# Subchondral Bone and Cartilage in Knee Osteoarthritis (STAR OA) Using HR-pQCT and MRI

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INTRODUCTION: Osteoarthritis (OA) is a prevalent joint disease, with knee OA being the most common subtype. OA affects the entire osteochondral unit, although the sequence of pathological changes remains unclear. Evidence suggests that the subchondral bone, composed of the subchondral plate and trabecular bone, contributes significantly to the development of the disease [1]. In pathologic samples from the tibial plateaus of advanced OA, μCT-based Individual Trabecula Segmentation (ITS) revealed trabecular rod loss and plate thickening, changes linked to altered mechanical properties [2]. Currently, clinicians evaluate the severity of knee OA and joint damage using magnetic resonance imaging MRI, which provides visualization of articular cartilage and bone, and conventional computed tomography (CT), which can assess subchondral bone changes and mineralization; however, both lack sufficient resolution to analyze individual trabeculae. High-resolution peripheral quantitative computed tomography (HR-pQCT) is a promising imaging modality that, combined with ITS, enables detailed microstructural assessment. This study aimed to assess regional changes in subchondral bone microarchitecture using ITS-based HR-pQCT and cartilage measurements from MRI across different severities of knee OA.

METHODS: Twenty-eight female subjects with varying OA status (Kellgren–Lawrence (KL) grades 0 to 4) were included in this cross-sectional study, which is part of an ongoing longitudinal study. After confirmation of the presence and severity of knee OA by radiograph, each patient underwent whole-knee scans using a second-generation HR-pQCT system (voxel size: 61 μm; Scanco Medical, Switzerland) and an MRI (3T GE Excite Sigma). Four regions of interest (ROIs), the medial and lateral tibial plateaus and femoral condyles, were defined based on anatomical landmarks. Average subchondral bone plate thickness (SBP Th.) was measured in the cortical layer of these ROIs. The underlying trabecular bone was selected as the 5 mm ROI immediately beneath the subchondral plate. Bone images were segmented using a Gaussian filter. ITS analysis was performed to quantitatively evaluate the trabecular microstructure, identifying and categorizing every individual trabecula based on its type (plate-like or rod-like structure), thickness, and orientation. MRI Osteoarthritis Knee Score (MOAKS) was used as a semi-quantitative method to score cartilage morphology and bone marrow lesions (BMLs) in corresponding ROIs [3]. The data were assessed for normative distribution using the Shapiro-Wilk test. Two-way ANOVA was used to assess subchondral bone parameters across KL grades, and correlations were evaluated with Pearson's pairwise test ($p < 0.05$).

RESULTS: Frequency of MOAKS scoring across compartments are summarized in Table 1. Cartilage morphology was most preserved in the medial tibia, while the lateral tibia showed more frequent moderate to severe damage (scores 2–3 in 10 subjects). BMLs were rarely observed in the medial femur and tibia, but were frequently in the lateral tibiae, with a prevalence of 30% and 10 subjects showing grade 3 BML cystic changes. A decreasing trend from KL 0/1 to KL 2 was observed in BV/TV, pBV/TV, rBV/TV, pTb.N, and pTb.Th., followed by an increase in KL 3 and 4 subjects (Fig. 1A). Pair-wise correlations between the MRI and X-Ray based OA gradings, along with subchondral trabecular and cortical bone measurements, were investigated. Figure 1B represents a correlation heat map for the medial and lateral tibia. A significant positive correlation was found between MOAKS cartilage surface loss and bone volume fraction (total BV/TV, plate BV/TV, and axial BV/TV) in both medial and lateral condyles. Lateral joint space narrowing was associated with most of the trabecular microstructural parameters.
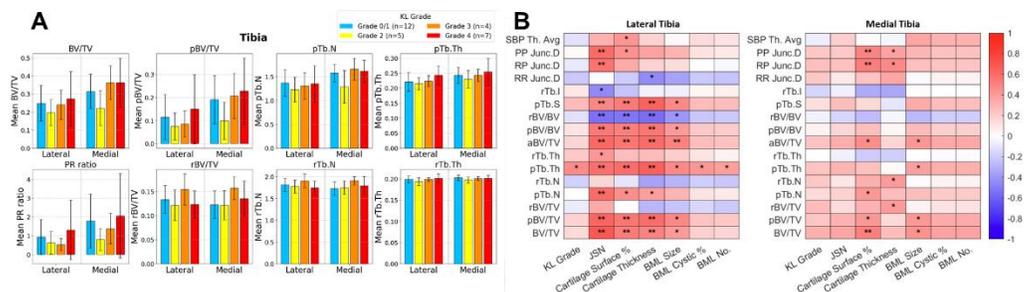
DISCUSSION: These are preliminary results from a cross-sectional clinical study that combines HR-pQCT, MRI, and X-ray assessments to comprehensively examine subchondral bone plate, trabecular bone, cartilage, and other osteoarthritis-related parameters. By examining ITS measured by HR-pQCT and MOAKS measured by MRI concurrently, we aim to identify correlations between structural changes and determine the temporal sequence of alterations across all stages of OA: early, moderate, and severe. Early OA is marked by trabecular loss, while later stages involve trabecular thickening. The trends observed in ITS parameters from KL 0/1 to grade 2 may reflect early OA alterations in subchondral trabecular bone. The one-by-one regression analysis revealed significant correlations between MOAKS cartilage scores and HR-pQCT-derived bone microstructural parameters and appears more responsive compared to KL grading. Strong correlations between cartilage loss and subchondral bone microstructure support a relationship between subchondral bone and knee OA progression. These initial findings suggest a relationship between subchondral bone parameters and the overlying cartilage in knee OA. Additionally, quantitative cartilage thickness analyses will be performed to further investigate the relationship between cartilage changes and subchondral bone. Study recruitment is also underway to include more male participants and to increase the number of subjects in the advanced stages of knee OA.

SIGNIFICANCE/CLINICAL RELEVANCE: These findings highlight the potential of ITS as a quantitative method to detect early subchondral bone changes in OA, supporting a whole-joint approach in clinical and observational studies.

REFERENCES: [1] Hu, Y. et al. *Bone Res* 2021, PMID: 33731688, [2] Chen, Y. et al. JBMR 2018, PMID: 29044705, [3] Hunter, D.J. et al. Osteoarthritis and Cartilage 2011, PMID: 21645627.

Table 1. Represents the frequency of MOAKS scoring across femoral and tibial compartments. **Figure 1. A)** ITS microstructural parameters for the medial and lateral tibia across KL grades. **B)** Correlation heat map between OA measurements and trabecular and cortical microstructural parameters in the medial and lateral tibia.