

# T1ρ and T2 Mapping Magnetic Resonance Imaging as Predictors of Cartilage Loss in Early Anterior Cruciate Ligament Injury

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## Learning Point of the Article:

T1ρ mapping primarily reflects proteoglycan loss, while T2 mapping indicates collagen matrix disruption and increased cartilage water content. Combined assessment of T1ρ and T2 values improves prediction of early cartilage loss and may aid in early intervention to prevent post-traumatic osteoarthritis.

## Abstract

**Introduction:** Early cartilage degeneration after anterior cruciate ligament (ACL) injury often precedes structural changes detectable on conventional imaging.

**Aim:** To evaluate the role of T1ρ and T2 mapping magnetic resonance imaging (MRI) in detecting early cartilage changes and predicting cartilage loss in ACL-injured knees.

**Materials and Methods:** A multicentric prospective observational study was conducted on 50 patients with early ACL injury. Quantitative MRI with T1ρ and T2 mapping was performed to assess cartilage composition and thickness. The study protocol was approved by the Institutional Ethics Committee, and written informed consent was obtained from all patients before inclusion.

**Results:** ACL-injured knees demonstrated elevated T1ρ and T2 values along with reduced cartilage thickness. Higher relaxation times correlated with early cartilage degeneration, particularly in patients with longer injury duration and associated meniscal pathology.

**Conclusion:** T1ρ and T2 mapping MRI are effective non-invasive tools for early detection of cartilage degeneration and may aid in predicting cartilage loss following ACL injury.

**Keywords:** Anterior cruciate ligament injury, cartilage degeneration, T1ρ mapping, T2 mapping, magnetic resonance imaging.

## Introduction

The anterior cruciate ligament (ACL) injury is a musculoskeletal condition, particularly among young people and athletes, and is a familiar cause of the pre-mature development of post-traumatic osteoarthritis (PTOA) of the knee [1]. The majority of patients who have ACL reconstruction (ACLR) and joint stability despite effective reconstructions and regaining of joint stability

experience gradual degeneration of cartilage, which leads to pain, functional losses, and reduction in quality of life 10-15 years following injury [2]. Traditional clinical assessment and the regular diagnostic magnetic resonance imaging (MRI) techniques lack sufficient data to reveal the initial biochemical and microstructural changes in the cartilage of the articular joint, which are precursors of irreparable morphological damage [3].

## Author's Photo Gallery



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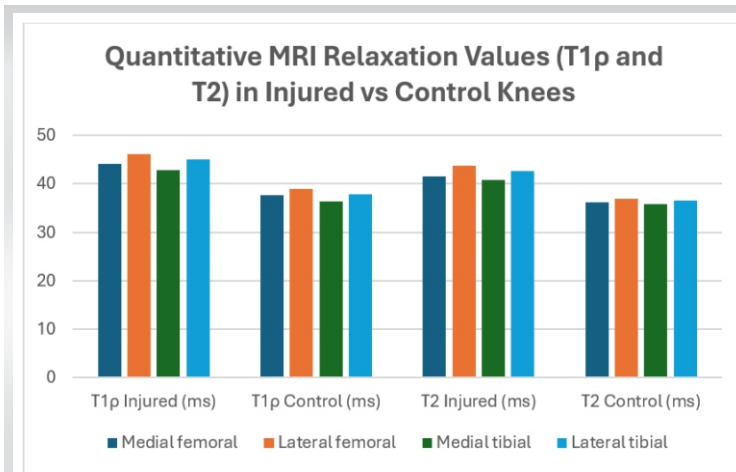
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**Figure 1:** Quantitative magnetic resonance imaging relaxation values (T1ρ and T2) in injured versus control knees.

Thus, there is currently an interest in more sophisticated quantitative MRI techniques that would be capable of identifying early cartilage degeneration at a potentially reversible stage and, therefore, be able to intervene at an opportune moment and achieve improved long-term outcomes after ACL injury [4]. Among these techniques, T1 rho (T1 rho) and T2 mapping MRI have been demonstrated to be promising non-invasive biomarkers of cartilage composition and cartilage integrity in vivo [5]. “T1r mapping, which is highly sensitive to the loss of proteoglycan of the cartilage extra-cellular matrix, is one of the first biochemical modifications to take place following the injury of a joint [6]. The degradation of the proteoglycans renders the cartilage vulnerable to compressive forces, and it is considered as one of the primary precipitating factors in the events of cartilage degeneration and the development of osteoarthritis [7]. On the other hand, T2 mapping primarily provides information about the collagen fibro-water structure, which provides data on cartilage hydration and collagen network integrity [8]. The first signs of cartilage destruction and disruption of the collagen structure and high mobility of water are typical of an ACL injury, even in the presence of no visible cartilage deficiencies in the standard MRI tests [9].

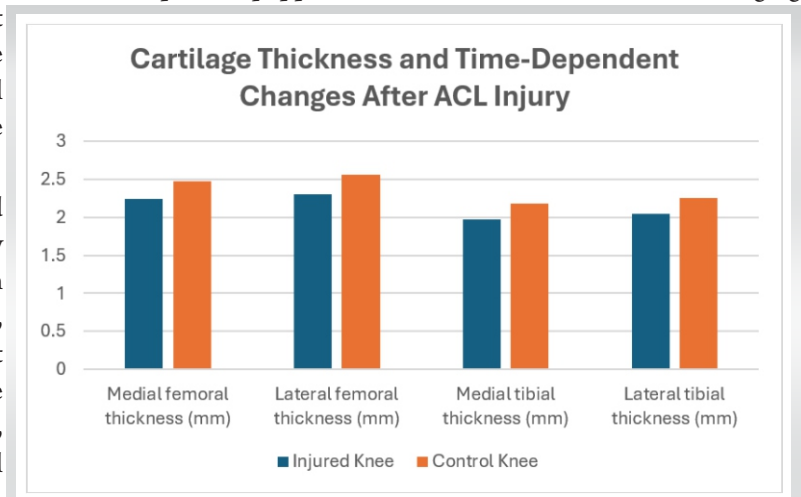
There are several longitudinal studies that have indicated that the T1rho and T2 relaxation times are significantly higher in the femur and tibia cartilage compartments in ACL or injured individuals than in healthy controls, suggesting the degeneration of the matrix within a short time following the injury [10]. It is noteworthy that the alterations have been noted in the pre- and post-ACLR, and thus it has been established that the surgical stabilization alone might not be adequate to inhibit the onward cartilage degeneration [11]. Additional emergent evidence suggests that post-ACL injury rise in

baseline T1r and T2 values is predictive of cartilage thinning, volume decrease, and time osteoarthritis radiographic features [12]. This prediction capability is particularly true in the early post-injury period when the standard imaging is normal, but cartilage biochemical changes are already progressing [13]. The capacity to utilize T1r and T2 mapping as early imaging biomarkers of cartilage loss might hence provide the necessary prognostic information, which may be a risk stratifier and in patient-specific management. The quantitative MRI techniques also present helpful evaluations of the efficacy of disease-modifying interventions, rehabilitation, and new cartilage preserving therapies of ACL-injured populations. However, T1r and T2 mapping have not been applied in clinical practice due to inconsistency in imaging regimes, difference in post-processing approaches, and variations in standardized thresholds to predict clinically significant cartilage loss despite potentials. In addition, comparative and auxiliary capabilities of T1r and T2 mapping in the signal of long-term cartilage consequences following early ACL injury are also being studied. In this way, T1 r and T2 MRI mapping of the cartilage in patients with early ACL injury are important predictors of cartilage loss that have to be thoroughly considered to gain a deeper insight into the post-traumatic cartilage degeneration, and facilitate the translation of quantitative MRI biomarkers into clinical and research practice.

## Materials and Methods

### Study design

The study was conducted as a multicentric prospective observational cohort study across the Departments of Orthopaedics and Radiology at multiple tertiary care teaching hospitals equipped with advanced musculoskeletal imaging



**Figure 2:** Cartilage thickness and time-dependent changes after anterior cruciate ligament injury.

**Table 1: Demographic profile and ACL injury characteristics (n=50)**

| Variable  | Value (%) |
|---|-----------|
| Age (years)   | 27.8±5.6  |
| Male  | 34 (68)   |
| Female  | 16 (32)   |
| BMI (kg/m <sup>2</sup> )                                    | 24.6±3.1  |
| Right knee involvement                                      | 28 (56)   |
| Left knee involvement                                       | 22 (44)   |
| Time since injury (months)                                  | 3.4±1.5   |
| Complete ACL tear   | 38 (76)   |
| Partial ACL tear  | 12 (24)   |
| Meniscal injury   | 21 (42)   |
| Bone contusion  | 18 (36)   |
| <b>BMI: Body mass index, ACL:Anterior cruciate ligament</b> |           |

facilities. The study protocol was approved by the Institutional Ethics Committees of all participating centers, and written informed consent was obtained from all patients before inclusion. The study was designed to evaluate the role of T1ρ and T2 mapping magnetic resonance imaging (MRI) as predictors of early cartilage degeneration following ACL injury. The study protocol was approved by the Institutional Ethics Committees of all participating centers, and written informed consent was obtained from all patients before inclusion in the study.

**Study setting**

The study was conducted as a multicentric investigation across the Departments of Orthopaedics and Radiology at multiple tertiary care teaching hospitals, all equipped with advanced musculoskeletal imaging facilities.

**Study duration**

The study was carried out over a period of 18 months, including participant recruitment, baseline clinical evaluation, MRI acquisition, image processing, and

data analysis.

**Participants**

Patients presenting with knee injury suggestive of ACL tear were screened for eligibility. Recruitment was performed after confirming ACL injury through clinical examination and conventional MRI.

**Inclusion criteria**

- Patients aged 18–40 years
- Patients with clinically and MRI-confirmed acute or subacute ACL injury
- Duration of injury ≤6 months
- No prior surgical intervention on the affected knee
- Willingness to provide written informed consent.

**Exclusion criteria**

- Evidence of advanced osteoarthritis (Kellgren–Lawrence grade ≥2)
- History of previous knee surgery or fracture involving the affected knee
- Concomitant ligament injuries requiring immediate surgical management
- Inflammatory arthritis or systemic connective tissue disorders
- Contraindications to MRI (e.g., pacemakers, metallic implants, claustrophobia).

**Study sampling**

A consecutive sampling method was used. All eligible patients presenting during the study period who fulfilled the inclusion criteria were recruited until the required sample size was achieved.

**Table 2: Quantitative MRI relaxation values (T1ρ and T2) in injured versus control knees**

| Cartilage compartment | T1ρ injured (ms) | T1ρ control (ms) | T2 injured (ms) | T2 control (ms) | P-value |
|-----------------------|------------------|------------------|-----------------|-----------------|---------|
| Medial femoral        | 44.2±5.8         | 37.6±4.9         | 41.5±4.9        | 36.2±4.1        | <0.001  |
| Lateral femoral       | 46.1±6.3         | 38.9±5.1         | 43.8±5.2        | 37.0±4.3        | <0.001  |
| Medial tibial         | 42.8±5.5         | 36.4±4.6         | 40.9±4.7        | 35.8±3.9        | <0.001  |
| Lateral tibial        | 45.0±6.0         | 37.8±4.8         | 42.6±5.0        | 36.5±4.2        | <0.001  |

**MRI: Magnetic resonance imaging**



**Table 3: Cartilage thickness and time-dependent changes after ACL injury**

| Parameter                      | Injured knee | Control knee | P-value |
|--------------------------------|--------------|--------------|---------|
| Medial femoral thickness (mm)  | 2.25±0.34    | 2.48±0.31    | 0.003   |
| Lateral femoral thickness (mm) | 2.31±0.36    | 2.56±0.33    | 0.002   |
| Medial tibial thickness (mm)   | 1.98±0.29    | 2.18±0.27    | 0.004   |
| Lateral tibial thickness (mm)  | 2.05±0.31    | 2.26±0.28    | 0.005   |
| Mean T1ρ ≤3 months             | 41.9±4.7     | –            |         |
| Mean T1ρ >3 months             | 46.3±5.9     | –            | 0.001   |

**ACL: Anterior cruciate ligament**

**Study sample size**

The total sample size for the study was 50 participants. The sample size was selected based on feasibility, availability of eligible patients within the study duration, and consistency with previous imaging-based observational studies assessing quantitative MRI biomarkers in ACL injury.

**Study groups**

Participants were categorized into two groups based on MRI findings:

- Group A: ACL-injured knees (affected knees)
- Group B: Contralateral uninjured knees or age-matched healthy controls (where applicable).

This grouping enabled comparison of quantitative cartilage parameters between injured and non-injured knees.

**Study parameters**

The primary study parameters included:

- T1ρ relaxation time values of articular cartilage
- T2 relaxation time values of articular cartilage.

Secondary parameters included:

- Cartilage thickness and volume measurements
- Compartment-wise cartilage assessment (medial femoral, lateral femoral, tibial, and patellar cartilage)
- Demographic variables, such as age, sex, body mass index, and time since injury.

**Study procedure**

Once the participants were enrolled, a comprehensive clinical assessment of the participants was conducted, which included history taking and physical examination of the knee joint. The ACL injury was initially confirmed by conventional MRI sequences to evaluate the related abnormalities in the meniscal or cartilage. Quantitative MRI acquisition of the T1rho and T2 mapping sequences with standardized imaging protocols followed this step. Trained radiologists who had no knowledge of clinical data manually (or semi-manually) segmented the cartilage areas of interest. Quantitative relaxation maps have been determined, and mean relaxation times of pre-determined cartilage compartments were observed.

**Study data collection**

The information on clinical data was captured on a structured pro forma, which contained demographic information, characteristics of the injury, and the clinical findings. Quantitative data were obtained using MRI and stored electronically, and brought out to be analyzed. Anonymization of all imaging data was done to protect the confidentiality of participants. The data quality checks were used to reduce variability in observers and allow uniformity in measurement.

**Data analysis**

The data collected were inputted into a spreadsheet, and statistical software was used to analyze the obtained data. Continuous variables were reported in terms of mean and the standard deviation, whereas the categorical variables were reported in terms of their frequencies and percentages. The statistical tests, such as the independent t-test or Mann-Whitney U test, were used to carry out comparative analysis

**Table 4: Correlation and predictive factors of early cartilage loss**

| Parameter                                  | Value            | P-value |
|--|------------------|---------|
| T1ρ versus cartilage thickness correlation | r=-0.54 to -0.62 | <0.001  |
| T2 versus cartilage thickness correlation  | r=-0.46 to -0.51 | ≤0.004  |
| Mean T1ρ with meniscal injury              | 47.1±5.6 ms      | 0.002   |
| Mean T2 with meniscal injury               | 44.0±5.1 ms      | 0.004   |
| Odds ratio – Elevated T1ρ                  | 3.8 (1.9–7.4)    | <0.001  |
| Odds ratio – Elevated T2                   | 2.9 (1.5–5.8)    | 0.002   |
| Odds ratio – Combined T1ρ+T2               | 5.2 (2.4–9.1)    | <0.001  |



between the groups. Correlation analysis was used to determine the association between T1rho and T2 values and cartilage thickness or cartilage volume. A P-value that was below 0.05 was taken as significantly important.

## Results

### Demographic profile and ACL injury characteristics

The study population consisted mainly of young adults with a predominance of males. Most patients had complete ACL tears, and a considerable proportion presented with associated meniscal injury and bone contusion, indicating complex joint trauma early after injury (Table 1).

### Quantitative MRI relaxation values (T1ρ and T2) in injured versus control knees

ACL-injured knees demonstrated significantly higher T1ρ and T2 relaxation values across all cartilage compartments compared with controls. These elevated values indicate early biochemical cartilage degeneration, including proteoglycan depletion and collagen matrix disruption (Table 2 and Fig. 1).

### Cartilage thickness and time-dependent changes after ACL injury

Significant cartilage thinning was observed in ACL-injured knees despite the absence of visible structural abnormalities on routine MRI. In addition, T1ρ values increased with time since injury, suggesting progressive biochemical cartilage deterioration in the early post-injury period (Table 3 and Fig. 2).

### Correlation and predictive factors of early cartilage loss

Higher T1ρ and T2 relaxation times showed a significant negative correlation with cartilage thickness, confirming that biochemical degeneration is associated with structural cartilage loss. The combined elevation of T1ρ and T2 demonstrated the strongest predictive value for early cartilage degeneration following ACL injury (Table 4).

## Discussion

The present research has shown that quantitative MRI methods, namely, T1rho and T2 mapping, are sensitive indicators of early cartilage degeneration following ACL injury, even in rather a short period after the injury. We found significantly increased T1ρ values in all femorotibial compartments compared to the control knees in our group of 50 patients with early ACL injury (mean time since injury 3.4 + 1.5 months), with medial femoral values of 44.2 + 5.8 ms and lateral

femoral values of 46.1 + 6.3 ms, and similarly increased T2 values (medial femoral 41.5 + 4.9 ms; lateral femoral 43.8 + 5.2 ms). These results indicate proteoglycan loss and collagen matrix breakdown earlier before morphologic abnormalities of the cartilage are observed. The findings are in good accord with the longitudinal studies of Williams et al., [14] proved that initial changes of cartilage T2 parameters after ACLR were the predictors of subsequent cartilage degeneration. The 6-month variation in mean T2 between 17 ACLR patients indicated that early T2 texture changes were related to 2-year changes in mean T2 ( $R = 0.80$ ,  $P = 0.0001$ ), and early T2 texture changes were associated with subsequent medial femoral cartilage thickness loss ( $R = 0.48 - 0.72$ ,  $P = 0.05$ ). Although our measurement did not encompass the analysis of the texture, the observed increases in the T2 values and the strong negative correlations between T2 relaxation times and cartilage thickness ( $r = -0.46 - 0.51$ ,  $P = 0.004$  or less) are in line with the trend of predictance of the biochemical changes of the early stages and subsequent structural damages as reported by Williams et al. [14]. Furthermore, the much smaller than normal cartilage thickness of our injured knees, which includes: Medial femoral thickness of 2.25 + 0.34 mm versus 2.48 + 0.31 mm in controls ( $P = 0.003$ ), endorses the idea that early compositional alterations observed by T2 mapping are clinically important predictors of subsequent cartilage alteration. The role played in the T1R mapping of early cartilage degeneration was further supported by the comparison with the results of Osaki et al., [15] where the T1R mapping was done on 49 ACL-injured knees and the values showed a rise with the number of years elapsed after the injury, especially after 2 years. Osaki et al. found criminally high results of T1 r in the anterior and middle of the medial femur condyle when patient duration of injury was over 2 years compared with those of patients injured under 12 weeks and 12 weeks-2 years ( $P = 0.05$ ) [2]. A comparable time-dependent effect was also found, even though our cohort looked at a much earlier phase after injury, the mean T1R values were significantly larger in patients measured more than 3 months after injury ( $46.3 \pm 5.9$  ms) than in patients measured <3 months ( $41.9 \pm 4.7$  ms;  $P = 0.001$ ). This stability implies that the degradation of proteoglycans starts early following ACL injury and evolves over time, which further supports a biological possibility of T14 as a sensitive indicator of early cartilage depletion. Effects of meniscal injury on cartilage health in our case are also in line with the study by Osaki et al., [15] who determined that patients with medial meniscus injury and a post-injury period of 12 weeks and longer had significantly higher T1 0 in the medial femur condyle than normal knees and ACL-injured knees, where there was no meniscal injury. The patients with comorbid meniscal tear also had significantly greater mean T1 0.47.1 +/- 0.56 ms vs. 42.9 +/

-0.48 ms;  $P = 0.002$ )[3.1] and T2 0.44.0 +/- -0.51 ms vs. 40.6 +/- -0.45 ms;  $P = 0.004$ )[4.1] in our analysis, which also points out that meniscal pathology has a compounding effect on cartilage matrix breakdown manifested as These results also confirm the idea that any changes in joint loading and shock absorption after meniscal damage hastens biochemical cartilage degradation in ACL injury. Our findings of a correlation between T1-elevation and cartilage early lesions are also aligned with the results of Hirose et al., [16] who assessed sagittal T1 maps in 23 individuals before and 1 year following ACLR. The baseline T1r values were found to be significantly higher in patients with cartilage lesions arthroscopically confirmed, with values of 40.7 ms, 38.0 ms at the medial femoral condylar site, in those with lesions, and 43.1 ms at the 1-year follow-up, respectively (Hirose et al., [16]) in patients with lesions versus 38.0 ms in patients without lesions ( $P = 0.025$ ). Compared to that, the mean medial femoral T1 - value in our ACL-injured patients (44.2 + 5.8 ms) relates closely with those of 1 year post-ACLR in the study by Hirose et al., although our patients were tested at a much earlier stage of the disease. This implies that significant changes in biochemical cartilages can be noticed shortly after ACL injury, and this is before surgery. The presence of the diagnostic performance of the T1 r and T2 mapping observed in our study is also justified by the results of Nishioka et al., [17] who proved that both T1 r and T2 mapping could identify International Cartilage Repair Society grade 1 cartilage lesions with high accuracy. It was found that cut-off values of 41.6 ms (T1rho) and 41.2 ms (T2) were identified, with T1rho having a sensitivity of 91.2 and specificity of 89.5, and T2 feasibility with a sensitivity of 76.5 and specificity of 81.6, based on Nishioka et al. finding of the use of arthroscopy as the reference standard. Interestingly, some of the compartments of our ACL-injured knees had a higher mean value of T1r and T2 than these cut-off values, and they suggest that there were initially present defects in the cartilage matrix without any gross morphological abnormalities. This observation confirms the finding that quantitative MRI techniques have a greater ability to detect minor cartilaginous damage than conventional morphological imaging.” Finally, the correlation between the degeneration of the meniscal and cartilage in our study is comparable to the longitudinal results of Knox et al., who evaluated T14 and T2 of the meniscus and cartilage of the 2 years after the ACL injury and reconstruction.

**Declaration of patient consent:** The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given the consent for his/ her images and other clinical information to be reported in the journal. The patient understands that his/ her names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

**Conflict of interest:** Nil **Source of support:** None

Knox et al. [18] reported that T1r/T2 signals more consistently showed increased signals in the anterior horn of the medial meniscus at all time points after reconstruction that were significantly positively correlated with medial tibial cartilage T1r/T2 values. On the same note, we were able to show that cartilage T14 and T2 were higher in patients with meniscal injury, which reflected the interrelationship of degeneration in meniscal and articular cartilage tissues. Taken together, the interpretation of the present findings, together with the previous studies, is that T1r and T2 mapping MRI is highly indicative of early and progressive degeneration of the biochemical cartilage following ACL injury, early cartilage thinning, and has a relationship with the chronicity of injury and meniscal pathology. These are quantitative imaging biomarkers and are thus promising in the early risk stratification, tracking disease progression, and implementation of timely interventions to prevent or delay the development of PTOA.

### Conclusion

T1p and T2 mapping MRI are sensitive, non-invasive imaging biomarkers capable of detecting early biochemical cartilage degeneration following ACL injury, even before structural changes become evident on conventional imaging. Elevated relaxation times and reduced cartilage thickness observed in this study indicate early matrix deterioration and progressive cartilage loss. The significant association of these parameters with time since injury and concomitant meniscal pathology highlights their role in identifying high-risk patients. Combined assessment of T1p and T2 values enhances predictive accuracy and may facilitate early risk stratification, monitoring of disease progression, and timely intervention to prevent PTOA.

### Clinical Message

Early biochemical cartilage degeneration occurs soon after ACL injury and can be detected using quantitative MRI techniques, such as T1p and T2 mapping. These imaging biomarkers allow identification of cartilage damage before morphological changes appear on conventional MRI.



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