Early Peripheral Osteophyte Lipping Drives Early Femoral Bone Surface Growth Following Anterior Cruciate Ligament Reconstruction

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INTRODUCTION: Post traumatic knee osteoarthritis (PTOA) develops in ~50% of the individuals following an anterior cruciate ligament reconstruction (ACLR) [1]. Alterations in knee bone shape have been proposed as early predictors of future osteoarthritis (OA) [2] preceding radiographic OA by at least 12 months [3]. Neural shape models (NSM) can precisely quantify 3D bone geometry and encode shape features into a single, reader- independent metric called the B-Score (higher B-Score strongly correlated with increased OA severity) [4]. Previous work showed that the ACLR knees exhibit higher B-Scores (more OA-like bone shape) as early as 3-months post ACLR suggesting early and subtle bone shape changes that may be precursor to PTOA onset [5]. However, the precise anatomical locations, morphological patterns, and magnitudes of early bone shape changes following ACLR remain unclear. Hence we aim to investigate early and longitudinal changes in bone surface area using NSMs in ACLR subjects and healthy controls from 3-weeks to 30 months following ACLR surgery.

METHODS: ACL injured and contralateral knees of 17 ACLR subjects (11M, age=38±11y, BMI=23.3±1.6 kg/m^2) were scanned at 3-weeks (baseline), 3, 9, 18, and 30 months following ACLR surgery (3T MRI GE scanner using quantitative double-echo in steady-state (qDESS) sequence: TE_1/TE_2=6/38 ms, TR=22 ms, flip angle=25°, slice thickness=1.5 mm). The right knee of sex, age, and BMI matched healthy controls was imaged at the same timepoints. The femur was automatically segmented on the qDESS images [6], and a NSM (trained on 6,325 knees from the Osteoarthritis Initiative (OAI) dataset) was fit to bone surfaces (Fig.1A). To quantify localized, longitudinal, changes in bone surface area, we identified consistent bone regions on an atlas of mean healthy femurs that was created by fitting the previously trained NSM to 505 knees from the OAI dataset with no structural damage (MRI Osteoarthritis Knee Score for cartilage morphology=0). For each point on this atlas, we computed the percentage of these healthy knees having overlying femoral cartilage at that location. We thresholded this percentage to define three femoral bone regions (Fig.1B)—Subchondral (points with >95% of the healthy knees having femoral cartilage, representing bone area immediately beneath the articular cartilage), periarticular (femoral cartilage-covered points in <0% but >95% of the healthy knees, capturing the marginal rim near the articular cartilage edge where osteophytes typically develop), and composite (the union of the subchondral and periarticular regions including any area of cartilage coverage across the healthy knees, denoting the entire bone–cartilage interface including the outer margin). Each bone region was further subdivided into anatomical subregions (Fig.1B)—anterior, medial-central, medial-posterior, lateral-central, and lateral-posterior based on previously established standards [7]. For each bone region, we computed surface area in every anatomical subregion for ACLR, contralateral, and healthy control knees at all timepoints. We used linear mixed effects models to assess the effect of knee, timepoint, and subregion on the subchondral, periarticular, and composite bone surface area. Pairwise comparisons with Tukey's corrections and effect sizes (partial eta squared, small: $\eta_p^2 \geq 0.01$, medium: $\eta_p^2 \geq 0.06$, and large: $\eta_p^2 \geq 0.14$) were computed when any fixed or interaction effects were significant.

RESULTS: In all anatomical subregions, ACLR knees exhibited greater increase in composite ($p<0.006$, $\eta_p^2=0.01$, 1.7%) and periarticular ($p<0.026$, $\eta_p^2=0.02$, 5.34%) bone surface areas over time compared to contralateral and healthy control knees. The rate of increase (slope) in the composite ($\eta_p^2=0.05$) and periarticular ($\eta_p^2=0.06$) bone surface area for the ACLR knees was significantly higher in the anterior ($p<0.001$, $p<0.001$), medial-posterior ($p=0.023$, $p=0.002$), and lateral-posterior ($p=0.008$, $p=0.001$) regions compared to the same anatomic subregions in contralateral and healthy control knees from 3 to 30 months. Subchondral bone surface area showed no significant ($p=0.154$) longitudinal change in any anatomical subregion.

DISCUSSION: ACLR knees showed modest yet larger increases in bone surface area compared to the contralateral and healthy control knees, indicating bone remodeling as early as 3 months post-ACLR surgery [8]. Steep increase in ACLR composite bone surface area longitudinally is primarily driven by increases in the periarticular region rather than subchondral plate enlargement [9]. Rise in periarticular surface area in the ACLR knees suggests early and progressive osteophyte lipping, particularly prominent in the trochlea, medial-posterior condyle, and lateral-posterior condyle—pattern in line with hallmarks of advanced knee OA [10].

SIGNIFICANCE/CLINICAL RELEVANCE: This study shows early and rapid increase in femoral bone surface area post-ACLR is mainly attributed to peripheral osteophyte lipping rather than flattening of subchondral plate. Thus, these results support the use of NSM-derived, reader-independent, shape metrics to serve as early biomarkers for PTOA risk stratification, or as quantitative endpoints for prevention and early-intervention trials.

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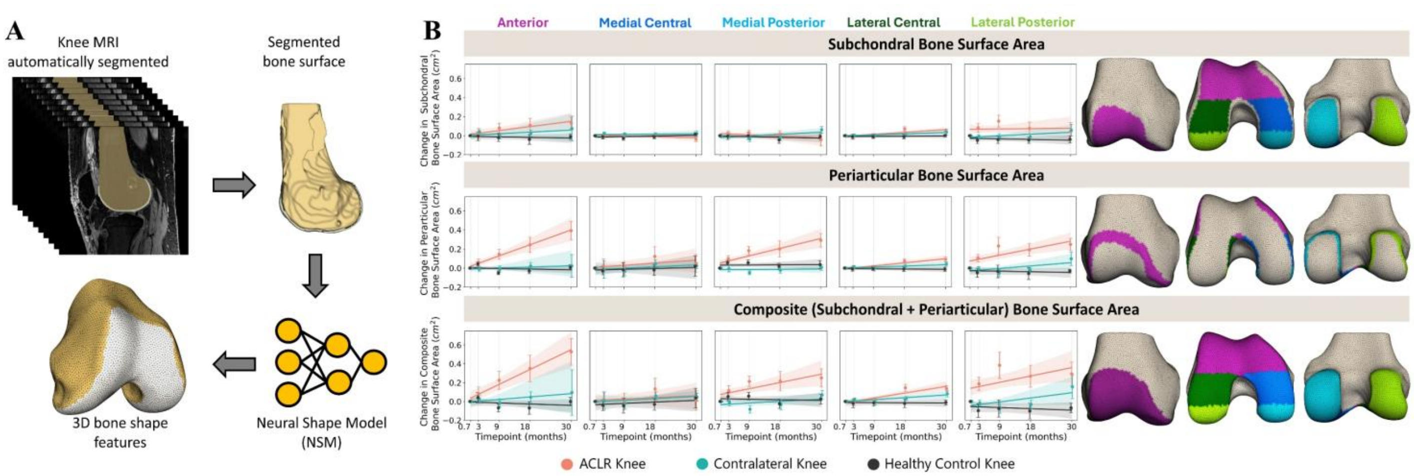

Figure 1: A) Pipeline illustrating neural shape model (NSM) fitting to automated femoral segmentations from knee MRI to extract 3D bone shape features. B) Femoral bone surface area changes in ACLR, contralateral, and healthy control knees at 3, 9, 18, and 30 months post-ACLR surgery. Surface area for subchondral, periarticular, and composite (subchondral + periarticular) bone regions that are subdivided into five anatomical subregions—anterior, medial central, medial posterior, lateral central, and lateral posterior. The dot and the error bars represent the raw mean and the standard errors at each timepoint with shaded regions representing the 90% CI of the linear regression fit.