Comparison of T1rho values versus T2 values on 3.0 Tesla MRI of healthy knee cartilage in order to detect initial signs of cartilage degeneration caused by loading

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Purpose

Introduction

Osteoarthritis (OA) is one of the most common causes of disability in developed countries, and the rate of OA increases as the population ages [1]. As the incidence of OA continues to increase, there is a tremendous need for noninvasive diagnostic tools for assessing early stage articular cartilage degeneration.

However, conventional magnetic resonance imaging (MRI) used to diagnose OA may not be sensitive enough for the subtle articular cartilage matrix alterations that occurs in the early stages of degeneration. To date, in vivo applications of clinical MR systems for the study of the subtle articular cartilage matrix alterations have been limited [2,3].

Several biochemical MRI methods have been proposed for early detection of alterations in the cartilage macromolecular content due to OA, including delayed gadolinium-enhanced MRI of the cartilage (dGEMRIC), T2 value and T1rho MRI [2,3]. dGEMRIC has been found to be specific for detecting early cartilage glycosaminoglycan loss. T1 mapping of the cartilage after contrast administration allows estimation of gadolinium diethylenetriamine pentaacetic acid concentration, which reflects the underlying negative fixed charge density of the cartilage [2,3]. Determination of the quantitative T2 values is a technique that has been reported to quantify the cartilage water content and collagen fibre orientation. Focal increase in T2 relaxation time has been associated with cartilage matrix damage. In particular, this increase has been associated with a loss of collagen integrity and increase in the cartilage water content. In future, quantitative T2 values may aid in diagnosis of early cartilage degeneration [2,3].

Recent studies have proposed that T1rho MRI is associated with a change in the macromolecular structure and composition, which is an initiating factor in cartilage degeneration. T1rho MRI, which probes the interaction between water molecules and their macromolecular environment, has the potential to identify early biochemical changes in the articular cartilage. Recent in vitro studies have reported correlations between the T1rho value and glycosaminoglycan content and have demonstrated a relationship between the T1rho value and mechanical properties of the cartilage, suggesting that T1rho values may be sensitive to early biochemical changes in cartilage degeneration [2,3]. For depiction of initial early OA changes, it is necessary to evaluate the sensitivity of the change in T1rho and T2 values for asymptomatic knee cartilage degeneration. Several studies have reported that T1rho values had more sensitivity than T2 mapping in knee cartilage damage in mild and progressive OA patients. However, few reports have shown greater sensitivity of T1rho values compared with that of T2 values for asymptomatic knee cartilage degeneration.
Aging and weight bearing promote changes in the cartilage that leads to OA. Morphological changes related to OA typically occur first in the medial knee compartment, and it is widely believed that weight bearing is greater in the medial knee compartment than in the lateral knee compartment [4]. However, previous studies have suggested that weight bearing has a positive influence on the cartilage and that normal cartilage adapts to weight bearing [5,6]. Assessment of the relationship between weight bearing and cartilage integrity would be of great value for accurate diagnosis and monitoring of early OA before morphological changes take place.

Two reports have stated that the biochemical MRI parameter T2 reflects the extent and location of degeneration of the collagen matrix; however, an age-related linear increase in knee cartilage T2 values in asymptomatic volunteers was reported only for volunteers over the age of 45 years [7,8]. Below the age of 45 years, there was no significant correlation between age and T2 values in the normal cartilage.

**Fig. 1**: Figure. 1 The hypothesis for the relationship between ageing and the cause of the observed T2-mapping change.

**References**: Department of Radiology, Kobe University School of Medicine - Kobe/JP

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This result can be explained by the degeneration process of cartilage components. The T2 value is affected mainly by the collagen and water content of the cartilage and is not very sensitive to changes in macromolecular concentrations, such as proteoglycan concentration [9,10]. In addition, some pathological studies have demonstrated that loss of proteoglycan is an initiating event in early OA [11] and that in the early stage of OA, the amount of collagen in the framework does not seem to be severely affected [12]. Furthermore, Temple et al. suggested that the cause of age-associated cartilage degeneration depends on the age group [13]. Mosher et al. concluded that damage to the type 2 collagen matrix leads to an elevation in the T2 value in persons over the age of 45 years [8]. Consequently, we can expect loss of proteoglycan before changes take place in collagen matrix contents along the pathway of asymptomatic age-related cartilage degeneration(Figure 1).

The purpose of the present study was to investigate the usefulness of T1rho and T2 values as biomarkers of early knee cartilage degeneration due to weight bearing in asymptomatic patients.

We hypothesized that the T1rho value has sufficient and greater sensitivity and specificity for detection of early and minor knee cartilage degeneration due to weight bearing than the T2 value, and that increase in the T1rho and T2 values due to weight bearing would be greater in the medial knee compartment than in the lateral knee compartment.
Material and Methods

Subjects

Thirty-three asymptomatic female volunteers (mean age ± standard deviation [SD]: 41.8 ± 12.7 years; range: 22-64 years) were examined using a 3.0-T MRI system (Koninklijke Philips Electronics N.V., Eindhoven, The Netherlands) for T1rho mapping. The inclusion criteria for all subjects were good health according to their medical history, physical examination and clinical laboratory data; normal body mass index (20-24 kg/m²); absence of a contraindication to MRI; Kellgren-Lawrence grade 0; absence of OA on MRI and radiography of both knees; intact joint function with full strength and no history of chronic or frequent knee pain (Figure 2).

- Thirty-three asymptomatic female volunteers (mean age ± SD: 41.8 ± 12.7 years)
- good health
- absence of contraindication to MRI
- no history of chronic or frequent knee pain
- normal BMI (20 - 24 kg/m²)
Fig. 2: Figure 2. The subjects of the study were 33 asymptomatic female volunteers.

References: Department of Radiology, Kobe University School of Medicine - Kobe/JP

After the nature of the procedure was explained, all participants provided their informed consent to participate in the study. All protocols were approved by the Committee of Human Research of our institution.

For eliminating the effects of ageing on cartilage degeneration and for assessment only of the effects of weight bearing on knee cartilage degeneration, the volunteers were classified into two subgroups by age—an over 50 age group and an under 50 age group. We expected that the rate of change in T1rho value would be higher than that of T2 mapping in the under 50 age group and vice versa in the over 50 age group.

MRI protocols and T1rho mapping parameters

The right knee of each patient was scanned for both T1rho values and T2 mapping under no load conditions at 30° of flexion. MRIs were performed in one continuous session without removing the subject from the scanner. All MRIs were implemented on a 3.0-T Philips Achieva QD R.3.1.1.2. MR scanner (Koninklijke Philips Electronics N.V., Eindhoven, Netherlands) using an 8-channel SENSE knee coil. The protocol included the following sequences: Sagittal T1-weighted spin-echo imaging [repetition time/echo time (TR/TE) = 700/13.5 ms, field of view (FOV) = 16 cm, matrix = 288 × 224, bandwidth = 15.63 kHz, number of excitations (NEX) = 2]; sagittal and axial 3D water excitation high-resolution spoiled gradient recalled echo (SPGR) imaging [TR/TE = 700/13.5 ms, FOV = 16 cm, matrix = 288 × 224, slice thickness = 1 cm, bandwidth = 15.63 kHz, NEX = 2]; sagittal fat-saturated T2-weighted fast spin echo imaging [TR/TE = 700/13.5 ms, FOV = 16 cm, matrix = 288 × 224, slice thickness = 3 mm, bandwidth = 16.5 kHz, echo train length = 8, NEX = 2].

Sagittal T1rho-weighted images were obtained using the spin-lock technique and spiral image acquisition. The following acquisition parameters were used: 3D balanced turbo-field-echo, 20 interleaves/slice, 4096 points/interleaf, FOV = 15 cm, matrix = 256 × 256, effective in-plane spatial resolution = 0.58 × 0.58 mm, slice thickness = 4 mm, number of slices = 20, TR/TE = 4.8/2.4 ms, time of spin-lock (TSL) =01/10/20/30/40 ms, flip angle = 50°, fat saturation = spectral pre-saturation of inversion recovery and spin-lock frequency = 759.5 Hz/pixel. The total acquisition time was 12.42 min (Figure 4). MRIs were performed in one continuous session without removing the subject from the scanner. Measurements were conducted in the evening between 5 and 7 p.m. T1rho mapping of the hyaline cartilage were reconstructed by fitting the T1rho-weighted image intensity pixel-by-pixel to the below mentioned equation (1) using an in-house Levenberg-Marquardt mono-exponential fitting algorithm written in C:

\[ S(TSL) \# \exp(-TSL/T1\text{rho}) \]
Where TSL is the time of spin lock and S is the signal intensity in a T1rho-weighted image with a certain TSL. MRIs were transferred to a Dell workstation (Dell Inc., Round Rock, TX, USA) for off-line quantification of the cartilage T1rho relaxation times.

**Cartilage MRI quantification**

Cartilage was manually segmented on sagittal spoiled gradient-echo MRI. The following four compartments were defined: the lateral femoral condyle with weight bearing, medial femoral condyle with weight bearing, lateral femoral condyle without weight bearing and medial femoral condyle without weight bearing.

![Segment](image)

**Fig. 3**: Figure.3 The T1rho and T2 mapping of the segmented cartilage.

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The equipment limitations forced us to draw round regions of interest (ROIs) as 1-mm squares. In addition, because a previous study investigated T2 mapping by employing 1-mm square ROIs for analysis of the knee articular cartilage degeneration [14], we
employed the same method. In all four segments, one ROI was established on the remaining full thickness of the cartilage (Figure 3). T1rho and T2 values were quantified in every ROI. Care was taken with the sagittal ROI so that joint fluid and subchondral bone were not sampled.

Statistical analysis

Results with $P < 0.05$ were considered statistically significant. All statistical analyses were performed using JMP software version 8.0 (SAS Institute, Cary, NC, USA) and SPSS software version 17.0 (SPSS, Chicago, IL, USA).

The under 50 and over 50 age groups were analysed independently. The mean and SD of the T1rho values and T2 mapping were calculated for four knee cartilage regions for all subjects. For repeated-measures analysis of variance, if there was a significant $P$ value, the Tukey-Kramer post hoc paired t-test was performed with an # of 0.05 to assess the relationship between the weight-bearing knee cartilage compartment and non-weight-bearing knee cartilage compartment T1rho values, the relationship between the weight-bearing knee cartilage compartment and non-weight-bearing knee cartilage compartment T1rho values, and the relationship between the weight-bearing knee cartilage compartment and non-weight-bearing knee cartilage compartment T1rho values in the medial and femoral knee cartilages; the same relationships were assessed for the T2 values.
Results

Conventional MRI

In all of the conventional MRI, such as proton density imaging, no subjects had symptomatic signal changes and morphological changes in the meniscus, cartilage and knee ligaments.

Lateral compartments

In both the under 50 and over 50 age groups, the T1rho and T2 values in the weight-bearing knee cartilage compartments were significantly higher than those in the nonweight-bearing compartments (Figures 4, 5).
Medial compartments

In the under 50 age group, the T2 values in the nonweight-bearing knee cartilage compartment were significantly higher than those in the weight-bearing knee cartilage compartment.

In the over 50 age group, there was no significant difference in the T2 values between the weight-bearing and nonweight-bearing knee cartilage compartments.

The T1rho value was significantly higher in the weight-bearing compartment than in the nonweight-bearing compartment in both the under 50 age group and over 50 age group (Figures 6,7).
Fig. 7: Figure 6 Results in medial compartment, under 50 age group

References: Department of Radiology, Kobe University School of Medicine - Kobe/JP
Fig. 6: Figure 7 Results in medial compartment, over 50 age group

References: Department of Radiology, Kobe University School of Medicine - Kobe/JP
Fig. 3: Figure 3 The T1rho and T2 mapping of the segmented cartilage.

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Conclusion

The present study demonstrated that T1rho values may be more sensitive than T2 values as biomarkers of early cartilage degeneration due to weight bearing in the knee cartilage in asymptomatic patients.
References


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