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Isotropic Morphometry and Multi-component T1 ρ Mapping of Human Knee Articular Cartilage, In Vivo at 3T

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Abstract

Background—The progressive loss of hyaline articular cartilage due to osteoarthritis (OA) changes the functional and biochemical properties of cartilage. Measuring the T1 ρ along with the morphological assessment can potentially be used as noninvasive biomarkers in detecting early-stage OA. To correlate the biochemical and morphological data, submillimeter isotropic resolution for both studies is required.

Purpose—To implement a high spatial resolution 3D-isotropic-MRI sequence for simultaneous assessment of morphological and biexponential T1 ρ relaxometry of human knee cartilage in-vivo.

Study Type—Prospective.

Population—Ten healthy volunteers with no known inflammation, trauma or pain in the knee.

Field Strength/Sequence—Standard FLASH sequence and customized Turbo-FLASH sequence to acquire 3D-isotropic-T1 ρ -weighted images on a 3T MRI scanner.

Assessment—The mean volume and thickness along with mono and biexponential T1 ρ relaxations were assessed in the articular cartilage of 10 healthy volunteers.

Statistical Tests—Non-parametric rank-sum tests. Bland-Altman analysis and coefficient of variation

Results—The mean monoexponential T1 ρ relaxation was 40.7 $\pm$ 4.8ms while the long and short components were 58.2 $\pm$ 3.9ms and 6.5 $\pm$ 0.6ms, respectively. The mean fractions of long and short T1 ρ relaxation components were 63.7 $\pm$ 5.9% and 36.3 $\pm$ 5.9%, respectively. Statistically significant ($p < 0.03$) differences were observed in the monoexponential and long components between some of the ROIs. No gender differences between biexponential components were observed ($p > 0.05$). Mean cartilage volume and thickness were 25.9 $\pm$ 6.4cm³ and 2.2 $\pm$ 0.7mm, respectively. Cartilage volume ($p = 0.01$) and thickness ($p = 0.03$) were significantly higher in male than female participants across all ROIs. Bland-Altman analysis showed agreement between two morphological methods with limits of agreement between -1000mm^3 and $+1100\text{mm}^3$ for volume, and -0.78mm and $+0.46\text{mm}$ for thickness, respectively.

Data Conclusion—Simultaneous assessment of morphological and multicomponent T1 ρ relaxation of knee joint with 0.7mm×0.7mm×0.7mm isotropic spatial resolution is demonstrated in-vivo. Comparison with a standard method showed that the proposed technique is suitable for assessing the volume and thickness of articular cartilage

Keywords

isotropic resolution; bicomponent T1 ρ relaxation; morphological assessment; articular cartilage

INTRODUCTION

Osteoarthritis (OA) of the knee is a degenerative joint disease that affects about 10% of adults aged over 60 years (1,2). The progressive loss of hyaline articular cartilage due to OA changes the functional and biochemical properties of cartilage and can eventually lead to destruction of cartilage (3,4). Magnetic resonance imaging (MRI) is more precise in diagnosing OA than other modalities such as radiography, arthrography, ultrasound and CT (5,6). The advantages of MRI includes its ability to achieve high soft-tissue contrast among different tissues in the knee joint and the ability to quantify morphological parameters such as cartilage thickness, area, and volume to assess disease progression in OA (7–9). However, the standard clinical MRI protocols for knee cartilage imaging such as T1-weighted spoiled gradient echo (SPGR) sequences and fat-saturated T2 or proton density-weighted fast spin echo (FSE) are unable to identify the early stages of the OA.

Measuring the spin-lattice relaxation time in the rotating frame (T1 ρ) and spin-spin relaxation (T2) relaxation times have been studied extensively as potential noninvasive biomarkers in detecting early-stage OA (6,10–13). The increase in water content and the loss of proteoglycans (PG) in early-stage OA results in an elevation of the T1 ρ and T2 relaxation times (6,10,14). A multicomponent model better represents the relaxation decay behavior than a monoexponential model, since the monoexponential relaxation shows the mean of relaxation in different water compartments in the cartilage while a multicomponent model distinguishes the relaxation time of different water compartments (e.g., free water, water tightly bound to PG and collagen macromolecules, etc.) (15). Previous morphological studies have shown the variations of the cartilage properties and its relationship with OA (16–18). To correlate multicomponent biochemical and morphological data, submillimeter isotropic resolution for both studies is required.

The small volume, and curved surfaces of articular cartilage necessitate imaging with high in-plane resolution and thin slices for accurate morphological as well as biochemical T1 ρ relaxometry measurements. Performing simultaneous morphological and multi-component relaxometry mapping of human knee cartilage with a single sequence is difficult due to long acquisition times. Several prior studies (14,19) utilized high-resolution morphology and low-resolution relaxometry respectively.

In this work, we aimed to demonstrate the feasibility of using a 3D-isotropic technique (3D-ISO) for simultaneous morphological and biexponential T1 ρ assessment of cartilage by measuring its volume, thickness, and multicomponent relaxation parameters.

MATERIAL AND METHODS

Human Subjects

The study was approved by the institutional review board (IRB) and complied with Health Insurance Portability and Accountability Act guidelines. All the participants provided written informed consent prior to participation in the study. Ten healthy volunteers (women $n=5$, men: $n=5$,) with no known inflammation, trauma or pain in the knee with a mean age ($\pm$ SD) of 26 ± 2 years (women: 25 ± 3 years, men: 26 ± 3 years), mean height of 168 ± 10 cm (women: 158 ± 6 cm, men: 178 ± 5 cm) and the mean weight of 71 ± 16 kg (women: 57 ± 10 kg, men: 86 ± 7 kg) participated in this study.

MRI Acquisition

The MR imaging was performed on a 3T clinical MRI scanner (Magnetom Prisma, Siemens Healthcare, Erlangen, Germany) with a 15-channel Tx/Rx knee coil (Quality ElectroDynamics, Cleveland OH). A 3D Cartesian Turbo-Flash sequence was customized to enable T1 ρ imaging with varying spin-lock durations (15). The T1 ρ preparation module consists of a 90° RF excitation pulse along the x -direction, followed by a 500Hz spin-lock pulse along the direction and a -90° along the x -axis. A 180° refocusing pulse was applied in the middle of the module to compensate for B_0 inhomogeneity. Moreover, the phase of the spinlock module was altered to compensate the B_1 inhomogeneity effect (15). Sagittal isotropic scans of the knee were obtained at 10 different spin-lock duration (t_{SL}) including t_{SL} : 2, 4, 6, 8, 10, 15, 25, 35, 45, and 55ms (Fig. 1). The sequence imaging parameters were as follow: repetition time/echo time =1500ms/4ms, flip angle= 8° , matrix size= $224\times 224\times 160$, voxel size= $0.7\text{mm}\times 0.7\text{mm}\times 0.7\text{mm}$, field of view (FOV) = $160\text{mm}\times 160\text{mm}$ and GRAPPA acceleration factor (AF)=3. The total acquisition time was 22:53minutes.

A morphologic scan was acquired using a 3D-FLASH sequence as a standard technique (20) to evaluate the accuracy of volume and thickness estimation from the proposed 3D-isotropic sequence. The imaging parameters were as follows: repetition time/echo time =16ms/7.2ms, flip angle= 12° , matrix size= $480\times 480\times 128$, voxel size= $0.33\text{ mm} \times 0.33\text{mm} \times 1\text{mm}$, FOV = $160\text{mm}\times 160\text{mm}$ and GRAPPA acceleration factor of AF = 2. The total acquisition time was 7:26min.

Cartilage Volume and Thickness Estimation

The mean cartilage volume and thickness were measured in 14 regions of interest (ROIs) including tibia, lateral and femoral cartilages and 11 smaller ROIs: Posterior-Lateral Femur (PLF), Central-Lateral Femur (CLF), Anterior- Lateral Femur (ALF), Posterior-Lateral Tibia (PLT), Anterior-Lateral Tibia (ALT), Posterior-Medial Femur (PMF), Anterior-Medial Femur (AMF), Posterior-Medial Tibia (PMT), Anterior-Medial Tibia (AMT), Inferior Patellar (IP), Superior Patellar (SP) cartilage (Fig. 2).

The T1 ρ weighted images with highest SNR ($t_{SL}=2\text{ms}$) were used for cartilage segmentation. The ROI masks were drawn manually on all the slices using ITK-SNAP (Version 3.6.0). Afterward, the segmentation masks were transferred to MATLAB

(MATLAB R2016a; MathWorks Inc., Natick, MA, USA) for volume and thickness measurement. The cartilage volume was calculated by multiplying the voxel size, the total number of voxels and the thickness was estimated by averaging the orthogonal distance from the subchondral bone surface to the articular cartilage surface in 1000 random points in different ROIs for each volunteer. The mean cartilage volume and thickness were calculated across all the volunteers on both 3D-ISO and 3D-FLASH images.

Multicomponent T1ρ Relaxation Mapping

In addition to cartilage volume and thickness, the mono and biexponential T1ρ relaxation were estimated pixel by pixel across the ROIs. The monoexponential relaxation time, T1ρ_{mono}, was calculated by fitting the monoexponential model to the data:

$$y(t_{sl}) = y_m e^{-\frac{t_{sl}}{T1\rho_{mono}}} + y_0 \quad (1)$$

Where $y(t_{sl})$ is the pixel signal intensity in the scan acquired at the spin-lock duration, t_{sl} . y_0 is the constant term that was forced to be equal to the noise.

Similarly, the biexponential relaxation components were estimated by fitting the biexponential model to the same data set using a nonlinear approach:

$$y(t_{sl}) = y_l e^{-\frac{t_{sl}}{T1\rho_{long}}} + y_s e^{-\frac{t_{sl}}{T1\rho_{short}}} + y_0 \quad (2)$$

Where T1ρ_{long} and T1ρ_{short} are the long and short relaxation time components, respectively. The relative fractions of the long (y_l) and the short (y_s) components were reported as

$$Y_{long} = \frac{y_l}{y_l + y_s} \text{ and } Y_{short} = \frac{y_s}{y_l + y_s}, \text{ respectively.}$$

Afterward, the pixels satisfying the below condition were included in the mean estimation (15):

$$T1\rho_{long} > 4 \times T1\rho_{short} \quad (3)$$

Statistical Analysis

The statistical analyses were performed using Minitab (Minitab 18 Statistical Software, Minitab Inc., USA). A non-parametric rank-sum test with a significance level (p-value) of 0.05 was applied to compare the relaxation components between different ROIs. Gender difference analysis was also performed to compare the T1ρ relaxation components as well as cartilage volume and thickness between male and female participants.

Bland-Altman plots (21), including 95% confidence intervals (estimated as 1.96 times the standard deviation of the differences) (22), were generated to quantify agreement between the estimated cartilage's thickness and volume from 3D-ISO and 3D-FLASH images.

As the measure of repeatability of cartilage thickness and volume, the experiment was repeated on four volunteers on two different days with a 3-week gap. For each subject, the mean and standard deviation (SD) were calculated across the two sessions and the coefficient of variation (CV) was calculated as $CV = SD/\text{mean}$. To depict the repeatability, root-mean-square coefficients of variation (rmsCV) for each ROI was calculated as (23):

$$\text{rmsCV} = \sqrt{\frac{\sum_{i=1}^N CV_i^2}{N}} \quad (4)$$

where CV_i is the CV of an individual volunteer and N is the total number of volunteers ($N = 4$), rmsCV% values less than 10% and 5% were interpreted as good, very good, respectively (24).

RESULTS

The representative examples of the T1ρ relaxation components map in sagittal, coronal, and axial planes are shown in Fig. 3 A summary of our descriptive statistics for the different ROIs is shown in Table 1 We expect that the long component corresponds to the water loosely bound to macromolecules while the short component is related to the water tightly bound to PG and collagen macromolecules. The short and long component mean fractions were 35% and 65%, respectively. The group histogram distribution of relaxation components in Fig. 4 show that the 95% confidence intervals of monoexponential, long and short component values were between [38.8ms–42.1ms], [6.2ms–6.7ms] and [56.7ms–59.7ms], respectively.

Fig. 5 shows the comparison of the T1ρ relaxation components for different ROIs. The pairwise statistically significant ROIs are shown with the black dashed line and the rank sum test p-values. The anterior tibial cartilage (ALT) had higher monoexponential relaxation compared to other ROIs. Moreover, its long component difference with IP, PLT and AMT were statistically significant. No significant difference was observed between 11 ROIs for the short component ($p > 0.05$).

The monoexponential T1ρ relaxation in patellar ($p = 0.01$) and medial tibia ($p = 0.03$) cartilage was significantly higher in females as compared to males. No gender difference ($p > 0.05$) was observed in biexponential T1ρ relaxation times across all 11 ROIs. The mean cartilage thickness and volume in different ROIs are shown in Table 2 for male and female participants. The global cartilage volume ($p = 0.01$) and thickness ($p = 0.03$) of male participants were significantly higher compared to females.

Analysis of the Bland-Altman plot demonstrated an average difference of 33mm^3 and -0.16mm with the 95% confidence interval of $\pm 1041\text{mm}^3$ and $\pm 0.62\text{mm}$ between 3D-FLASH and 3D-ISO measurements for cartilage volume (Fig. 6) and thickness (Fig. 7), respectively.

The regression between the difference and the average showed a negative relationship for cartilage volume ($\text{Volume_Difference} = 161.67 - 0.09 \times \text{Volume_Mean}$) and positive relationship for thickness ($\text{Thickness_Difference} = -0.05 + 0.09 \times \text{Thickness_Mean}$). Only a few data points were outside the 95% tolerance intervals.

The inter-subject repeatability results (rmsCV%) for cartilage thickness and volume for all of the ROIs are showed in Fig. 8 The experiments showed a rmsCV smaller than 10% in all 11 regions for both thickness and volume measurements.

DISCUSSION

In this study, we presented an isotropic 3D-MRI technique for simultaneous morphological and biochemical assessment of the human knee cartilage. The morphological and compositional measurements can be quickly registered and correlated in the same voxels for more comprehensive and accurate assessment of cartilage tissue properties. Moreover, the isotropic spatial resolution allowed the multiplanar reformatting of the scans and evaluation of the relaxation, volume and thickness in any plane and hence the complete coverage of the surface of the articular cartilage.

The main advantage of this method was its ability of simultaneous 3D-T1 ρ relaxation mapping and morphological estimation with isotropic high-resolution. Although our in-plane resolution was still lower than the standard Osteoarthritis Initiative (OAI) protocol for quantitative cartilage morphology studies (20,25–29) (0.7mm vs. <0.35mm in 3D-FLASH (25–27) and 3D-DESS (28,29)), its ability of simultaneous measurement of T1 ρ relaxation time provides additional information in the reduced total scan time. Moreover, the Bland-Altman analysis showed that the estimated cartilage volume and thickness of the cartilage were in agreement with the estimated values from the 3D-FLASH sequence. The negative regression relationship for the volume indicated a tendency for 3D-ISO to overestimate the cartilage volume while the positive relationship for thickness showed a tendency for the 3D-ISO technique to underestimate the thickness. On the other hand, our spatial resolution was higher than many of the reported T1 ρ relaxation studies (15,19,30,31). In studies with higher in-plane resolution and voxel size such as Nozaki study (31), their larger slice thickness (3mm vs. 0.7mm) leads to higher partial volume effect (PVE) and as a result less accuracy in comparison with our technique.

The smaller slice thickness in this study decreases the partial volume effects (PVE) and as a result, the T1 ρ estimation error. Additionally, acquiring more temporal data points (10 t_{SL}) instead of 4–6 in other studies (10,11,14,19,31) leads to more accurate relaxation mapping. The isotropic submillimeter resolution of this sequence justifies its longer scan time (~23 min) in comparison to another study (~15min), as it could eliminate the need for acquiring multiple time-consuming 2D acquisitions in different planes or an additional 3D high-resolution scan for morphological assessment.

The estimated range of the cartilage's volume and thickness in our study is in agreement with previous studies (7,32,33). However, some differences were observed that might be due to the difference in the physical size of the volunteers (32) as well as the different thickness

estimation methods used in previous work (33). We observed that men had higher cartilage thickness and volume than women which is also in agreement with previous studies (34,35).

This study has several limitations. First, only the asymptomatic healthy volunteers were recruited, and further validation in patients with knee OA is warranted. Moreover, the relatively small number of volunteers analyzed in this work might affect the statistical results. The condition used for excluding pixels in biexponential analysis can also generate some bias (15).

In conclusion, a 3D isotropic turbo-flash based sequence was implemented for simultaneous in vivo morphological, mono and bicomponent T1 ρ relaxation mapping analysis of the human knee articular cartilage. The biexponential T1 ρ components in combination with cartilage volume and thickness assessment with isotropic 0.7mm×0.7mm×0.7mm resolution could potentially be used to increase the specificity for detection of early osteoarthritis.

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References

1. Krasnokutsky S, Belitskaya-Lévy I, Bencardino J, et al. Quantitative magnetic resonance imaging evidence of synovial proliferation is associated with radiographic severity of knee osteoarthritis. *Arthritis Rheum.* 2011; 63(10):2983–2991. [PubMed: 21647860]
2. Scott D, Kowalczyk A. Osteoarthritis of the knee. *BMJ Clin Evid.* 2007; 2007
3. Bonnin M, Chambat P. Osteoarthritis of the Knee. Springer Science & Business Media; 2008.
4. Peat G, McCarney R, Croft P. Knee pain and osteoarthritis in older adults: a review of community burden and current use of primary health care. *Ann Rheum Dis.* 2001; 60(2):91–97. [PubMed: 11156538]
5. Gabrielle Blumenkrantz B, Jesus Lozano B, Julio C-G, Ries M, Majumdar S. In vivo T1 ρ and T2 mapping of articular cartilage in osteoarthritis of the knee using 3 tesla MRI. *Osteoarthritis Cartilage.* 2007; 15(7):789–797. [PubMed: 17307365]
6. Wang L, Regatte RR. T1 ρ MRI of human musculoskeletal system. *J Magn Reson Imaging.* 2015; 41(3):586–600. [PubMed: 24935818]
7. Sittek H, Eckstein F, Gavazzeni A, et al. Assessment of normal patellar cartilage volume and thickness using MRI: an analysis of currently available pulse sequences. *Skeletal Radiol.* 1996; 25(1):55–62. [PubMed: 8717120]
8. Morgan S, Waterton J, Maciewicz R, et al. Magnetic resonance imaging measurement of knee cartilage volume in a multicentre study. *Rheumatology.* 2003; 43(1):19–21. [PubMed: 12923282]
9. Sharma L, Song J, Felson DT, Shamiyeh E, Dunlop DD. The role of knee alignment in disease progression and functional decline in knee osteoarthritis. *JAMA.* 2001; 286(2):188–195. [PubMed: 11448282]
10. Li X, Benjamin Ma C, Link TM, et al. In vivo T1 ρ and T2 mapping of articular cartilage in osteoarthritis of the knee using 3 T MRI. *Osteoarthritis Cartilage.* 2007; 15(7):789–797. [PubMed: 17307365]
11. Regatte RR, Akella SV, Lonner J, Kneeland J, Reddy R. T1 ρ relaxation mapping in human osteoarthritis (OA) cartilage: comparison of T1 ρ with T2. *J Magn Reson Imaging.* 2006; 23(4): 547–553. [PubMed: 16523468]

12. Nishioka H, Nakamura E, Hirose J, Okamoto N, Yamabe S, Mizuta H. MRI T1 ρ and T2 mapping for the assessment of articular cartilage changes in patients with medial knee osteoarthritis after hemicallotasis osteotomy. *Bone Jt Res.* 2016; 5(7):294–300.
13. Monu UD, Jordan CD, Samuelson BL, Hargreaves BA, Gold GE, McWalter EJ. Cluster analysis of quantitative MRI T2 and T1 ρ relaxation times of cartilage identifies differences between healthy and ACL-injured individuals at 3T. *Osteoarthritis Cartilage.* 2017; 25(4):513–520. [PubMed: 27720806]
14. Wang L, Chang G, Xu J, et al. T1 ρ MRI of menisci and cartilage in patients with osteoarthritis at 3T. *Eur J Radiol.* 2012; 81(9):2329–2336. [PubMed: 21908122]
15. Sharafi A, Xia D, Chang G, Regatte RR. Biexponential T1 ρ relaxation mapping of human knee cartilage in vivo at 3 T. *NMR Biomed.* 2017
16. Favre J, Erhart-Hledik JC, Blazek K, Fasel B, Gold GE, Andriacchi TP. Anatomically Standardized Maps Reveal Distinct Patterns of Cartilage Thickness With Increasing Severity of Medial Compartment Knee Osteoarthritis. *J Orthop Res.* 2017 n/a-n/a.
17. Omoumi P, Michoux N, Roemer FW, Thienpont E, Vande Berg BC. Cartilage thickness at the posterior medial femoral condyle is increased in femorotibial knee osteoarthritis: a cross-sectional CT arthrography study (Part 2). *Osteoarthritis Cartilage.* 2015; 23(2):224–231. [PubMed: 25450850]
18. Omoumi P, Michoux N, Thienpont E, Roemer FW, Vande Berg BC. Anatomical distribution of areas of preserved cartilage in advanced femorotibial osteoarthritis using CT arthrography (Part 1). *Osteoarthritis Cartilage.* 2015; 23(1):83–87. [PubMed: 25450851]
19. Zarins ZA, Bolbos RI, Pialat JB, et al. Cartilage and meniscus assessment using T1 ρ and T2 measurements in healthy subjects and patients with osteoarthritis. *Osteoarthritis Cartilage.* 2010; 18(11):1408–1416. [PubMed: 20696262]
20. Eckstein F, Guermazi A, Gold G, et al. Imaging of cartilage and bone: promises and pitfalls in clinical trials of osteoarthritis. *Osteoarthritis Cartilage.* 2014; 22(10):1516–1532. [PubMed: 25278061]
21. Altman DG, Bland JM. Measurement in Medicine: The Analysis of Method Comparison Studies. *J R Stat Soc Series D (The Statistician).* 1983; 32(3):307–317.
22. Bland JM, Altman DG. Measuring agreement in method comparison studies. *Stat Methods Med Res.* 1999; 8(2):135–160. [PubMed: 10501650]
23. Glüer C-C, Blake G, Lu Y, Blunt BA, Jergas M, Genant HK. Accurate assessment of precision errors: How to measure the reproducibility of bone densitometry techniques. *Osteoporos Int.* 1995; 5(4):262–270. [PubMed: 7492865]
24. Atkinson G, Nevill AM. Statistical Methods For Assessing Measurement Error (Reliability) in Variables Relevant to Sports Medicine. *Sports Med.* 1998; 26(4):217–238. [PubMed: 9820922]
25. Eckstein F, Buck RJ, Burstein D, et al. Precision of 3.0 Tesla quantitative magnetic resonance imaging of cartilage morphology in a multicentre clinical trial. *Ann Rheum Dis.* 2008; 67(12):1683–1688. [PubMed: 18283054]
26. Graichen H, Eisenhart-Rothe R, Vogl T, Englmeier K-H, Eckstein F. Quantitative assessment of cartilage status in osteoarthritis by quantitative magnetic resonance imaging: Technical validation for use in analysis of cartilage volume and further morphologic parameters. *Arthritis Rheum.* 2004; 50(3):811–816. [PubMed: 15022323]
27. Eckstein F, Charles HC, Buck RJ, et al. Accuracy and precision of quantitative assessment of cartilage morphology by magnetic resonance imaging at 3.0T. *Arthritis Rheum.* 2005; 52(10):3132–3136. [PubMed: 16200592]
28. Wirth W, Nevitt M, Hellio Le Graverand MP, et al. Sensitivity to change of cartilage morphometry using coronal FLASH, sagittal DESS, and coronal MPR DESS protocols – comparative data from the osteoarthritis initiative (OAI). *Osteoarthritis Cartilage.* 2010; 18(4):547–554. [PubMed: 20060948]
29. Schneider E, Nevitt M, McCulloch C, et al. Equivalence and precision of knee cartilage morphometry between different segmentation teams, cartilage regions, and MR acquisitions. *Osteoarthritis Cartilage.* 2012; 20(8):869–879. [PubMed: 22521758]

30. Stahl R, Luke A, Li X, et al. T1rho, T2 and focal knee cartilage abnormalities in physically active and sedentary healthy subjects versus early OA patients—a 3.0-Tesla MRI study. *Eur Radiol*. 2009; 19(1):132–143. [PubMed: 18709373]
31. Nozaki T, Kaneko Y, Hon JY, Kaneshiro K, Schwarzkopf R, Yoshioka H. Comparison of T1rho imaging between spoiled gradient echo (SPGR) and balanced steady state free precession (b-FFE) sequence of knee cartilage at 3T MRI. *Eur J Radiol*. 2015; 84(7):1299–1305. [PubMed: 25956494]
32. Nishimura K, Tanabe T, Kimura M, Harasawa A, Karita K, Matsushita T. Measurement of articular cartilage volumes in the normal knee by magnetic resonance imaging: can cartilage volumes be estimated from physical characteristics? *J Orthop Sci*. 2005; 10(3):246–252. [PubMed: 15928885]
33. Cohen ZA, McCarthy DM, Kwak SD, et al. Knee cartilage topography, thickness, and contact areas from MRI: in-vitro calibration and in-vivo measurements. *Osteoarthritis Cartilage*. 1999; 7(1):95–109. [PubMed: 10367018]
34. Faber SC, Eckstein F, Lukasz S, et al. Gender differences in knee joint cartilage thickness, volume and articular surface areas: assessment with quantitative three-dimensional MR imaging. *Skeletal Radiol*. 2001; 30(3):144–150. [PubMed: 11357452]
35. Karvonen R, Negendank W, Teitge R, Reed A, Miller P, Fernandez-Madrid F. Factors affecting articular cartilage thickness in osteoarthritis and aging. *J Rheumatol*. 1994; 21(7):1310–1318. [PubMed: 7966075]

Fig. 1.
A representative example of isotropic $T1\rho$ weighted MRI images in sagittal, coronal, and axial plane at different spinlock durations. The MR signal decays with time due to $T1\rho$ relaxation.

Fig. 2. Cartilage regions of interest. (a) 2D view (left to right) medial, lateral and patellar cartilages (b) 3D view from two different angles to show medial and lateral ROIs.

Fig. 3. A representative example of relaxation maps in the sagittal, coronal, and axial plane. (a) mono (b) long and (c) short relaxation components maps.

Fig. 4.
T1 ρ histogram distributions over articular cartilages. (a) mono, (b) short, and (c) long components.

Fig. 5.

Box plot shows the $T1\rho$ relaxation times components between different 11 ROIs. The line in the middle of each box is the median and the bars extending from each box are the maximum and minimum values. The dash line with numbers show the pairwise rank sum test between two ROIs (**PLF**: Posterior-Lateral Femur; **CLF**: Central-Lateral Femur; **ALF**: Anterior- Lateral Femur; **PLT**: Posterior-Lateral Tibia; **ALT**: Anterior-Lateral Tibia; **PMF**: Posterior-Medial Femur; **AMF**: Anterior-Medial Femur; **PMT**: Posterior-Medial Tibia; **AMT**: Anterior-Medial Tibia; **IP**: Inferior Patellar; **SP**: Superior Patellar).

Fig. 6.

(a) Scatterplot of cartilage volume measurement from the 3D-FLASH sequence (FL) plotted against 3D-ISO measurements (ISO). Linear regressions indicated a tendency for 3D-ISO to overestimate volume. Strong coefficients of determination (R^2) demonstrated that 3D-ISO scans are well suited to measure articular cartilage volume. (b) Bland-Altman plot shows data for mean volume thickness plotted against difference.

Fig. 7.

(a) Scatterplot of cartilage thickness measurement from the 3D-FLASH sequence (FL) plotted against 3D-ISO measurements (ISO). Linear regressions indicated a tendency for 3D-ISO to underestimate thickness. Strong coefficients of determination (R^2) demonstrated that 3D-isotropic images are well suited to measure articular cartilage thickness. (b) Bland-Altman plot shows data for mean cartilage thickness plotted against difference.

Fig. 8. Inter-subject repeatability of morphological evaluation of (a) cartilage thickness and (b) cartilage volume. The root-mean-square coefficient of variation (rmsCV) is less than 10% in the all 11 regions of interests (ROIs).

Table 1

Descriptive statistics of mono and biexponential relaxation times in 15 regions of interest.

ROI	T1 ρ _{mono} (ms)		T1 ρ _{short} (ms)		T1 ρ _{long} (ms)		Y _{short} (%)		Y _{long} (%)	
	Mean $\pm$ SD	($\pm$ 95% CI)	Mean $\pm$ SD	($\pm$ 95% CI)	Mean $\pm$ SD	($\pm$ 95% CI)	Mean $\pm$ SD	($\pm$ 95% CI)	Mean $\pm$ SD	($\pm$ 95% CI)
PLF	37.7 $\pm$ 5.1	(34.1,41.4)	5.6 $\pm$ 0.7	(6.1,7.1)	59.0 $\pm$ 3.8	(56.2,61.7)	38.7 $\pm$ 8.3	(31.3,46.1)	61.3 $\pm$ 8.3	(53.9,68.7)
CLF	35.0 $\pm$ 0.3	(27.7,41.4)	5.7 $\pm$ 1.1	(4.9,6.5)	57.3 $\pm$ 8.7	(51.0,63.5)	41.7 $\pm$ 5.4	(36.3,47.1)	58.3 $\pm$ 15.3	(43.0,73.6)
ALF	43.2 $\pm$ 4.3	(40.1,46.2)	6.4 $\pm$ 0.6	(5.9,6.8)	59.1 $\pm$ 4.2	(56.0,62.0)	29.6 $\pm$ 7.0	(22.6,36.6)	70.4 $\pm$ 7.0	(63.4,77.4)
PLT	39.7 $\pm$ 5.8	(35.6,43.9)	6.9 $\pm$ 0.4	(6.6,7.2)	56.0 $\pm$ 1.8	(54.7,57.2)	36.3 $\pm$ 6.0	(30.3,42.3)	63.7 $\pm$ 6.0	(57.7,69.7)
ALT	50.7 $\pm$ 4.2	(47.8,53.8)	6.1 $\pm$ 0.5	(5.7,6.5)	63.7 $\pm$ 3.2	(61.4,66.0)	36.0 $\pm$ 7.0	(29.0,43.0)	64.0 $\pm$ 7.0	(57.0,71.0)
PMF	37.1 $\pm$ 6.8	(32.5,41.7)	5.8 $\pm$ 1.4	(4.8,6.7)	58.4 $\pm$ 8.5	(52.3,64.5)	37.4 $\pm$ 6.2	(31.4,43.4)	62.6 $\pm$ 6.2	(56.6,68.6)
AMF	44.1 $\pm$ 5.3	(40.2,47.9)	6.2 $\pm$ 0.7	(5.6,6.7)	61.1 $\pm$ 4.2	(58.1,64.1)	40.7 $\pm$ 11.7	(29.0,52.4)	59.3 $\pm$ 11.7	(47.6,71.0)
PMT	42.2 $\pm$ 6.0	(37.9,46.5)	6.5 $\pm$ 0.7	(5.9,7.1)	58.7 $\pm$ 3.5	(56.2,61.3)	34.9 $\pm$ 7.6	(27.3,42.5)	65.1 $\pm$ 7.6	(57.5,72.7)
AMT	39.7 $\pm$ 6.1	(35.3,44.0)	6.8 $\pm$ 0.8	(6.1,7.4)	55.8 $\pm$ 4.9	(52.3,59.3)	37.0 $\pm$ 11.1	(25.9,48.1)	63.0 $\pm$ 11.0	(51.9,74.1)
IP	38.5 $\pm$ 3.8	(35.8,41.3)	6.8 $\pm$ 0.7	(6.3,7.3)	56.2 $\pm$ 4.2	(53.2,59.2)	37.3 $\pm$ 8.1	(31.3,43.3)	62.7 $\pm$ 9.0	(56.7,68.7)
SP	40.1 $\pm$ 3.5	(37.5,42.6)	6.5 $\pm$ 0.6	(6.1,6.9)	58.4 $\pm$ 3.9	(55.5,61.1)	36.0 $\pm$ 7.6	(29.0,43.0)	64.0 $\pm$ 7.6	(57.0,71.0)
Patella	39.3 $\pm$ 3.0	(37.3,41.4)	6.7 $\pm$ 0.6	(6.3,7.1)	57.3 $\pm$ 3.3	(55.1,59.5)	36.7 $\pm$ 7.7	(30.7,42.7)	63.3 $\pm$ 7.7	(57.3,69.3)
Tibia	43.1 $\pm$ 4.0	(40.2,45.9)	6.7 $\pm$ 0.4	(6.3,6.8)	58.5 $\pm$ 2.9	(56.5,60.6)	36.0 $\pm$ 7.9	(29.0,43.0)	64.0 $\pm$ 7.9	(57.0,71.0)
Femur	39.4 $\pm$ 4.6	(36.1,42.8)	6.1 $\pm$ 0.7	(5.6,6.7)	58.9 $\pm$ 5.2	(55.1,62.6)	37.6 $\pm$ 10.8	(26.8,48.4)	62.4 $\pm$ 10.8	(51.6,73.2)
Global	40.7 $\pm$ 4.8	(38.8,42.1)	6.5 $\pm$ 0.6	(6.2,6.7)	58.2 $\pm$ 3.9	(56.7,59.7)	36.3 $\pm$ 5.9	(30.3,42.3)	63.7 $\pm$ 5.9	(57.7,69.7)

SD: Standard Deviation; CI: Confidence Interval; **PLF**: Posterior-Lateral Femur; **CLF**: Central-Lateral Femur; **ALF**: Anterior-Lateral Femur; **PLT**: Posterior-Lateral Tibia; **ALT**: Anterior-Lateral Tibia; **PMF**: Posterior-Medial Femur; **AMF**: Anterior-Medial Femur; **PMT**: Posterior-Medial Tibia; **AMT**: Anterior-Medial Tibia; **IP**: Inferior Patellar; **SP**: Superior Patellar

Table 2

Mean± SD and 95% confidence intervals of volume and thickness of articular cartilage of women and men in different ROIs

ROI	Volume(mm ³) Mean± SD (±95% CI)		Thickness(mm) Mean± SD (±95% CI)	
	Female (n=5)	Male (n=5)	Female (n=5)	Male (n=5)
PLF	2634.40 ± 326.06 (2229.54,3039.25)	2973.20 ± 175.24 (2755.61,3190.79)	1.41 ± 0.21 (1.15,1.67)	1.70 ± 0.26 (1.36,2.03)
CLF	2264.20 ± 454.10 (1700.36,2828.04)	3279.80 ± 454.50 (2715.46,3844.14)	1.52 ± 0.13 (1.35,1.69)	1.60 ± 0.17 (1.37,1.80)
ALF	3024.60 ± 679.23 (2181.22,3868.98)	5554.40 ± 1176.74 (4093.28,7015.52)	2.08 ± 0.19 (1.83,2.32)	2.76 ± 0.95 (1.57,3.93)
PLT	1574.20 ± 309.04 (1190.48,1957.92)	2868.40 ± 235.28 (2576.26,3160.54)	2.06 ± 0.27 (1.72,2.40)	2.33 ± 0.47 (1.74,2.92)
ALT	1944.00 ± 412.62 (1431.66,2456.34)	3752.00 ± 576.62 (3036.03,4467.97)	1.61 ± 0.24 (1.31,1.91)	1.95 ± 0.68 (1.09,2.79)
PMF	1675.40 ± 375.30 (1209.40,2141.40)	2399.60 ± 285.88 (2044.63,2754.57)	1.50 ± 0.18 (1.26,1.73)	1.73 ± 0.28 (1.37,2.08)
AMF	1948.60 ± 153.44 (1758.08,2139.12)	2729.00 ± 278.11 (2383.68,3704.32)	1.38 ± 0.08 (1.27,1.49)	1.62 ± 0.15 (1.42,1.81)
PMT	1174.80 ± 168.17 (965.98,1383.61)	1653.20 ± 229.13 (1368.69,1937.70)	1.43 ± 0.13 (1.26,1.59)	1.48 ± 0.10 (1.34,1.61)
AMT	1037.98 ± 148.86 (853.15,1222.81)	1775.00 ± 202.86 (1523.12,2026.88)	1.45 ± 0.15 (1.26,1.64)	1.53 ± 0.15 (1.33,1.72)
IP	1347.89 ± 173.41 (1132.48,1563.12)	2096.40 ± 285.26 (1742.20,2450.59)	2.96 ± 0.31 (2.57,3.35)	3.27 ± 0.27 (2.92,3.61)
SP	1599.80 ± 214.03 (1334.04,1865.56)	2543.80 ± 333.03 (2130.29,2957.31)	2.99 ± 0.32 (2.58,3.40)	3.24 ± 0.73 (2.33,4.16)
Patella	2947.60 ± 343.97 (2520.50,3374.70)	4640.20 ± 606.50 (3887.13,5393.27)	2.98 ± 0.29 (2.62,3.34)	3.26 ± 0.44 (2.70,3.81)
Tibia	5622.98 ± 369.35 (5164.37,6081.59)	10048.60 ± 754.61 (9111.62,10985.58)	1.64 ± 0.16 (1.44,1.84)	1.82 ± 0.30 (1.43,2.20)
Femur	11547.20 ± 944.51 (10374.43,12719.97)	16936.00 ± 1449.98 (15135.60,18736.39)	1.58 ± 0.13 (1.41,1.75)	1.88 ± 0.28 (1.52,2.23)
Global	20117.78 ± 1513.60 (18238.40,21997.16)	31624.80 ± 2440.40 (28594.65,34654.95)	2.06 ± 0.69 (1.68,2.45)	2.32 ± 0.76 (1.89,2.74)

SD: Standard Deviation; **CI:** Confidence Interval; **PLF:** Posterior-Lateral Femur; **CLF:** Central-Lateral Femur; **ALF:** Anterior- Lateral Femur; **PLT:** Posterior-Lateral Tibia; **ALT:** Anterior-Lateral Tibia; **PMF:** Posterior-Medial Femur; **AMF:** Anterior-Medial Femur; **PMT:** Posterior-Medial Tibia; **AMT:** Anterior-Medial Tibia; **IP:** Inferior Patellar; **SP:** Superior Patellar