

## Bone Curvature Changes of the Knee in OA Subjects as on Detected on MRI Can Predict Who Will Progress to TKR in Five Years Time: Data From the OAI

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**Purpose:** Osteoarthritis (OA) is a multifactorial joint disease process with a spectrum of manifestations. In the knee, end-stage disease is characterized by joint space narrowing, articular cartilage (AC) and meniscal maceration, synovial hypertrophy and bone curvature changes – typically flattening – of the subchondral, articular surfaces. These bone curvature changes serve as a biomarker of disease severity. This work examines the relationship between bone curvature changes – as detected on MRI – as a biomarker for end-stage OA, defined here as the need for total knee replacement (TKR) within five years of the detection of these curvature changes.

**Methods:** Case and control pairs were selected from 4,796 participants from the Osteoarthritis Initiative (OAI), a multicenter population-based cohort study designed to identify biomarkers of knee OA development and/or progression. End-stage cases (n=119) were participants who received a TKR, confirmed by radiography and/or a review of hospital records. Matched controls were selected with the same Kellgren-Lawrence (KL), sex and age within 5 years. Time-points included the defining event (TO), where a TKR was performed, and available preceding time-points. OAI 3D WE DESS sagittal images (Siemens) were used for curvature measurements at each time-point. Measurements for total and sub-regional articulating bone surfaces were obtained using segmentation software (CiPAS, Qmetrics). Longitudinal KL scores were obtained as well. Mean and standard deviation of curvature and joint space longitudinal measurements for case and control cohorts were analyzed using a generalized estimating equation model (SAS: GENMOD) to account for the interdependence between longitudinal outcomes.

**Results:** There were statistically significant differences ( $p < 0.05$ ) between case and control pairs for end-stage OA. For end-stage OA, there were statistically significant differences for the whole femur and for the central medial femoral condyle. In general, the involved cortices of the cohort who advanced to TKR were more flat compared with the control group at the initial time of examination (Fig 1), although in some cases the initial exam of the TKR cohort revealed greater curvature centrally, over a relatively narrow region.

**Conclusion:** The eventual TKR cohort had bony curvature changes significantly different at the time of the initial MR examination from a similarly matched cohort. Initial changes of the femur were greater indicator of eventual TKR than was the tibia; overall, the femur showed greater plasticity than did the tibia in end-stage disease. Indeed, standard deviation curvature changes that were significantly different in the TKR cohort were seen only for the entire femur and in the central medial femur. The femur and this region and the changes observed in it served as an effective biomarker for end-stage OA, as defined here by the need for TKR. Further analyses with prospective design will serve to validate the robustness of curvature changes as detected on MRI as a biomarker for ensuing end-stage.

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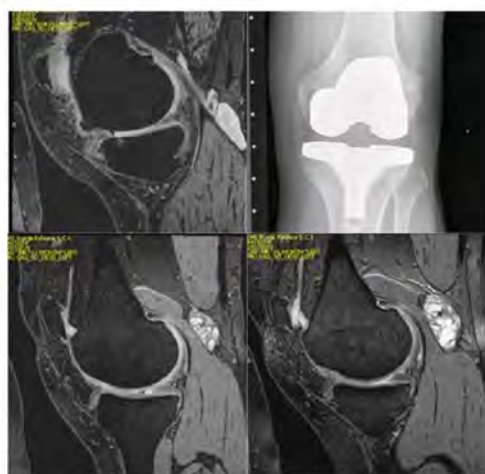


Figure 1: Top Left: Sagittal MRI of left knee through medial femoral condyle at three years prior to TKR demonstrates severe flattening of the medial femoral condyle, especially centrally. The articular cartilage and medial meniscus are macerated, all findings of end-stage disease; Top Right: Same knee three years later, at TO, demonstrates a TKR; Bottom Left: Sagittal MRI of a left knee in a matched control demonstrates maintenance of femoral curvature, despite articular cartilage and meniscal disease; Bottom Right: Sagittal MRI of same knee at TO demonstrates maintenance of the femoral curvature and persistent articular cartilage and meniscal disease.