold, $p<0.001$), and IL4 (3.8-fold, $p<0.001$). In contrast, IL6/sIL6r treatment for 24-hrs only increased release of IL4 (1.3-fold, $p=0.012$) and reduced mean levels of IL13 (1.3-fold, $p=0.057$). IL6/sIL6r + Yoda1 for 2-hrs prevented some of the IL6 induced increase in IFN-g (1.3-fold, $p<0.001$), IL10 (1.4-fold, $p=0.034$), and IL4 (1.4-fold, $p=0.025$) but levels remained significantly higher than control levels. IL6/sIL6r + Yoda1 for 24-hrs increased release of IL2 (1.3-fold, $p=0.006$) and IL1β (1.2-fold, $p=0.039$).

CONCLUSIONS: This study highlights the importance of the Piezo1 mechanosensitive channel in linking mechanical and inflammatory pathways in osteocytes. Yoda1 mediated an increase in IL6 signaling

directly linking mechanical activation of Piezo1 and inflammation, which may contribute to mechanically induced joint degeneration in diseases such as osteoarthritis. Understanding the role of Piezo1 in osteocyte signaling is important since mechanisms underlying abnormal joint mechanics are poorly understood despite it being the major risk factor for developing osteoarthritis.

In-vivo kinematics of the lumbar spine measured using biplane videoradiography and magnetic resonance imaging

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Objectives: Spinal disorders, such as low back pain, incur a substantial societal and economic burden, with an estimated 619 million affected by back pain globally in 2020[1]. Currently, there is a lack of understanding about these disorders and their treatments which is further impeded by the challenge of measuring in-vivo spine biomechanics. Biplane Videoradiography (BVR) is an imaging technique that allows direct measurement of the individual vertebra during dynamic activities. To use this technique to evaluate the in-vivo biomechanics of spine disorders, it is first necessary to characterise the lumbar spine kinematics in a healthy population. The objective of this study is to develop an in-vivo imaging protocol to quantify the kinematics of the lumbar spine during different activities of daily living. *Methods:* Ethical approval for this study was obtained from the London Bridge Research Ethics Committee. For the development of the protocol one healthy volunteer was recruited and written informed consent was received. The participant underwent Magnetic Resonance imaging (MRI) (Magnetom 3T Prisma, Siemens) using a T1 VIBE sequence which was manually segmented into 3D vertebra and pelvis models (Simpleware Scan IP, Synopsis). Anatomical coordinate systems were applied[2] to each individual vertebra. BVR (10Hz, 3.33ms, 85kVp and 320ma) and simultaneous marker-based motion capture (Qualisys) were obtained during different range of motion (ROM) activities and other activities of daily living. Bone position and orientation for the five lumbar vertebrae were calculated by manual matching of 3D bone models to X-ray images (DSX Suite, C-motion, Inc.). Intervertebral kinematics were calculated in MATLAB (MathWorks, Inc.) based upon the recommended International Society of Biomechanics standards[3]. A 10kg stoop lift and side bending activity were chosen to develop the protocol. *Results*: An imaging protocol was developed to enable quantification of in-vivo lumbar spine kinematics. The preliminary results showed that, during the 10kg stoop lift, L1-L2 had the largest ROM for flexion-extension (8°) compared with L2-L3 (4°), L3-L4 (6°) and L4-L5 (5°). During the side bending activity only L3-L5 was visible in the BVR volume. L3-L4 was found to have the highest peak lateral bend of 10°, compared with L4-L5 (6°) and L5-S1 (0°), contributing to the overall lateral bending between L3-S1 of 16°. These results demonstrate the various contributions of different vertebra towards overall lumbar spine motion during different activities. *Conclusion*: An in-vivo imaging pipeline combining BVR and MR imaging was successfully developed. Future work will apply this protocol on up to 15 healthy volunteers and to analyse additional activities including twisting, lateral lift, and backward bending. Additionally, the coupling of in-vivo kinematics will be investigated to understand relative vertebra motion and how this may change due to injury or disease. *References:* [1]Ferreira, M. L. et al. Lancet Rheumatol. (2023).

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INFLUENCE OF MECHANICAL LOADING ON HUMAN OSTEOCHONDRAL TISSUE EXPLANTS

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Objectives: Osteoarthritis (OA) is a debilitating chronic disease, the development of disease modifying treatments are hampered due to gaps in understanding disease pathophysiology. Mechanical loading is an important risk factor for OA. To date, its study using physiologically relevant human tissues is lacking, with most studies using animal models, or in vitro systems that lack the matrix-cell connections essential for mechanotransduction. Here, a human osteochondral explant model was developed to maintain viability and phenotype of chondrocytes, osteoblasts and osteocytes during culture, enabling application of compressive and hydrostatic load. Methods: Osteochondral explants (7mm diameter) were harvested from patients undergoing knee arthroplasty for OA from regions of cartilage graded ICRS 0/1 and 2/3. Samples were either fixed immediately or cultured in low glucose DMEM, FBS free media in normoxia (21% O2) or physioxia (5% O2) for 2 weeks (compressive study) or 1 week (hydrostatic study) before application of load. Samples were subjected to either high magnitude compressive load (1.5-3MPa, 1Hz) or low magnitude hydrostatic load (0.6-0.9MPa 1Hz) for 30 mins and returned to culture for 24 hours post-loading prior to fixation, EDTA decalcification and paraffin embedding. RNA was extracted for qRT-PCR for anabolic and catabolic factors. Histological staining and immunohistochemistry (IHC) were applied to investigate cellular phenotype and matrix composition. IHC data was analyzed using modified Q-Path protocol specifically for low cellularity tissues. Results: Viability was retained in all regions of the osteochondral explant following 3 weeks in culture, with low caspase 3 staining (<18%), and positive total message RNA in situ hybridisation. Collagen type II immunopositivity was observed within cartilage within cells and matrix in similar staining in cultured (0/1:47%; 2/3:35%) and directly extracted tissues (0/1:49%; 2/3:33%). MMP 13 immunopositive staining was present especially within chondrocytes in high grade tissues (0/1:10% v/s 2/3:42%). Tissues from high grade regions retained significantly higher catabolic cytokine and enzyme expression than low grade regions ($P<0.05$), whilst low grade osteochondral explants showed significantly higher expression of anabolic factors ($P<0.05$). Following culture tissues retained collagens and GAGs matching the ECM composition observed in directly extracted tissues. Hydrostatic loading decreased cellular immunopositivity for collagen type II and increased catabolic cytokine immunopositive staining within low grade tissues (IL-1:20% non-load, 41% loaded). Whilst compressive loading increased collagen type II but not aggrecan in both low grade and high-grade tissues, and decreased catabolic factors including IL-1, MMP3 & 13 at gene and immunopositivity in high grade tissues and IL-1 within osteocytes across low grade and high-grade tissues ($P<0.05$) (Figure 1). Conclusion: This study has developed an osteochondral explant model for human tissues which retains viability and cell phenotype of chondrocytes, osteoblasts and osteocytes for up to 3 weeks in culture, with excellent retention of normal matrix expression. Mechanical loading using both hydrostatic and compressive loading systems induced changes in cellular phenotype with a switch to more anabolic conditions following compressive mechanical loading and catabolic following

hydrostatic loading. This culture system can be applied to develop an improved understanding of mechanotransduction within osteochondral tissues and differential regulation between non-degenerate and degenerate tissues.

Using Mesendoderm Progenitor Cells Seeded in Hydrogel Biomaterial as a strategy to Regenerate the Intervertebral disc

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BACKGROUND: Low back pain, the leading cause of disability worldwide and is strongly associated with degeneration of the intervertebral disc (IVD). We have previously demonstrated than an injectable biomaterial 'NPgel' can induce regeneration within organ culture systems of goat and human cadaveric IVDs. The combination of this biomaterial with embryonic precursors for the cells within the nucleus pulposus (NP), could be an attractive regeneration strategy. This study investigates the viability and phenotype of mesendoderm progenitor cells (MEPCs) generated from induced pluripotent stem cells (iPSC), within NPgel in vitro to determine the ability of NPgel to drive differentiation to matrix producing cells under conditions which mimic the IVD. Furthermore, the safety and short-term efficacy was then investigated within an ovine model of disc degeneration. METHODS: iPSC were differentiated into MEPCs using culture on laminin coated plates and CHIR stimulation, and MEPCs were seeded into NPgel and cultured for upto 4 weeks at 5% O2. Histological and immunohistochemical analysis was performed to investigate MEPCs viability, phenotype, and extracellular matrix synthesis. An ovine model of disc degeneration was induced through nucleotomy in a block design in 4 adult sheep, with degeneration induced in 5 lumbar discs within each animal. After 5 weeks to enable degeneration to establish, 2 sheep were treated in 3 alternating lumbar discs with NPgel injection, and 2 sheep treated with NPgel+MEPC injection. The remaining n=2 degenerate discs in each animal remained as untreated degeneration only controls. MRI of lumbar spines was undertaken prior to sacrifice to evaluate disc height and Pfirmann grading, peripheral blood collected haematological, biochemical, metabolic and immunological (lymphocyte/monocytes) evaluation prior to induction of degeneration, post degeneration (5wks) and post treatment (2 months). Three months following treatment sheep were sacrificed and spines processed for: macroscopic Thompson grading, Histological grading, and immunohistochemical assessment. RESULTS: MEPCs cultured within NPgel survived and were immunopositivity for brachyury, and Sox 9, and following 4-weeks in culture showed immunopositively staining for Aggrecan and Collagen type II. Ovine in vivo treatment with NPgel+MEPCs showed a slight increase in disc height index. No adverse reactions were seen locally within IVD tissue or systemically with no induction of systemic activation of T cells or monocytes. Histological grading showed similar degeneration in IVDs treated with NPgel alone or NPgel+MEPC. A signifanct increase in GAG was seen in the NP tissue following treatment with NPgel+MEPC compared to NPgel alone, which was accompanied with an increase in aggrecan immunopositivity. DISCUSSION: NPgel was shown to support the differentiation of iPSC-MEPCs towards

notochordal/nucleus pulposus cells and were delivered safely to an animal model of disc degeneration, this could have potential to be injected into patients that suffer from disc degeneration. ACKNOWLEDGEMENTS: This project has received funding from the European Union's Horizon 2020 research and innovation program under grant agreement No 825925. CONFLICT OF INTEREST: CLM and CS are inventors on the patent for NPgel which has been licensed to Orthoson Ltd.

The biomechanical outcomes of fresh osteochondral allograft (FOCA) for articular cartilage defects of the knee – A systematic review

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Objectives: Fresh osteochondral allograft (FOCA) is a surgical treatment option for patients with symptomatic osteochondral lesions of the knee. Research has shown the treatment to be effective in defects >2cm^2 , and improvements in clinical outcomes have been reported post-operatively. Two common symptoms of osteochondral lesions are locking of the knee and joint instability. While FOCA aims to eliminate these mechanical symptoms, the biomechanical outcomes of the procedure remain poorly understood. This systematic review aimed to collate and interpret the available literature on the biomechanical outcomes of patients who have undergone FOCA. The purpose of this review was to better understand the success of FOCA at restoring knee function and mobility. Methods: Systematic searches of the literature were performed in Ovid MEDLINE, Embase, and Web of Science databases (Search Date: March 29, 2024). The search terms '(Knee OR knee joint) AND (FOCA OR fresh osteochondral allograft OR fresh OCA)' were used. Following PRISMA guidelines, publications were screened initially by title and abstract, and later by review of the full text. Studies were included in the review if they contained any objective variable that would be considered a biomechanical or functional outcome, such as knee range of motion, knee strength, or parameters of gait. Data from eligible papers were extracted by one author and verified by a second author. The NIH Quality Assessment Tool was used to assess the quality of each eligible paper. Results: In total, eight studies met the inclusion criteria. All eligible studies were case reports (n=4) or case series (n=4) of fair (n=4) or good (n=4) quality. On average, the papers included 10 participants with a follow up time of 49±33.5 months. Although knee range of motion was reported in all eligible papers, it was not possible to calculate the average change in range of motion over time from the available data, as the methodologies and ways of reporting this variable varied across the publications. However, knee range of motion was reported to improve post-operatively in each study. Generally, the post-operative range of motion was reported to be >125°. One study also reported an improvement in knee strength following FOCA, while two others commented on improvements to gait, although little numerical data was provided. Conclusion: This review has identified an ongoing gap in our knowledge of the biomechanical outcomes of FOCA . This is especially true for dynamic activities of daily living. The limited reporting of improvements to knee range of motion suggest that FOCA has the potential to improve patient quality of life through improved knee function and mobility. However, further research with larger patient groups are required to corroborate the data in

the existing literature. This knowledge is important for optimising functional outcomes of FOCA via evidence-based rehabilitation programmes.

Risk factors associated with long-term outcome of ACI therapy for Patellofemoral defects

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Objectives: Patellofemoral joint (PFJ) chondral lesions are common and reduce the activity levels and quality of life for patients. Cartilage injury in the PFJ is complex to manage due to the anatomy of the joint and the high biomechanical forces which act on it. When the PFJ is abnormally aligned, such as trochlear dysplasia, patella alta or increased tibial tubercle trochlear groove (TTTG) distance, the biomechanical forces are increased and the chance of patellar instability heightens, increasing the risk of cartilage injury. Autologous chondrocyte implantation (ACI) has shown positive results in femoral condyle defects. However, for PFJ defects, the results vary in success rate. Identifying factors that influence the long-term outcome of ACI within the PFJ would allow informed decisions on whether the therapy justifies the cost, rehabilitation commitment, and likely outcome for the patient. This study aimed to investigate potential risk factors such as patient demographics, knee alignment and concurrent surgery on the short-term and longitudinal outcome of ACI therapy for PFJ chondral defects. Methods: All patients who underwent ACI treatment of the PFJ at The RJAH Orthopaedic Hospital were included. Lysholm scores were collected at baseline and annually post ACI until final follow-up or arthroplasty (failure). Patients were excluded if they had: Major knee trauma. ACI therapy to isolated compartment other than the PFJ. No follow-up Lysholm scores. A linear mixed model with random intercept and slope was used, using Lysholm score as a dependent variable and demographic/clinical baseline characteristics as independent fixed effects variables. Backward stepwise selection of fixed effects variables was conducted, removing at each step the variable most reducing Akaike's Information Criterion (AIC), until no variable could be removed without increasing the AIC. Exploratory variables included: Baseline characteristics (Age at ACI, sex, BMI, smoker status, baseline Lysholm, MRI alignment measurements, history of microfracture/alignment surgery and history of instability). Surgical characteristics (Concurrent procedure(s) at time of stage II ACI). Defect characteristics (Location, ICRS grade, cell number implanted and diameter (mm)). Results: Of the 149 patients treated, 121 were eligible for analysis. There were 44 females and 77 males and an average age of 38.2 ± 8.7 years. Several variables such as younger patients ($p = 0.049$), lower BMI ($p = 0.004$), trochlear defects ($p < 0.001$), lower cell number implanted ($p < 0.001$), higher baseline Lysholm ($p < 0.001$) and normal trochlear dysplasia ($p = 0.038$) were significantly associated with improved Lysholm scores 1-year post ACI. Longitudinally, older age ($p = 0.041$), non-smokers ($p < 0.001$), lower baseline Lysholm ($p = 0.022$), normal TTTG distance ($p = 0.023$), soft tissue intervention ($p = 0.013$) and no previous surgery ($p < 0.001$) demonstrated a significant increase in Lysholm score with each progressive follow-up year. Conclusion: This study explored a longitudinal dataset of patient outcomes, up to 20 years post ACI therapy, for PFJ cartilage defects. The analysis

identified several variables that affect short term and longitudinal Lysholm outcome. Further work to identify optimum cell seeding density per defect size is needed.

Knee Arthroplasty Documentation Audit Against GIRFT, BASK & BOA Guidelines

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Title: Knee Arthroplasty Documentation Audit - *Background:* Working in the elective Trauma and Orthopaedic wards involves a rapid turnover of patients undergoing surgical procedures, primarily arthroplasties. We have observed challenges in locating certain pertinent information in Operation Notes and noted frequent omissions. Addressing this issue is imperative, as comprehensive documentation not only aids in understanding and managing complications but also fulfils professional and legal obligations.This audit focuses on knee arthroplasties, being the most prevalent elective surgeries in the department, with the potential for extending similar templates to other procedures. *Aim:* Knee arthroplasty documentation audit against guidelines from GIRFT, BASK, and BOA Best Practice for Knee Arthroplasty Surgery to assess and address deficits in documentation to fulfil professional & legal requirements. - *Method/Clinical Management:* Data were retrospectively collected from operation notes of knee arthroplasties performed on 41 randomly selected patients in each cycle across Orthopaedic Surgical Unit St. Woolos Hospital and Trauma and Orthopaedics Unit C7W Royal Gwent Hospital. - *Discussion*: The audit on Knee Arthroplasty Surgery Documentation reveals both strengths and areas for improvement in our current practices. While certain sections of operation notes consistently meet standards, such as detailing surgical teams and post-operative plans, others display variability or consistent omissions. These discrepancies underscore the need for a standardized approach to documentation, ensuring comprehensive records that support patient care, mitigate risks, and fulfil professional and legal requirements. These discrepancies underscore the need for a standardized approach to documentation, ensuring comprehensive records that support patient care, mitigate risks, and fulfil professional and legal requirements. Regular audits should be conducted to monitor adherence to documentation standards, with a commitment to continuous improvement. By prioritizing thorough documentation practices, we aim to enhance patient safety, facilitate effective communication among healthcare providers, and uphold the highest standards of care delivery.We appreciate the collaborative effort of all stakeholders in this audit and look forward to implementing the recommendations outlined to enhance the quality and consistency of knee arthroplasty surgery documentation.

Does Socioeconomic Status Influence Patient Reported Outcome Measures after Bone Marrow Aspirate Concentrate Treatment of Ankle Cartilage Defects?

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Objectives A relationship between lower socioeconomic status (SES) and poorer clinical outcomes is becoming widely recognised. Previously, we identified that patient reported outcomes following cell therapy in the knee are worse in individuals with a lower SES. Therefore, it is important to consider the potential influence of SES on cartilage repair surgical outcomes.Bone marrow aspirate concentrate (BMAC; RegenGlobal, UK) is used as a single-step minimally manipulated cell therapy in our centre to treat patients with ankle cartilage defects, offering promising short-term outcomes. The currently recognised predictors of BMAC treatment outcome in the ankle are shorter time from symptom onset and presence of larger defect areas. This study aimed to investigate the relationship between SES and functional outcomes after BMAC treatment for repair of ankle cartilage defects. Methods This retrospective study was conducted on patients who received BMAC treatment between 2015 and 2020 in out centre. Patients' demographics, postcodes, baseline and 12-month follow-up Manchester Oxford Foot and Ankle Questionnaire (MOXFQ) were collected. Index of Multiple Deprivation (IMD) scores were identified via postcodes and used to represent geographical area SES. All data were analysed using R version 4.3.2. Non-parametric data were transformed using Box-Cox transformations. Fisher's Exact test, Kruskal-Wallis rank sum tests and one-way analysis of variance were used to assess the distribution of demographic factors and baseline scores across IMD quintiles. Multivariable linear regression models were used to analyse the relationship between IMD scores, income and employment status with follow-up functional outcomes, adjusting for demographic factors and baseline scores. Any missing data were handled using the full information maximum likelihood method. Two-tailed p-values below 0.05 were assumed to indicate statistical significance. Results The study identified 84 (42 male and 42 female) patients who had BMAC treatment. The median age of the patient group was 36.5(range 15-72) years, with a median BMI of 28 (range 19-49) kg/m^2 and a median IMD score of 20.3 (range 1.9-56.0). Only 7% of the participants indicated they were smokers at the time of outcome collection. No significant differences were found when comparing gender, age, BMI, smoking status of patients, time from symptom onset and baseline MOXFQ scores from different IMD quintiles (p=0.29, p=0.65, p=0.71, p=0.38, p=0.13 and p=0.23, respectively). The regression models found no evidence that IMD scores, income and employment status were related to patient functional outcomes (p=0.90, p=0.29 and p=0.63, respectively). However, baseline MOXFQ scores were recognised as strong predictors for 12-month follow-up scores in IMD, income and employment status models (all p<0.0001). Conclusions Patients who received BMAC treatment were evenly spread in IMD quintiles in terms of numbers, demographic factors and baseline scores, showing that our patients were from diverse socioeconomic backgrounds. No evidence was found that IMD scores, income and employment status were related to patient functional outcomes, when accounting for demographic factors and baseline scores. This finding

suggests that BMAC treatment may be suitable for patients from all backgrounds in our centre. However, the study had a small sample size and therefore validation in larger, independent cohorts is needed.

An Investigation into the Clinical Utility of Intramedullary Reaming Samples for Diagnosis of Metastatic Bone Disease.

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Background: Histological diagnosis of skeletal metastases is essential in guiding appropriate treatment for patients, providing information on primary source, grade and prognosis. It is common practice to send intramedullary tissue samples during fixation of suspected pathological fractures to confirm or exclude the presence of metastatic bone disease. There is variation in techniques in which intramedullary samples are obtained, with biopsies being the gold standard for analysis. Despite this, it is often intramedullary reamings that are sent for pathological analysis. There is conflicting evidence regarding the reliability of reaming samples, with literature suggesting reamings may not provide accurate histological diagnosis, often due to poor sample quality. Our aim was to investigate the clinical value of intramedullary reaming samples sent during fixation of suspected pathological fractures and compare these results to bone
biopsies.

Methods: We retrospectively analysed (n=17) seventeen consecutive cases from March 2023 to March 2024 from a single district general hospital in which intramedullary samples were sent for suspected pathological fractures. In all patients included the indication for sampling was due to clinical and radiological suspicion of skeletal
malignancy.

Results: Nine cases used intramedullary reaming and eight cases used bone biopsies as sampling methods. Pathology reports were issued for all (n=17) seventeen cases. Of the nine reaming samples, seven patients had a known primary malignancy. Within this group of seven, reaming samples confirmed metastatic disease was present in three patients. Four samples had no evidence of malignancy. With these four patients, there was evidence of bony metastasis on radiographs , leading us to conclude these results were false negatives. The remaining two patients out of the nine reaming samples had no known malignancy and no pathological evidence of metastatic bone
disease.

Within the eight bone biopsy samples, six patients had a known primary malignancy, three of these six samples confirmed metastatic bone disease. The remaining three biopsy samples showed an absence of malignancy. Within these 3 negative cases, all were sent due to an increased PSA in the background of prostate cancer. The remaining 2 cases had no known cancer. One biopsy showed evidence of known Paget's disease and the other showed no evidence of
malignancy.

Conclusions: Our findings highlight the clinical value of reaming samples to diagnose metastatic bone disease may be limited. As discussed in other publications investigating bone sampling, reaming samples should be used in conjunction with clinical context and other diagnostic tools to achieve confirmation of metastatic bone disease.

Effect of Chlorhexidine Wound Irrigation in Reducing Early Surgical Site Infection in Implant Orthopaedic Surgeries: A Randomized Clinical Trial

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Objectives: Surgical site infections (SSIs) in orthopaedic implant surgeries continue to pose significant challenges, leading to increased morbidity and strain on healthcare resources especially in developing countries. In this study, we aimed to compare the efficacy of chlorhexidine wound irrigation vs normal saline in orthopaedic implant surgeries.

Methods: This is a single-center, prospective randomized clinical clinical trial in patients undergoing orthopaedic surgeries with implant placements. The trial protocol design was approved by the ethics committee of National Hospital Abuja (NHA/EC/033/2020) and was conducted at National Hospital Abuja, Nigeria. The participants were randomized into two groups: one receiving 0.05% Chlorhexidine Gluconate (CHG) solution and the other receiving normal saline for wound irrigation. The exclusion criteria were open fractures, antibiotic treatment at the time of implant placement for a concomitant disease or infection, local and/or systemic symptoms of infection within one week of planned surgery, cancer, uncontrolled diabetes, immunosuppressant use, pregnancy, revision surgeries, polytrauma. The incidence of early SSIs within 30 days postoperatively was the primary outcome measured.

Results: A total of 50 patients were enrolled. Early SSI was recorded in one patient in each group. There was no significant difference between both solutions compared in preventing early SSIs in orthopaedic implant surgeries. Prolonged duration of surgery, and lowerlimb surgeries were the common denominators in both patients.

Conclusions: Based on the findings, the use of dilute chlorhexidine gluconate solution may not be recommended. The incidence of early SSIs was lower than regional studies and comparable to developed countries. These findings contribute valuable insights into optimizing infection prevention strategies in orthopaedic implant surgeries.

Abstracts for Posters

Does Listing Isolated ACL Repairs as Low Priority Lead to Subsequent Meniscal Pathology?

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Introduction: Anterior cruciate ligament (ACL) ruptures often result in knee instability, causing meniscal pathology if untreated. New guidance suggests lower priority surgery for ACL tears without meniscal pathology seen at the time they are added to the surgical waiting list. This study examined the risk of developing meniscal pathology with postponed surgery. Methods: We conducted a retrospective cohort study from January 2018 to March 2024 of all consecutive patients who had undergone ACL reconstruction at our unit. We categorised patients based on pre-operative MRI findings of meniscal pathology and their time from addition to the waiting list, to surgery. Surgical notes were searched to determine if meniscal tears were identified intra-operatively. Non-parametric testing determined baseline and clinical differences between groups. A binary logistic regression model determined the risk of developing meniscal pathology with delayed surgery. Results: From 272 patients, 15.1% developed meniscal tears identified intra-operatively that were not present on the initial MRI scan, with a male to female ratio of 3:1. Additionally, 5% had pathology on MRI not seen during surgery. Median time to diagnosis was 16 days, and median time between listing and operation was 162 days. Age and time to diagnosis didn't significantly affect outcomes between groups ($p>0.05$). BMI differences were not significant overall but were significant when high leverage points (BMI>43) were removed ($p= 0.038$). Binary logistic regression, accounting for gender and BMI, showed that for each additional day on the waiting list, the chance of developing a meniscal tear increased by 0.3% ($p= 0.013$). Conclusion: This study highlights the risk factors and progression of meniscal pathology following delayed ACL reconstruction surgery. While patient age and time to diagnosis showed no significant impact, BMI and waiting list duration are important factors. With a delay of a month to surgery, the likelihood of developing a meniscal tear increases by nearly 10%. These findings emphasise the importance of early clinical intervention and highlights potential revaluation of the current guidance.

Getting It Right Every Time – Compliance with Data and Patient Reported Outcomes on the British Spine Registry from 2018 to 2022.

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Introduction: The British Spine Registry (BSR) collects data to monitor outcomes of spinal procedures in both adult and paediatric populations. Good data compliance has growing importance to understanding the success of spinal procedures. Our study aimed to assess compliance with BSR data entry and patient reported outcomes (PROMs) in our spinal surgery practice, isolating predictors of good adherence and long-term completion. Methods: This retrospective cohort study included spinal procedures recorded on theatre scheduler reports (January 2018-March 2022) that were performed by the same group of spinal surgeons in adult and paediatric settings across 3 different hospitals. The BSR was reviewed for data entry completion and PROMs completion at 4 timepoints, along with contact availability. Standards of 80% were set as stated in the best practice tariff. Results: 85% of all operations performed were recorded. PROMs completion across 3 pathways (Idiopathic Scoliosis, Spinal Trauma and Spinal Elective) averaged 33% over pre-operative, post-operative, 6-months and 1-year timepoints. PROMs completion decreased from 61% to 42% at 1 year follow-up in the paediatric pathway and 44.5% to 19% in adult pathways. Binary logistic regression demonstrated pre-operative completion was a significant predictor of 6-month completion (OR: 2.9; OR:3.4; OR:4.8; $p<0.05$). Furthermore, 6-month completion predicted increased 1 year completion (OR:20.5; OR:9.9; OR:6.1; $p<0.05$) across all pathways. 93% of patients had phone or email contacts available. Mobile/Email availability did not predict greater completion in the paediatric pathway ($p>0.05$) but did predict adherence in adult pathways (OR:6.6; OR:25.0; $p<0.05$). Discussion: PROMs completion on the BSR is currently low and falling. Pre-operative PROMs completion increases adherence to longer term follow-up in both paediatric and adult spinal pathways. Without early engagement and completion, future compliance is likely unsuccessful. Local initiatives to increase pre-operative and immediately post-operative PROMs engagement, alongside updated active contact information, could lead to better compliance with PROMs completion. National and regional engagement to reproduce this study across wider spinal units (posed as a national collaborative study) will allow discussion and implementation of standardised best practices. Furthermore, increased PROMs compliance on the BSR could provide extremely beneficial for the optimal use of outcome data via such registry.

The management of osteoporotic vertebral fractures at a District General Hospital

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Introduction-Most common osteoporotic fracture affecting 1/5th of the elderly population Only 20-30% of patients with OVFs are presented to hospital while 2.2 million remain undiagnosed in theUK, as the diagnosis is usually opportunisticAround 66,000 OVFs occur annually in the UK with increase by 18,000 cases a year predicted till 2025.There is a 20% chance of another OVF in the next 12 months and 3 times more likely to sustain hip fracture.OVFs can sometimes be poorly tolerated by infirm elderly patients, leading to significant morbidity and 8 times increase in age-adjusted mortality.Materials and Methods-To classify (AO-OF) the fracture severity and patents with ovfs in a 12-month period, To assess follow-up status and if kyphoplasty was offered to patients with significant pain within 6 weeks as per NICE [TAG279] guidelines and from evidence of VAPOUR trial.To introduce the recent Royal Osteoporosis Society and GIRFT guidelines onmanagement of symptomatic osteoporotic vertebral fracturesResults-Total no. of patients- 62Initial pain assessment=40Pain assessed at ≤6 weeks- 21Duration from decision to operate to kyphoplasty 8.7 weeks11% had kyphoplasty of which 50% noted improvement in pain11 deathsConclusion-To improve pain assessment on admission of patients with acute osteoporotic vertebral fracturesTo follow GIRFT guidelines for early assessment and intervention in patients with osteoporotic vertebral fractures to improve pain, mobility and early discharge from hospital

Exploring the Microstructural, Tribological, and corrosion characteristics of Titanium-Niobium Pentoxide Composites for Biomedical Applications

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The introduction of high porosity in titanium scaffolds significantly reduces their strength, rendering them potentially unsuitable for load-bearing biomedical applications. To address the need for biocompatibility, low elastic modulus, and adequate strength in orthopaedic implant materials, it is essential to develop new titanium-based materials with improved strength. This study presents the development of a niobium pentoxide (Nb2O5) reinforced titanium composite using powder metallurgy for biomedical use. The Nb2O5 reinforced titanium composites (Ti-Nb2O5) exhibit considerably higher strength compared to pure titanium. Cell culture experiments indicated that the Ti-Nb2O5 composite offers excellent biocompatibility and cell adhesion, with human osteoblast-like cells growing and spreading well on its surface. Our findings suggest that the Nb2O5 reinforced titanium composite is a highly promising implant material due to its superior mechanical strength and biocompatibility.

Primary Synovial Chondromatosis

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Background: Primary synovial chondromatosis: It is a benign monoarticular disorder of unknown origin that is characterized by synovial metaplasia and proliferation resulting in multiple intra-articular cartilaginous loose bodies of relatively similar size, not all of which are ossified (5)It affects approximately 1 in 100,000 people (1).

Presenting complaint: 21 years male with a 3 years history of painful swelling around his right big toe which has gradually increased in size over the last 12 months. No proceeding trauma or history of inflammatory arthritis. On examination, the swelling was tender without any skin discoloration. Range of movement was restricted.

Clinical management: Given the unusual appearances and recent interval growth, a surface based paraosseous osteosarcoma or bizarre parosteal osteochodromatous prolifiration was suspected and an opinion from a regional bone tumour centre was sought. The patient underwent a CT guided biopsy. Histological diagnosis was primary synovial chondromatosis. Subsequently the patient had surgical excision a good result

Atypical Femur Fractures In Post-Menopausal Patients Taking Bisphosphonates and Their Indication When to Start After Holiday Period of 5 Years and Its Effects

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Introduction1.Postmenopausal women are particularly at risk of fractures from osteoporosis, a systemic skeletal condition that causes bone fragility. This group has increased osteoporotic fractures because to hormonal variations, specifically a drop in oestrogen levels after menopause, which demineralises bone (Walker and Shane, 2023). This type of fracture can cause severe pain, illness, death, and medical bills. They usually affect the wrist, pelvis, and vertebrae. M Bisphosphonates prevent fractures and increase bone density by inhibiting bone resorption (Khan et al., 2022). Bisphosphonates like ibandronate, zoledronic acid, alendronate, and risedronate enable customised treatment due to their dosage and formulation possibilities.Despite lowering fracture risk, bisphosphonates can cause uncommon but dangerous atypical femur fractures. Without trauma, these radiographic-pattern femur fractures can occur in the subtrochanteric or diaphyseal area (Grygorieva et al., 2023). Multiple studies have linked bisphosphonates to atypical femur fractures, raising safety concerns, especially when taken long-term. To improve osteoporosis therapy and limit bisphosphonate hazards, one must understand the epidemiology, risk factors, and aetiology of atypical femur fractures (Hart, 2023). Methods Search StrategyA comprehensive search strategy will be used to find relevant studies for this systematic review. The databases PubMed, Embase, and Cochrane Library will be examined. The search strategy will include atypical femur fractures, bisphosphonates, osteoporosis, treatment duration, and fracture risk. Boolean operators (AND, OR) produce acceptable word combinations. The search strategy initially yielded 1,200 articles from the selected databases. Duplicate articles were removed, leaving 800 entries for inquiry. All 800 articles were then evaluated for inclusion and exclusion. Studies on atypical femur fractures in postmenopausal women using bisphosphonates were investigated. The research focused on determining the ideal treatment duration and start time. Randomised controlled trials, cohort studies, case-control studies, and systematic reviews fulfilled inclusion requirements. Systematic review evaluates bisphosphonate duration and timing on bone mineral density and fracture risk. Bisphosphonates minimise the risk of fractures, according to Brown (2021) and Morkos et al. Researchers recommend maintaining bone-health medicines. Saag et al. (2021) stress that quitting bisphosphonate therapy momentarily stimulates bone turnover and eventually reduces bone mineral density. Toro et al. (2023) analyse fracture liaison services and their capacity to reduce fracture risk, emphasising the need of healthcare practitioners adopting preventative measures after the holidays despite concerns about bone loss after cessation. The results emphasise the need for prescription bisphosphonate therapy for fracture prevention and the hazards and benefits of long-term usage and drug cessation. Conclusion:This succinct review summarises various bisphosphonate long-term efficacy studies. It also stresses the need of medication adherence, especially during holidays, to avoid bone resorption and preserve bone mineral density. The study also shows that extended bisphosphonate medication may cause infrequent but substantial atypical femur fractures. Clinical environments require close monitoring and individualised risk assessment. Checking bone health markers and following treatment regimens periodically can help give the finest medical care in the future. and prevent fractures in susceptible groups. Evidence-based

recommendations and a patient-centered approach can help healthcare practitioners manage postmenopausal women with osteoporosis and avoid fractures. This will enhance therapy and decrease side effects.

Optimising Post-op Imaging in HemiArthroplasty

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Introduction:A postoperative x-ray is frequently checked immediately after a hip hemiarthroplasty to verify proper placement of the implant and reliability of ordering an additional x-ray 24 hours post-surgery as a routine protocol has not been definitively established. However, early detection of a serious complication is a crucial factor, the additional radiation exposure, increased health care costs, and potential patient discomfort it causes raises concerns whether it is worth the value (Teisberg et al., 2020). There is no universal consensus on the optimal timing of postoperative imaging for our patients to balance early detection of a serious complication against those concerns (Baumann et al., 2018). In addition, uniformity was lacking in the criteria utilised to judge postoperative x-rays as either predicted postoperative changes or the earliest possible signs of trouble leading to dissimilarities in care decisions and results (Corona-Cedillo et al., 2021). The purpose of the present investigation is to evaluate the effectiveness of routinely performed 24-hourpostoperative radiographs in the early detection of complications following a hip hemiarthroplasty. The results will be compared between groups of patients who receive postoperative X-rays and groups of patients who do not receive postoperative X-rays. The objectives of this study are, • To evaluate whether both in theatre , and 24-hour postoperative X-rays can detect early complications such as implant dislocation/misplacement,periprosthetic fracture and mal alignment, following hip hemiarthroplasty.• To investigate the impact of X-rays early in the postoperative period on clinical decision-making and improved patient management.• To evaluate the cost effectiveness of implementation of routine X-rays and also the impact on healthcare resource utilisation .METHODS:Data collection for this study involved the review of a total of 1154 X-rays of patients who underwent hemiarthroplasty for neck of femur fractures due to falls at a single tertiary care trauma unit. Inclusion criteria included patients who had immediate postoperative X-ray in the theatre and departmental X-ray on the next day when weight bearing is allowed. Exclusion criteria included revision surgery and any other surgery for femur fractures. The X-rays were independently reviewed by 2 orthopaedic consultants for complications such as dislocation and periprosthetic fractures. Conclusion Data analysis was carried out using patient postoperative medical records of 1154 patients who have undergone hemiarthroplasty for Neck of Femur. Data is analysed using SPSS statistical software to allow the statistical tests and calculations to be carried out so as to find the diagnostic accuracy of X-rays and by default it has facilitated in reliability and validity of the study results. The data has been analysed statistically using pertinent methods like descriptive statistics and frequency analysis. CONCLUSION:The main aim of this study is to observe the need for post-operative X-rays specifically in theatre. This study is based on a single-centre retrospective radiologic review. The collected data was analysed using SPSS software. Day 1 post operative , inter departmental, post mobilisation hip x-rays are reliable, cost

effective, less time consuming , require less manual handling ,better quality and aresufficient enough to out rule implant related complications , in patients post Bipolar Hip Hemiarthroplasty

The importance and clinical significance of Kager's fat bad in the diagnosis of acute Tendo Achilles rupture

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Acute Tendo Achilles ruptures makes up 1.8 % of the traumatic load in the emergency load in Emergency departments.The diagnosis of Acute Tendo Achilles rupture is challenging in the emergency situation ,as it depends on clinical suspicion then ultrasound or MRI if available for confirmation.In majority of hospitals Scans are rarely available in the emergency departments. So in this study we have tried to find out importance and clinical significance of Kager,s triangle and disruption of its fat pad in the diagnosis of Acute Achilles tendon ruptures on the lateral ankle xrays which are easily accessible in the emergency departmentsMethods: We went retrospectively through the xrays of all patients operated in our set up from 2018 till date. Data selection was done by fetching the charts of these patients. And then going through X-rays done in the emergency department.Inclusion criteria was all patients who had xrays done in ED as primary investigation. Excluding patients who lack X-rays and the one who got US and MRI as their primary investigation.After all the search we found out 109 patients out 243 who full filled the criteria and were confirmed as having disruption of Kager's fat pad by the radiologist. Patients data was anonymised and Research Ethics committee approval was taken.Later patients were called to find out their progress by filling out a questionnaire , which includes questions like type of injury ie sports related or non sports related, when started playing sports, any limp, any issues , any other complication , satisfaction after surgery. Discussion: Achilles tendon injuries are always challenging to diagnose.Whether partial or full needs scans for prompt diagnosis. Xrays diagnosis in an emergency situation , once approved will not only help in the prompt diagnosis but will also aid in the start of the treatment rather than waiting hours for the scans and then to decide treatment . This will not only be time effective but cost effective and convenient as well. And not only this early initiation of the treatment will also help prevent patients from getting complications due to delay in the treatment ,as all modes of treatment for the Tendo Achilles ruptures depends on the accurate diagnosis.Conclusion: From the above retrospective cohort we concluded that disruption of Kager's triangle and fat pad on the lateral ankle xrays done in the emergency department in acute setting , can be taken as a significant finding for the diagnosis of Acute Achilles Tendon rupture.Considering it for the diagnosis will not only save time , but will also save resources as well. Once promptly diagnosed it will urge us to start treatment reducing frustration for the patient and their family by cutting unnecessary delays in the treatment. However because this is done retrospectively further investigation is required on prospective background In order to find out reliability and sensitivity .

Minimally Invasive Surgery for Diabetic Foot Disease: A systematic review

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Background: Diabetic foot disease is a common life altering complication of diabetes mellitus that results from a combination of neuropathy, angiopathy, and structural deformities. Minimally invasive surgeries (MIS) are known to have shortened recovery time, reduced length of stay in hospital, reduce peri operative complications and in some cases general anaesthesia can be avoided, all of which would benefit diabetic patients. Current evidence-based guidance on the use of minimally invasive surgeries (MIS) in managing diabetic foot disease is limited. Objectives: To systematically review all studies on the use of MIS in managing diabetic foot disease affecting various anatomical locations, and to compile data on ulcer healing, recurrence, complication rates. Methods: A systematic literature search of Medline (PubMed), Embase, Scopus and Cochrane Library from inception until 1st April 2024, using the keywords 'diabetes', 'diabetic foot', 'minimally invasive surgery', 'minimally invasive procedure'. Articles were reviewed for demographic details and surgical outcomes. PRISMA guidelines were adhered to and reported. Results: Thirty-two studies were included in the review: 12 reported on forefoot interventions, 4 on midfoot interventions, 4 on hindfoot interventions, 3 on ankle interventions and 9 on lower limb interventions. Forefoot MIS, such as distal metatarsal osteotomies, phalangeal osteotomies and flexor tenotomies, showed significant improvements in ulcer healing times (mean 1.5-3.7 weeks) and reduced recurrence rates (0-21%). Midfoot MIS included Taylor Spatial Frame external fixator with percutaneous arthrodesis, solid bolt fixation and metatarsal ray resection. These interventions demonstrated promising outcomes with minimal complications, particularly in managing Charcot neuroarthropathy. MIS techniques in hindfoot and ankle explored were percutaneous cannulated screw fixation, minimally invasive plate osteosynthesis, tibiotalocalcaneal arthrodesis, vertical contour calcanectomy and combination of subtalar arthroereisis with Achilles tendon lengthening. They showed favourable results in lowering post-operative infections (0-9%) and raising functional scores (improved American Orthopaedic Foot & Ankle Society scores of 44.8). Lower leg MIS, including percutaneous Achilles tendon lengthening, showed improved plantar forefoot ulcers healing (30 to 57.5 days) and lower recurrence rates (0-38%) compared to total contact cast. Conclusion: MIS exhibits a promising role in the management of diabetic foot disease and ulcers, especially when paired with rigorous patient selection criteria and preoperative patient optimisation through a multidisciplinary team approach.

Associations between weight loss pre-hip or pre-knee arthroplasty and peri- and post-operative outcomes

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Objectives: Obesity is associated with increased complications after arthroplasty. However, it is unknown whether these risks are mitigated by pre-operative weight loss. Our systematic review and meta-analysis explore the association between pre-arthroplasty weight loss and peri- and post-operative outcomes. Methods: We searched medical databases and grey literature for studies of hip/knee arthroplasty patients who underwent medical and/or surgical weight loss prior to surgery. Exclusion criteria included articles pre-2010, case studies, upper limb or revision arthroplasty, and articles not published in English. Outcome measures included incidence of wound infection, pulmonary embolus, deep vein thrombosis (DVT) and revision surgery up to 90 days post-arthroplasty. The intervention group included patients living with obesity who lost weight pre-arthroplasty. The control group consisted of patients of any BMI who underwent arthroplasty without intervention. Results: We included 21 articles, with 50,672 patients in the intervention group and 1,446,755 patients in the control group. Pre-arthroplasty weight loss was associated with an increased risk of revision surgery (Odds Ratio (OR) 1.32, p=0.0004) and DVT (OR 1.37, p=0.00001). However, there was no association between pre-arthroplasty weight loss and superficial wound infection (OR 1.08, p=0.54), deep wound infection (OR 0.97, p=0.79) or pulmonary embolism (OR 0.93, p=0.38). Conclusions: These data suggest that weight loss prior to arthroplasty does not reduce the risk of perioperative complications and may increase the risk of DVT and revision surgery. However, well-designed and adequately powered prospective studies are required to establish the risks and benefits of pre-arthroplasty weight loss in people living with obesity.

Associations between pre-operative clinical data and radiographic osteoarthritis with fatty acids composition in dogs with naturally occurring cranial cruciate ligament disease

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Osteoarthritis (OA) secondary to cranial cruciate ligament (CrCL) disease/rupture is prevalent in dogs causing joint inflammation and pain. Fatty acids are important energy sources and cell membrane components, and critically impact animal health. Polyunsaturated fatty acids (PUFAs) are metabolised into bioactive lipid mediators or oxylipins which are involved in inflammation, wound healing, and pain, thus potentially playing a role in OA. Generally, saturated FAs, omega-6 (or n-6) PUFAs, such as arachidonic acid (C20:4n-6, AA), and AA derivatives (prostaglandins and leukotrienes) have pro-inflammatory effects whereas unsaturated FAs, omega-3 PUFAs, such as eicosapentaenoic acid (C20:5n-3, EPA), docosapentaenoic acid (C22:5n-3, DPA) and docosahexaenoic acid (C22:6n-3, DHA) and oxylipins derived from them (resolvins, maresins and protectins) are anti-inflammatory. PUFAs have been shown to have pro-resolving functions restoring tissue homeostasis after inflammatory reactions (Brouwers et al. 2015), and EPA, DHA and alpha-linolenic acid (C18:3n-3, ALA) described in canine OA management (Mehler et al. 2016). Objectives: 1) to collect discarded synovial fluid (SF) and serum from dogs undergoing CrCL surgery (ethics: RCVS:2017/14/Alves); 2) to analyse lipids and FAs in SF and serum; 3) to score radiographic OA and lameness at time of surgery; 4) to correlate clinical findings with the relative amounts of omega-3 and -6 PUFAs. Methods: Total lipids were extracted from SF and serum with chloroform/methanol (1:2, by volume), and FAs analysed by gas chromatography. CrCL disease pre-operative lameness scores were graded as: (1) mild, (2) moderate (easily visible), (3) marked (encumbered), (4) non-weightbearing lameness. Blinded OA scoring was performed on pre-operative orthogonal radiographs based on 15 assessment points with an integer numeric scale from 1 to 4 [15-60, no OA to severe OA]. Results: The data were obtained in 9 dogs [3 male (2 neutered), 6 female (5 neutered), various breeds, 2.08-10 years, 17.1-45.5Kg]. Lameness scores varied from 1 to 3 (average 1.89±0.89) and radiographic OA scores from 24 to 36 (average 29.33±4.27). High levels of omega-6 AA (from 12.07% to 21.76% of the total FAs) were found in SF and correlated with those in serum. The levels of omega-3 PUFAs were variable possibly reflecting dietary differences. Spearman correlations showed that OA score correlated positively with AA in SF (rs 0.85, P=0.005) and negatively with ALA in SF (rs -0.75, P=0.024), EPA in serum (rs -0.71, P=0.037) and DHA in SF (rs -0.73, P=0.03) and serum (rs -0.72, P=0.034). Linoleic acid (C18:2n-6, LA) in SF were negatively correlated with AA in SF (rs -0.82, P=0.011) and DPA in SF and serum (rs -0.93, P=0.001 and rs -0.77, P=0.021). Principal component analysis showed PC1 (44.10% of variance) was positive for EPA, LA, DHA, ALA and negative for AA, DPA, OA and lameness scores, whereas PC2 (22.63% of variance) was positive for dihomo-gamma-linolenic acid (C20:3n-6, DGLA) and weight and negative for LA, ALA and OA scoring. Conclusions: Higher OA radiographic scores were associated with higher AA and lower ALA and DHA levels in the SF. These FAs represent potential biomarkers or therapeutic targets for OA associated with CrCL disease in dogs.

Applications of Artificial Intelligence (AI) to human orthopedic knee data: a systematic scoping review uncovering the true current role of AI in healthcare

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Objectives. Given the rapid rise of artificial intelligence (AI) in orthopaedic clinical decision-making, it is crucial to understand current trends, applications, best practices for quality reporting, and opportunities for further research in this field. This understanding will enhance the global impact of AI in healthcare, revealing both its potential and limitations. With knee joint problems being highly prevalent and the knee being the most studied lower limb joint using AI models, this review focuses on the current use of AI in orthopaedic care specifically related to the knee. *Methods*. We adopted Joanna Briggs Institute methodology. Our report uses the PRISMA extension for scoping review guidelines. We registered the review protocol with the Open Science Framework (https://osf.io/xz9ka).Three databases (MEDLINE, EMBASE, and ISI Web of Science) were searched for studies published between 2008-2024. Studies were included if they were published in English, involved adult human patients (>18yo), and reported orthopaedic knee interventions where an AI algorithm, including traditional machine learning, artificial neural networks, and deep learning approaches, was utilized to diagnose knee conditions, predict clinical outcomes, or directly aid in these processes. Data extracted included study demographics, orthopaedic knee condition assessed, AI algorithms used, and the purpose of the algorithm. *Results*. Of the 2761 studies screened, only 30% (n=816) used AI in a way that had a direct clinical application; these final included studies used imaging data (56%), non-imaging data (40%), or both (3%). Among the included studies, 66% focused on using AI to make a clinical diagnosis, with 34% using AI to make a clinical prediction; and the most common knee pathology studied was osteoarthritis (71%), followed by soft tissue damage (i.e., meniscal tears) (15%). Furthermore, 81% were used for pre-operative applications; and deep learning, mostly utilizing pre-trained networks, was the most popular algorithm used (43%), followed closely by traditional machine learning algorithms (39%). Of the 15% of screened studies that used AI indirectly, 25% focused on identifying, 42% on segmenting, and 17% on measuring clinical features within orthopaedic knee data. *Conclusions*. Despite a significant increase in the use of AI models in recent years, only 30% of published papers used AI algorithm/s to directly diagnose knee conditions, predict clinical outcomes, or directly aid in these processes. AI has the potential to improve the efficiency, accuracy, and precision of patient care, however, generalization, global applicability, and overall use of models are currently limited by poor reporting standards (and potentially poorly designed models) which can restrict the real-world applicability. Future research should focus on improving reporting standards and developing fairer, more transparent, and explainable AI approaches. Additionally, research could investigate the role of AI algorithms in intra-operative/post-operative and non-imaging-based investigations, and to better define the role of AI models in clinical research.

Complex shoulder arthroplasty: a review of glenoid reconstruction with custom patient specific implants

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Background: Management of severe glenoid bone loss during shoulder arthroplasty can be challenging.Although mild to moderate glenoid defect and in some cases, even severe glenoid defects can be reconstructed with glenoid bone grafting, this is not possible in certain large, complex glenoid defects. Recent advances in technology have provided useful tools that allows custom reconstruction of these challenging glenoid defects. Objectives: To review our management of complex glenoid defect that were not suitable for glenoid bone grafting and requiring custom glenoid prosthesis. Methods: We reviewed the indications for surgery, characterisation of glenoid defect (using Walch, Antuna, Seebauer and Kocsis classification), surgical techniques, post operative course, complications and outcomes in patients who underwent custom glenoid reconstruction during arthroplasty. Results: 8 patients underwent reconstruction of the glenoid using custom glenoid component during reverse shoulder arthroplasty during 2021-2023. Indication for surgery included severe glenoid bone loss due to inflammatory arthritis, haemophiliac arthritis, failed arthroplasty and idiopathic osteoporosis. 3-D CT reconstruction was carried out in all cases with close liaison with design engineers to establish optimal implant, central peg and peripheral screw position with the objective to restore centre of rotation and adequate soft tissue tensioning. Patient specific instrumentation and 3D printing was carried out in all cases.The procedures were carried out using standard deltopectoral approach in 5 and extensile deltopectoral approach with clavicular osteotomy in the other three cases. Patients were followed up at 2 weeks, 6 weeks, 6 months and yearly. Radiological and functional assessment was performed. There were no postoperative infections. The first design of the implant resulted in dislocation and further changes to the custom components were made. No dislocations were noted in the subsequent 7 cases. There was significant improvement in the preoperative symptoms and average range of movements. Conclusions: Severe glenoid bone loss was successfully managed with custom prosthesis in our series. Implantation in severe defects requires extensive surgical exposure with a longer period of post operative rehabilitation before complete recovery. Early results indicate noticeable improvement in function and shoulder stability. Medium to long term outcomes should be closely monitored to establish the longevity of the implant.

Exploration of chromosomal aberration in ASCOT trial patient cells using eSNP Karyotyping

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Objective: As part of the ASCOT trial, autologous cells – either chondrocytes or bone marrow mesenchymal stromal cells (MSCs) - were harvested from patients and cultured to expand the cell population in a GMP laboratory facility before being re-implanted into the patients. There is potential for this ex vivo growth to impact the genetic stability of the cells, which can influence their phenotypes. Using data which is readily available from gene transcript analysis, this can be explored using bioinformatics approaches. Methods: This analysis uses RNA sequencing data in order to examine samples for any abnormal chromosomal aberrations. The expressed Single Nucleotide Polymorphism (eSNP) protocol used was described by Weissbein et al., 2016. Paired end sequencing files for each sample were mapped against HG38 using HISAT2 default parameters. The resultant BAM files underwent various pre-processing steps using GATK, PicardTools and R to produce a filtered variant call format (VCF) output which can be visualised within R. Both chromosomal duplication and loss of heterozygosity (LOH) were able to be identified from the RNA-sequencing files by visualising the VCF data on plots and calculating p-values for significant results using t-tests. Results: To date, this analysis has been completed on 88 samples (44 MSCs and 44 Chondrocyte samples) from 66 patients (40 men and 26 women) within the ASCOT cohort. Analysis of the complete trial cohort is expected to be ready for presentation at BORS.RNA sequencing data revealed subtle changes thought to be indicative of duplication and loss of heterozygosity events. Of the 88 samples where analysis has been completed, there were 7 in which chromosomal duplications were identified, and 73 where LOH were identified, all within chromosome 21p. Given the novelty of this application, further validation is currently in progress. Discussion: One limitation to this analysis is that it is highly reliant on the read depth of the sequencing files inputted into the analysis. Whilst the overall read depth was deemed sufficient for this analysis, chromosome 21p is a particularly small arm, and as such will be prone to a smaller read depth, and therefore an increased likelihood of technical errors at this site. Whilst 73 samples analysed to date had LOH of chromosome 21p identified, the accuracy of this result requires further investigation in order to have confidence in this output. This will be achieved using additional open-source RNA-Seq files from a cohort exhibiting a genetic disease where there is an expected outcome at chromosome 21 to confirm the methodology, as well as using traditional karyotyping on these samples to corroborate both the LOH results, and the 7 samples with chromosome duplications, as well as any results of interest identified within the remaining cohort. Conclusion: The use of RNA-Seq files to screen for chromosomal aberrations is a useful tool. Both duplications and LOH can be identified without further data generation, however there are still significant limitations with this approach which need to be addressed prior to this technique being effectively used in place of traditional karyotyping.

Advancing Osteochondral Tissue Supply Chain Transport Conditions for Clinical Allografts

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Objectives

Osteochondral injuries are debilitating. At present osteochondral allografting (OCA) is indicated for the treatment of osteochondral defects in the knee on a case-by-case basis in the NHS. OCA is the process of implanting cadaveric bone and cartilage into a patient in a one-step procedure to treat large (≥2cm) osteochondral defects, demonstrating excellent long term clinical outcomes (>15 years). At present, OCAs must be implanted within the clinically relevant window (28 days post-harvest from a donor) to maintain a chondrocyte viability >70%; a metric which has been correlated to positive outcomes in animal models. Through analysing multiple waste samples from clinically implanted grafts, our group has established that the chondrocyte viability is well below the industry 70% threshold. OCAs regularly have 12-14 days of shelf-life remaining once they have undergone the necessary serological and microbiological testing at US tissue banks. Thus, there is a small clinical window of opportunity for transplantation, this is compounded further by complex logistics and medico-legal requirements greatly reducing the availability and utilisation of OCAs in the UK. The overarching aim of this study is to maintain chondrocyte viability thereby prolonging the storage time of OCAs and increasing their utilisation in the UK.

Methods

Human osteochondral cores have been fabricated and stored in a manner which replicates OCA industry standards. After prolonged storage, multiple longitudinal assessments have been utilised to probe the tissue and cellular characteristics of stored articular cartilage. Confocal microscopy was used to assess localised cell death and in-situ viability and histological assessments examined the cellular and biochemical changes in the tissue. Tissue desiccation tests have also been used to provide an accurate water content value. Finally, tissue digestion using collagenase was undertaken to release cells for viability analysis.

Results

Viability assessments using in-situ viability and trypan blue exclusion corroborate one another and have shown that chondrocyte viability decreases with increased storage time. Both modalities determined that chondrocyte viability can fall below the 70% threshold before the clinically relevant cut off 28 days. Furthermore, histological staining and confocal microscopy demonstrated that chondrocyte cell death is most prevalent in the middle and deep zones of the articular cartilage. Tissue desiccation revealed that the water content of articular cartilage can increase by as much as 20% during storage time up until days 21-28, where it then begins to decrease. At its maximum (day 28) the water content of articular cartilage accounted for 88% of total tissue weight.

Conclusions

These preliminary analyses indicate that with storage time, the chondrocyte viability decreases. However, cell death is least prevalent in the superficial zone. This work demonstrates the importance of understanding the effects of storage and transportation on the quality of OCA tissues for transplantation. Additionally, studies are needed to better understand how the OCA tissue quality relates to clinical outcomes for patients. Future work will aim to optimise storage and transport conditions to improve cell viability, particularly focused on addressing issues with transport of OCAs from commercial US suppliers to the UK.

Contrast-enhanced ultrasound (CEUS) reveals perfusion of human bone fracture in acute phase healing: a pilot study

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Abstract

Objectives Bone fractures are common injuries with reported non-union rates of up to 9%. Current treatments for non-unions and at-risk fractures include surgery or low-efficacy options such as low intensity pulsed ultrasound. Average treatment costs are up to £17,200 and involve significant morbidity. Microbubbles are widely used in ultrasonography as contrast agents and can deliver therapeutics to desired locations through the loading of agents and local micron scale cavitation effects on cell membranes. Contrast enhanced ultrasound has been used to determine the cause of established fracture non-unions, though this is not in widespread use clinically in the fracture setting. This study aimed to test the hypothesis that peripherally injected microbubbles are detectable in acute fracture sites.MethodsAdulte patients between the ages of 18 and 75 who had sustained an isolated acute humeral shaft fracture were recruited to undergo contrast enhanced ultrasound imaging of the fracture site within 28 days of injury. They underwent ultrasound imaging and peripheral injection of commercially available SonoVue (Bracco, Italy) microbubbles. B-mode and contrast mode images were captured together with time-intensity curve analysis of regions of interest to assess for the presence of microbubbles at the fracture site.ResultsTen patients were recruited, 8 underwent humeral shaft fracture scans with 7 analysed. All fracture sites demonstrated increased contrast signal following injection. The mean Peak Intensity (PI) was 1.95×10^{-6} ($\pm 1.6 \times 10^{-6}$ AU). The wash-in volume of microbubbles was greater than the wash-out volume in all cases, with a mean difference of 1.4×10^{-5} ($\pm 1.7 \times 10^{-5}$) (p=0.015 Wilcoxon Test). There was a noticeable decrease in PI and Time to Peak (TtP) with age of fracture, although this was not statistically significant ($R^2 = 0.44$, $p = 0.1$; $R^2 = 0.24$, $p = 0.26$,

respectively).ConclusionsThis pilot study demonstrates that commercially available microbubbles are able to perfuse acute fractures in ultrasonographically detectable quantities using commercially available equipment. This is a key step in demonstrating the viability of using microbubbles therapeutically to influence the healing of acute fractures. The intensity of contrast signal appears to decline with time from injury, possibly due to reduced blood supply or changing tissue echodensity within the fracture.

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