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Patterns of Cartilage Degeneration in Knees with Medial Tibiofemoral Offset

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ABSTRACT

Objective: To determine if radiographic medial tibiofemoral offset (MTFO) is associated with: 1) magnetic resonance imaging (MRI) pathology of cartilage, meniscus, and ligament; and 2) a distinct pattern of lateral cartilage degeneration on MRI.

Materials and Methods: Three hundred consecutive adult knee MRIs with anteroposterior (AP) radiographs were retrospectively reviewed, and 145 studies were included. MTFO was defined as a medial extension of the medial femoral condyle beyond the articular surface of the medial tibial plateau on weight-bearing AP radiographs. The patients were then divided into the MTFO (n=61) or no-offset (n=84) groups. On MRI data obtained on a 1.5-Tesla system, articular cartilage of the femoral condyle and tibial plateau were graded using a modified Outerbridge classification (36 sub-regions similar to whole-organ MRI Score (WORMS) system). In addition, MR pathology of the ACL, MCL, LCL, medial and lateral menisci, were determined.

Results: Significantly increased (ANOVA $p<0.007$) MR grade of the ligaments, menisci, and cartilage in the MTFO group (ranging from 0.3 to 2.5) compared to the control group (0.2 to 1.1). Color maps of the cartilage grades suggested a marked difference in both severity of degeneration and regional variations between the groups. MTFO group exhibited focally increased cartilage grades in the central, non-weight regions of lateral compartment (region p=0.07 to 0.12, interaction p=0.05 to 0.1).

Conclusion: MTFO is associated with overall degeneration of the knee and features a distinct lateral cartilage degeneration pattern, which may reflect non-physiologic contact of the cartilage between the lateral tibial eminence and lateral central femoral condyle.

INTRODUCTION

Osteoarthritis (OA) of the knee is the most common joint disease in the elderly [1], affecting 10-13% of the world population over age 60, and is characterized by loss of articular cartilage [2]. While the etiology of knee OA is unclear, mechanical factors that affect load transmission through the tibiofemoral joint may play major roles. These may include joint congruity [3], body weight [4], valgus and varus alignment [5], as well as ligamentous and meniscal tears [6], all of which can influence tibiofemoral contact location and load magnitude.

Coronal tibiofemoral subluxation of the knee has been studied in the context of ligament deficiency [7, 8], but rarely as a separate risk factor for knee OA. Khamaisy et al. [9] analyzed anteroposterior (AP) radiographs of 113 patients and 40 healthy subjects and found that both mild OA and severe OA knees had significantly greater coronal subluxation than normal controls. In another study by the same group, higher subchondral bone density was reported in knees with coronal subluxation [10]. While these studies found a general association between coronal malalignment and radiographic knee degeneration, the type of subluxation (i.e., medial vs. lateral) topographic pattern of cartilage degeneration has not been investigated in detail. These would further help to understand how mechanical factors affects specific regions of the knee.

Topographic characterization of cartilage degeneration requires volumetric imaging techniques such magnetic resonance image (MRI). MRI is highly sensitive to cartilage degeneration [11, 12], and is used clinically [13, 14] Using volumetric MR data [15], studies such as Whole-Organ MRI Score (WORMS) [16] and OA Initiative [17] have defined and evaluated sub-divisions of anatomic regions of the knee, to provide a more detailed picture of knee health than it is possible with plain radiography.

In our study, we sought to determine if radiographic medial tibiofemoral offset (MTFO; **Figure 2D-F**) of femoral condyle with respect to tibial plateau is associated with: 1) the pathology of cartilage, meniscus, and ligament on MRI; and 2) a distinct pattern of lateral cartilage degeneration on MRI that is consistent with a medial-shearing motion of the knee. We hypothesized that in knees exhibiting MTFO, shearing of cartilage between central regions of lateral condyle and lateral tibial tubercle will occur, resulting in greater lateral compartment degeneration in the central regions.

MATERIALS AND METHODS

This retrospective study was approved by the Institutional Review Board (IRB #blinded for review) and is compliant with the regulations of the Health Insurance Portability and Accountability Act (HIPAA). The requirement for informed patient consent was waived.

Study population

In this retrospective study, 300 knee MRI examinations of adult patients performed between October 2016 and January 2017 were initially included at random. During a preliminary inspection, following exclusion criteria were applied as detailed in the flowchart (**Figure 1**): (a) age under 35 year old (to age-match the experimental groups); (b) history of acute knee injury; (c) the presence of anterior cruciate ligament

(ACL), medial collateral ligament (MCL) or lateral collateral ligament (LCL) tears that could cause a severe joint laxity and instability; (d) ACL reconstruction or any knee instrumentation; (e) bone fracture on radiograph or MRI; (f) rheumatologic disorder or active synovitis; (g) incomplete MR examination; (h) the lack of weight-bearing radiographs of the knee within 6 months of MRI; (i) an evidence of knee internal or external rotation on lateral radiograph; and (j) the presence of large medial tibial osteophytes, defined as size greater than 3 mm on weight-bearing AP radiograph. Of 300 initial examinations, 145 cases were included in the study. The patients were categorized into offset and non-offset groups based on radiographic evaluation in the following section.

Imaging

Weight-bearing AP radiographs (**Figure 2AD**) within 6 months from the date of MRI, along with knee MRI, were available for assessment. All MR images were acquired on a General Electric Signa HDXT 1.5 MRI scanner (General Electric, Milwaukee, WI) using a Transmit/Receive 8-channel phased-array knee coil. The patient was placed in supine position with knee fully extended and the foot oriented perpendicular to the table. Spin echo sequences with proton density (PD) or T2-weighting were used, with or without fat saturation (FS), as detailed in **Table 1**.

Image evaluation

All the images were reviewed by two musculoskeletal radiologists (initials blinded for review) with 7 and 18 years of experience. Four weeks after the main readout, a mutual consensus reading was held for any discordant assessment between readers.

Radiographic evaluation of MTFO: The radiographic MTFO was assessed on the weight-bearing AP radiographs. The MTFO was defined as the presence of a medial offset (**Figure 2D, arrow**) from the cortex of the medial tibial plateau to the most medial edge of the articular surface of the medial condyle. Subjects were grouped into those without MTFO (no offset group) and with a detectable MTFO (offset group).

Cartilage evaluation: Medial and lateral tibiofemoral joint surfaces were divided into 36 regions using a modified WORMS [16] system (**Figure 3A**). There were nine regions in each of medial femoral condyle, lateral femoral condyle, medial tibial plateau, and lateral tibial plateau. For example, the regions in the medial femoral condyle were anterior-central, anterior-middle, anterior-medial, middle-central, middle-middle, middle-medial, posterior-central, posterior-middle, and posterior-medial (**Figure 3A**). In the coronal plane, we used the meniscus coverage to define medial/middle and lateral/middle cartilage divisions, while the tibial eminence was used to define the central division of the medial and lateral compartment (**Figure 3B**). In the sagittal plane, we again used meniscus coverage to define anterior, middle, and posterior divisions (**Figure 3CD**). For brevity, the trochlear cartilage was not included in the analysis.

On PD and T2 FS images, cartilage grading was carried out in each region, using a five-point scale according to the modified Outerbridge classification (ICRS 2000)[20, 21] as follows: grade 0 normal signal and intact surface, grade 1, inhomogeneous high signal with intact cartilage surface; grade 2, superficial ulceration, fissuring or fibrillation, or <50% of surface thickness; grade 3, ulceration, fissuring or fibrillation, or >50% of surface thickness; and grade 4 full thickness chondral loss.

The ligaments (ACL, MCL, and LCL) were graded as being normal (grade=0) or degenerate (grade=1) with an altered interstitial signal [22]. The meniscus was graded according to WORMS criteria [18], as follow; 0 = intact menisci, 1 = minor radial tear, 2 = nondisplaced tear, 3 = displaced tear, partial maceration or partial resection, and 4 complete maceration, destruction or complete resection. The presence of medial meniscus extrusion was diagnosed when the meniscal body was found to overhang the medial tibial plateau on coronal plane.

Statistics

Statistical analysis was performed using commercially available software (Systat 12, Systat Software Inc., San Jose, CA). Patient demographics were summarized, and the difference between offset and no-offset groups were determined using analysis of variance (ANOVA) for continuous variables, or chi-square test for proportional data. The inter-reader agreement of MR grading was evaluated with Cohen’s kappa coefficient. The Cohen’s kappa coefficient was defined as followed 0–0.20 as slight, 0.21–0.40 as fair, 0.41–0.60 as moderate, 0.61–0.80 as substantial, and 0.81–1 as excellent agreement [18].

To determine if the knees with MTFO exhibit more severe knee degeneration, mean MR grades of menisci (medial and lateral), and tibiofemoral articular cartilage (medial and lateral compartments) of no-offset vs. offset groups were compared using analysis of variance (ANOVA). Since an initial analysis showed a significant difference in age between the groups, the age was added as a covariate to account for the difference.

The proportion of samples exhibiting medial meniscus extrusion was compared using chi-square test. A p-value of < 0.05 was used to denote statistical significance.

To assess visually if there exists a distinct pattern of regional cartilage degeneration in the offset group, we first generated colormaps showing the cartilage grades in the 36 regions of the knee (**Figure 4**). Further, to determine statistically if there is an increased cartilage degeneration in the non-weight bearing central region of the lateral condyle, we performed a planned comparison using repeated measures ANOVA (region as a repeated factor and MTFO as a between factor), to compare the cartilage grade of the Mid-Cen region to the other 8 regions within the lateral condyle. This was then repeated for the lateral and medial tibial plateau and the medial femoral condyle.

RESULTS

The incidence of MTFO, defined as the extension of the medial femoral condyle beyond the articular surface of medial tibial plateau more than 0 mm, was 61 out of 145 knees. The age between MTFO and control groups was not significantly different (54.4 ± 12.0 years old vs 55.7± 12.4 years old, p=0.6). There were no significant differences between groups in proportion of sexes or the body mass index (**Table 2**).

Inter-reader agreement

MR grading of cartilage, menisci, and ligaments demonstrated an excellent inter-reader agreement (kappa coefficient ranged 0.86 to 0.99).

Severity of knee degeneration associated with MTFO

The analysis of the various structures between two groups is summarized in **Table 3**. MR grades of all major tissues of the knee (except for ACL) were significantly higher (i.e., more degenerated) in the MTFO group compared to the controls. The mean pathologic grade of ligaments, menisci, and cartilage in the MTFO ranged from 0.3 to 2.5, while the grades in the control group ranged from 0.2 to 1.1. In particular, medial meniscus grade of the MTFO knees was 2.3, suggesting severely degenerated or torn menisci, and a likelihood of altered mechanical axis due to instability.

Pattern of cartilage degeneration with MTFO

Colormaps of the cartilage grades (**Figure 4**) showed marked difference in both the severity of degeneration and the regional variations. It can be seen that in the no offset group (**Figure 4A**), the Mid-Cen and Mid-Mid regions have similar grades within the lateral condyle and the tibial plateau, while those regions in the MTFO group (**Figure 4B**) exhibited greater cartilage degeneration grades in the Mid-Cen regions. This was also confirmed statistically. In the lateral femoral condyle, cartilage grade of Mid-Cen region tended to be higher (p=0.12) than Mid-Mid region, in a translation-dependent manner (interaction p=0.1). Findings were similar (region p=0.07, interaction p=0.05) in the lateral tibial plateau. We did not find similar region-dependent increase in cartilage grade within the medial femoral condyle or the medial tibial plateau, only overall increases.

DISCUSSION

Our study found an association of MTFO, as assessed on radiographs, with significant degeneration of the knee, evident by higher MR grading of lateral and medial articular cartilage, as well as the major stabilizers including the ACL, MCL, LCL, and meniscus. Furthermore, our study revealed in patients with TMFO a unique pattern of a markedly greater degeneration at the central regions of the tibial and femoral cartilage of the lateral compartment.

Our results agree with past studies that evaluated the association between tibiofemoral subluxation and knee cartilage degeneration. In a study by Khamaisy et al. [9], 113 osteoarthritis patients were retrospectively evaluated for coronal plane tibiofemoral subluxation and found that the tibiofemoral subluxation is related to knee osteoarthritis. However, the study did not distinguish medial vs. lateral subluxation and used only anteroposterior radiographs to estimate the severity of osteoarthritis. While difficult to compare directly, ACL injury is strongly associated with subsequent knee degeneration [19-21], as well as with tibiofemoral subluxation on the coronal plane [22-24]. Our study also showed significantly greater knee degeneration in MTFO subjects, suggested by higher MR grades of cartilage, ligaments, and menisci. In addition, our study expands on past work by assessing the topographical pattern of cartilage degeneration.

Additionally, we found in MTFO knees a distinct pattern of cartilage degeneration characterized by higher MR grades in the central non-weight-bearing region of the lateral compartment of the tibial plateau and femoral condyle, compared to their respective weight-bearing regions. This pattern likely reflects an abnormal shift in the tibiofemoral contact, from the middle (i.e., normally weight-bearing) region to the central regions between the tibial eminence and central femoral condyle. This finding supports a recent study from Hosseini et al. [7] investigating the deformation of cartilage during knee flexion in healthy volunteers, revealing no considerable contact between the cartilage of the tibial eminence and femur. Therefore, it would seem plausible that, in subjects with MTFO, repetitive medial-lateral shearing of the femur onto the tibia in the central region may induce localized damage. Somewhat similar patterns of cartilage degeneration are also seen in ACL deficient knees [8], which may have increased coronal subluxation [7] as well as rotational instability [25-27].

As an ancillary finding, our study revealed markedly greater degeneration of the medial meniscus in the MTFO group compared to a minimal degeneration in the no offset group. This may suggest a significant role of the medial meniscus in the horizontal stabilization of the tibiofemoral joint. A recent cadaveric study by Tachibana et al. [28] found an association between complete radial tears of the lateral meniscus and tibiofemoral mediolateral shift, which suggests that without preserved ring structure of the meniscus, the mediolateral axis of the tibiofemoral joint is no longer stable. Furthermore, in cases of degenerative horizontal tear of the meniscus, Arno et al. [29] found an association between horizontal cleavage lesions of the medial meniscus with a medial shift of tibiofemoral contact area of the medial compartment. Therefore, severely degenerated menisci might not only cause local cartilage degeneration by increased contact pressure at the weight-bearing region, [30] but also indirectly cause remote cartilage degeneration by reduction of tibiofemoral stabilization.

Our study has several limitations. First, it is a retrospective, cross-sectional study where the initiation and progression of OA could not be followed. Second, the study included a largely male cohort of greater than 80%, which may lead to gender bias due to slightly lower prevalence of OA in men [31, 32]. However, the distribution of sexes in each of the group was not statistically different. Third, the study population consists only of patients referred to MR imaging. Therefore, these patients are more likely to have severe degeneration. Lastly, our study used a semiquantitative cartilage assessment method, and quantitative techniques such as T2 mapping may be used in the future to reveal greater differences between groups. Nonetheless, the interobserver agreement in our study was excellent.

In conclusion, in patients featuring radiographic MTFO, we found both an overall increase in knee degeneration, as well as a distinct pattern of cartilage degeneration in the central non-weight bearing region of the lateral tibiofemoral compartment. The pattern of degeneration is consistent with the concept of coronal micro-instability in MTFO, causing an abnormal contact in the central regions of the lateral compartment.

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TABLES

	TR (ms)	**TE (ms)**	**FOV (mm)**	**Slice (mm)**	**Matrix**
Sagittal PDw	3250	30	130-160	2.5	512x256
Sagittal fat saturated T2w	4000	60	130-160	4	320x320
Coronal FS T2w	3850	70	150-160	4	320x256
Axial FS PDw	3000	30	130-160	4	320x320
Sagittal PDw CUBE	2000	36	130-160	1.6	256x256

Table 1. MR sequence parameters.

	No offset group (mean ± SD, n=84)	**MTFO group (mean ± SD, n=61)**	**P-value**
Age (years old)	54.4 ± 12.0	55.7 ± 12.4	0.552
Sex (M:F)	73:11	51:10	0.577
Body Mass Index	31.0 ± 6.1	31.9 ± 6.7	0.445

Table 2. Patient characteristics.

MR Grade	No offset group (mean ± SD, n=84)	MTFO group (mean ± SD, n=61)	P-value
lateral cartilage	0.26 ± 0.82	0.67 ± 1.27	<0.00001
medial cartilage	0.37 ± 0.99	1.19 ± 1.57	0.00027
ACL	0.17 ± 0.38	0.28 ± 0.45	0.15336
MCL	0.50 ± 0.85	1.15 ± 0.97	0.00004
LCL	0.73 ± 0.96	1.05 ± 0.99	0.06282
lateral meniscus	0.57 ± 1.17	1.33 ±1.39	<0.00001
medial meniscus	1.09 ± 1.25	2.49 ± 1.29	0.00006
medial meniscus extrusion	30 (35.7%)	43 (70.5%)	0.00003

Table 3. Mean MR grades of cartilage, ligaments and menisci for no offset and MTFO groups.

FIGURE LEGENDS

Figure 1: Flowchart of data exclusion and group selection.

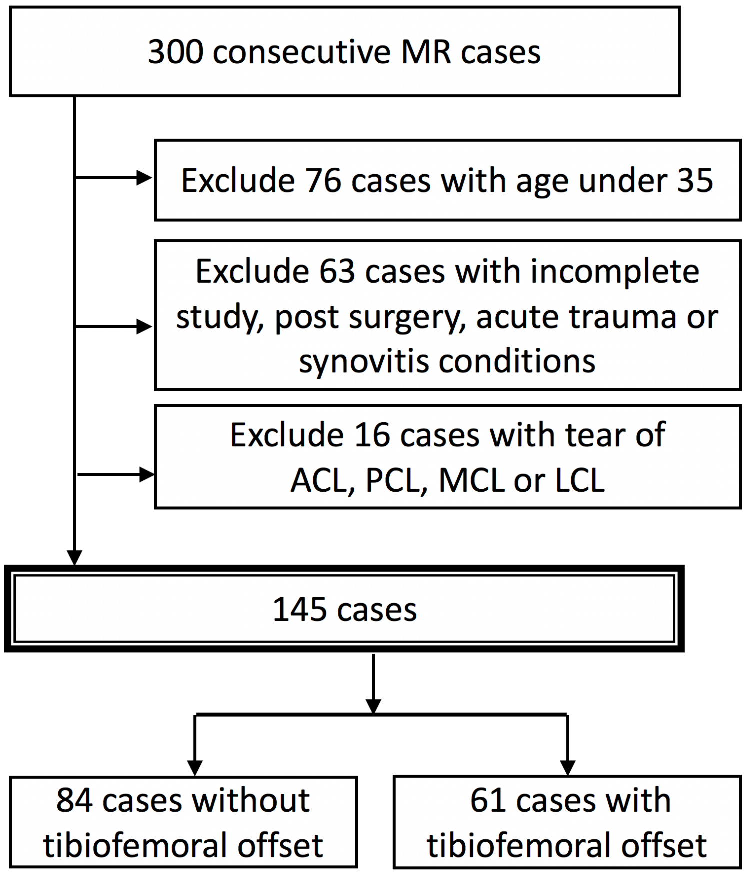
Figure 2. Representative images and illustration of no offset (**A, B, C**) and MTFO (**D, E, F**) groups. Weight-bearing radiographs (**A, D**), coronal MR image with T2 weighting and fat saturation (**B, E**), and illustrations (**C, F**). 52-year-old male patient without radiographic offset (**A**) shows no degeneration of the ACL or the tibiofemoral articular cartilage (**B**), and likely has a normal mechanical axis (**C**). 60-year-old male patient with a radiographic MTFO (**D**, arrow), seen as a medial offset of the femoral condyle (**D**, solid line) from the cortex of the medial tibial plateau (**D**, dotted line). The patient exhibited a mild cartilage loss at the central region of the lateral compartment of the femur (**E**, arrowheads) and mild mucinous degeneration of the ACL (**E**, asterisk). (**F**) Conceptual illustration of a knee with MTFO, showing an alteration of the contact area (red) between the femur and tibia due to the offset (**F,** arrows). The cartilage in the central region of the lateral compartment may become more vulnerable to degeneration in this case compared to no offset case (**C**).

Figure 3. Tibiofemoral cartilage regional assessment. Cartilage surface was divided into 36 regions (**A**), using the meniscus coverage seen in coronal (**B**) and sagittal (**C, D**) MR images. (**B**) On the coronal T1w image of the knee, the medial (Med), middle (Mid), and central (Cen) of the medial compartment and central (Cen), middle (Mid), and lateral (Lat) of the lateral compartment were defined using the body of menisci and tibial eminence as landmarks. (**C**) On the sagittal PDw MR image of the knee at medial

compartment, the anterior (Ant), middle (Mid) and posterior (Pos) were defined using the anterior and posterior horn of medial meniscus as landmarks. (**D**) On the sagittal PDw MR image of the knee at lateral compartment, the anterior (Ant), middle (Mid) and posterior (Pos) were defined using the anterior and posterior horn of lateral meniscus as a landmark.

Figure 4. Color map showing regional MR grade of cartilage in no offset (**A**) and MTFO (**B**) groups, suggesting not only the overall severity, but also different regional patterns, of cartilage degeneration between groups. The cartilage was graded using the Modified Outerbridge classification (grade 0 to 4), and the menisci were graded base on WORMS classification (grade 0 to 4). In the no offset group, the Mid-Cen (**A**, asterisk) and Mid-Mid (**A**, triangle) regions have similar grades within the lateral condyle and the tibial plateau, while those regions in the MTFO group (**B**) exhibited greater increases in the Mid-Cen regions (**B**, asterisk). In the medial femoral condyle and medial tibial plateaus, there were no such region-dependent increase in cartilage grade, only the overall increases, in the MTFO group.

FIGURES



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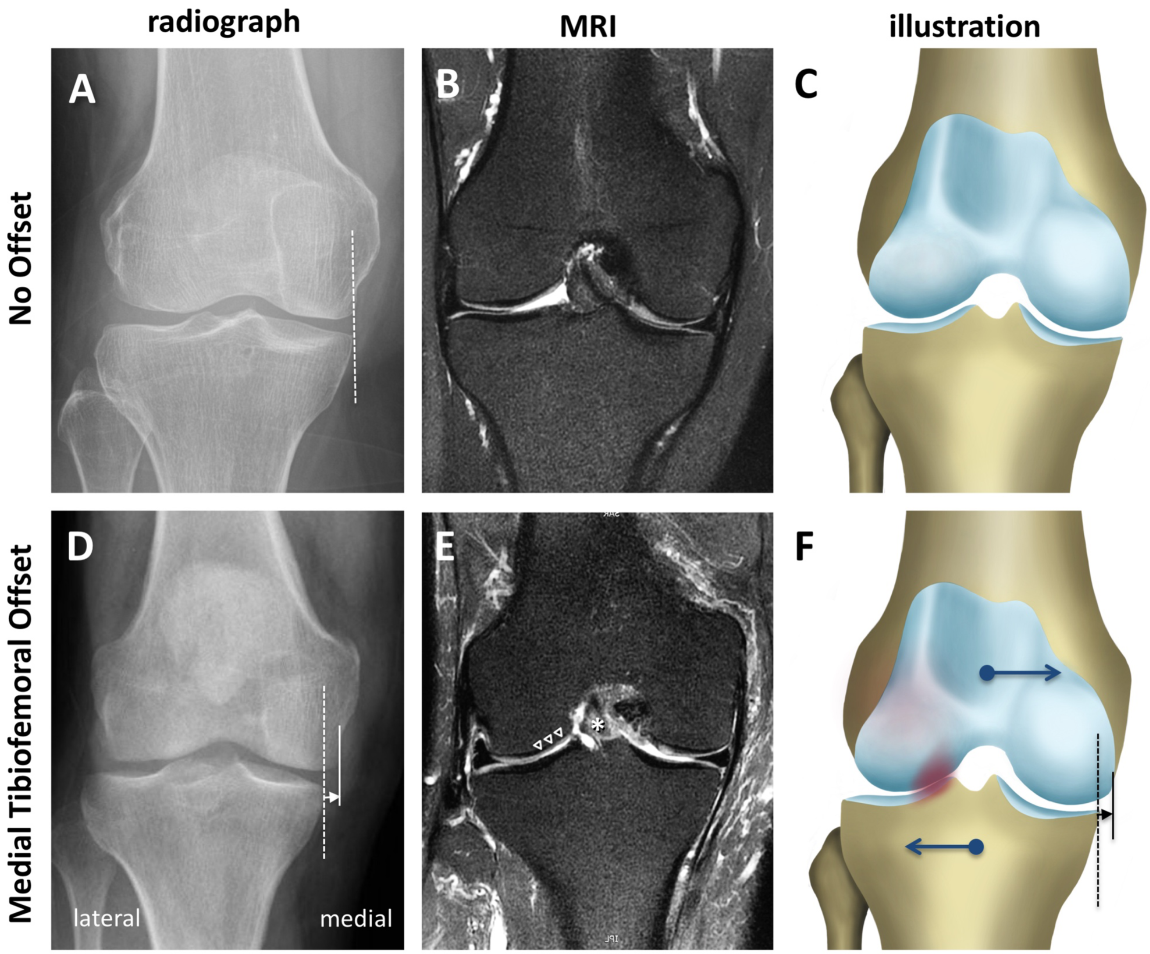

Figure 2: Representative images and illustration of no offset (**A, B, C**) and medial tibiofemoral offset or MTFO (**D, E, F**) groups. Weight-bearing radiographs (**A, D**), coronal MR image with T2 weighting and fat saturation (**B, E**), and illustrations (**C, F**). 52-year-old male patient without radiographic offset (**A**) shows no degeneration of the ACL or the tibiofemoral articular cartilage (**B**), and likely has a normal mechanical axis (**C**). 60-year-old male patient with a radiographic MTFO (**D**, arrow), seen as a medial offset of the femoral condyle (**D**, solid line) from the cortex of the medial tibial plateau (**D**, dotted line). The patient exhibited a mild cartilage loss at the central region of the lateral compartment of the femur (**E**, arrowheads) and mild mucinous degeneration of the ACL (**E**, asterisk). (**F**) Conceptual illustration of a knee with MTFO, showing an alteration of the contact area (red) between the femur and tibia due to the offset (**F,** arrows). The cartilage in the central region of the lateral compartment may become more vulnerable to degeneration in this case compared to no offset case (**C**).

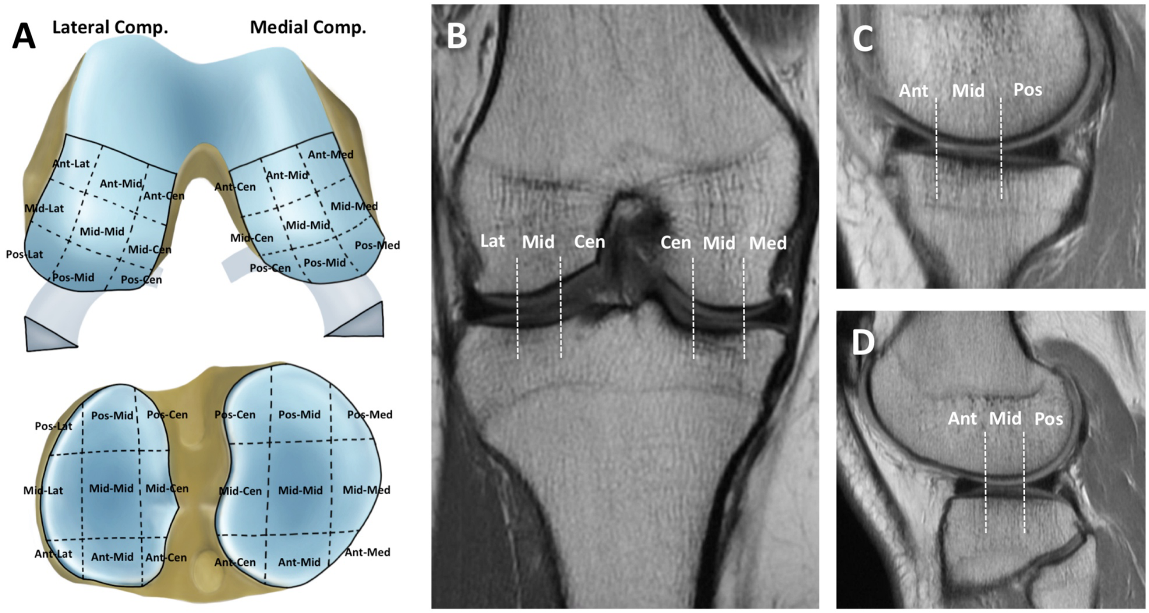

Figure 3. Tibiofemoral cartilage regional assessment. Cartilage surface was divided into 36 regions (**A**), using the meniscus coverage seen in coronal (**B**) and sagittal (**C, D**) MR images. (**B**) On the coronal T1w image of the knee, the medial (Med), middle (Mid), and central (Cen) of the medial compartment and central (Cen), middle (Mid), and lateral (Lat) of the lateral compartment were defined using the body of menisci and tibial eminence as landmarks. (**C**) On the sagittal PDw MR image of the knee at medial compartment, the anterior (Ant), middle (Mid) and posterior (Pos) were defined using the anterior and posterior horn of medial meniscus as landmarks. (**D**) On the sagittal PDw MR image of the knee at lateral compartment, the anterior (Ant), middle (Mid) and posterior (Pos) were defined using the anterior and posterior horn of lateral meniscus as a landmark.

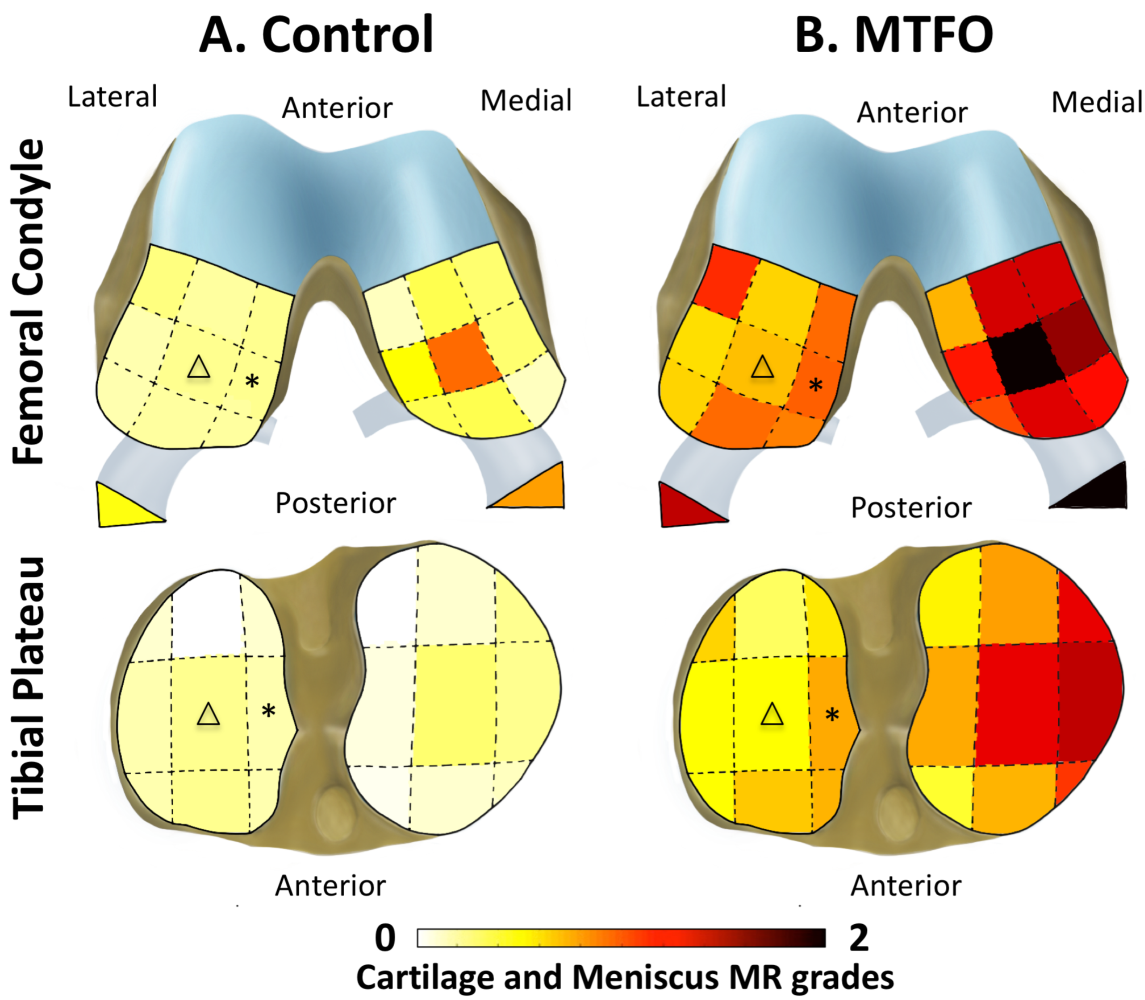

Figure 4. Color map showing regional MR grade of cartilage in no offset (**A**) and MTFO (**B**) groups, suggesting not only the overall severity, but also different regional patterns, of cartilage degeneration between groups. The cartilage was graded using the Modified Outerbridge classification (grade 0 to 4), and the menisci were graded base on WORMS classification (grade 0 to 4). In the no offset group, the Mid-Cen (**A**, asterisk) and Mid-Mid (**A**, triangle) regions have similar grades within the lateral condyle and the tibial plateau, while those regions in the MTFO group (**B**) exhibited greater increases in the Mid-Cen regions (**B**, asterisk). In the medial femoral condyle and medial tibial plateaus, there were no such region-dependent increase in cartilage grade, only the overall increases, in the MTFO group.