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A pilot study with 3D T1ρ-mapping for quantitative evaluation of cartilage after open-wedge high tibial osteotomy

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ABSTRACT

Purpose: To evaluate the recently developed three-dimensional (3D) T1ρ-mapping technique for the quantitative evaluation of cartilage changes after open-wedge high tibial osteotomy (OWHTO).
Method: Eleven patients with medial knee osteoarthritis and spontaneous osteonecrosis of the medial femoral condyle underwent T1ρ magnetic resonance imaging. The full-thickness cartilage of the medial femoral condyle (MFC), lateral femoral condyle, medial tibial condyle, and lateral tibial condyle, and the trochlea and patella were set as regions of interest; mean T1ρ values were calculated using two-dimensional (2D) and 3D analyses. The state of cartilage injury was evaluated using the International Cartilage Repair Society grading system (ICRS grade). T1ρ values before OWHTO and after hardware removal were compared using the Wilcoxon signed-rank test. The correlation between T1ρ values and the ICRS grade was explored using the Spearman rank correlation coefficient.
Results: Cartilage repair at the MFC was observed in a high proportion of patients (82%), but 2D analysis did not reveal a significant difference after surgery at any site. In contrast, 3D analysis revealed a significant decrease in T1ρ values after surgery at the MFC (before surgery: 44.1 ms; after surgery: 38.9 ms; $p = 0.016$), but no significant difference at any other site. In the MFC, there was a positive correlation between 3D T1ρ values and arthroscopic findings before and after surgery (rs = 0.62, $p < 0.01$), which was absent from the 2D T1ρ values.
Conclusions: 3D T1ρ-mapping may be an effective tool for detecting changes in cartilage quality after OWHTO.

1. Introduction

High tibial osteotomy (HTO) is extremely effective for the improvement of pain and recovery of function in patients with medial knee osteoarthritis and is associated with favorable long-term outcomes [1]. HTO achieves these therapeutic effects by correcting varus malalignment and eliminating overloading from the medial compartment. In 1979, Fujisawa et al. introduced arthroscopy for post-HTO evaluation and were the first to report the regeneration of cartilage-like tissue by following offloading of the medial compartment about 1 year after osteotomy [2]. Many reports of regenerated cartilage in the medial compartment after HTO have since emerged; however, almost all have been based on qualitative evaluations using arthroscopic findings, and no method for quantitative evaluation of regenerated cartilage has yet been established.

In recent years, open-wedge high tibial osteotomy (OWHTO) with locking plates has become an increasingly popular treatment for varus knee osteoarthritis (OA). Although this procedure can only achieve a limited correction angle, it avoids osteotomy of the fibula and is less invasive than other procedures such as closed wedge osteotomy. However, in cases with a large correction angle, OWHTO can also induce patella infera, and there are concerns over the possibility of progressive cartilage degeneration in the patellofemoral joint [3]. There is not yet any consensus on the optimal knee alignment target for young athletes

Abbreviations: %MA, percentage of the mechanical axis; 2D, two-dimensional; 3D, three-dimensional; FTA, femoral tibial angle; HTO, high tibial osteotomy; ICRS, International Cartilage Repair Society; IS, Insall-Salvati; LFC, lateral femoral condyle; LTC, lateral tibial condyle; MFC, medial femoral condyle; MRI, magnetic resonance imaging; MTC, medial tibial condyle; OA, osteoarthritis; OWHTO, open-wedge high tibial osteotomy; ROIs, regions of interest; SONK, spontaneous osteonecrosis of the knee.

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with early knee OA, and some controversy remains over which conditions are indicated for OWHTO. To resolve these issues, non-invasive methods are needed to evaluate changes in articular cartilage over time after OWHTO.

Progress has recently been made in compositional cartilage evaluation methods. Of these methods, T2-mapping, T1ρ-mapping, and dGEMRIC use MRI to evaluate cartilage quality and are attracting interest [4–12]. Compared with dGEMRIC, T1ρ MRI does not require double contrast medium dosing and is less invasive. T1ρ-mapping can also evaluate proteoglycan concentration compared with T2-mapping, which evaluates collagen orientation. T1ρ-mapping can therefore potentially provide an earlier evaluation of cartilage degeneration. Compared with T2, T1ρ is also more sensitive to changes in cartilage degeneration. The larger dynamic range of T1ρ-mapping can potentially provide a better quantitative evaluation of cartilage degeneration, and T1ρ-mapping has promising applications in assessing cartilage degeneration and determining therapeutic effects of treatment on cartilage degeneration [4–8].

Few studies have used these MRI techniques to evaluate changes in cartilage quality after HTO. While some studies using T1ρ MRI have been reported, they are few in number. Previous studies have also been limited by evaluating a defined area using two-dimensional (2D) image analysis, and three-dimensional (3D) image analysis was not used in any studies. Previous reports using 2D analysis showed that the fibrocartilage-like repair tissue appeared on the articular surface of the medial compartment after hemicallotasis osteotomy by MRI T1ρ- and T2-mapping [9]. However, using conventional 2D image analysis to evaluate cartilage in a defined area limits the scope of the evaluation and may not provide accurate lesion localization or an accurate assessment of cartilage damage severity [9]. Thus, 3D image analysis technology may be useful for evaluating the physiological effect of loading distribution on knee joint cartilage. We therefore created a 3D T1ρ-mapping method; then, we evaluated the usefulness of this 3D method in a pilot study.

The objective of this study was to explore the utility of 3D image analysis by using both conventional 2D image analysis and our newly developed 3D T1ρ-mapping analysis method to perform a quantitative analysis of cartilage changes, such as regenerated cartilage-like tissue, due to alignment changes after OWHTO. We hypothesized that there would be a correlation between a qualitative evaluation of cartilage before and after OWHTO and a quantitative evaluation based on T1ρ values obtained by 3D image analysis. We also predicted that 3D image analysis could be used to quantitatively evaluate changes in cartilage quality resulting from regeneration or degeneration after OWHTO, which is difficult to achieve with 2D image analysis. The change in regenerative cartilage in the MFC before and after surgery was evaluated as the primary outcome measure, and degenerative cartilage changes in the PF joint and lateral joint were evaluated as secondary outcome measures.

2. Methods

2.1. Patients

This prospective cohort study investigated patients who underwent OWHTO for spontaneous osteonecrosis of the knee (SONK) involving the medial femoral condyle or medial knee OA between September 2019 and December 2020. Eleven patients (6 men, 5 women; mean age at surgery: 59.2 ± 7.5 [42–69 years]) participated in the study. All surgeries were performed by a single doctor with extensive experience and knee specialization. This study was approved by the institutional review board of our institution and conformed to the Declaration of Helsinki. All patients provided written informed consent for participation in the study. The eligibility criteria were SONK or knee OA with mild deformity (Kellgren-Lawrence grade I or II), ongoing knee pain or edema, resistance to at least 3 months of conservative therapy, high disease activity, and patients not requiring a large correction angle of 15°or greater. The exclusion criteria were as follows: contraindications for MRI examination, patients with osteoarthritis in the patellofemoral joint or lateral compartment of femorotibial articulation, and patients with a history of knee surgery. All patients underwent radiographic examination before surgery and after hardware removal approximately 1 year after the initial surgery. In this study, the follow-up period was up to the day of the post-MRI examination after implant extraction. Image analysis (X-rays and MRI scans) was performed by a different orthopedic surgeon.

2.2. Surgical technique

An additional microfracture and resurfacing procedure was performed at arthroscopy before OWHTO in cases where the subchondral bone was exposed and hardened. In preoperative planning for OWHTO, the target postoperative mechanical axis was set at 62.5% from the medial edge of the proximal tibial articular surface. A medial longitudinal incision approximately 6 cm in length was made, and the superficial layer of the medial collateral ligament was released subperiosteally; medial opening-wedge osteotomy was performed, the osteotomy site was fixed with a locking plate (TriS plate, Olympus Terumo Biomaterials, Japan), and the osteotomy gap was filled with β-tricalcium phosphate (OSferion60, Olympus Terumo Biomaterials, Japan) [13]. Partial weight bearing was started as postoperative pain allowed, and full weight bearing was permitted 2–3 weeks after surgery.

2.3. Radiographic evaluation

Radiographic evaluation (X-rays) was performed before surgery and approximately 1 year after surgery (after hardware removal). Lower limb alignment was evaluated based on the femoral tibial angle (FTA) and percentage of the mechanical axis (%MA). Patellar height was evaluated based on the Insall-Salvati (IS) ratio with a 30° flexed knee in the lateral view. The posterior tibial slope was evaluated based on the posterior tibial angle. The slope of the tibial articular surface was evaluated based on the medial proximal tibial angle.

2.4. Articular cartilage assessment

All patients underwent arthroscopy before OWHTO surgery and before hardware removal. Articular cartilage in the weight-bearing area of the medial femoral condyle (MFC), lateral femoral condyle (LFC), medial tibial condyle (MTC), lateral tibial condyle (LTC), and articular cartilage in the trochlea and patella was assessed using the International Cartilage Repair Society (ICRS) grading system (grade 0: normal cartilage, grade 1: superficial lesions [1A, superficial fibrillation or softening; 1B, superficial fissures and laceration], grade 2: defect<50% of the cartilage depth, grade 3: defect more than 50% of the cartilage depth, and grade 4: defect down to the subchondral bone). Articular cartilage grades were compared between the initial and second arthroscopies. Degeneration, regeneration, and unchanged were defined as an increase, decrease by 50% or more, and no change in ICRS grade, respectively, before and after surgery.

2.5. MRI protocol

All MRI examinations were performed using an 8 Channel Sense Knee coil (Philips) and a 3 Tesla MRI scanner (Achieva 3 Tesla, Philips, Best, Netherlands). To eliminate the effects of body movement, the affected limb was fixed at 10° flexion in a neutral rotational position when installing the knee coil for MRI. All imaging was performed in the sagittal plane, and sagittal slices were set perpendicular to the tibial posterior condylar axis that is connected to the posterior edge of the medial and lateral tibial condyles. The MRI protocol included two sequences, and the acquisition parameters were as follows: (1) 3D T1ρ-weighted fast field echo images (spin-lock pulse amplitude = 500 Hz; repetition time [TR] = 5.2 ms; echo time [TE] = 2.6 ms; visual field = 140 × 140 mm; matrix size = 256 × 256; slice thickness = 3 mm; time of spin-lock [TSL] = 1, 10, 20, 30, 40 ms; bandwidth = 0.7 kHz/pixel; scan time = 3 min 15 s).

(2) Proton density fat saturated images (TR = 1803 ms; TE = 40 ms; visual field = 170 × 170 mm; matrix size = 288 × 218; slice thickness = 3 mm; scan time = 54 s).

The total scan time was about 20 min, including 54 s for proton density fat saturated imaging and 16 min and 15 s for T1ρ-weighted fast field echo imaging. Because of the time required, we limited the imaging studies to the two methods above.

2.6. MRI data analysis

Data were transferred to an offline computer for image analysis. T1ρ-mapping was performed using an AZE Virtual Place system (Cannon medical systems corporation, Otawara, Japan) and constructed based on the following single-index fitting algorithm:

S(TSL) = S0 × exp (-TSL / T1ρ),

where TSL is the spin-lock time, S is the signal intensity on T1ρ–weighted images with a prescribed TSL, and S0 is the signal intensity at the shortest TSL.

2.7. 2D analysis

The regions of interest (ROIs) were the load-bearing full-thickness cartilage in the MFC, LFC, MTC, and LTC, and full-thickness cartilage of the patella and trochlea in a sagittal slice, as defined by hand segmentation. The ROI was established as follows: we selected a sagittal central slice for the MFC, LFC, MTC, and LTC that was passed through the center of the weight-bearing cartilage surrounded by the anterior and posterior margins of the meniscus in the sagittal slice (Fig. 1a). We selected a sagittal central slice for the patella and trochlea that passed through the central ridge of the patella (Fig. 1b). We also added two slices that neighbored the central slice anteriorly and posteriorly. T1ρ relaxation times (ms) in the ROIs that were set for each image were measured using the AZE virtual place system (Cannon medical systems corporation, Otawara, Japan) for T1ρ-mapping. We calculated the average T1ρ relaxation times for the three slices.

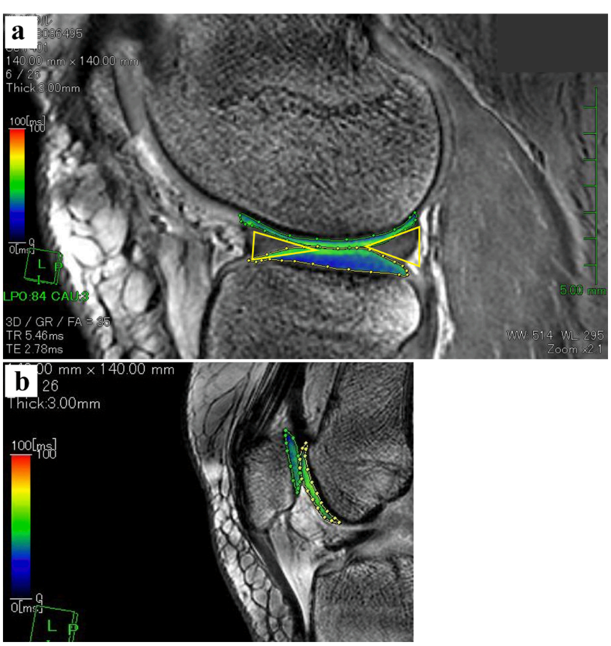

Fig. 1. Patella and tibiofemoral 2D-T1ρ maps, a: Tibiofemoral 2D-T1ρ maps, ROI: We selected a sagittal central slice for the MFC, LFC, MTC, and LTC that passed through the center of the weight-bearing cartilage surrounded by the anterior and posterior margins of the meniscus (yellow line) in the sagittal slice, b: Patella 2D-T1ρ maps, ROI: We selected a sagittal central slice for the patella and trochlea that passed through the central ridge of the patella, The colormap represents T1 values in ms. MFC = medial femoral condyle; MTC = medial tibial condyle; LFC = lateral femoral condyle; LTC = lateral tibial condyle; 2D = two-dimensional; ROI = region of interest.

2.8. 3D analysis

First, the AZE Virtual Place system (Cannon medical systems corporation, Otawara, Japan) was used to manually extract cartilage regions from all captured sagittal section images, and a 3D morphological model was created for the femur, tibia, and patella. Weight-bearing full-thickness articular cartilage at the MFC, MTC, LFC, and LTC, and full-thickness cartilage at the trochlea and patella were manually set as ROIs. The ROIs were set as follows: Anatomical landmarks (A) were used to specify the trochlea point and the anterior and posterior horns of the medial and lateral meniscuses on a 2D plan, and a 3D plan was created by incorporating the 2D images (Fig. 2b and 2c). The MFC, MTC, LFC, LTC, and trochlea were extracted from the 3D plan (Fig. 2d). The AZE Virtual Place system (Cannon medical systems corporation, Otawara, Japan) was then used to measure T1ρ relaxation times (ms) at the ROIs set in each image. ROI measurements were performed by two different, non-surgical observers with no prior knowledge of the clinical or radiographic findings.

The change in regenerative cartilage in the MFC was evaluated as the primary outcome measure, and degenerative cartilage changes in the PF joint and lateral joint surfaces were evaluated as secondary outcome measures.

2.9. Statistical analysis

The Shapiro-Wilk test was performed, and each radiographic evaluation before and after surgery followed a normal distribution, while the T1ρ values before and after surgery did not follow a normal distribution. Each item identified by radiographic evaluation before surgery and after hardware removal was compared using a paired *t*-test, and data are presented as the mean and standard deviation. T1ρ values before surgery and after hardware removal were compared using the Wilcoxon signed-rank test, and data are presented as the median and interquartile range. Arthroscopic findings at each site were compared using the Steel–Dwass test. The correlation between T1ρ values and arthroscopic findings (ICRS grade) was explored using the Spearman rank correlation coefficient. Intra- and inter-observer agreement on T1ρ values within the ROIs were evaluated using intra-and inter-class correlation (ICC) testing. ICC estimates and their 95% confidence intervals were calculated using the SPSS statistical packages version 23 (SPSS Inc, Chicago, IL). The inter-rater reliability was calculated based on mean-rating ($k = 2$), absolute agreement, and a two-way random-effects model. The intra-rater reliability was calculated based on the mean of two measurements, absolute agreement, and a two-way mixed effects model. ICC values<0.5, between 0.5 and 0.75, between 0.75 and 0.9, and greater than 0.90 indicate poor, moderate, good, and excellent reliability, respectively [14]. A post hoc power analysis was conducted on the pre- and post-operative results of T1ρ values for the MFC using *GPower* 3.1 software. Statistical significance was set at $p < 0.05$. All analyses were performed using SPSS statistics software version 26 (IBM Corp., Armonk, NY).

3. Results

3.1. Subject characteristics

There were 11 patients included in this study; six were male and five were female. Six patients had medial knee OA while the rest had SONK. The mean patient age was 59.2 years (range: 42–69 years), and all

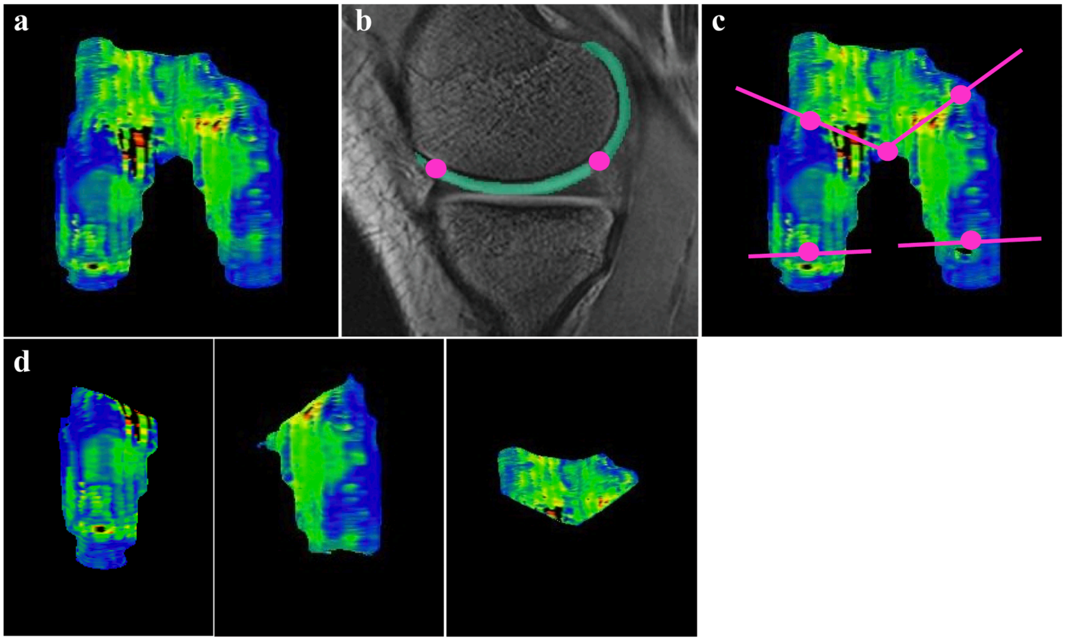

Fig. 2. Femoral 3D-T1ρ maps, a: 3D image of the distal femur, b: 2D image of the lateral view of the distal femur, The purple dots indicate the anterior and posterior horns of the meniscus. c: Borderline between the MFC, LFC, and trochlea in ROI setting. Anatomical landmarks were used to specify the trochlea point and anterior and posterior horns of the medial and lateral meniscuses on a 2D plan. d: 3D images of the extracted MFC, LFC, and trochlea. MFC = medial femoral condyle; MTC = medial tibial condyle; LFC = lateral femoral condyle; LTC = lateral tibial condyle; 3D = three-dimensional; ROI = region of interest.

patients were Japanese. The mean weight was 73.2 kg (range 58.0–94.7 kg), and the mean length was 1.66 m (range 1.50–1.807 m). The mean body mass index was 26.6 kg/m^2 (range 23.5–29.4 kg/m^2). The Kellgren-Lawrence scores were grade I in three patients and grade II in three patients. The mean change in knee alignment after OWHTO was 11.6° (range, 7°–15°) and the mean time to hardware removal was 455 days (range: 280–749 days).

3.2. Radiographic assessment

The radiographic measurements are presented in Table 1. In terms of FTA, %MA, and medial proximal tibial angle, all were significantly improved after surgery and showed proper alignment ($p < 0.01$). The IS ratio was not significantly different after surgery, showing no postoperative progression to the patella infera. There was also no significant change in the posterior tibial angle after surgery.

3.3. Arthroscopic evaluation of articular cartilage

We performed ablation and microfracture during arthroscopy in three patients. Second-look arthroscopic findings revealed a high percentage of patients with cartilage repair at the MFC (82%), which was significantly higher than the percentage of patients with cartilage repair at other sites ($p < 0.01$, MTC 9%, LFC, LTC, trochlea, and patella 0%). Concerning the lateral articular surfaces, LTC degeneration was observed in only one patient, and no progression of cartilage degeneration was found in any other patient. Concerning the patellofemoral joint, trochlea degeneration was observed in three patients and patella degeneration in two patients, although unchanged was the most common finding (Figs. 3 and 4).

Table 1
X-ray evaluation of OWHTO patients (n = 11) preoperatively (pre-op) and 1 year after surgery (post-op) between September 2019 and December 2020.

	Pre-op	Post-op	*p*-value
FTA (°)	179 ± 3.1	170 ± 2.2	<0.01
%MA (%)	24 ± 9.7	61 ± 7.7	<0.01
IS	0.94 ± 0.08	0.93 ± 0.09	NS
TPS (°)	9.6 ± 3.7	10.3 ± 3.8	NS
MPTA (°)	84.6 ± 3.1	92.1 ± 2.0	<0.01

pre-op = pre-operatively; post-op = post-operatively; FTA = femoral tibial angle; %MA = percentage of the mechanical axis; IS ratio = Insall-Salvati ratio; TPA = posterior tibial angle; MPTA = medial proximal tibial angle; NS = not significant. Date are reported as mean ± standard deviation.

3.4. Qualitative evaluation of the cartilage matrix using T1ρ-mapping

3.4.1. 2D T1ρ-mapping

A reliability analysis showed ICC values of 0.978 for intra-observer agreement on T1 ρ values (95% CI 0.970–0.985) and 0.943 for inter-observer agreement (95% CI 0.920–0.960); the level of reliability can be regarded as “excellent”. T1ρ values (ms), the qualitative evaluation of the cartilage matrix by T1ρ-mapping, are compiled in Table 2. There was no significant change in mean T1ρ values 1 year after surgery versus before surgery in the MFC. There was also no significant change in mean T1ρ values 1 year after surgery versus before surgery in the MTC, LFC, LTC, trochlea, and patella (Table 2); however, the results of a post hoc power analysis of the secondary outcome measures showed that the power did not reach 0.8. There was a positive correlation between T1ρ

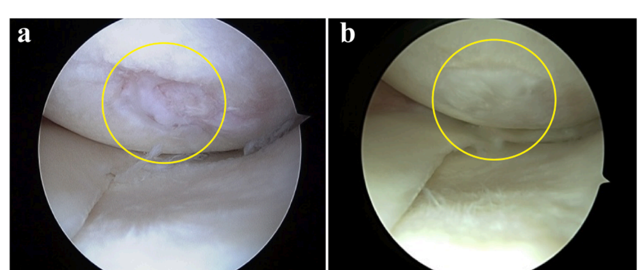

Fig. 3. Arthroscopic findings before and after OWHTO. a: Before OWHTO. There is cartilage damage at the medial femoral condyle (yellow line).b: After OWHTO. Regenerated cartilage is seen in the medial femoral condyle (yellow line). OWHTO = open-wedge high tibial osteotomy.

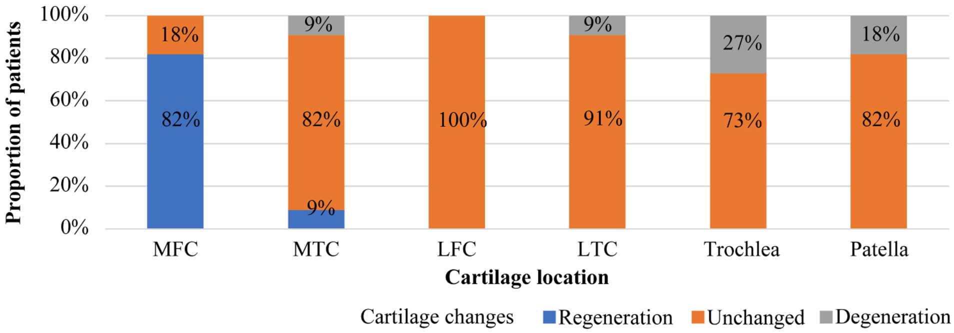

Fig. 4. Percentage of articular cartilage changes during second-look arthroscopy, Cartilage changes after OWHTO: Degeneration, regeneration, and unchanged were defined as an increase, decrease by 50% or more, and no change in ICRS grade, respectively, before and after surgery. LFC = lateral femoral condyle; LTC = lateral tibial condyle; MFC = medial femoral condyle; MTC = medial tibial condyle; OWHTO = open-wedge high tibial osteotomy; ICRS = International Cartilage Repair Society.

Table 2
T1ρ evaluation of OWHTO patients (n = 11) preoperatively (pre-op) and 1 year after surgery (post-op) between September 2019 and December 2020.

	MFC	MTC	LFC	LTC	Trochlea	Patella
2D analysis						
pre-op	40.7 (38.0–44.6)	41.0 (39.4–43.3)	38.9 (37.7–40.1)	37.1 (35.5–41.2)	43.3 (39.2–47.1)	37.9 (34.9–40.5)
post-op	41.1 (36.2–42.3)	43.6 (38.5–45.8)	40.2 (39.2–41.5)	39.2 (37.3–45.4)	42.3 (40.2–45.7)	39.4 (37.5–45.2)
p-value	NS	NS	NS	NS	NS	NS
3D analysis						
pre-op	44.1 (40.9–46.2)	41.3 (39.5–46.6)	40.8 (38.8–42.0)	38.5 (36.8–42.0)	41.4 (38.0–46.7)	40.4 (37.4–45.0)
post-op	38.9 (38.5–41.4)	46.7 (39.7–50.0)	38.4 (37.8–41.3)	39.8 (37.1–44.8)	41.6 (41.5–44.7)	41.3 (39.2–45.5)
p-value	0.016	NS	NS	NS	NS	NS

pre-op = preoperatively; post-op = postoperatively; MFC = medial femoral condyle; MTC = medial tibial condyle; LFC = lateral femoral condyle; LTC = lateral tibial condyle; NS = not significant. The unit of the T1ρ value is ms. Date are reported as the median and interquartile range.

values and arthroscopic findings (ICRS grade) before and after surgery at all sites (rs = 0.45, $p < 0.01$) (Fig. 5). There was no significant correlation between T1ρ values and arthroscopic findings (ICRS grade) before and after surgery in the MFC (Fig. 6).

3.4.2. 3D T1ρ-mapping

A reliability analysis showed ICC values of 0.901 for intra-observer agreement on T1 ρ values (95% CI 0.863–0.928), and 0.885 for inter-observer agreement (95% CI 0.503–0.955); the level of reliability can be regarded as " moderate" to " excellent." In the MFC, there was a significant decrease in T1ρ values 1 year after surgery (38.9 ms [38.5–41.4 ms]) compared with before surgery (44.1 ms [40.9–46.2 ms]) ($p = 0.016$); the results of a post hoc power analysis showed a high power of 0.85. Concerning the lateral articular surfaces, there was no significant difference in T1ρ values at either the LFC or LTC 1 year after surgery. Considering patellofemoral articular surfaces, there was no significant difference in T1ρ values at either the trochlea or patella 1 year after surgery (Table 2); however, the results of a post hoc power analysis of the secondary outcome measures showed that the power did not reach 0.8. There was a positive correlation between T1ρ values and arthroscopic findings (ICRS grade) before and after surgery for all sites (rs = 0.56, $p < 0.01$; Fig. 7). There was a positive correlation between T1ρ values and arthroscopic findings (ICRS grade) before and after surgery at the MFC (rs = 0.62, $p < 0.01$; Fig. 8).

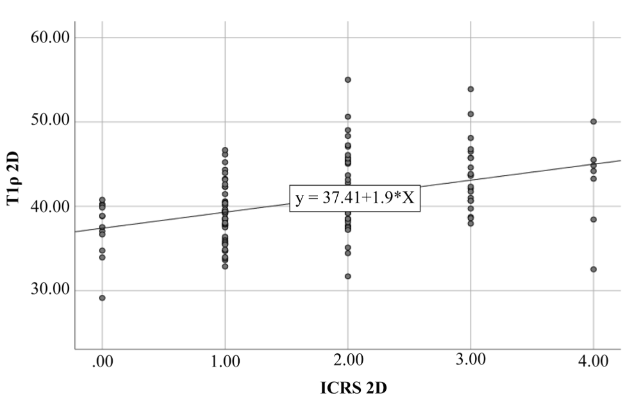

Fig. 5. Correlation between T1ρ values of 2D T1ρ-mapping and arthroscopic findings in all regions, Y-axis: T1ρ value; x-axis: ICRS grade, ICRS = International Cartilage Repair Society; 2D = two-dimensional.

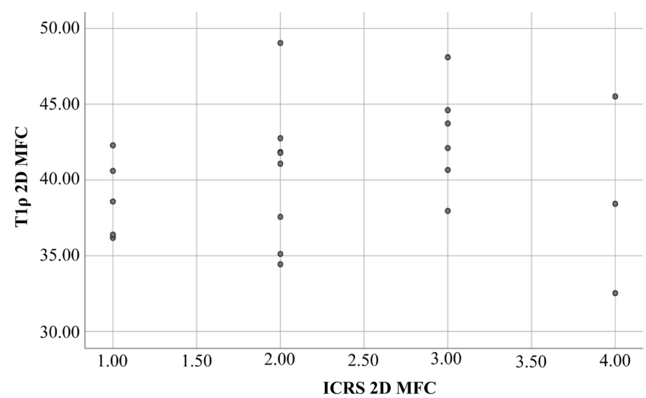

Fig. 6. Correlation between T1ρ values of 2D T1ρ-mapping and arthroscopic findings in the MFC Y-axis: T1ρ value; x-axis: ICRS grade. ICRS = International Cartilage Repair Society; MFC = medial femoral condyle; 2D = two-dimensional.

4. Discussion

This pilot study used T1ρ-mapping to quantitatively evaluate cartilage before and after OWHTO. The objective of this study was to explore

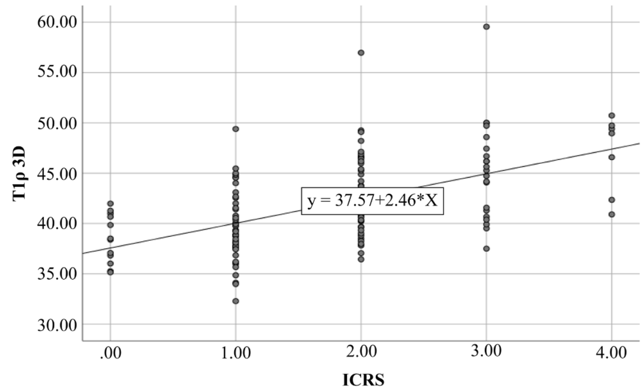

Fig. 7. Correlation between T1ρ values of 3D T1ρ-mapping and arthroscopic findings in all regions, Y-axis: T1ρ value; x-axis: ICRS grade, ICRS = International Cartilage Repair Society; 3D = three-dimensional.

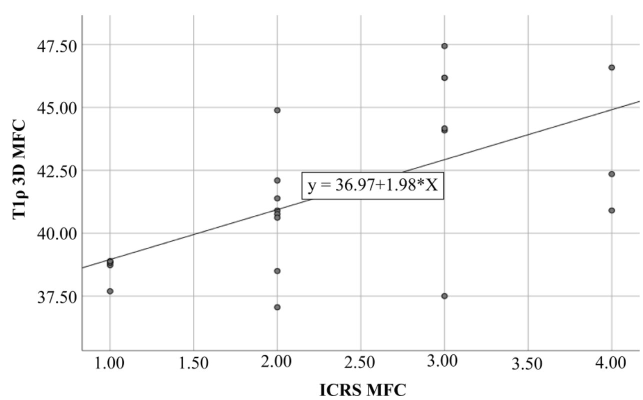

Fig. 8. Correlation between T1ρ values of 3D T1ρ-mapping and arthroscopic findings in the MFC, Y-axis: T1ρ value; x-axis: ICRS grade, ICRS = International Cartilage Repair Society; MFC = medial femoral condyle; 3D = three-dimensional.

the utility of 3D image analysis by using both conventional 2D image analysis and our newly developed 3D T1ρ-mapping analysis method to perform a quantitative analysis of cartilage changes, such as of regenerated cartilage-like tissue after OWHTO. The most important finding was that qualitative evaluation by arthroscopy after OWHTO revealed significant cartilage repair at the MFC, and quantitative evaluation by 3D T1ρ-mapping reflected this arthroscopic finding by revealing a significant improvement in T1ρ values at the MFC; hence, a correlation was found between the qualitative cartilage evaluation and quantitative evaluation based on T1ρ values. This finding supports our hypothesis that there is a correlation between the qualitative evaluations of cartilage before and after OWHTO and a quantitative evaluation based on T1ρ values obtained by 3D image analysis. Furthermore, we observed no significant change in the patellofemoral joint or lateral compartment in patients who underwent OWHTO with consideration of appropriate indications. To the best of our knowledge, this is the first published study to use 3D T1ρ-mapping to quantitatively evaluate cartilage changes after OWHTO.

We used 3D T1ρ-mapping to quantitatively evaluate cartilage repair after OWHTO, and the results reflected arthroscopic findings by revealing significant improvement at the MFC. Kumagai et al. investigated the state of cartilage tissue regeneration at medial articular surfaces in 131 knees approximately 20 months after OWHTO and found regeneration in 71% of MFCs. Body mass index, ICRS grade before surgery, and postoperative lower limb alignment were cited as factors that affected cartilage regeneration [15]. Good production of regenerated cartilage has been reported to occur with proper alignment, which reduces stress on weight-bearing surfaces [16,17]. Second-look arthroscopy findings in the present study revealed regenerated cartilage at the MFC in significantly more patients than in other sites (MFC 82%, $p < 0.01$). Given that proper postoperative alignment was achieved in the present study, similar to previous studies (FTA 170°, %MA 61%), regenerated cartilage was probably produced at the MFC because of the reduced load in the medial compartment.

Previous studies have reported that fibrillated cartilage is regenerated after HTO [16,18,19]. However, Wakabayashi et al. performed a histological evaluation of regenerated cartilage after HTO and observed hyaline cartilage in 27% of knees in an eburnation group (KL grade IV) and hyaline cartilage in 96% of knees in a fibrillation group (KL grade III) [20]. Okahashi et al. also performed a histologic evaluation of regenerated cartilage after HTO and observed regenerated hyaline-like cartilage in six patients [21]. We did not perform a histologic evaluation, but in cases with early to-mild knee OA of KL grade I or II, such as those in this study, regenerated cartilage is likely to include hyaline cartilage. Evaluation by T1ρ-mapping, which is sensitive to proteoglycans, is probably sensitive to regenerated cartilage proteoglycan, otherwise known as hyaline-like cartilage.

Recently, new MRI techniques capable of providing a detailed understanding of molecular structural changes in articular cartilage have been introduced in routine clinical practice, and have been used to facilitate early diagnosis of cartilage degeneration and quantitative evaluation of cartilage degeneration severity, which are difficult to achieve using conventional methods. Among these MRI techniques, the use of T2-mapping, T1ρ-mapping, and dGEMRIC for quantitative evaluation of cartilage has been reported [4–8,10,22]. Theologis et al. reported reduced T1ρ values in deep layers of repaired cartilage during follow-up examinations 1 year after microfracture surgery, which was suggestive of maturation concerning proteoglycan content [11]. This could indicate that the improvement in T1ρ values observed in our study after surgery is due to the sensitivity of 3D T1ρ-mapping to the maturation of proteoglycan content in regenerated cartilage. Meanwhile, Parker et al. evaluated femorotibial joint cartilage by dGEMRIC at 6 months and 1 year after OWHTO, but found no significant change in MFC after surgery [12]. Nishioka et al. also used T1ρ- and T2-mapping for the quantitative evaluation of cartilage after hemicallotasis osteotomy. They observed no significant difference in T1ρ values after hemicallotasis osteotomy, but T2 values were significantly reduced 1 year after surgery, which shows effective detection of regenerated cartilage-like tissue [9].

The findings of these studies differ from our 3D image analysis findings. Almost all such studies have evaluated cartilage using one or several sagittal or coronal section images of the knee joint in the MRI plane. We believe that using sectional images makes it difficult to reproduce patient position and direction sufficiently enough to allow for a comparison to be made between individuals or to longitudinally examine cartilage changes.

The present study found no correlation between T1ρ values and arthroscopic findings before and after surgery in the MFC using 2D image analysis, but revealed a positive correlation with 3D image analysis ($rs = 0.62$, $p < 0.01$). The reason for this finding is probably because 3D image analysis evaluated the articular surface and was therefore sensitive to regenerated cartilage and tissue changes in the surrounding cartilage. We also observed no significant difference in T1ρ values after surgery with 2D image analysis, but a significant difference with 3D image analysis. While the number of patients and follow-up period in this pilot study may be insufficient to establish the utility of 3D image analysis for clinical application, our findings provide support for future comparative trials to demonstrate the clinical benefits of 3D image analysis. There was a positive correlation between the 3D analysis findings and arthroscopic findings, but not a strong correlation. This was likely due to the limitations of qualitative arthroscopic evaluation of cartilage changes based on gross findings.

Furthermore, the 3D method did not reveal a significant difference in

T1ρ values after OWHTO at the lateral articular surfaces or patellofemoral joint. The absence of a significant difference in T1ρ values after OWHTO at lateral articular surfaces shows that although the mechanical axis passes through the lateral compartment after OWHTO, there is no overloading on the lateral side. Ziegler et al. investigated the effect of OWHTO on the lateral compartment in animal experiments with sheep [23]. They compared OWHTO correction angles of 4.5° valgus and 9.5° valgus and reported no degenerative findings in the lateral compartment in either group after surgery, either macroscopically or microscopically. In the present study, although %MA was corrected to 61%, there was no significant increase in T1ρ values in the lateral compartment, which indicates that OWHTO achieved an appropriate distribution of overloading and that no overloading occurred on the lateral side.

There was also no significant change in T1ρ values at the trochlea or patella after OWHTO. OWHTO with a large correction angle has, in most cases, been reported to induce a lower patellar position that increases contact pressure on the patellofemoral joint, which can potentially progress to osteoarthritis [24]. The present study observed no significant difference in T1ρ values at the trochlea or patella after surgery, probably because the patients selected for this study exhibited no OA or patella infera and did not require excessive correction; hence, there was no postoperative progression to patella infera and no effect on the patellofemoral joint. Accordingly, our findings also highlight the potential use of 3D T1ρ-mapping in assessing indications for surgery. The strength of this study is that we quantitatively evaluated the postoperative cartilage changes using T1ρ-mapping and suggested the usefulness of 3D analysis for the first time. However, as there were limitations on the strength of evidence for the secondary outcomes due to the small number of cases, the results should be interpreted with caution. Further research will be necessary in the near future.

This study has some limitations. First, the small number of subjects and short follow-up period may not be sufficient to prove the usefulness of 3D image analysis. In particular, the results for the secondary outcomes may need to be interpreted with caution. However, we believe that the findings this pilot study are important because they suggest that 3D analysis may be able to detect regenerated cartilage with a power of over 80%. Further research using a larger patient population with longer follow-up periods is recommended.

Second, ICC values of inter-observer agreement for 3D image analysis was 0.885, but the 95% CI was 0.503–0.955, and the level of reliability was "moderate" to "excellent," which was lower than that of the 2D image analysis. The inter-observer agreement may inevitably be lower than 2D image analysis because 3D image analysis extracts many slices manually. For better reproducibility in the future, it is necessary to study methods such as automatic extraction of cartilage. In addition, further investigations, including accuracy analyses, are required to assess the efficacy of this 3D analysis. Third, microfracture surgery and resurfacing were performed in some patients. Although a previous study found no difference in cartilage regeneration in patients who underwent OWHTO and OWHTO combined with microfracture surgery [25], we cannot determine whether cartilage regeneration arose due to the change in alignment provided by OWHTO or due to the microfracture procedure. Fourth, in this study, the 2D analysis did not segment the entire cartilage as in previous reports, and only used three slices [9]. Two-dimensional (2D) mapping of cartilage from the multi-slice data might have been more appropriate for comparison with the 3D analysis. Finally, it is unclear whether 3D T1ρ-mapping correlates with histological evaluation because regenerated cartilage was not evaluated histologically. Therefore, further studies are needed to demonstrate the effectiveness of 3D T1ρ-mapping by evaluating its correlation with histological findings.

In conclusion, qualitative evaluation by arthroscopy after HTO revealed significant cartilage repair at the MFC, and quantitative evaluation by 3D T1ρ-mapping reflected these arthroscopy findings, revealing a significant improvement in T1ρ values at the MFC; thus, a correlation was observed between the qualitative evaluation of cartilage and quantitative evaluation based on T1ρ values. After OWHTO, there was no significant reduction in T1ρ values at the lateral articular surfaces or the patellofemoral joint. These findings suggest that 3D T1ρ-mapping may be an effective tool in detecting changes in cartilage quality after OWHTO. As a prospect, the use of 3D T1ρ-mapping may be useful in determining the optimal correction angle and target alignment for OWHTO, or it may be useful in determining a more suitable surgical technique for patients by comparing it with other osteotomy techniques such as distal tibial tubercle osteotomy. In order to determine the usefulness of this evaluation method, further investigation is needed, including accuracy analyses (2D vs. 3D) and comparisons with other imaging methods (T2 mapping).

CRediT authorship contribution statement

Tsuyoshi Yamasaki: Data curation, Formal analysis, Investigation, Visualization, Writing – original draft, Writing – review & editing. **Munehiro Ogawa:** Data curation, Methodology, Resources, Project administration, Supervision, Validation. **Kensuke Okamura:** Validation. **Yusuke Inagaki:** Supervision. **Yasuhito Tanaka:** Supervision.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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