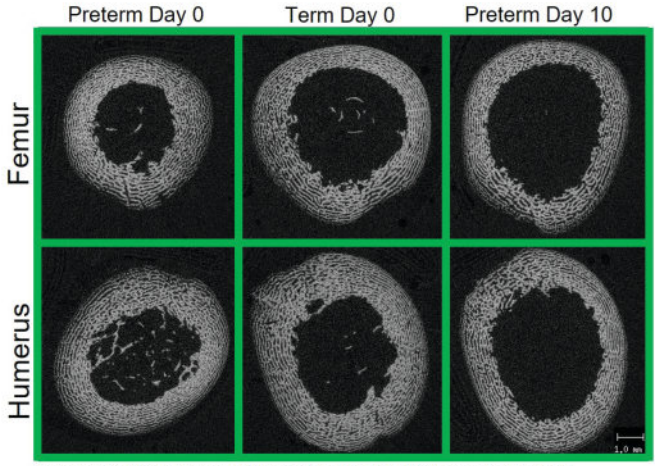
Preterm pigs had 35% less body mass and about 17% shorter and thinner humeri and femora than term pigs on postnatal day 0. Deficits in body mass and bone lengths and widths in preterm pigs were resolved by term-corrected age (postnatal day 10), suggesting catch-up growth had occurred postnatally. Both cortical bone area and total cross-sectional area at the humeral mid-diaphysis were reduced by 29% and 25%, respectively, in preterm compared to term pigs on postnatal day 0, and these properties did not fully rebound by term-corrected age. Humerus cortical thickness and polar moment of inertia were each reduced (10% and 50%, respectively) in preterm compared to term pigs on postnatal day 0 and remained lower on average in preterm pigs on postnatal day 10. Similar patterns were observed for bone structure of the femora, but the deficits appeared to more fully recover. While overall body mass and bone size tended to recover by term-corrected age in preterm pigs, other bone structural properties, particularly in the humerus, did not fully recover to the level observed in term pigs at birth. This suggests that catch-up bone growth occurs during the early postnatal period in preterm pigs, but decrements in cross-sectional properties may indicate that preterm bones are at increased risk for fracture.



Representative cross-sections at the mid-diaphysis. Scale bar 1mm.

Disclosures: M. Tsukamoto, *None*

SUN-128

Whole-exome sequencing implicates a variant in lysyl oxidase like 4 in the pathogenesis of familial atypical femur fractures Wei Zhou[1], Denise van de Laarschot[1], Jeroen van Rooij[1], Marijke Koedam[2], Hanh Nguyen[3], Andre G. Uitterlinden[1], Peter R. Ebeling, MBBS, MD[4], Rajesh V. Thakker[5], Piet Geusens[6,7], Bram CJ van der Eerden[2], Annemieke Verkerk[2] and Maria Carola Zillikens*[1], [1]Department of Internal Medicine, Erasmus MC, University Medical Center, Netherlands,[2]Department of Internal Medicine, Erasmus MC, Erasmus University Medical Center, Netherlands,[3]Department of Medicine, The University of Melbourne, Australia,[4]Department of Endocrinology, Monash Health, Australia,[5]Radcliffe Department of Medicine, Academic Endocrine Unit, University of Oxford, United Kingdom,[6]Biomedical Research Institute,University Hasselt, Belgium,[7]Department of Internal Medicine, Maastricht University, Netherlands

Atypical femur fractures (AFFs) are rare adverse events associated with the use of bisphosphonates but the pathophysiology is unclear. They have been reported to cluster in families and have occurred in patients with monogenetic bone diseases even without bisphosphonate use, suggesting an underlying genetic susceptibility. The aim of this study was to identify a genetic cause for AFF in a Caucasian family with three siblings with bisphosphonate-associated AFFs among seven family members with osteoporosis. By whole-exome sequencing, we identified a rare missence variant c.G1063A (p.Gly355Ser) in lysyl oxidase like 4 (LOXL4) among 64 heterozygous rare, protein-altering variants shared by the three siblings with AFFs. This variant was also found in a fourth sibling with a low-trauma femur fracture above the knee, not fulfilling all the ASBMR criteria of AFF but it was not present in the other family members with osteoporosis but without an AFF. The same variant in LOXL4 was also found in one of 73 unrelated European AFF patients. LOXL4 is involved in collagen and elastin cross-linking and likely relevant for bone repair mechanisms. Skin fibroblast-derived osteoblasts from the unrelated patient with the LOXL4 variant expressed less collagen type I and elastin, while osteogenic differentiation and mineralization were enhanced compared with controls. We hypothesize that this LOXL4 variant may affect collagen deposition in bone and healing of microcracks, eventually leading to AFFs. In summary, family-based whole-exome sequencing implicates a variant in LOXL4 in AFFs but not in osteoporosis. The findings need further replication in larger AFF cohorts and more functional evaluations.

Disclosures: W. Xia, *None*

SUN-130

See Friday Plenary Number FRI-130

SUN-132

See Friday Plenary Number FRI-132

SUN-134

Identifying a Geometrical Risk Factor for Mechanical Complication Development Following Adult Spinal Deformity Surgery Fatemeh Alavi*[1], Christopher Nielsen[2], Stephen Lewis[2], Raja Rampersaud[2] and Angela M. Cheung[3,4], [1]Osteoporosis Program, Schroeder's Arthritis Institute,University Health Network (UHN), Canada,[2]Division of Orthopaedics, Schroeder's Arthritis Institute,University Health Network (UHN), Canada,[3]Department of Medicine and Joint Department of Medical Imaging,University of Toronto, Canada,[4]Osteoporosis Program, Schroeder's Arthritis Institute, University Health Network (UHN), Canada

Despite achieving satisfactory clinical outcomes following adult spinal deformity (ASD) surgery, high rate of mechanical complications such as proximal junctional kyphosis (PJK) remains challenging. The multifactorial nature of these complications makes it difficult to identify their etiology and predict their development. While several risk factors for PJK have been identified, research into the primary contributors is still ongoing. We hypothesized that the preoperative orientation of the level above upper-instrumented vertebrae (UIV+1) has an impact on vertebral loading at this level and development of PJK. The aim of this study was to determine the local drivers for PJK development through musculoskeletal (MSK) analysis and clinical assessments. In this retrospective study, 35 patients [average age 66.5 (SD 11.4 yrs), 70% females] underwent lower thoracic to pelvis fusions with a minimum of 2-y follow-up (FU) were included. We stratified the patients based on their preoperative orientation of UIV+1 into two groups: posteriorly and non-posteriorly inclined. Incident PJK development and adjacent forces at UIV+1 were studied among both groups. Patient-specific OpenSim MSK models were created from pre- and immediate post-op EOS images. Vertebral loading was calculated using static optimization under up-right standing posture and normalized to weight. There were no differences in age, sex, BMI and FU duration between the two groups. PJK developed in 3 out of 13 patients with preoperative posteriorly inclined UIV+1 (23%), while in 16 out of 22 patients without preoperative posteriorly inclined (72.7 %) up to the final FU. Average normalized shear at UIV + 1 in the posteriorly inclined group was 0.13 and 0.06 in PJK and non-PJK patients, while average normalized shear was 0.27 and 0.15 in PJK and non-PJK patients without posteriorly inclined. Pearson chi-square test demonstrated that post-op shear, UIV+1 orientation and PJK development are highly associated (p values <0.005). Non-posterior orientation of UIV+1 was determined to be an important sagittal alignment risk factor for increasing post-op adjacent shear loading and PJK development accordingly. Future prospective studies should determine if UIV+1 orientation is prognostic for PJK development. Identifying low-risk patients with posteriorly inclined UIV+1 preoperatively may reduce the need for PJK mitigation procedures during ASD surgery, potentially improving cost efficiency within healthcare systems.

Disclosures: F. Alavi, *None*

SUN-135

Impact of Masticatory Function on Mandibular Bone Architecture in Sprague-Dawley Rats: A Preliminary Study Maxime Bedez*, Jérôme Delattre, Alexandrine During and Cécile Olejnik, Marrow Adiposity and Bone Laboratory (MABLab), University of Lille, France

This study is designed to investigate whether masticatory function influences changes in the microarchitecture of the mandible bone. By examining variations in bone structure under different masticatory loads, the research seeks to understand the extent to which chewing activities contribute to maintaining or altering the structural integrity of mandibular bone tissue. This exploration is critical in assessing the potential mechanical roles of mastication in preserving bone quality against conditions such as osteoporosis. In this study, nine female Sprague-Dawley rats (10-months-old) were equally divided into three groups : a group receiving either hard (H) AIN-93G pellets plus wood (W) sticks (group H+W), powdered soft (S) AIN-93G diet plus wood sticks (group S+W), or powdered AIN-93G diet only (group S), for 2 months. After sacrifice, mandibles were extracted and stored at -80°C. Mandible microarchitecture was studied using a Skyscan 1172 micro-CT scanner (Bruker, Belgium) and analyzed using CTAn 1.19 software with a segmentation done by Otsu method. Regions of interest (ROI) were designated using Avizo 2019.4 and CTAn 1.18 software. ROIs were defined on the buccal side near the third molar for the cortical bone, and between the roots of the first molar for the trabecular bone. The analysis enabling the quantification of classical structural parameters like bone volume fraction (BV/TV) and trabecular morphology (Tb.Th, Tb.N). In the cortical bone, BV/TV values were similar (between 99.89%, and 99.96%) for the three groups. In the trabecular bone, BV/TV values were 67.1%, 60,4%, and 66.4% respectively for the H+W, S+W, and S groups, with corresponding trabecular thickness Tb.Th values of 0.23mm, 0.17mm, and 0.22mm and trabecular number Tb.N values of 2,93mm-1, 3,74mm-1, and 3,01mm-1. Due to the small sample size, statistical analysis was