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Bias of Cartilage T₂ Values Related to Method of Calculation

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Abstract

Purpose—To determine how different methods for calculating T₂ affect the resulting T₂ values of patellar cartilage.

Materials and Methods—T₂-weighted images of patellar cartilage for 10 subjects were acquired using 2 MRI scanners. T₂ values of patellar cartilage were calculated using linear, weighted and non-linear fitting algorithms for a mono-exponential decay equation. T₂ values were also calculated for the superficial, middle and deep zones of the cartilage

Results—All three methods of calculation resulted in significantly different T₂ values ($p < 0.0001$). The weighted calculation produced the highest T₂ values and the non-linear calculation produced the lowest T₂ values. The average difference of T₂ value between the methods was under 5 ms. Similar results were found in a zonal analysis of the tissue. The non-linear calculation of T₂ consistently had the best fit to the acquired data.

Conclusion—The T₂ value of patellar cartilage depends on the method of calculation. It is unclear if larger T₂ value differences would be seen in subjects diagnosed with osteoarthritis. This study highlights the potential difficulty of comparing different studies to one another based on the method of T₂ calculation.

Keywords

Cartilage; T₂; osteoarthritis; patella; MRI

Introduction

Magnetic resonance imaging is a powerful tool for in-vivo evaluation of articular cartilage. MRI is a non-invasive and non-ionizing imaging modality capable of producing images of soft tissues in the human body. An additional benefit of MR images is the potential of high contrast between adjacent anatomy in the images. Several studies have previously investigated the diagnostic potential of MR images for detection of OA (osteoarthritis) (1,2). T₂-weighted images have been successful in identifying Outerbridge grades 3 and 4 chondromalacia, however, T₂-weighted images also tend to underestimate surface fibrillation and surface defects (1,2). Quantitative measures of cartilage quality in patients with OA may be beneficial for tracking disease progression (3,4). Change of the transverse relaxation time constant, T₂,

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of articular cartilage has been proposed as a medical imaging biomarker for OA (4). T_2 values of articular cartilage are dependent upon local water content and collagen fiber orientation (5). During the OA process, the water content of cartilage increases and the superficial fibers of the articular surface become fibrillated. Both of these factors lead to an increase of T_2 value.

Significant work has been performed evaluating T_2 values of articular cartilage in asymptomatic subjects (6) and subjects with OA (7), subjects of different age groups (8) and of different genders (9) at clinically relevant field strengths (1.5–3T). T_2 values have also been assessed for correlation with radiographic stage of OA (7) and joint space width (10). The intra- and inter-examiner repeatability of T_2 value calculation has also been performed (11). Additional work has been performed at high magnetic field strength (~7–9T) on in-vitro specimens examining regional differences of T_2 values of articular cartilage through the depth of the tissue and the magic angle effect on calculated T_2 values (12–14). Although a considerable amount of research of T_2 values has been performed, direct comparison of results from different studies may be difficult. For example, T_2 values are relatively insensitive to field strength, however a previous report found slightly lower T_2 values at higher field strengths (15). The T_2 values from an imaged volume may also differ depending on the image acquisition parameters for a single pulse sequence. Our laboratory currently uses a multi-slice multi-echo fast spin echo (FSE) sequence for T_2 quantification (16,17). With our scanning sequence, an increase of echo time (TE) will decrease the SNR of FSE images and an increase of echo train length (ETL) will increase the blurring of images (18). Notably, an additional factor which may influence the resulting T_2 value is the method which is chosen to calculate T_2 .

Different numerical methods for calculating cartilage T_2 values have been used in the literature. The most common method to calculate T_2 formulates a linear solution to a mono-exponential decay equation to solve for apparent spin density and T_2 value (6,9,12,14,16,19–22). Other studies have used a weighted method (16) or a non-linear least squares fitting method (8,23–25) for the same calculations. T_2 values may also be solved with a 3 parameter model (5) by using non-linear methods. The 3 parameter model uses a mono-exponential decay equation to fit echo time data to signal intensity data to solve for apparent spin density, T_2 and an offset value for signal intensity. The differences of resulting T_2 values and the interpretation of the variations from these four methods of calculation are unknown.

To the best of our knowledge, no studies have been performed using musculoskeletal MR data to evaluate how the method of T_2 calculation affects the resulting T_2 values. Therefore, the purpose of this study was to determine how different methods for calculating T_2 effect the resulting T_2 values of patellar cartilage. While previous investigators have commented on different sampling strategies for analysis (26), the focus of the current study was to evaluate different post-processing techniques for T_2 . We hypothesized the calculated T_2 values depend on the method of calculation when using images from a clinically relevant MR imaging protocol.

Methods

Subjects

Following local institutional review board (IRB) approval with informed consent, 10 male volunteers (30.6 ± 3.8 y.o., 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.

Data Acquisition

MR images of each subject's right patella were obtained using two separate 1.5T clinical scanners (GE Signa System, Milwaukee, WI). Six subjects were scanned using one scanner

and the remaining subjects were scanned using a second scanner. An MR compatible knee positioning device composed of plexiglass was used to center the knee within the MR scanners and to prevent knee motion during scanning. A dedicated transmit-receive knee coil was used for all imaging. A series of axial T₂-weighted images were acquired using a multi-slice multi-echo fast spin echo (FSE) pulse sequence (16). Images were acquired across 11 slice locations centered on the patella. Imaging parameters for T₂ mapping were: TR = 1500 ms, slice thickness = 2mm, slice spacing = 4mm, in-plane resolution = 0.49mm × 0.49mm, FOV = 12 cm × 12 cm, acquisition matrix = 256 × 160 (zero filled to 256×256), BW = 31.25 MHz, 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 ms – 62.53 ms with 7.82 ms increments. The TEs used for the second scanner was TE = 8.48 ms – 67.84 ms with 8.48 ms increments. The acquisition time for the T₂ mapping images was approximately 5 minutes. The series was acquired as part of an ongoing study in our laboratory which had a total imaging time of approximately 1 hour.

Data Analysis

Custom written software (MATLAB, Natick, MA) was used to calculate T₂ values using three different methods for each set of MR images obtained from each subject. Patellar cartilage was manually segmented at each slice location by the same individual for all subjects enrolled in the study. 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. A previous study has shown the intra- and inter-examiner repeatability of T₂ calculations to be 0.6 ± 2.4 ms and 0.7 ± 3.1 ms (mean ± st.dev.), respectively (11). On average, the segmentation took approximately 20 to 30 minutes each individual. Image slices at the proximal and distal poles of the patella were not included in the analysis due to potential volume averaging.

The T₂ value and apparent spin density (S₀) of patellar cartilage were calculated on a pixel-by-pixel basis by fitting the echo time (TE) data and the corresponding signal intensity (S) data at each TE to a mono-exponential decay equation:

$$S(TE_i) = S_0 \cdot e^{(-TE_i/T_2)} \quad (\text{eq. 1})$$

The characteristic equation of T₂ decay is a specific form of the generalized exponential equation:

$$y_i = A e^{Bx_i} \quad (\text{eq. 2})$$

with variables substituted as:

$$y_i = S(TE_i), x_i = TE_i, A = S_0, \text{ and } B = -\frac{1}{T_2} \quad (\text{eq. 3})$$

Equation 1 was solved for T₂ using three different computational algorithms: linearized least squares, weighted linearized least squares and non-linear least squares.

The linearized least squares method first takes the natural log of both sides of Equation 2 and a cost function is then defined as the sum of the residuals at each increment of x_i (27):

$$\Phi(\ln(A), B) = \sum_{i=1}^n \{\ln(y_i) - \ln(A) - Bx_i\}^2 \quad (\text{eq. 4})$$

The partial derivatives of equation 4 with respect to $\ln(A)$ and B are obtained, set equal to zero, and are solved simultaneously to obtain the final solution for the linearized least squares method:

$$\ln(A) = \frac{\sum_{i=1}^n x_i^2 \sum_{i=1}^n \ln(y_i) - \sum_{i=1}^n x_i \sum_{i=1}^n x_i \ln(y_i)}{n \sum_{i=1}^n x_i^2 - \left(\sum_{i=1}^n x_i \right)^2} \quad (\text{eq.5})$$

and

$$B = \frac{n \sum_{i=1}^n x_i \ln(y_i) - \sum_{i=1}^n x_i \sum_{i=1}^n \ln(y_i)}{n \sum_{i=1}^n x_i^2 - \left(\sum_{i=1}^n x_i \right)^2} = -\frac{1}{T_2} \quad (\text{eq.6})$$

The weighted linear least squares method is similar to the linear least squares method described above however, a weight factor is assigned at each increment of x_i . This is performed since a linearized fitting gives greater weights to data points which have small values of y_i . The cost function for the weighted curve fitting is defined by the residuals of the data and best fit line as:

$$\Phi(\ln(A), B) = \sum_{i=1}^n w_i \{ \ln(y_i) - \ln(A) - Bx_i \}^2 \quad (\text{eq.7})$$

where w_i is the assigned weight factor at each increment of x_i . The partial derivatives of Equation 7 with respect to $\ln(A)$ and B are obtained, set equal to zero, and are solved simultaneously to obtain the final solution for the weighted linear least squares method (28):

$$\ln(A) = \frac{\sum_{i=1}^n x_i^2 w_i \sum_{i=1}^n w_i \ln(y_i) - \sum_{i=1}^n x_i w_i \sum_{i=1}^n w_i x_i \ln(y_i)}{\sum_{i=1}^n w_i \sum_{i=1}^n x_i^2 w_i - \left(\sum_{i=1}^n x_i w_i \right)^2} \quad (\text{eq.8})$$

and

$$B = \frac{\sum_{i=1}^n w_i \sum_{i=1}^n w_i x_i \ln(y_i) - \sum_{i=1}^n x_i w_i \sum_{i=1}^n w_i \ln(y_i)}{\sum_{i=1}^n w_i \sum_{i=1}^n x_i^2 w_i - \left(\sum_{i=1}^n x_i w_i \right)^2} = -\frac{1}{T_2} \quad (\text{eq.9})$$

The selection of the numerical value assigned to the weight may be chosen by the user. If the weights are selected as:

$$w_i = 1/\sigma^2(\ln(y_i)) \quad (\text{eq.10})$$

where $\sigma^2(\ln(y_i))$ is the variance of $\ln(y_i)$, then Equations 8 and 9 become the χ^2 best-fit to the data, resulting in an optimal solution for $\ln(A)$ and B (29). For our study, the weights were taken to be the squared signal intensity measured at each TE (30).

The third method used was a non-linear least squares solution to Equation 1 (31). Unlike the previous two methods of solution, the natural log of both sides of the equation was *not* performed to linearize the equation. The cost function to be minimized is defined as:

$$\Phi(A, B) = \sum_{i=1}^n \{ y_i - A e^{Bx_i} \}^2 \quad (\text{eq.11})$$

In this case, the cost function is only a function of A and B . The cost function is minimized by setting the partial derivatives of $\Phi(A, B)$ with respect to A and B equal to zero, and simplifying to:

$$\sum_{i=1}^n y_i e^{Bx_i} - A \sum_{i=1}^n e^{2Bx_i} = 0 \quad (\text{eq.12a})$$

$$\sum_{i=1}^n x_i y_i e^{Bx_i} - A \sum_{i=1}^n x_i e^{2Bx_i} = 0 \quad (\text{eq.12b})$$

The resultant equations are non-linear in the unknown variables A and B. Initially, the LSQNONLIN function in the MATLAB optimization toolbox was used to solve iteratively for T_2 using the Levenberg-Marquardt algorithm. This optimization method of solution was a computationally time consuming process for a pixel-by-pixel analysis for multiple regions of interest (ROIs). We subsequently implemented an algorithm published by Li and Hornak for the non-linear T_2 calculations (32). The algorithm reduced the non-linear solution for T_2 to a single working equation:

$$Z(T_2) = \sum_{i=1}^n \sum_{j=1}^n [S_i e^{-TE_i/T_2} TE_j e^{-2TE_j/T_2} - S_j TE_j e^{-TE_j/T_2} e^{-2TE_i/T_2}] \quad (\text{eq.13})$$

where $S_i = S(TE_i)$, from Equation 1. The location at which $Z(T_2) = 0$ is the T_2 value for the defined dataset. The single zero of this function may be solved using a standard bisection method algorithm (33). We found the method of Li and Hornak to be significantly faster than the LSQNONLIN function. In addition, the Li and Hornak method calculated T_2 values were nearly identical to the Levenberg-Marquardt algorithm during initial tests. The maximum difference of T_2 value (re-analysis error) was typically less than 0.05 ms (Figure 1). All non-linear T_2 values for this study were calculated using the method of Li and Hornak as a result of the reduced calculation time and minimal difference of calculated T_2 values.

The coefficient of determination (R-squared value) was calculated for all methods of T_2 calculation as a measure of goodness of fit of the method of solution (34). R-squared ranges from 0.0, indicating a poor fit of the data, to 1.0, indicating a perfect fit to the data.

For each algorithm, patellar cartilage pixels with T_2 values greater than 200 ms were considered outliers and were excluded from statistical analysis (35). The percentage of pixels considered outliers for a whole patella was typically less than 0.5% of all of the pixels analyzed. An average bulk T_2 value and bulk R-squared value generated from all analyzed pixels of each patellar image slice for each of the three methods described was used for statistical analysis.

An automated program was used to separate the cartilage of each image into deep, middle and superficial zones (7). The deep zone was considered as 0%–30% of depth of the tissue, the middle zone was considered as 30%–70% depth of the tissue and the superficial zone was considered as 70%–100% depth of the tissue (36). An average T_2 value and R-squared value generated from pixels in each zone was used for a regional statistical analysis.

Noise Analysis

An initial analysis was performed to evaluate the signal to noise ratio (SNR) of the images of the entire dataset. SNR was calculated as the mean signal intensity of cartilage pixels divided by the standard deviation of the signal intensity located outside the imaged knee anatomy (18). The results of the SNR analysis are shown in Table 1. A subset of 160 images (8 echo images for 20 image slices) from the total dataset were used to determine the effect of noise on calculated T_2 values when using the linear, weighted and non-linear methods. Since the average SNR of all echo images was > 3 units, each of the 20 image slices had random Gaussian noise added to each of the 8 echo images (37). The noise data was generated from a normal distribution with a mean of zero and standard deviation of 0, 10, 20, and 30 units. Random Gaussian noise of the same standard deviation was applied to each echo image, and the T_2 calculations were repeated using the same ROIs previously used from the initial analysis.

Statistical Analysis

An initial two-tailed t-test was performed to determine if T_2 values calculated using images from the two separate scanners were similar. No differences of T_2 values were found for all methods of calculation: $p=0.38$ for the linear calculation, $p=0.81$ for the weighted calculation

and $p=0.52$ for the non-linear calculation. Due to the lack of systematic bias of the T_2 values from both scanners, the two datasets were combined for subsequent statistical analyses.

A one-way repeated measures analysis of variance (ANOVA) was performed to determine the effect of method of calculation on bulk T_2 value. In addition, a two-way repeated measures ANOVA was performed to determine the effects of cartilage zone and method of calculation on resulting T_2 value. These one-way and two-way ANOVAs were repeated using the R-squared values of the curve fits. In addition, a two-way repeated measures ANOVA was performed to determine the effect of the level of noise standard deviation and method of T_2 calculation on the resulting T_2 values. Significance for all statistical tests was set at $p < 0.05$. A Student-Neuman-Keuls (SNK) multiple comparison test was performed when statistical significance was achieved in the ANOVA tests (SAS Institute, Inc.)

The power of the study was calculated using a custom written MS Excel worksheet. For simplicity, the power analysis was based on a pairwise comparison of means using a paired t-test using a type I error of 0.05 and a two sided test of hypothesis. The harmonic mean and weighted standard deviation of the linear T_2 values and non-linear T_2 values were calculated (38) and used in the power analysis. We selected these groups for the power analysis based on the minimal difference between their group mean values to give the lower limit of power of the study. The sample size of our study enabled us to detect a 1.3 ms difference of T_2 values between the methods of calculation with a power of 80%.

Results

The method of calculation had a significant effect on calculated bulk T_2 value ($p < 0.0001$). All three methods of T_2 calculation resulted in significantly different T_2 values. The non-linear calculation resulted in the lowest T_2 values (37.7 ± 4.1 ms, mean $\pm$ st.dev.), the weighted calculation resulted in the highest T_2 values (42.2 ± 4.0 ms), and the linear calculation resulted in intermediate T_2 values (38.8 ± 3.3 ms, Figure 2).

The method of calculation also significantly affected the bulk R-squared values ($p < 0.0001$). The non-linear solution resulted in the best curve fittings and was significantly better than the weighted solution. Furthermore, the weighted solution had a significantly better fit to the data than the linear solution (Figure 3).

The statistical results for the zonal analysis were similar to the results for the bulk analysis (Table 2). T_2 values were significantly different by the method of calculation ($p < 0.0001$) as well as tissue depth ($p < 0.0001$). There was a significant interaction of these effects, $p < 0.0001$. All three methods of T_2 calculation resulted in significantly different T_2 values. The non-linear calculation resulted in the lowest T_2 values and the weighted calculation resulted in the highest T_2 values (Table 2). All three zones of patellar cartilage had significantly different T_2 values. The superficial cartilage layer had the highest T_2 values and the deep cartilage layer had the lowest T_2 values.

The two-way ANOVA demonstrated that the R-squared values were significantly affected by the method of calculation ($p < 0.0001$) and tissue depth ($p < 0.0001$). There was a significant interaction of these effects, $p < 0.0001$. The non-linear solution resulted in a significantly better fit to the data than the weighted solution and the weighted solution had a significantly better fit to the data than the linear solution. The curve fittings of the deep and middle zones were significantly better than curve fitting in the superficial zones.

Although the interaction between type of calculation and depth of cartilage for T_2 and R-squared values was statistically significant, closer examination of factor interaction plots

revealed that this interaction was quantitatively small: < 1.5 ms for T_2 values and < 0.016 units for R-squared values.

Finally, the two-way repeated measures ANOVA for analyzing the effect of noise on T_2 values found the standard deviation of the noise to significantly affect the resulting T_2 values ($p < 0.0001$). Similarly, the method of T_2 calculation was significant ($p < 0.0001$), as was the interaction of these two factors ($p < 0.0001$). Further investigation found the increase in magnitude of T_2 due to noise was < 1 ms. The magnitude of differences due to method of calculation were similar to the results from the larger (entire) dataset. An interaction plot of method of calculation versus applied noise indicated small increase of T_2 due to these two factors, < 1 ms, even though the interaction was significant.

Discussion

Our laboratory is interested in determining the applicability of cartilage T_2 values and cartilage T_2 maps in a clinical setting. This study evaluated how different methods of calculating T_2 values may alter the T_2 values. Based on the results reported in this study, the method of calculation significantly affects the resulting T_2 value. A weighted calculation results in higher T_2 values than a linear or a non-linear method, and a linear calculation results in higher T_2 values than a non-linear method. In addition, the non-linear method resulted in the best fitting of a mono-exponential decay curve to the dataset rather than the weighted or linear methods.

Previous investigators have calculated MR time constants using the ratio of signal intensities at two TE values (39) or with multiple TEs and multiple TRs (26,40). These methods may increase the accuracy of the time constant calculation; however, the time requirement for image acquisitions at each slice location for multiple TRs may not be feasible during a normal clinical exam. The scanning time for this study was approximately 5 minutes. We feel that the time requirement of this scanning series is suitable to incorporate T_2 mapping into a clinical exam without eliminating other scanning series due to time constraints. It may be beneficial to determine how calculating T_2 using acquisitions with multiple TEs and TRs influence the clinical interpretation of the T_2 values.

Other studies have calculated T_2 differently based on image datasets with multiple TEs. Additional post-processing methods for calculating T_2 include using a bi-component model (41–43) or a Gaussian distribution model (42). Modeling cartilage T_2 using a bi-component model may require a large number of echo images to distinguish short and long components of cartilage T_2 , while a Gaussian model of signal decay requires considerable computational time and may not be feasible clinically (42).

Investigators have also used the method of non-negative least squares (NNLS) to map a spectrum of T_2 values (44). In this method, a range of initial T_2 values are required for the NNLS optimization to solve for the apparent spin density of each value of T_2 . This method requires a large dataset spanning a wide range of TEs to accurately calculate the magnitude of spin density for each distinct T_2 value. In addition, data interpretation would prove difficult due to the user dependent selection and distribution of T_2 values.

The present study used a fast spin echo (FSE) pulse sequence for image acquisition and T_2 calculations (16) while previous investigators have commonly used a spin echo (SE) pulse sequence (22,45,46). The reduced scanning time afforded by an FSE versus an SE sequence is a clear benefit for scanning in a clinical setting, but the FSE sequence has potential for the formation of stimulated echos. The accumulation of stimulated echos has been shown to artificially increase calculated T_2 values (16). The increase of T_2 values using an FSE sequence was confirmed on our scanning equipment using a T_2 phantom composed of agarose doped with varied amounts of copper sulfate. Although the FSE sequence may result in higher T_2

values, examining the *accuracy* of the T_2 values was not the focus of the present study. Rather, we focused on the *measurement bias* of the T_2 values when using a multi-slice multi-echo FSE pulse sequence for image acquisition.

Several assumptions were made for calculating T_2 values in this study. We assumed no movement of the subject during scanning, ideal RF and slice selection pulses, uni-exponential T_2 relaxation of cartilage, uniformity of the B_0 field, lack of partial volume effects, and the absence of systematic errors during image acquisition (47). All of these factors must be considered when determining the accuracy of the calculated T_2 . Currently, our interest was focused on examining different post-processing methods for T_2 . Any error associated with image acquisition or reconstruction would be present in all of the post-processing methods when solving for T_2 .

Our results indicate it may difficult to directly compare T_2 values from one study to another based on the method of T_2 calculation. Furthermore, it is possible for studies which use T_2 mapping as a quantitative measure of cartilage health to have different statistical results based on the method of calculation. The maximum difference of T_2 values in this study was found between the non-linear and weighted methods of calculation. The average difference between these two methods was 4.5 ms. The results also indicate that the T_2 analysis methods in are robust to noise, with little change in the resulting magnitude of the calculated T_2 value.

Previous studies which evaluated the effect of exercise (22) or alternative loading of joint cartilage (48,49) using scan-rescan protocols found differences of T_2 on the order of 0.6 ms to 9.6 ms. Two of these studies used the linear fitting method for calculating T_2 (22,48) while the method used by the third study was unspecified (49). It is uncertain if a non-linear solution for T_2 may alter the findings of these studies. Investigators should clearly indicate which method of T_2 calculation was used in a study. The calculation methods used in this study were straight forward and may be implemented easily in numerous programming languages. Furthermore, the results of this study are important for examining T_2 of cartilage as a biomarker for OA.

The different post-processing methods for T_2 calculation may result in different clinical interpretation of OA on a subject-by-subject basis. For example, elevated T_2 values have been found associated with advanced degeneration of articular cartilage (46). Using a non-linear method to solve for T_2 may result in a lower T_2 value and underestimate the amount of degeneration. In addition, it is unclear how the results would change in subjects diagnosed with OA.

This study demonstrates the method chosen to calculate patellar cartilage T_2 values significantly influences the resulting T_2 value. Our future work will continue to focus on examining different factors which affect cartilage T_2 values, as well as the applicability and interpretation of cartilage T_2 mapping in a clinical environment.

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Figure 1.

A Bland-Altman plot comparing pixel-by-pixel differences of patellar cartilage T_2 values from one subject enrolled in the study. T_2 values were calculated with non-linear optimization (T_{2opt}) and the method of Li and Hornak (T_{2nl}) (32). The mean $\pm$ std of differences is $-0.0001 \text{ ms} \pm 0.0019 \text{ ms}$, with upper and lower limits of agreement of 0.004 ms and -0.004 ms , respectively, as indicated by the dashed lines. Maximal differences between the two methods of calculation were less than 0.05 ms .

Figure 2.

Bar plot of mean $\pm$ st. dev. of T₂ values by method of calculation. All three methods of T₂ calculation resulted in significantly different T₂ values. The non-linear calculation resulted in the lowest T₂ values.

Comparison of R-Squared Values By Method of Calculation

Figure 3.

Bar plot of mean $\pm$ st. dev. of R-squared values by method of calculation. All three methods of T_2 calculation resulted in significantly different R-squared. The non-linear calculation resulted in the best fit solution of T_2 than the weighted or linear calculation methods.

Table 1

SNR of Image Data

Echo Number	SNR
1	17.3 ± 3.1
2	13.8 ± 2.3
3	10.0 ± 1.8
4	8.26 ± 1.4
5	6.4 ± 1.1
6	5.4 ± 1.0
7	4.3 ± 0.8
8	3.8 ± 0.7

Note: SNR values expressed as mean ± st.dev.

Table 2**T₂ and R-Squared Values By Cartilage Depth**

Depth of Patellar Cartilage	Method of Calculation	T ₂ (ms) [†] (Ave. ± St.Dev.)	R-Squared [‡] (Ave. ± St. Dev.)
Superficial	Linear	42.7 ± 4.6	0.858 ± 0.032
	Weighted	46.7 ± 5.2	0.864 ± 0.031
	Non-Linear	42.5 ± 5.4	0.882 ± 0.023
Middle	Linear	38.7 ± 4.5	0.863 ± 0.028
	Weighted	42.7 ± 5.1	0.872 ± 0.029
	Non-Linear	38.5 ± 5.2	0.891 ± 0.022
Deep	Linear	33.7 ± 3.2	0.855 ± 0.035
	Weighted	36.9 ± 4.0	0.868 ± 0.036
	Non-Linear	32.3 ± 4.2	0.895 ± 0.024

[†]Note: T₂ values were significantly different by method of calculation at each tissue depth (p<0.001)

[‡]Note: R-Squared values were significantly different by method of calculation at each tissue depth (p<0.0001)