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Examiner repeatability of patellar cartilage T_2 values

Matthew F. Koff^a, Sebastien Parratte^a, Kimberly K. Amrami^b, and Kenton R. Kaufman^{a,*}

^aDepartment of Orthopedic Surgery, Mayo Clinic, Rochester, MN 55901, USA

^bDepartment of Radiology, Mayo Clinic, Rochester, MN 55901, USA

Abstract

Aim—The purpose of this study was to evaluate the intra- and interexaminer resegmentation precision of patellar cartilage T_2 mapping measurements in healthy subjects.

Materials and Methods— T_2 -weighted images of patellar cartilage for 10 subjects were acquired. Two individuals manually segmented patellar cartilage at each slice location twice, once on each of two separate days. Bulk average and zonal T_2 values for the superficial, middle, and deep layers of cartilage were calculated. The root mean square (RMS) and coefficient of variation (COV) were calculated using the repeated measurements of each slice of each subject by each examiner.

Results—The intraexaminer bulk T_2 differences were 0.2 ± 1.0 ms, with an RMS error of 0.7 ms and a COV of 1.9%. The differences of interexaminer bulk T_2 values was 1.0 ± 1.4 ms, with an RMS error of 1.2 ms and a COV of 3.3%. The superficial zone of cartilage had the highest zonal variability of T_2 values. The average interexaminer T_2 values for the superficial, middle and deep zones were 42.2 ± 5.6 , 38.1 ± 5.3 and 31.9 ± 4.6 ms, respectively.

Conclusion—The interexaminer variability of calculated T_2 values highlights the difficulty of interpreting significant differences of T_2 values which are similar in magnitude. The repeatability measurements of patellar cartilage T_2 values were less than reported intersession T_2 repeatability.

Keywords

Reproducibility of results; MRI; Cartilage; Patella

1. Introduction

The World Health Organization has declared the 2000–2010 decade as the bone and joint decade with the goal of improving the understanding, the prevention and the treatment of musculoskeletal disorders [1]. Osteoarthritis, one of the most common musculoskeletal diseases, is a main target of this program. In 1997, an estimated 16% of the US population had a form of arthritis, and its prevalence is expected to further increase in the near future [1]. Therapeutic innovations developed for management of the early stage of osteoarthritis (OA) as well for surgical management of advanced cartilage lesion [2] require an objective quantitative method to confirm their validity and usefulness [3–7]. Clinical scores can be used as outcome measures for surgical procedures, but these methods only provide an indirect and subjective evaluation of the articular cartilage [8].

New methods of medical imaging may provide an objective quantitative method for evaluation of the cartilage status. Magnetic resonance imaging (MRI) is a powerful noninvasive evaluative

*Corresponding author. Tel.: +1 507 284 2262; fax: +1 507 266 2227. E-mail address: E-mail: kaufman.kenton@mayo.edu (K.R. Kaufman).

tool for imaging cartilage, especially the evolving MRI technique of T_2 relaxation time mapping [3–7,9–12]. The MRI time constant T_2 represents the rate of internuclear dephasing between excited hydrogen dipoles [13]. The stratification of T_2 through the depth of articular cartilage reflects the arrangement of the Type II collagen fibers within the collagen matrix as well as water content of the tissue [5,12]. T_2 mapping has been demonstrated to be sensitive to degenerative changes of cartilage [3,5,12,14]. A current goal is to use T_2 relaxation time for the clinical evaluation of regional cartilage heterogeneity and for discrimination between healthy and diseased cartilage [3,4,9,10].

Determining the precision error and reproducibility of an imaging method is a fundamental step before use of the imaging technique in routine clinical practice. Eckstein et al. [15] proposed a multifaceted analysis of the reproducibility of a new imaging technique, including: (a) technical precision — defined as repeated analysis of an identical dataset within one session; (b) resegmentation precision — defined as repeated image analysis of an identical dataset in different image analysis sessions, days or weeks apart; (c) interscan test–retest precision — defined as analysis of two datasets with repositioning between the scans; (d) long-term acquisition precision — defined as analysis of at least two datasets acquired in different imaging sessions, days or weeks apart; (e) overall precision — representing the error of (b)+(c) or (b)+(d); (f) interobserver precision — defined as image analysis performed by different observers; and (g) interscanner precision — defined as image analysis with similar evaluated the interscan test–retest precision as well as long-term acquisition precision of cartilage T_2 values [4]; however, the resegmentation precision has not been evaluated.

Resegmentation precision of T_2 values assesses the reproducibility of the measurement methodology due to changes in technical or human performance during the segmentation process. This type of precision is especially necessary in evaluating the applicability of T_2 mapping within a clinical setting, as different radiologists may produce varying results for quantitative cartilage analysis (Fig. 1). The resegmentation precision may be further evaluated by intraexaminer reproducibility and interexaminer reproducibility. These different measurements of T_2 mapping precision evaluate the induced additional sources of error when the image analysis is performed by different observers over different days. This type of analysis is important since different readers may have different perceptions about what should and should not be considered cartilage during the segmentation process [3]. To the best of our knowledge, the intra- and interexaminer resegmentation precision of cartilage T_2 values have not been reported. Therefore, the purpose of this study was to evaluate the intra- and interexaminer resegmentation precision of patellar cartilage T_2 mapping measurements in healthy subjects. The specific goals of the study were to (1) evaluate global (bulk) tissue T_2 values and depth dependent resegmentation intraobserver precision error of patellar cartilage T_2 values, and (2) evaluate global and depth dependent interobserver precision error of patellar cartilage T_2 values.

2. Methods and materials

2.1. Subjects

Following local institutional review board approval with informed consent, 10 male volunteers (31 ± 4 years old, range 25–36) were enrolled in the study. All subjects had no pain, stiffness or other symptoms of OA in the knee which was scanned.

2.2. Data acquisition

Magnetic resonance (MR) images of each subject's right patella were obtained using a 1.5-T clinical MRI scanner (GE Health Systems, Milwaukee, WI, USA). Six subjects were scanned using one scanner, and the remaining subjects were scanned using a second scanner. A

dedicated transmit–receive knee coil was used for all imaging. An MR-compatible knee positioning device was used in both scanners to ensure consistency of knee position and flexion angle relative to the knee coil. A series of axial T_2 -weighted images were acquired using a multislice multiecho fast spin echo (FSE) pulse sequence [11]. Images were acquired across 11 slice locations centered on the patella. Imaging parameters were: Repetition time (TR)=1500 ms, slice thickness=2 mm, slice spacing=4 mm, in-plane resolution=0.49×0.49 mm, field of view=12×12 cm, acquisition matrix=256×160 (zero filled to 256×256), Bandwidth (BW)=31.25 MHz, Array Spatial Sensitivity Encoding Technique (ASSET) acceleration=1. Eight echo images were acquired at each slice location. The echo times (TEs) used for the first scanner was TE=7.82 – 62.53 ms, with 7.82-ms increments. The TEs used for the second scanner was TE=8.48 – 67.84 ms, with 8.48-ms increments. The acquisition time for the T_2 mapping images was approximately 5 min. A single MR technologist acquired the images for all subjects. The series was acquired as part of an ongoing study in our laboratory, which had a total imaging time of approximately 1 h.

2.3. Data analysis

Two individuals processed the data at each slice location twice, once on each of two separate days. The different data analysis sessions were separated by more than 24 hours. All data processing by the two individuals was performed independently from one another. One individual had experience of analyzing over 800 cartilage T_2 maps, and the second individual had experience of analyzing over 100 cartilage T_2 maps. Custom written software (MATLAB, Natick, MA, USA) was used to process the image data. Patellar cartilage was manually segmented at each slice location [9]. The first echo image was used to delineate the deep cartilage from the underlying subchondral bone, and the last echo image was used to delineate the superficial cartilage from the surrounding joint space. Image slices at the proximal and distal pole of the patella were not included in the analysis due to potential volume averaging. T_2 values were calculated on a pixel-by-pixel basis by fitting the TE to the corresponding signal intensity data (SI) using a monoexponential decay equation:

$$SI(TE) = S_0 \cdot \exp(-TE/T_2).$$

The solution for T_2 was calculated using a nonlinear least squares fitting algorithm [11]. A bulk average T_2 value was calculated from all pixels within the individual slices and used for bulk repeatability analysis. In addition, a semi-automated program [9] separated the cartilage within each slice into a deep zone (0–30% depth), middle zone (30–70% depth) and superficial zone (70–100% depth). Briefly, the program fit a spline to the most superficial pixels and a spline to the deep pixels within the cartilage region of interest (ROI) defined previously by the examiner. Next, the program individually parameterized the splines to calculate (x,y) coordinates at 80 equally spaced points. Using the (x,y) coordinates of corresponding parametric points on the superficial and deep splines, the program then calculated (x,y) coordinates at 30% and 70% depths on a line which connected the two splines. Therefore, the (x,y) coordinates of the superficial most pixels and the (x,y) coordinates of the calculated points at 30% depth created an ROI representing the deep zone of cartilage, the (x,y) coordinates of the deep pixels and the calculated (x,y) coordinates at 70% depth created an ROI representing the superficial zone of cartilage and the calculated (x,y) coordinates of the points at 30% and 70% depths represented the middle zone of cartilage. An average T_2 value within each cartilage zone was used for zonal repeatability analysis. Finally, the number of pixels within an ROI defined by each examiner for each image plane was calculated, as well as the percentage of common pixels within the ROIs defined by both examiners. On average, the data processing took approximately 20–45 minutes for each patella.

2.4. Statistical analysis

Bland–Altman plots [16] were generated to evaluate intra- and interexaminer repeatability of bulk and zonal T_2 values. These plots, which display the difference between two measurements on the ordinate and the average of two measurements on the abscissa, are effective at highlighting trends and differences between two independent measurements of a single variable. A repeatability coefficient was calculated from the Bland–Altman analysis as 1.96 times the standard deviation of the differences [16,17].

Additional numerical measures of intra- and interexaminer variability were calculated using the root mean square (RMS) error and coefficient of variation (COV) of the bulk and zonal T_2 values. The RMS and COV were calculated using the repeated measurements of each slice of each subject by each examiner, as outlined previously by Gluer et al. [18]. In addition, a two-sample, two-tailed t test was performed to detect significant differences of the number of pixels within the ROIs defined by the individual examiners.

3. Results

A preliminary two-sample t test of the calculated T_2 values was performed to evaluate the effect of using different scanners for data acquisition. No significant difference of T_2 value was found due to using different scanners for image acquisition ($P=.68$, mean difference: -0.2 ± 4.3 ms). Subsequently, the data from both scanners was pooled together for repeatability analysis.

A total of 66 slices of data from all subjects were available for analysis. The average bulk T_2 calculated by the first examiner was 37.9 ± 4.4 ms (mean $\pm$ S.D.). The average bulk T_2 calculated by the second examiner was 36.9 ± 4.1 ms. The differences of intraexaminer bulk T_2 values was 0.2 ± 1.0 ms, with a coefficient of repeatability of 2.0 ms, an RMS error of 0.7 ms and a COV of 1.9% (Table 1, Fig. 1). The differences of interexaminer bulk T_2 values was 1.0 ± 1.4 ms, with a coefficient of repeatability of 2.8 ms, an RMS error of 1.2 ms and a COV of 3.3% (Table 1). The Bland–Altman plots for the intra- and interexaminer repeatability of bulk patellar cartilage T_2 values show a random distribution of the data points indicating no underlying relationship between the method of segmentation by each examiner (Fig. 2).

The repeatability of zonal T_2 values was dependent upon the cartilage zone of interest. The superficial zone of cartilage had the highest variability of all three zones of tissue analyzed. The average T_2 values for the superficial, middle and deep zones were 42.2 ± 5.6 , 38.1 ± 5.3 and 31.9 ± 4.6 ms, respectively. The inter-examiner Bland–Altman plots for each cartilage zone display larger differences of data between the two examiners for the superficial zone, as compared to differences for the middle and deep zones (Fig. 3). The intraexaminer coefficient of repeatability of the superficial zone was more than 1.5 ms greater than the middle and the deep zones (Table 1). Similarly, the interexaminer coefficient of repeatability of the superficial zone was almost 3 ms greater than the middle and deep zones (Table 1). The superficial zone also had the largest COV for intra- and interexaminer repeatability, 3.1% and 5.0%, respectively. In general, the middle zone had the best repeatability and COV than the other two zones. Overall, the bulk T_2 evaluation tended to result in better repeatability, RMS and COV than the zonal T_2 evaluation.

There was no significant difference between the number of pixels segmented by each examiner for all analyzed image slices ($P=.4$). On average, the first examiner defined 534.6 ± 241.8 pixels, 86.0 $\pm$ 7.6% of which were common to the pixels defined by the second examiner. The second examiner defined 510.5 ± 227.3 pixels, 89.2 $\pm$ 7.1% of which were common to the pixels defined by the first examiner. Visual inspection of the ROIs did not indicate anatomical areas where pixels were commonly over- or undersampled by an individual examiner.

4. Discussion

This study evaluated the intra- and interexaminer resegmentation variability and repeatability of patellar cartilage T_2 values. Understanding the resegmentation repeatability of T_2 values is important since changes of T_2 values over time may be influenced by examiners defining different ROIs within image data sets in addition to the natural progression of pathology.

The results of the current study aid in interpreting significant differences and changes of T_2 in experimental protocols. The current analysis found the range of interexaminer coefficient of repeatability to be between 2.0 and 5.8 ms for bulk- and depth-dependent comparisons. This coefficient of repeatability is similar to previous reports of T_2 changes due to joint loading [19,20], producing changes from <1 to approximately 4 ms, or differences due to gender [21], producing differences of approximately 2 ms. Furthermore, the coefficient of repeatability was slightly less than the change of cartilage T_2 through the depth of the tissue as reported in previous studies [9,22,23]. Therefore, based on the current interexaminer coefficient of repeatability, if a study finds a significant difference between two sample groups and the mean difference is at most 6 ms, then the results may depend upon the individual who processed the data. The data set should be reprocessed by a second individual to verify the significant difference which was initially found. If a study finds a significant difference between two sample groups and the mean difference is greater than 6 ms, then the differences are likely due to genuine changes of the biological composition of the tissue rather than the individual processing the data set.

The current analysis found better repeatability in the middle and deep zones of cartilage than in the superficial zone of the tissue. We attribute this result to our method of manual image segmentation. Our method used the first echo image to delineate the articular cartilage from the underlying subchondral bone surface. Defining the subchondral bone surface was facilitated since the low T_2 value of bone produced an obvious dark boundary with the articular cartilage. The last echo image was used to differentiate the articular surface from the surrounding joint space. However, defining the articular surface proved to be difficult in several slices due to focal degeneration of the articular surface. The degeneration produced an indistinct boundary between the articular surface and surrounding joint space. As a result, the ease of defining the deep zone combined with the difficulty of defining the articular surface and the semiautomated program for defining the middle zone produced the variability of the depth dependent T_2 values seen in the study.

Using manual segmentation, the intra- and interexaminer errors (COV and RMS) tended to be less in magnitude than a previous study which reported intra- and intersession analysis of bulk, zonal and regional T_2 values [4]. In evaluating session dependent T_2 values, Glaser et al. [4] acquired a series of 3D T_1 -weighted fast low-angle-shot water excitation images and a series of T_2 mapping images. The water excitation images were registered to the T_2 mapping images to optimize the overlap of anatomic structures. The transformed water excitation images were then used to define cartilage ROIs for T_2 calculations. This potentially time-intensive methodology resulted in a range of bulk patellar T_2 COV values of 2.76% to 5.37%. In addition, the zonal dependent patellar T_2 COVs were calculated as 4.68%, 3.89% and 3.92% for the superficial, middle and deep zones of cartilage, respectively. The zonal dependent patellar T_2 RMS errors were calculated as 1.95, 1.43 and 1.02 ms for the superficial, middle and deep zones of cartilage, respectively. These values calculated by Glaser et al. tend to be larger than our current observer dependent COV and RMS values. Interpretation of T_2 data with knowledge of intersession repeatability and interexaminer repeatability is important for the application of T_2 in a clinical setting. Combining our results with the results of Glaser et al. indicates that comparing scans across scanning sessions may have a greater effect on the

variability of calculated T_2 values than the effect of different examiners defining the cartilage ROIs for analysis.

The T_2 COV values compare well to studies which have used other imaging techniques to quantify OA. The COV for the current T_2 repeatability analysis ranged between 1.8% and 5.0%. Previous studies which used radiographs to evaluate joint space width measurements in the knee produced COVs ranging from 0.86% to 12% [24–27]. The COV of repeated cartilage volume measurements using MRI data has been reported to be 1.0–6.7% [28]. The similar magnitudes of intra- and interexaminer T_2 repeatability COV with these previous quantitative studies indicates the potential of using T_2 mapping to accurately track the progression of OA within diarthrodial joints.

The analysis of pixels common to each examiner indicated that one examiner typically defined slightly larger ROIs during image analysis. The average pixel count difference between the two examiners was relatively low — approximately 24 pixels. The pixel count difference may be attributed to the level of experience of the two examiners. We do not believe the pixel count difference adversely affected the T_2 repeatability analysis, since a majority of the pixels (>86%) were common to both examiners.

The current sample of subjects was composed of young healthy subjects asymptomatic for OA. It is likely that the resegmentation error would change if subjects with confirmed OA were evaluated. We would anticipate larger values for the coefficient of repeatability, COV and RMS errors for bulk and depth dependent T_2 values if OA were present within the joint [28].

This study provides one measurement of bulk and zonal T_2 mapping repeatability. The current results indicate good agreement between measurements by a single observer and between two observers. Additional studies which evaluate T_2 mapping repeatability of cartilage during OA or after cartilage repair are needed in order to provide support for T_2 mapping in the clinical environment.

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Fig. 1.

(Top) Representative patellar cartilage T_2 maps of a slice from one subject as processed separately by Examiners 1 and 2. There is a bulk T_2 value difference of 1.9 ms between the examiners. (Bottom) Pixels of each T_2 map are shown superimposed on one another. The overlapping portions of the regions of interest defined by Examiners 1 and 2 are shown in yellow. Pixels unique to Examiners 1 and 2 are shown in red and blue, respectively. The image shows that Examiner 1 defined a larger region of interest than Examiner 2, resulting in a different bulk T_2 value.

Fig. 2. Bland–Altman plots for bulk T_2 value intraexaminer repeatability (left) and interexaminer repeatability (right). The mean difference of each plot is shown as a solid line and the upper and lower limits of agreement are shown as dashed lines. The intraexaminer coefficient of repeatability is 2 ms, and the interexaminer repeatability is 2.8 ms.

Inter-Examiner Reproducibility of Zonal Patellar Cartilage T_2 Values

Fig. 3.

Bland–Altman plots of depth dependent T_2 value interexaminer repeatability for the superficial (left), middle (center) and deep (right) zones of cartilage. The mean difference of each plot is shown as a solid line and the upper and lower limits of agreement are shown as dashed lines. The middle and deep zones had greater measures of repeatability than the superficial zone.

Table 1

Repeatability of patellar cartilage T_2 values

Repeatability measurement	Cartilage zone	T_2 Difference (mean $\pm$ S.D.) (ms)	RMS error (ms)	Coefficient of repeatability (ms)	Coefficient of variability
Intraexaminer	Bulk	0.2 $\pm$ 1.0	0.7	2.0	1.9%
	Superficial	0.2 $\pm$ 1.9	1.3	3.7	3.1%
	Middle	0.1 $\pm$ 1.0	0.7	1.9	1.8%
	Deep	0.3 $\pm$ 1.1	0.8	2.1	2.5%
Interexaminer	Bulk	1.0 $\pm$ 1.4	1.2	2.8	3.3%
	Superficial	0.5 $\pm$ 3.0	2.1	5.8	5.0%
	Middle	0.9 $\pm$ 1.5	1.2	2.9	3.2%
	Deep	1.0 $\pm$ 1.3	1.2	2.5	3.7%