T2* mapping of anterior cruciate ligament in osteoarthritic knee joint: comparison with oblique coronal T2-weighted image, operative and pathologic results

Poster No.: C-0952
Congress: ECR 2013
Type: Scientific Exhibit
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Keywords: Musculoskeletal joint, MR, Imaging sequences
DOI: 10.1594/ecr2013/C-0952

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Purpose

Magnetic resonance imaging (MRI) is a widely used imaging modality providing information about the natural structure and injuries of the anterior cruciate ligament (ACL) (1). Anatomic and embryologic studies show that the native ACL consists of two distinct functional bundles, termed the anteromedial (AM) and posterolateral (PL) bundles, based on their tibial insertions(2-4). The ability to reliably and accurately detect AM and PL bundles on MR images is of particular interest. The use of additional oblique planes of view for the evaluation of AM and PL bundles offers a potential means of improving evaluations, even using low field strength magnets(5). In this study, we evaluated AM and PL bundles separately using oblique coronal images.

The differentiation of partial and complete tears is important because this can influence patient management and prognosis (6, 7). However, several authors (8, 9) have suggested that standard or oblique MRI slices are not sufficiently accurate to satisfactorily differentiate complete and partial tears. Also, chronic tears may have potentially confusing appearances due to bridging fibrosis, which resembles the normal ACL, although acute tears can be accurately differentiated from intact ligaments (10-12). On the other hands, a complete ACL tear in those with established knee osteoarthritis may arise from mechanisms that differ from those of acute ACL tears in younger persons. Reactive bone formation in the intercondylar notch in osteoarthritic knees causes the notch to narrow and reduce in height. This can cause damage to the ACL due to the shear forces generated during flexion and extension (13, 14). Although not as common or as widely studied as complete tears of the ACL, partial ACL tears are substantial injuries that commonly progress to complete tears and resultant symptomatic knee laxity within 1 year of initial injury (6). Therefore we undertook to investigate the statuses of AM and PL bundles including partial and complete tears, using standard T2-weighted sequences and by T2* mapping in the oblique coronal plane in osteoarthritic knee joints.

T2*, the effective T2 shortened by phase dispersion from both main and local magnetic field inhomogeneities, captures fast-T2 relaxations (T2* < 10 ms) that reflect spin-spin interactions between protons bound to collagen and degree of collagen fibril-alignment (15). Similar to T2, T2* describes the transverse relaxation of tissues. However T2* is always shorter than T2. Furthermore, T2* may provide us with different information about tissues than T2 or T1# (16). Although, T2* mapping has been used for the evaluation of cartilage, we considered that could be beneficial for determining the severities of ligament disruption and degeneration in patients with a partial ACL tear. furthermore, microscopic evidence of ACL degeneration is not well documented in the literature. Accordingly, the purpose of this study was to investigate the efficacy of T2* mapping for the evaluation of ACL status in osteoarthritic knee joints, and to compare this with oblique coronal T2-weighted imaging (WI) and with respect to pathologic and operative results.
Methods and Materials

Patients

This study was approved by our hospital ethics committee, and informed consent was obtained from all patients.

From January through June 2011, we prospectively selected patients scheduled for total knee arthroplasty due to severe osteoarthritis (Kellgren-Lawrence grades 3 and 4). Patients with inflammatory or infectious arthritis, and those with a history of a previous knee injury or previous knee surgery were excluded. Initially, 61 ACLs were harvested from 58 patients (49 women, 9 men, age range; 52-84 years, mean age; 70.4 years). Cases in which pathologic and imaging studies were difficult to perform due to severely deformed or missed bundles were excluded. Finally 53 ACLs in 50 patients (43 women, 7 men, age range; 55-84 years, mean age; 69.3 years) were included in this study.

In addition, 10 healthy volunteers (8 men, 2 women, age range; 25-35 years, mean age; 30.4 years) without any knee joint symptom or previous knee injury were included.

MR examinations

All patients underwent MR examinations one day before surgery. MR imaging was performed with a 1.5 T magnet (Magnetom Avanto TIM; Siemens Medical Systems, Erlangen, Germany) using a dedicated send/receive 8-channel phased array knee coil.

The MR imaging protocol consisted of oblique coronal turbo spin echo T2-weighted and T2* mapping images. Oblique coronal planes were obtained in the plane parallel to the course of the femoral intercondylar roof on sagittal scout images to maximize visualization of the AM and PL bundles of the ACL. Although the use of sagittal oblique MRI, parallel to the long axis of the ACL, has been advocated by some authors, we used oblique coronal MRI parallel to the femoral intercondylar roof, as was previously used by Hong et al's (17).

Oblique coronal T2-weighted imaging parameters were TR/TE 3000 ms / 101 ms, 3-mm slice thickness, 384 x 269 matrix, 160 x 160 mm field of view (FOV), and an echo train length (ETL) of 7. The total scanning time for this sequence was 3 minutes 23 seconds. Oblique coronal T2* mapping parameters were TR/TE of 689 / 4.2, 3-mm slice thickness, 256 x 179 matrix, 180 x 180 mm FOV, ETL of 1 and the total scanning time for this sequence was 3 minutes 32 seconds.

Imaging analysis
Oblique coronal T2-weighted MR images were reviewed by consensus of two musculoskeletal radiologists with 9 and 2 years of MRI experience on a PACS monitor. The two reviewers were unaware of pathologic results or gross findings.

To evaluate ACL status, AM and PL bundles were analyzed separately. As previously described (2, 5) it was found that the AM and PL bundles originated from the anterior-proximal and posterior-distal aspect of the femoral attachment. At the tibial insertions, the AM bundle inserted anteromedially and the PL bundle posterolaterally. Image analyses of oblique coronal T2-weighted image were performed using different two methods as previously described (6, 18, 19). First, the statuses of the AM and PL bundles were graded using a 5-point system (grades 0-4) for comparison with pathologic findings. A grade 0 indicated an intact bundle, that is, a continuous band of low signal intensity from the femoral to the tibial attachments; a grade 1 indicated abnormal high intrasubstance signal or a subtly wavy contour with definable intact ligamentous fibers in less than quarter of a bundle; grade 2 indicated a signal change and a wavy contour in less than half of a bundle; grade 3 a signal change and a wavy or lax contour or severe atrophy affecting more than half of a bundle; and grade 4 indicated a complete disruption or complete replacement of the bundle by an edematous mass. Second, ACL tear statuses were simply classified as normal (grade 0, 1), partial (grade 2, 3), or complete tear (grade 4) for comparison with gross finding in the operative field.

On T2*-mapping images, we measured regions of interest (ROIs) on AM and PL bundles at a workstation (Leonardo, Siemens Medical Solution). An ROI was drawn over the whole area of bundles in each image slice. Corresponding oblique coronal T2-weighted images served as references for the accurate placement of ROIs within bundles. If AM or PL bundles are visible in more than one slice, the mean value of summed ROI values in each slice was obtained and used in the analysis. To standardize the procedure, all measurements were performed by a single investigator. To test the reproducibility of measurements, ROI measurements were carried out a second time for each AM and PL bundle by the radiologist who had performed the original assessment. The radiologist was blinded to histologic and operative gradings and to first measurement results.

Operation and Pathology

ACL statuses were determined by two orthopaedic surgeons (KDJ, SJT), who separated AM and PL bundles, before and after ACL harvest in the operative field. The analysis list was as follows; the presence or absence of synovial coverage and synovial inflammation, and continuity, fraying, delamination and shrinkage of bundles. Gross findings also were graded according to the imaging grades; grade 0 - normal appearance, grade 1 - only one finding among synovial problem such as no synovial coverage or synovial inflammation, fraying or delamination with maintenance of continuity, grade 2 - a synovial problem plus delamination or fraying with maintenance of continuity, grade 3 - a synovial problem plus fraying or delamination and shrinkage with maintenance of continuity, and grade 4 - discontinuity or poor fiber delineation due to severe shrinkage. In addition, for comparison
with imaging grades, we also modified the above grading with normal (grade 0, 1), partial (grade 2,3) or complete tear (grade 4).

ACLs were harvested by sharp incision from the bone-ligament junctions of femurs and tibiae. Proper specimen orientation was maintained by placing a mark on the anterior tibial side of harvested ligaments. AM and PL bundles were gently separated by one pathologist (C.K.W), in consultation with an orthopaedic surgeon (K.D.J). Each specimen was fixed in 10% formalin, embedded in paraffin, cut longitudinally, and stained with Hematoxylin and Eosin for histological evaluations.

Histological appearance was evaluated using a semiquantitative scoring system, which included the amount of loose collagen fiber, fibrosis, cystic changes, chondroid metaplasia and mucoid degeneration. The degenerative changes were categorized as normal, slight, mild, moderate or marked according to Kleinbart's criteria (20). Normal (0) was defined as no microscopic abnormalities, slight (1) when microscopic changes were observed in one high-power microscopic field (magnification ×400), mild (2) when histologic changes were noted in several fields, moderate (3) when a significant portion of the ligament was involved, and marked (4) when there was a confluence of the microscopic fields. The sections were examined and graded by the pathologist in a blind manner.

**Statistical analysis**

Linear regression analysis and Pearson correlation coefficients were used to establish the correlation between the ROI values of AM or PL bundles on T2* mapping images and pathologic, operative grades and imaging grades on T2-weighted MR images. In addition, the correlations between ROI values, pathologic, gross and imaging grades, and age and sex were sought using linear regression analysis. Wilcoxon's signed-rank test was used to investigate the difference between 1st and 2nd measurements of ROI values. Kappa statistics were used to evaluate degree of agreement between pathologic grades, visual grades from operative fields or gross specimens, and imaging grades on oblique coronal T2-weighted and T2* mapping images. Level of agreement were assessed using kappa values as previously described by Landis and Koch: a negative kappa value was interpreted as poor agreement, 0.00 - 0.20 as slight agreement, 0.21 - 0.40 as fair agreement, 0.41 - 0.60 as moderate agreement, 0.61 - 0.80 as substantial agreement, and greater than 0.81 as almost perfect agreement. Using operative findings as reference standards, sensitivity, specificity, and accuracy of oblique coronal T2-weighted images and T2* mapping images for the diagnosis of complete and partial tears about each AM and PL bundle were calculated using simple bundle status. Statistical software (SPSS version 13; SPSS Inc.) was used for analyses and statistical significance was accepted for p values < 0.05.
Fig. 1: A 58-year-old female patient underwent total knee arthroplasty due to a KL osteoarthritis score of 3 and severe knee pain. Oblique coronal T2-weighted MR image of the anteromedial (AM) bundle (arrowheads) showing poorly differentiated fibers, an undulating course, and mild swelling in more than half of the bundle (imaging grade 3).
Fig. 2: A 58-year-old female patient underwent total knee arthroplasty due to a KL osteoarthritis score of 3 and severe knee pain. In the corresponding T2* mapping image, the ROI value was 25.
Fig. 3: Fig 3. A 58-year-old female patient underwent total knee arthroplasty due to a KL osteoarthritis score of 3 and severe knee pain. Oblique coronal T2-weighted MR image of the posterolateral (PL) bundle (arrowheads) showing more prominently conglomerated fibers and swelling of almost the whole bundle (imaging grade 4).
Fig. 4: A 58-year-old female patient underwent total knee arthroplasty due to a KL osteoarthritis score of 3 and severe knee pain. In the corresponding T2* mapping image, the ROI value was 24.6.
**Fig. 5:** Pathologic examination of both bundles (x 40, H&E stain) revealed marked change with an extensively degenerative area. Most of the bundle had been replaced by cystic lesions (arrows, grade 4). In the operative field (not shown), the AM bundle appeared normal (grade 0) and the PL bundle showed only synovial detachment (grade 1).
Results

By linear regression analysis, correlations between age and sex and ROI values and pathologic, operative and imaging grades were all insignificant (p > 0.05). Furthermore, the difference between 1st and 2nd ROI measurements was insignificant (AM bundle; p = 0.236, PL bundle; p = 0.824). The mean ROI values of the AM and PL bundles of the ten normal volunteer on T2* mapping images were 17.9 (range, 16.8 - 20.2) and 17.9 (range, 16.2 - 20), respectively. The mean ROI values of AMB and PLB on T2* mapping images and corresponding pathologic, operative and T2-weighted imaging grades are presented in table 1. Histologic results showed that 58 % (31 of 53) of the AM bundles and 62 % (33 of 53) of the PL bundles exhibited moderate to severe degenerative changes (grades 3-4). In operative fields, the number of patients with grade 3 (moderate partial tear) and grade 4 (complete tear) was four and seven for AM bundles, and five and five for PL bundles. On oblique coronal T2-weighted images, 13 and 10 patients in AM bundle, and 9 and 12 patients in PL bundle were interpreted as grade 3 and 4, respectively.

According to table 1, higher pathologic grades had higher mean ROI values for both AM and PL bundles and this result was statistically significant (AM bundle; Pearson’s coefficient = 0.557 (p = 0.00), PL bundle; Pearson’s coefficient = 0.384 (p = 0.005)). The correlation between ROI values and operative grades was prominently linear for AM bundles (Pearson's coefficient = 0.513 (p = 0.000)), but poor for PL bundles (Pearson’s coefficient = 0.254) and statistically insignificant (p = 0.093). The correlation between ROI values and imaging grades on T2-weighted MR images was linear for AM bundles (Pearson’s coefficient = 0.362 (p = 0.008), but negligible for PL bundles (Pearson’s coefficient = 0.040 (p = 0.774)).

Table 1. Mean ROI values of AM and PL bundles of anterior cruciate ligaments on T2* mapping images and corresponding pathologic, operative and imaging grades.

<table>
<thead>
<tr>
<th>Grade</th>
<th>AM bundle</th>
<th>PL bundle</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>P</td>
<td>O</td>
</tr>
<tr>
<td>0</td>
<td>19.9*</td>
<td>25.1 (19.5-36.5)</td>
</tr>
<tr>
<td></td>
<td>(n = 1)</td>
<td>(n = 23)</td>
</tr>
<tr>
<td>1</td>
<td>23</td>
<td>28.6</td>
</tr>
<tr>
<td></td>
<td>(19.8-27.4)</td>
<td>(19.9-36.7)</td>
</tr>
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</table>
We also examined correlations between pathologic grades and imaging grades on oblique coronal T2-weighted images, T2* mapping images and operative grades for AM and PL bundles. Results are represented in Table 2.

Table 2. The correlation between pathologic and imaging grades for oblique coronal T2-weighted images, T2* mapping images, and operative grades. (n = Pearson’s correlation coefficient)

<table>
<thead>
<tr>
<th></th>
<th>AM bundle</th>
<th>PL bundle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathology &amp; T2WI</td>
<td>0.482 (p = 0.000)</td>
<td>0.315 (p = 0.022)</td>
</tr>
<tr>
<td>Pathology &amp; †T2* map</td>
<td>0.445 (p = 0.001)</td>
<td>0.247 (p = 0.074)</td>
</tr>
<tr>
<td>Pathology &amp; operative findings</td>
<td>0.331 (p = 0.027)</td>
<td>0.311 (p = 0.036)</td>
</tr>
<tr>
<td>Operative findings &amp; T2WI</td>
<td>0.562 (P = 0.000)</td>
<td>0.634 (P = 0.000)</td>
</tr>
<tr>
<td>Operative findings &amp; †T2* map</td>
<td>0.725 (p = 0.000)</td>
<td>0.514 (p = 0.000)</td>
</tr>
</tbody>
</table>

Note. †; imaging grades
Except the correlation between pathologic grades and imaging grades on T2* mapping images in PL bundle, imaging grades on MR images and visual grades on operative field had significant correlation with pathologic grades about each AM and PL bundle. However, all kappa values were < 0.3, which indicated only fair to slight agreement (see Table 3).

Table 3. Agreements between imaging and pathologic and macroscopic grades in the operative field.

<table>
<thead>
<tr>
<th></th>
<th>AM bundle</th>
<th>PL bundle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operative findings &amp; T2WI</td>
<td>0.168 (p = 0.003)</td>
<td>0.094 (p = 0.128)</td>
</tr>
<tr>
<td>Operative findings &amp; T2* map</td>
<td>0.3 (p = 0.000)</td>
<td>0.211 (p = 0.002)</td>
</tr>
<tr>
<td>Pathology &amp; T2* map</td>
<td>-0.005 (p = 0.940)</td>
<td>0.039 (p = 0.568)</td>
</tr>
<tr>
<td>Pathology &amp; T2WI</td>
<td>0.082 (p = 0.335)</td>
<td>0.163 (p = 0.062)</td>
</tr>
<tr>
<td>Operative findings &amp; pathology</td>
<td>0.071 (p = 0.201)</td>
<td>0.016 (p = 0.776)</td>
</tr>
</tbody>
</table>

Using operative results as standard references, for complete tears, the sensitivity, specificity and accuracy of oblique T2-weighted MR imaging were 100, 94, and 96 %, respectively for AM bundles and 100, 90, and 92 %, respectively for PL bundles, and for incomplete tears, these were 71, 59, and 63 %, respectively for AM bundles and 80, 62, and 67 %, respectively for PL bundles. The sensitivity, specificity and accuracy of T2* mapping for complete tears were 86, 93, and 92 %, respectively for AM bundles and 80, 79, and 79 %, respectively for PL bundles and for incomplete tears, corresponding values were 53, 74, and 68 % for AM bundles and 56, 76, and 70 % for PL bundles.
**Fig. 1:** A 58-year-old female patient underwent total knee arthroplasty due to a KL osteoarthritis score of 3 and severe knee pain. Oblique coronal T2-weighted MR image of the anteromedial (AM) bundle (arrowheads) showing poorly differentiated fibers, an undulating course, and mild swelling in more than half of the bundle (imaging grade 3).
Fig. 2: A 58-year-old female patient underwent total knee arthroplasty due to a KL osteoarthritis score of 3 and severe knee pain. In the corresponding T2* mapping image, the ROI value was 25.
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Fig. 5: Pathologic examination of both bundles (x 40, H&E stain) revealed marked change with an extensively degenerative area. Most of the bundle had been replaced by cystic lesions (arrows, grade 4). In the operative field (not shown), the AM bundle appeared normal (grade 0) and the PL bundle showed only synovial detachment (grade 1).
Conclusion

Magnetic resonance imaging (MRI) is the most commonly used and highly valued noninvasive imaging procedure for suspected injuries to the ACL (21). The main factors in determining the detection of the ACL by MRI are field strength and plane of view. Although Kwon et al. (8) reported that additional oblique planes are useful for the evaluation of ACL tears, most previous studies have concluded that it is not clear which planes and sections are most appropriate for accurate MRI evaluation of the ACL. Moreover, the separation of ACL into AM and PL fiber bundles has now been widely accepted as a basis for understanding ACL function. On routine MR images, the AM bundle is usually the one that can be evaluated and the PL bundle is less frequently observed (5). Because oblique sagittal and oblique coronal imaging have been used to delineate the ACL more clearly (17, 22), we used the oblique coronal plane for separate evaluations of AM and PL bundles. In patients with a severely atrophic or attenuated ACL or when the ACL exhibited a prominent angulated or wavy course or a severely edematous condition, the clear differentiation of these two bundles was difficult. Nevertheless, we were able to analyze both the AM and PL bundles in most cases. Furthermore, since these bundles have different biomechanical functions, the histological appearance of each bundle of the ACL in osteoarthritic knee should be investigated, and thus, we investigated each bundle during our histologic examination.

The ability to accurately differentiate complete, partial, and isolated AM tears and isolated PL tears would undoubtedly aid preoperative planning (23, 24). Several investigators have found MR to be useful for the assessment of the double-bundle anatomy of the intact, normal ACL, but data is lacking regarding its ability to detect isolated AM or PL bundle tears in patients with a history of ACL injury (25). In addition, isolated ruptures of the AM and PL bundles are difficult to diagnose during arthroscopy, and a potential cause of controversy (6). Relatively few MR studies have considered complete and partial tears separately, but these were performed using 1.5T or lower field strength systems, which have not been shown to be accurate enough to differentiate complete and partial ACL tears, or to identify partial ACL tears (6, 7, 18). According to our results, histologic, macroscopic in the operative field and radiologic grades were inconsistent, despite being significantly correlated. In some cases, the ACL did not show high-grade partial or complete rupture on MR images or in the operative field, despite a high grade pathologic condition. These findings demonstrate that the functional role of a histologically degenerated but morphologically intact ACL is questionable, and suggest that a severely degenerative state might not cause direct high-grade partial or complete disruption on standard MR images or in macroscopic view.

In the present study, we used T2* mapping to objective evaluate of ACLs. T2 relaxation time reflects the specificity of tissue by describing the attenuation of transverse magnetization of tissue. Specifically, it is a measure of MR signal intensity during different echo times, and specific values are calculated using a formula (26). T2 mapping has the
potential to quantitatively evaluate deteriorations in molecular composition (27), and T2 is sensitive to water content and the arrangement of the collagen network structure (28). On the other hand, T2* is the relaxation time obtained with a gradient-echo pulse sequence that comprises both T2 relaxation and coherent dephasing effects, which arise from spins within a voxel having different precession frequencies due to local field variations, within the net T2* decay (29). To measure T2* relaxation, a series of images with different TEs must be acquired. TEs between 0.008 and 40 ms have been used to date (30). In the present study, we used 4.2 ms TE for T2* mapping images and the total scanning time for this sequence was 3 minutes 32 seconds. According to the results obtained, the pathologic grades and T2* values of the ACL bundles were significantly and linearly correlated. In terms of the correlation between T2* values and operative and radiologic grades, only the AM bundle showed a significant correlation. Therefore, these results suggest that T2* values well demonstrate the severity of ACL degeneration. However, in some cases, ROI values and pathologic grades showed a negative linear correlation. We supposed that in the severe fibrotic state, ROI values are lower, despite higher pathologic grades.

Hovis et al. (31) found that severity of degeneration in the knee joint did not differ between complete and non-complete ACL groups, and also, found that usually mild and moderate OA was associated with abnormalities of the ACL, and that symptomatic OA was associated more so with severe knee degeneration. These findings are important for surgeons considering cruciate-conserving arthroplasty or unicompartmental arthroplasty in osteoarthritic knees. In our study, according to operative results, 79 % (42/53) of AM bundles and 81 % (43/53) of PL bundles were less than grade 2. Regarding imaging results, 43 % (23/53) of AM bundles and 39 % (21/53) of PL bundles were more than grade 3. These results are contrary to those of several previous reports (32), in which, it was suggested that ACL rupture probably occur a prior to the development of knee OA in most subjects. However, according to our pathologic results, 58 % (31/53) of AM bundles and 62 % (33/53) of PL bundles were more than grade 3, which concurs with the findings of Mullaji et. al. (33), who found a statistically significant positive correlation between radiologic grade of arthritis and histologic grade of ACL degeneration.

There were some limitations in the present study. First, the number of patients included was relatively small. Second, the differentiation of AM and PL bundles was problematic as in cases of severely degenerative or atrophic ACL states, clear separation of the two bundles was difficult on all images, in the operative field, and during tissue preparation for pathologic examinations. However, vague boundary regions between bundles were excluded from pathologic and imaging analyses. Third, we could not perform the isotropic three-dimensional (3D) MR sequences used at 3T, because T2* mapping software was only available for a 1.5 T MR system. Isotropic 3D sequences enable multiplanar reconstructions along the ACL, and could aid diagnosis, especially for clinical applications of the double-bundle concept (34). Further study using more recent techniques and a 3 T-MR system is needed. Fourth, all patients enrolled underwent total knee arthroplasty for severe osteoarthritis. Thus, ACL status was evaluated from an osteoarthritic perspective, and additional study of ACL injuries with a history of acute trauma is needed.
In summary, the finding that higher pathologic grades are associated with greater mean ROI values for AM and PL bundles suggests that T2* mapping reasonably reflects degree of bundle degeneration. In addition, for AM bundles, operative and imaging grades were found to be linearly correlated with ROI values. On the other hand, relations between the grades obtained using imaging, pathology and macroscopy in the operative field were highly variable, despite the significance of the correlations between pathologic, macroscopic and imaging grades for AM and PL bundles. Furthermore, for complete tears, the sensitivity, specificity and accuracy of oblique coronal T2WI and T2* mapping were high, whereas for incomplete tears, they were relatively low. Therefore, pathologic grades may differ from operative grades because pathologic grades represent degrees of bundle degeneration rather than the presence or absence of a tear. However, we found that T2* maps provide more accurate information regarding the degree of degeneration of ACL bundles. In addition, we found that the severity of degeneration by pathology does not reflect the completeness of tears in the arthroscopic or operative field, which indicates that elevated ROI values on T2* maps and increased signal intensities on T2W-images are not directly linked to tear status. To differentiate partial and complete tears, other imaging techniques should be combined. However, we suggest that the higher grades by pathology or an elevated ROI on a T2* map, indicate a greater risk of a tear or a rapidly developing bundle tear.

References


**Personal Information**