Purpose: Both high tibial osteotomy (HTO) and knee joint distraction (KJD) are surgical techniques intending to unload the more affected femorotibial compartment (MAC) in patients with knee osteoarthritis (OA). While HTO permanently unloads the medial compartment by overcorrecting the leg axis, whilst putting more load on the lateral compartment, KJD temporarily unloads both compartments by separating the tibia and femur for 5 millimeters for 6 weeks. Both techniques have been shown to improve pain and function as well as to successfully delay knee arthroplasty. In a previous randomized controlled trial (RCT), clinical effects of both treatments were shown similar and both resulted in a statistically significant increase in weight-bearing radiographic joint space width (JSW) in the MAC. In the current study, a subgroup of patients was evaluated using extended imaging modalities, specifically MRI and computed tomography. Here, we report two-year change in cartilage thickness after treatment with KJD vs. HTO by quantitative MRI. It is hypothesized that KJD is more effective in rebuilding cartilage in the MAC while avoiding deleterious effects on cartilage in the less affected compartment (LAC).

Methods: 33 patients treated for tibiofemoral OA (16 KJD, 17 HTO) were included. Standardized semi-flexed weight-bearing radiographs and 3T MRIs with 3D spoiled gradient recalled imaging sequence with fat suppression (SPGR-fs) were acquired before and two years after surgical treatment. Cartilage thickness in the knee was measured using Chondrometrics Works 3.0 software, with longitudinal changes determined for 16 femorotibial subregions (5 tibial, 3 femoral, in the MAC and LAC, respectively). The readers were blinded to the type of intervention and acquisition order. Location-independent analysis was used to determine the total (summed) thinning and thickening score across all subregions. Further, the percentage of denuded bone area in the MAC was measured. On the radiographs the mean and minimum JSW in the MAC were measured with KIDA software.

Results: Baseline patient characteristics were similar between KJD and HTO patients, except for the Kellgren-Lawrence grade (Median(IQR): KJD 3(1), HTO 2(1); p=0.02). With KJD, the mean cartilage thickness in the MAC and in the central subregion of the MAC (cMAC) increased (both p<0.05; figure 1A/C), and the percentage of denuded bone area decreased (p=0.01; figure 1B). With HTO, in contrast, the mean cartilage thickness slightly decreased in the MAC and cMAC, and the percent denuded bone area increased (all p<0.05; figure 1). KJD showed a significantly better response in cartilage thickness gain in the MAC and cMAC, and in denuded bone area decrease than HTO, also when corrected for baseline values and Kellgren-Lawrence grade (all p<0.01). In the LAC, there was no change in cartilage thickness for either intervention (KJD -0.05±0.05; HTO -0.01±0.03; both changes p>0.33) or denuded bone area (KJD 0.10±0.15; HTO 0.26±0.18; both p>0.16). Subregion analysis showed an increase in mean cartilage thickness in most MAC areas in KJD, while a decrease was observed with HTO (figure 2). The total thickening score for KJD amounted to 1.44±0.25mm vs. only 0.51±0.13mm for HTO (difference p=0.003) while the thinning score for KJD was half vs. HTO (-0.64±0.16 vs. -1.20±0.17 mm; p=0.03). The radiographic JSW in the MAC increased in both KJD (mean MAC 1.73±0.45 to 2.63±0.40; minimum 0.23±0.12 to 1.43±0.30; both p<0.01) and HTO (mean MAC 1.86±0.33 to 2.95±0.39; minimum 0.68±0.30 to 1.45±0.40; both p<0.03). There were moderate correlations between two-year changes in MRI cartilage thickness and minimum and mean radiographic JSW measurements in the MAC for KJD patients (both R>0.47; p=0.045 and p=0.083 resp.), while for HTO there was no statistically significant association between the two (both R<0.25 and p>0.29).

Conclusions: In this subgroup of patients, KJD showed significant cartilage gain two years after treatment, as expressed by mean cartilage thickness and percentage of denuded bone area in the MAC. HTO, however, was unable to stop the cartilage thickness loss and increase in denuded bone area in the MAC. Both treatments showed no negative effects on cartilage in the LAC. Our findings suggest that the radiographic medial JSW increase previously reported in HTO may be predominantly a result of a mechanical axis shift, and not one of cartilage gain. This interpretation is supported by the absence of correlations between MRI cartilage measurement and radiographic JSW changes in this group. These results support the hypothesis that in knee OA patients KJD is more efficient in rebuilding cartilage thickness in the MAC than high tibial osteotomy.

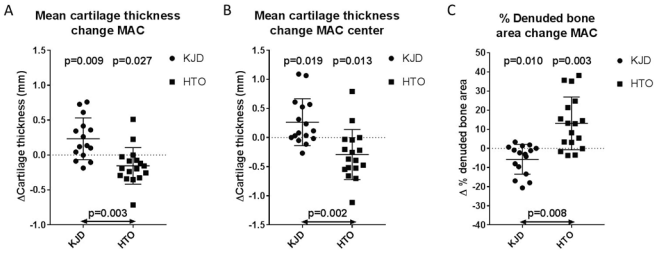

Figure 1: (A) Two-year change in mean cartilage thickness in the more affected compartment (MAC) for patients treated with knee joint distraction (KJD) and high tibial osteotomy (HTO). (B) Two-year change in mean cartilage thickness in the center of the MAC for KJD and HTO patients. (C) Two-year change in percentage of denuded bone area for KJD and HTO patients.
In all graphs, the p-values above treatment groups indicate significant two-year changes while the p-values between treatment groups indicate the differences between each two groups, corrected for baseline values and Kellgren-Lawrence grade.

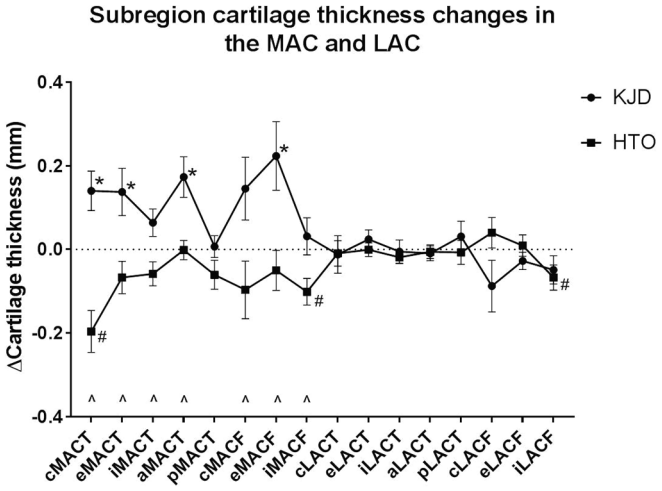

Figure 2: Two-year change in mean cartilage thickness per area for patients treated with knee joint distraction (KJD) and high tibial osteotomy (HTO). Significant changes compared to baseline are indicated with * for KJD patients and # for HTO patients. Significant differences per area between KJD and HTO are indicated with ^.
MAC = more affected compartment, LAC = less affected compartment, T = tibia, F = femur, c = central, e = external, i = internal, a = anterior, p = posterior.

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DIFFUSE TIBIOFEMORAL CARTILAGE CHANGE PRIOR TO THE DEVELOPMENT OF ACCELERATED KNEE OSTEOARTHRITIS: DATA FROM THE OSTEOARTHRITIS INITIATIVE

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Purpose: At least 1 in 7 adults who develop accelerated knee osteoarthritis (AKOA) receive a knee replacement at a median of 2.3 years from the first signs of radiographic progression. Hence, adults with AKOA present with a shortened window for intervention. Developing prognostic tools to detect who is at risk for incident AKOA is a critical step towards identifying optimal targets for

disease prevention. Traditional compartmental articular cartilage assessments that provide a mean estimate of cartilage change throughout an entire region may fail to accurately describe longitudinal cartilage alterations since this approach combines cartilage locations that may experience either an increase or decrease in cartilage thickness. We aimed to compare the spatial distribution of tibiofemoral cartilage change between adults who developed AKOA versus typical knee osteoarthritis (KOA) prior to the development of radiographic KOA.

Methods: We conducted a case-control study using data from the Osteoarthritis Initiative. We identified 129 participants who had at least one radiographically normal knee at baseline (Kellgren-Lawrence [KL] grade < 1). Participants were classified based on rapidity of radiographic progression during the first 48 months: AKOA=KL progression to >3 within 12 months (n=44), typical KOA=any other KL increase (n=40), and No KOA=no change in KL grade (n=45). Using a semi-automated program, we assessed the percent change in tibiofemoral cartilage on a 3-dimensional dual-echo steady-state magnetic resonance sequence at 36 informative locations (Figure 1). The key timeframe was two to one year prior to the radiographic onset of AKOA or typical KOA. We operationally defined meaningful longitudinal cartilage change as a location experiencing: 1) > the 95th percentile change (i.e. largest cartilage thickening), or 2) < the 5th percentile change (i.e. largest cartilage thinning) in each respective location of the no KOA group. Operationally, an individual had diffuse cartilage change if at least half of the 4 tibiofemoral regions (i.e. medial/lateral tibia/femur) had a meaningful longitudinal change (i.e. increase, decrease) in multiple (i.e., >1) informative locations. We performed a binary logistic regression to determine if diffuse tibiofemoral cartilage change (predictor) was associated with group (AKOA or typical KOA). We qualitatively described the spatial patterns of tibiofemoral regions experiencing diffuse cartilage change in the AKOA and typical KOA groups. To compare spatial distribution of cartilage change, we determined the percentage of adults with AKOA and typical KOA presenting with any meaningful cartilage change (thickening or thinning), as well as separately for thickening and thinning, at each of the 36 informative locations and qualitatively described the differences in the spatial distribution of cartilage change between groups.

Results: Table 1 highlights the group demographics. There was a non-significant trend that adults with diffuse tibiofemoral cartilage change were 2.2 times more likely to develop AKOA when compared to adults who develop typical KOA (Odds Ratio (OR) [95% Confidence Limits] = 2.2 [0.90,5.14]). There appeared to be a greater percentage of adults with AKOA (13.6%; 6/44 total) presented with involvement in the entire medial tibiofemoral compartment (i.e. both femur and tibia) when compared to the adults with typical KOA (2.5%; 1/40 total; Figure 2). Cartilage damage change simultaneously occurring in the medial femur and lateral tibia represented the most common pattern of cartilage change in the AKOA group (27.3%; 12/44) and this pattern appeared to be less prevalent in the typical KOA group (12.5%; 5/40; Figure 2). The AKOA group had more locations (9/36) with >20% of adults experiencing any meaningful cartilage change compared to typical KOA (4/36) (Figure 3). When comparing the spatial distribution of meaningful cartilage change, the commonly affected informative locations (i.e. >10% of adults, Figure 2) infrequently overlapped between AKOA and typical KOA: overlapping thickening = 50% (i.e. 4/8), thinning = 35% (i.e. 5/14).

Conclusions: We found preliminary evidence that adults who developed AKOA may present with more diffuse and spatially heterogeneous pre-radiographic tibiofemoral cartilage change compared to adults who developed typical KOA. These data may suggest that AKOA may be a subset of KOA with different instigating structural events compared to typical KOA.

Table 1. Demographics at Two Years prior to the Index Visit

Variable	Accelerated Knee OA *n=44*	Typical Knee OA *n=40*	No Knee OA *n=45*
Age (years), mean (SD)	64.4 (8.7)	57.6 (8.4)	56.6 (7.5)
BMI (kg/m^2), mean (SD)	29.6 (4.9)	28.9 (5.0)	27.2 (5.2)
WOMAC Pain, mean(SD)	1.4 (2.5)	2.1 (3.0)	1.8 (2.6)
KL Grade 0, n(%)	12 (27%)	23 (58%)	30 (67%)
Female, n(%)	29 (65%)	27 (68%)	29 (64%)

OA = osteoarthritis, WOMAC = Western Ontario and McMaster's Osteoarthritis Index; KL Grade 0 = Frequency of Kellgren-Lawrence Grade 0 (i.e. could only be 0 or 1)

Figure 1. Spatial Distribution of the 36 Informative Tibiofemoral Cartilage Locations. Three-dimensional representation of the informative locations on the femur (A) and tibia (B), as well as the two-dimensional (C) representative of these locations derived from the magnetic resonance images.

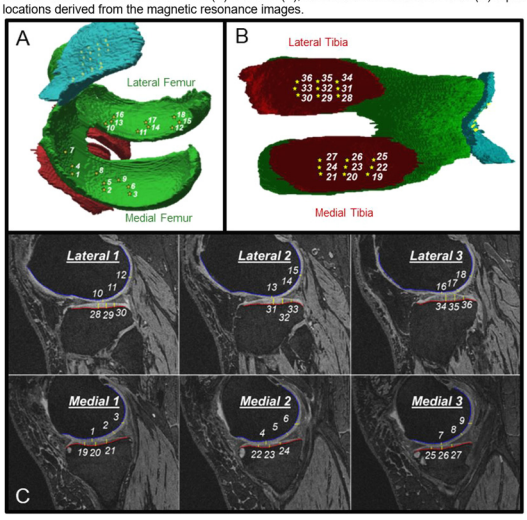

Figure 2. Different Patterns of Tibiofemoral Regions Experiencing Diffuse Cartilage Change Between Accelerated and Typical Knee OA Groups. Outlines the patterns of tibiofemoral compartment involvement and their frequency in adults with accelerated and typical knee OA with diffuse cartilage damage change. Shaded region indicates a region is experiencing multiple locations with cartilage change. M=medial, L=lateral, F=femur, T=tibia.