



Published in final edited form as:

Magn Reson Imaging. 2008 November ; 26(9): 1215–1220. doi:10.1016/j.mri.2008.02.017.

A comparative study at 3 Tesla of sequence dependence of T₂ quantitation in the knee

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Abstract

Objective—T₂ mapping has been used widely in detecting cartilage degeneration in osteoarthritis. Several scanning sequences have been developed in the determination of T₂ relaxation times of tissues. However, the derivation of these times may vary from sequence to sequence. This study seeks to evaluate the sequence dependent differences in T₂ quantitation of cartilage, muscle, fat and bone marrow in the knee joint at 3 Tesla.

Methods—Three commercial phantoms and ten healthy volunteers were studied using 3T MR. T₂ relaxation times of the phantoms, cartilage, muscle, subcutaneous fat, and marrow were derived using spin echo (SE), multi-echo spin echo (MESE), fast spin echo (FSE) with varying echo train length (ETL), spiral, and spoiler gradient (SPGR) sequences. The differences between these times were then evaluated using a student's t-test. In addition, the SNR efficiency and coefficient of variation of T₂ from each sequence were calculated.

Results—The average T₂ relaxation time was 36.38 ± 5.76 ms in cartilage and 34.08 ± 6.55 ms in muscle, ranging from 27 to 45 ms in both tissues. The times for subcutaneous fat and marrow were longer and more varying, ranging from 41 to 143 ms and 42 to 160 ms, respectively. In FSE acquisition, relaxation time significantly increases as ETL increases (P < 0.05). In cartilage, the SE acquisition yields the lowest T₂ values (27.52 ± 3.10 ms), which is significantly lower than those obtained from other sequences (P < 0.002). T₂ values obtained from spiral acquisition (38.27 ± 6.45 ms) were higher than those obtained from MESE (34.35 ± 5.62 ms) and SPGR acquisition (31.64 ± 4.53 ms). These differences, however, were not significant (P > 0.05).

Conclusion—T₂ quantification can be a valuable tool for the diagnosis of degenerative disease. Several different sequences exist to quantify the relaxation times of tissues. Sequences range in scan time, SNR efficiency, reproducibility, and 2D or 3D mapping. However, when choosing a sequence for quantitation, it is important to realize that several factors affect the measured T₂ relaxation time.

Keywords

Magnetic Resonance Imaging; T₂; quantitation; articular cartilage

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Introduction

Osteoarthritis (OA) is a degenerative disease that results in morphological and biochemical changes in tissues of the joint, including cartilage, subchondral bone and bone marrow. In cartilage, it has been shown that biochemical changes in the proteoglycan and collagen matrix can precede morphological changes that happen at later stages of the disease. Therefore, detecting biochemical changes and small intracartilagenous lesions are critical for diagnosing OA and monitoring the disease progression as well as for evaluating therapeutic procedures.

Magnetic Resonance Imaging (MRI) has proven to be a useful non-invasive tool in imaging joint diseases. It provides multi-planar capabilities, high spatial resolution, and superior sensitivity to soft-tissue details. In addition to detecting structural changes, advanced MRI techniques have been shown to have the potential of probing biochemical changes in the tissue. In particular, spin-spin or T_2 relaxation times, have been correlated with increase of water contents and damage to collagen network in cartilage during osteoarthritis (1–4).

Although T_2 quantitation has been widely used in clinical trial due to its potential correlation with cartilage biochemistry, different scan sequences and acquisition parameters can result in different measured relaxation times. In order to develop a platform from which to diagnosis disease based on relaxation time, it is essential to identify how the quantitation of T_2 relaxation times of musculoskeletal tissues varies as different scanning parameters are used.

There are several factors that can affect T_2 quantification. Insufficient sampling of the T_2 decay curve, RF and static field inhomogeneities, stimulated echoes, and T_1 effects can all attribute to the incorrect quantitation of in vivo relaxation times (5). Currently the most commonly used T_2 quantification sequences are spin-echo (SE) and fast spin-echo (FSE) sequences (6). Several pulse sequences have been developed in the determination of T_2 relaxation times in musculoskeletal system. These sequences include the multi-echo spin-echo (MESE) sequence (7) and spiral sequence (8). Additionally, T_2 relaxation time appears to decrease slightly as the magnitude of static magnetic field increases (8,9). Although many clinical MR scanners operate at 1.5 T, 3.0 T scanners are becoming more prevalent in the clinical setting. Studies show an increase of signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) efficiencies as static magnetic field increases (8,10,11). Therefore, a high-field quantitation carries with it the advantage of increased sensitivity.

Even though the differences in T_2 quantification using different sequences and parameters are known, comparisons of T_2 values based on different sequences are very limited. Maier et al (7) and Mendlik et al (12) have compared T_2 quantification based on SE and several multi-echo (ME) sequences at 1.5 T. To the best of our knowledge, no previous studies have systematically investigated measurement differences (T_2 values, SNR and reproducibility) using sequences mentioned above (SE, FSE, MESE and spiral). In addition, with the increasing application of 3 T scanners in clinical settings, it is important to document tissue T_2 relaxation times differences at this field strength.

All of the sequences mentioned are two dimensional (2D) acquisitions. A 3D acquisition may be desired, however, in T_2 relaxation time quantitation. Three-dimensional imaging is free from artifacts caused by slice crosstalk. Therefore 3D sequences can generally have a thinner slice thickness, and consequently may provide a more accurate assessment of tissue relaxation properties.

The goal of this study was therefore twofold: 1) to evaluate the consistency of T_2 quantification in healthy musculoskeletal tissues, including cartilage, muscle, bone marrow and subcutaneous fat, in the knee using different sequences at 3.0 Tesla, including SE, FSE, MESE and spiral

acquisition; 2) to evaluate a new 3D T_2 quantitation method, and to compare the results with currently available 2D sequences.

Materials and Methods

Phantoms and Subjects

Three commercial cylindrical T_2 phantoms (Diagnostic Sonar, Livingston, UK) with different T_2 values spanning the expected relaxation times of tissues of interest were studied. Each phantom was scanned from three to four times to investigate the reproducibility and quantification accuracy for each sequence. The phantoms were repositioned between scans at different location (center, left or right to the isocenter of the scanner).

The right knees of 10 healthy volunteers (6 males, 4 females, ages 21–31 years, mean age 27 years) were studied. All of the subjects had no clinical knee OA symptoms or other knee injuries. All of the volunteers provided informed consent in accordance with the rules by the Committee on Human Research at our institution.

All scans were implemented on a 3.0 T GE Excite Signa MR scanner (Waukesha, WI, USA) using a quadrature transmit/receive knee coil (Clinical MR Solutions, Brookfield, WI, USA).

Imaging Protocol

Phantoms and subjects were scanned using 7 separate sequences in axial plane: a spiral acquisition with a T_2 preparation sequence (8), a multi-echo multi-slice spin echo sequence (7), a single-echo spin echo sequence, a fast spin echo sequences with varying echo train lengths (ETL = 4, 8, 16) and a 3D T_2 quantification based on spoiled gradient echo (SPGR) acquisition developed in this study. The acquisition parameters for each sequence are described in detail as follows:

The T_2 preparation of the spiral sequence was consisted of a 90 tip-down pulse, a train of equally spaced 180 pulses, and a (−90) tip-up pulse. Different TEs were generated by changing either the number of the 180 pulses or the interval between the 180 pulses (8). The acquisition parameters for the spiral sequence were: TR/TE = 2000/6.61, 17.26, 27.92, 49.25 ms, 14 interleaves/slice, 4096 points/interleaf, FOV = 14 cm, effective in-plane resolution = 0.6×0.6 mm, slice thickness = 4 mm, skip = 4 mm, number of slices = 14–16. The total acquisition time was approximately 11 min.

The acquisition parameters for the MESE were: TR/TE = 2000/7.84, 15.68, 23.52, 31.36, 39.2, 47.04, 54.88, 62.72 ms, matrix = 256×192 , with all other parameters the same as the spiral sequence. Total acquisition time was approximately 9 min.

The acquisition parameters for the SE sequence were: TR/TE = 2000/16.9, 33.8, 50.7, 67.6 ms, matrix = 256×256 with all other parameters the same as the MESE sequence. Total acquisition time was approximately 9 min.

The TR/TE and acquisition time for the FSE of ETL 4, 8, and 16 were 2000/15.26, 30.52 ms, 5 min; 2000/15.26, 45.79 ms, 2 min; 2000/15.26, 76.32 ms, 1 min respectively. Only two echoes were acquired in FSE sequences due to limitation of the FSE sequence on the scanner. Large slice gap (4mm) was prescribed for all the 2D sequences in order to minimize quantification inaccuracy caused by potential cross-talk artifact. The matrix size was 256×256 .

The T_2 quantitation sequence based on 3D SPGR was composed with two parts: a nonselective T_2 preparation and a 3D SPGR acquisition in an elliptic-centric trajectory in segmented k-space. The T_2 preparation sequence was the same as what was used in the spiral T_2 sequence.

The data was acquired right after the T_2 preparation, during the transient signal evolving towards the steady state. The number of α pulses after each T_2 magnetization preparation was defined as views per segment (VPS). There was a relatively long delay (time of recovery, T_{rec}) between each magnetization preparation to allow enough and equal recovery of the magnetization before each $T_{1\rho}$ preparation. The acquisition parameters were: TR = 9.3 ms, $T_{rec} = 1.5$ s, TE = 6.61, 17.26, 27.92, 49.25 ms, flip angle = 12, bandwidth = 31.25 KHz, matrix = 256×256 , slice thickness = 4mm, NEX = 1, VPS = 48. The total acquisition time was approximately 10 min.

Image Post-Processing

Images were transferred to a Sun workstation (Sun Microsystems, Palo Alto, CA) for off-line post-processing. Regions of Interest (ROIs) were drawn around tissues of marrow, muscle, subcutaneous fat, and cartilage in slices where they were largest, as seen in Figure 1. For the cartilage tissue, the ROI was drawn in the slice where the patellar cartilage was the thickest. The marrow ROI was drawn in the slice with the largest femoral bone area. Similarly, subcutaneous fat and muscle ROIs were drawn where their regions were the largest. In order to minimize the effects of chemical shifts, JJ coupling effects, and changes in magnetic susceptibility on signal intensities, care was taken to insure that ROIs were not drawn in regions of the interfaces between the tissue being measured and surrounding tissue. Figure 1 shows the image of one knee with typical definition of ROI of these tissues.

A T_2 map was reconstructed by fitting the image intensity pixel-by-pixel to the equation below using a Levenberg-Marquardt mono-exponential fitting algorithm developed in-house:

$$S \propto e^{-(TE/T_2)} \quad (1)$$

We ignored the relaxation times derived from the spiral and SPGR sequences in the subcutaneous fat and marrow regions because the spiral sequence contains a spectral-spatial pulse which suppresses signal in fat, and similarly, our SPGR sequence also contains fat suppression.

Statistical Analysis

Mean, Median, and Standard Deviations of T_2 values were calculated for each tissue. A student's t-test was used to compare the relaxation times acquired with different sequences. The Coefficient of Variance (CV) was also calculated across each tissue and across all sequences using the formula:

$$CV = \frac{SD(M_1, M_2, \dots, M_k)}{Mean(M_1, M_2, \dots, M_k)} \quad (2)$$

where M_i = Mean T_2 relaxation time of the i^{th} subject for a particular tissue

The Signal to Noise Ratio (SNR) efficiency was evaluated using the formula:

$$SNR \text{ efficiency} = \frac{SNR}{\sqrt{\text{Total Imaging Time}}} \quad (3)$$

where $SNR = \frac{\text{Mean Tissue Signal}}{SD \text{ of noise}}$

Because there were different voxel sizes among the sequences, SNR was normalized to voxel size.

Results

Phantom

The average CV of T_2 quantification was lower than 8% in all three phantoms for all sequences, showing a good overall reproducibility, as seen in Table 1. After combining data from different sequences, the average CV was the highest (5.6%) in phantom #3, indicating the worst reproducibility. This phantom has the longest T_2 relaxation time (103 ms) and the longest T_1 relaxation time (926 ms). A high CV of 13.6% was observed in the FSE sequence with ETL = 16 in this phantom. After combining data from different phantoms, the average CV was the lowest in the MESE (1.3%) and SPGR (1.3%) acquisitions, and the highest in the FSE acquisition with ETL = 16 (6.7%).

Figure 2 shows the T_2 quantitation by different sequences in the phantoms as compared with the T_2 relaxation times provided by the manufacturer. The SE acquisition significantly underestimated the T_2 values. The average underestimate of the three phantoms was -21.0%. The T_2 values obtained with FSE sequences increased with ETL, showing a 6.8%, 13.6% and 20.9% average overestimate by using the sequence with ETL = 4, 8 and 16, respectively. The T_2 quantitation with MESE, spiral and SPGR show relatively good accuracy, with an average underestimate of -1.5%, -4.4% and -5.8% respectively. The quantitation of phantoms did not depend on their placements within the magnet bore.

In vivo

The average cartilage T_2 relaxation time is 36.38 ± 5.76 ms from all subjects ranging from 27 to 45 ms. The average muscle T_2 times is 34.08 ± 6.55 ms, ranging from 27 to 45 ms. The times for subcutaneous fat and marrow were longer and more varying, ranging from 41 to 143 ms and 42 to 160 ms, respectively. The T_2 relaxation times obtained from each sequence are shown in Figure 3.

As ETL increases, the relaxation time of cartilage in the FSE acquisitions increases, as shown in figure 3(a). This trend was the same as that in phantoms. There was a significant difference ($P = 8.4 \times 10^{-7}$) between the FSE with ETL = 4 (37.25 ± 5.01 ms) and the FSE with ETL = 8 (41.08 ± 5.07 ms). There was also a significant difference ($P = 1.7 \times 10^{-6}$) between the FSE with ETL 8 (41.08 ± 5.07 ms) and the FSE with ETL = 16 (44.59 ± 5.50 ms).

In cartilage, the SE acquisition yields the lowest T_2 values (27.52 ± 3.10 ms), which is significantly lower than those obtained from other sequences ($P < 0.002$). T_2 values obtained from the spiral sequence (38.27 ± 6.45 ms) were higher than those obtained from MESE (34.35 ± 5.62 ms) and SPGR acquisition (31.64 ± 4.53 ms). These differences, however, were not significant ($P > 0.05$).

T_2 relaxation times in muscles were lower than those in cartilage, while the values in marrow and subcutaneous fat were higher than those in cartilage. A similar trend of T_2 relaxation time values using different sequences were observed in these tissues, as indicated in Figure 3(a) and (b).

The SNR efficiency was the greatest in the FSE sequence with ETL = 16 for all tissues, except for muscle, where the MESE sequence maintained the greatest SNR efficiency. In all tissues, the SE sequence maintained the lowest SNR efficiency, as shown in Figure 4.

The CV in all sequences were all below 8%, as seen in Table 1. The highest CV, 12.3%, was observed in subcutaneous fat using the Fast Spin Echo sequence with 4 echoes. The lowest CV was observed in marrow, 0.7%, using the MSME sequence. In cartilage, the lowest CV was observed using the SPGR sequence. The spiral, SE, and MESE sequences produced similar CVs, but the FSE sequences produced the worst CVs.

Discussion

In this study, different sequences were used to quantify T_2 relaxation time at 3T in musculoskeletal tissues, including cartilage, muscle, bone marrow and subcutaneous fat. A new 3D T_2 mapping technique based on SPGR sequence was also proposed. The T_2 relaxation time for each tissue or phantom was different for the different sequences. However the magnitude and the direction of sequence dependent difference between the T_2 times were consistent across all tissues. For example, SE gives lowest T_2 times for all tissues and FSE with 16 echoes gives the highest times. The FSE sequences tend to overestimate T_2 relaxation time for all tissues.

In the Spin Echo sequence, we found a correspondence to previously reported values, except for the times found for subcutaneous fat (13). In this study, subcutaneous fat was a 38.8% lower than previously reported values. However, this discrepancy could be attributed to our lower TR and lower number of echoes in the SE sequence.

The MESE sequence yielded an increase in relaxation times of tissues, when compared with the SE sequence. An increase of 24.8% was seen in cartilage. This increased T_2 relaxation time of MESE corresponds to the results in a previous study at 1.5T (7) where the authors observed a 10–13% increase in T_2 using MESE sequences. The increased T_2 values may be due to stimulated echoes generated in the multi-echo sequences. In this study, however, we also observed a significant underestimation of T_2 values when compared with the known relaxation times provided by the manufacturer of the phantoms. Potential reasons of this underestimation include the imperfect slice profile in the SE sequence and the limited number of echoes.

One consistent trend in the determination of T_2 relaxation times is the increase of measured T_2 time as echo train length of the fast spin echo sequence increases. The fast spin echo sequence was part of an existing pharmaceutical protocol, which prompted us to test its performance. The estimated higher T_2 values that we show with FSEs in phantoms and cartilage is consistent with the literature (6). Utilizing the student's t test, the mean relaxation time of fast spin echo with 8 echo train lengths is significantly higher than fast spin echo with 4 echo train lengths in all tissues. Similarly, fast spin echo with 16 echo train lengths is significantly higher than fast spin echo with 8 echo train lengths in all tissues. Our FSE results correlate with the literature regarding slower T_2 decays, resulting in abnormally high signal intensities in later echoes due to stimulated echo pathway created by the imperfect refocusing pulses in a multi-echo sequence (5,7,14). Other factors that affect the quantification accuracy in a multi-echo sequence include static field inhomogeneities and the error propagation introduced by off-resonance effects (15).

The relaxation times of cartilage and muscle in the spiral sequence correspond to findings in the literature with a study implemented at 3T (8). However, there is a significant difference between spin echo T_2 for marrow and fat compared to T_2 measured using fast spin echo and spiral sequences. This could be due to the unsaturated fat and saturated fat interactions, J-J coupling, in the preparatory part of the sequences modulating the T_2 estimate. This clearly warrants further investigation.

A 3D T_2 mapping technique based on SPGR acquisition has been proposed in this study. The data acquisition is right after the T_2 magnetization, during the transient signal evolution towards

the steady state. Thus acquiring data using centrally reordered phase encoding is critical so that the low spatial frequencies are sampled first. Although its SNR efficiency was mediocre when compared to other sequences, it achieved the lowest CV for the cartilage and muscle tissues. Three-dimensional T₂ mapping may allow us to have thinner slices compared with 2D acquisition, and therefore provide more reliable information, e.g., on cartilage degeneration in osteoarthritis.

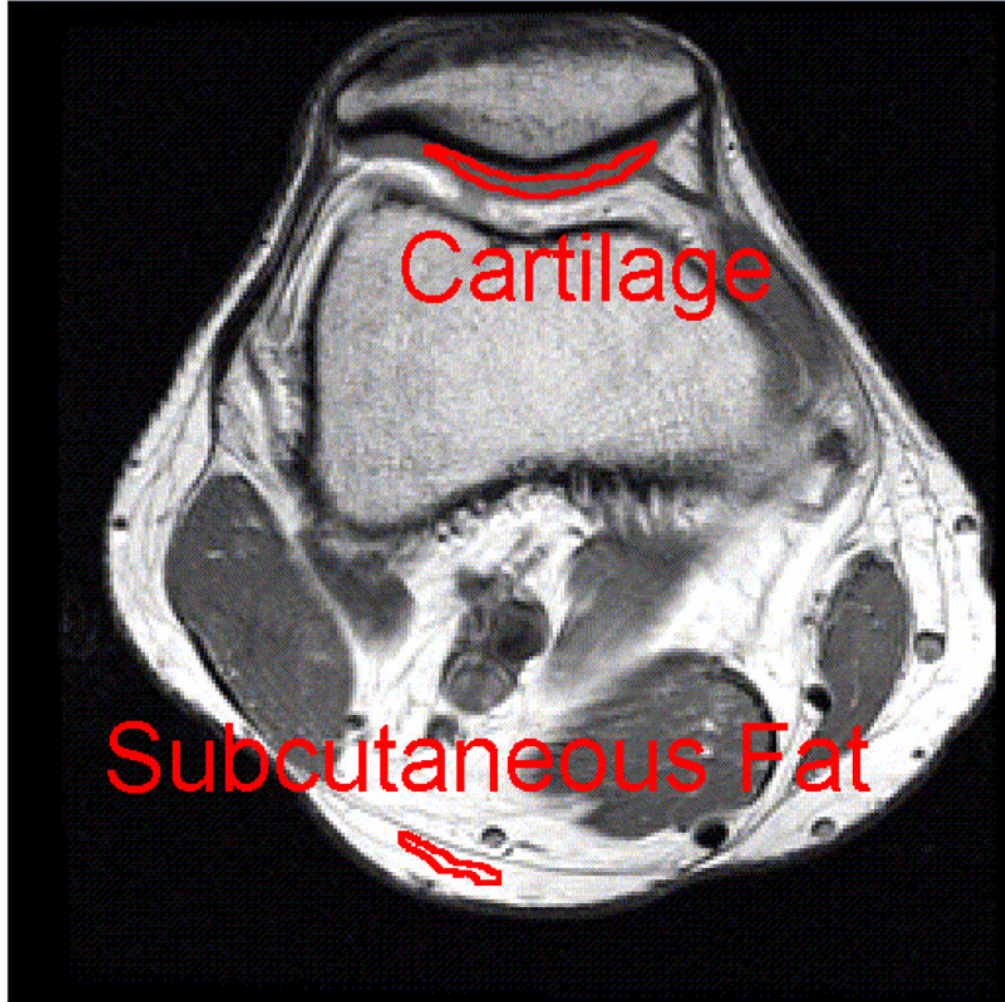
In conclusion, this study has examined the in vivo T₂ quantitation at 3T using different 2D and 3D mapping techniques. The results from this study suggest that, when attempting to quantify, it is important to consider that different sequences have several factors that affect T₂ quantitation. Moreover, different scanners can add additionally variability in T₂ quantitation. From this study, it is vital to note that when comparing studies, for example, the OsteoArthritis Initiative dataset (16) compared to a smaller natural history study (17), it is not appropriate to compare the actual relaxation times, but the trends of relaxation times may be more appropriate.

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(a)



(b)

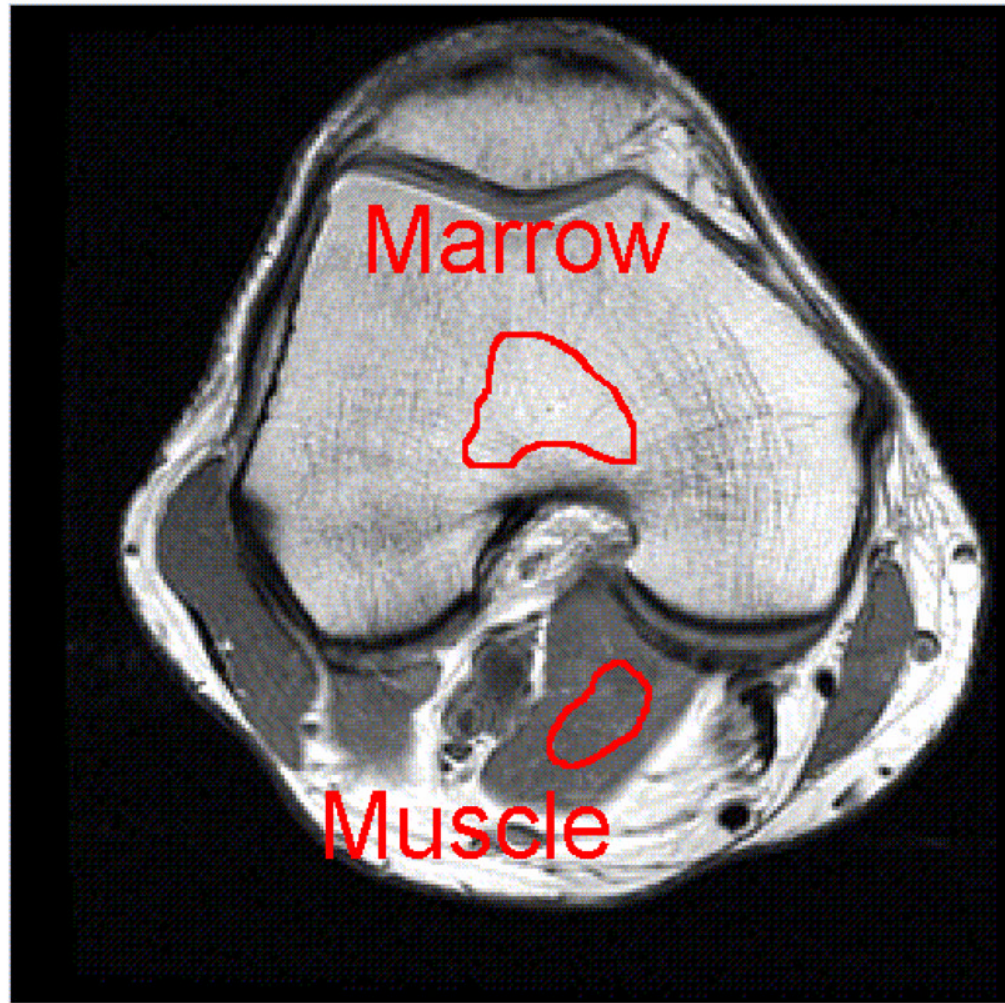


Figure 1.

An example of Region of Interest (ROI) selection in one subject. The tissues examined are (a) cartilage and subcutaneous fat, and (b) marrow and muscle. ROIs are taken in slices where the tissues are the largest. ROIs are manually segmented well within the boundaries of surrounding tissues to reduce the effects of chemical shift and magnetic susceptibility on relaxation times.

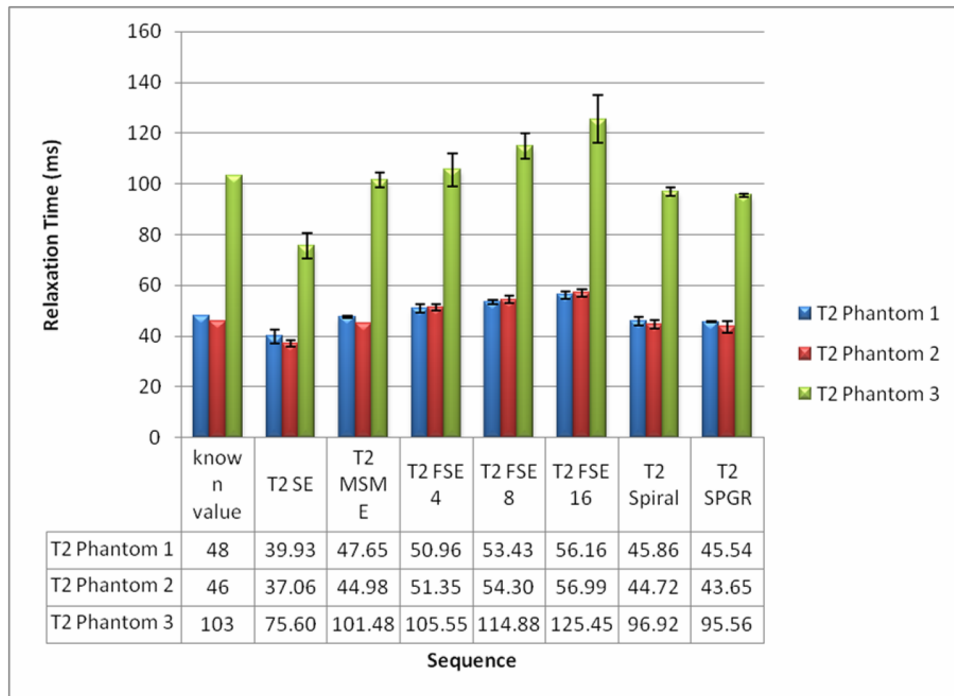
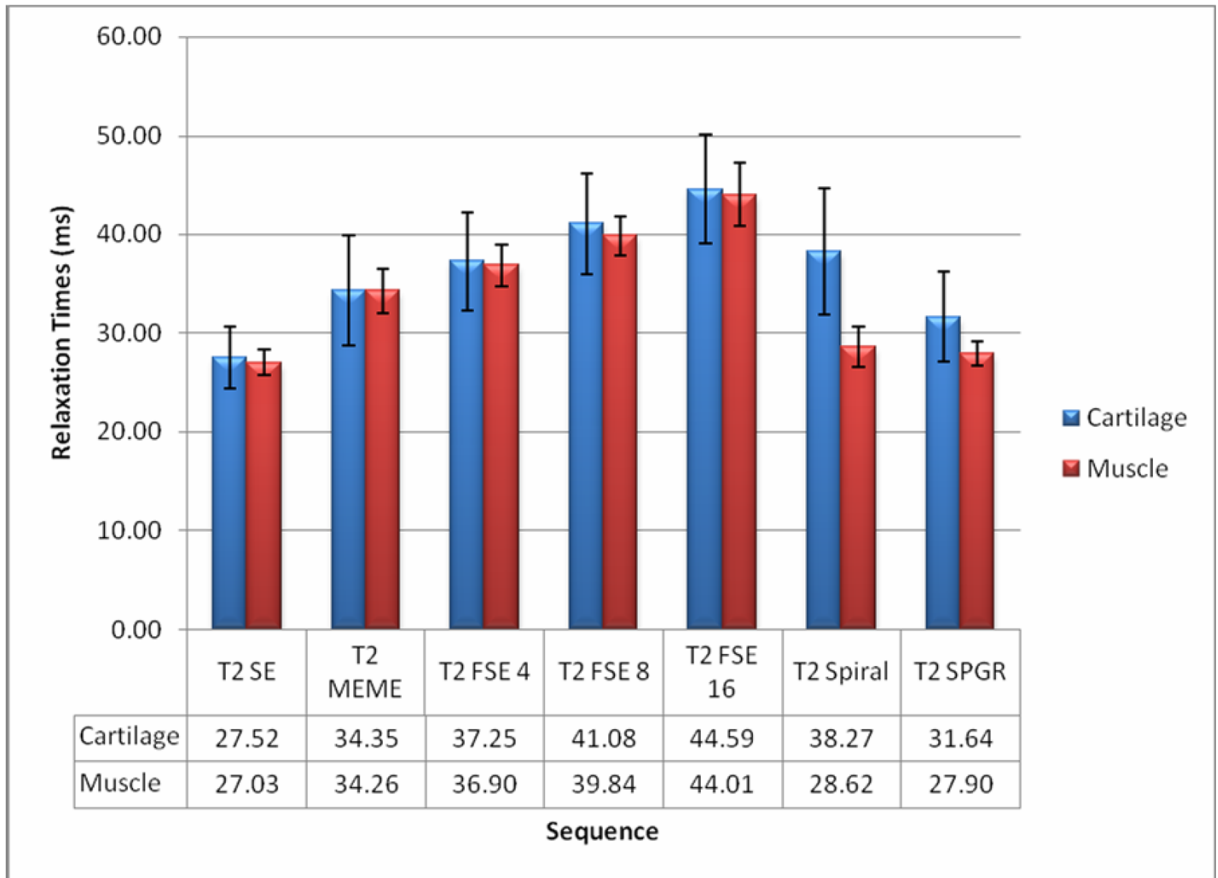


Figure 2. Relaxation times of three separate commercial phantoms with known times.

(a)



(b)

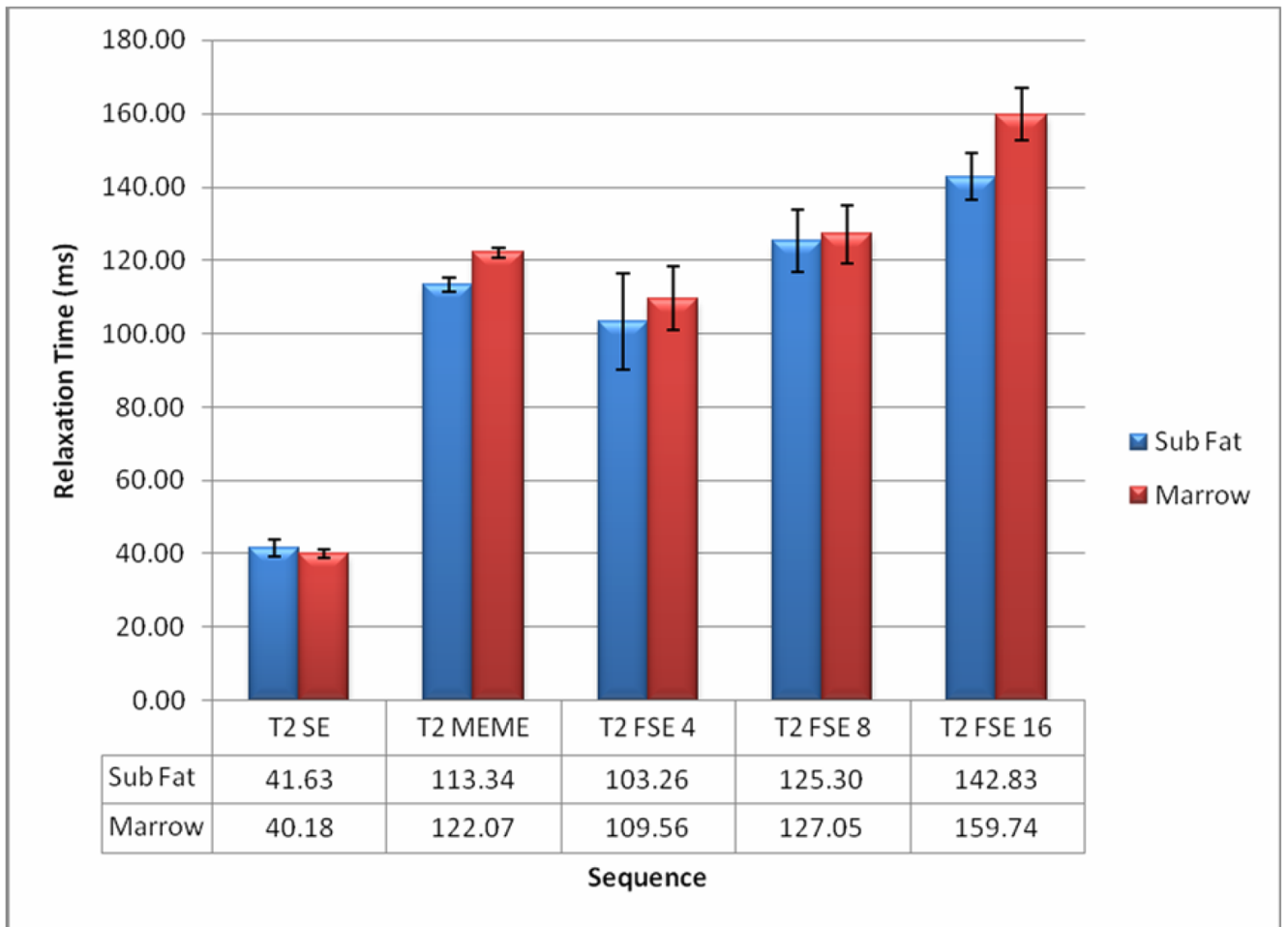


Figure 3. In vivo relaxation times of (a) cartilage and muscle, and (b) subcutaneous fat and marrow.

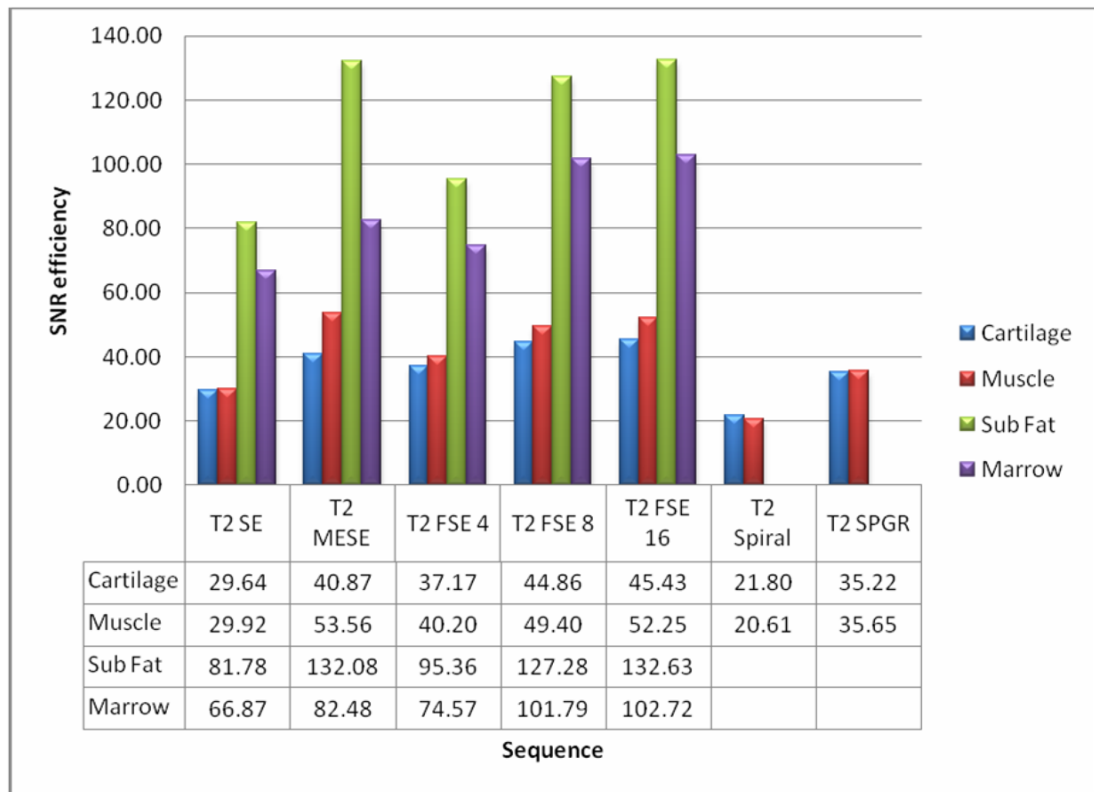


Figure 4. In vivo Signal to Noise Ratio (SNR) across all sequences and tissues.

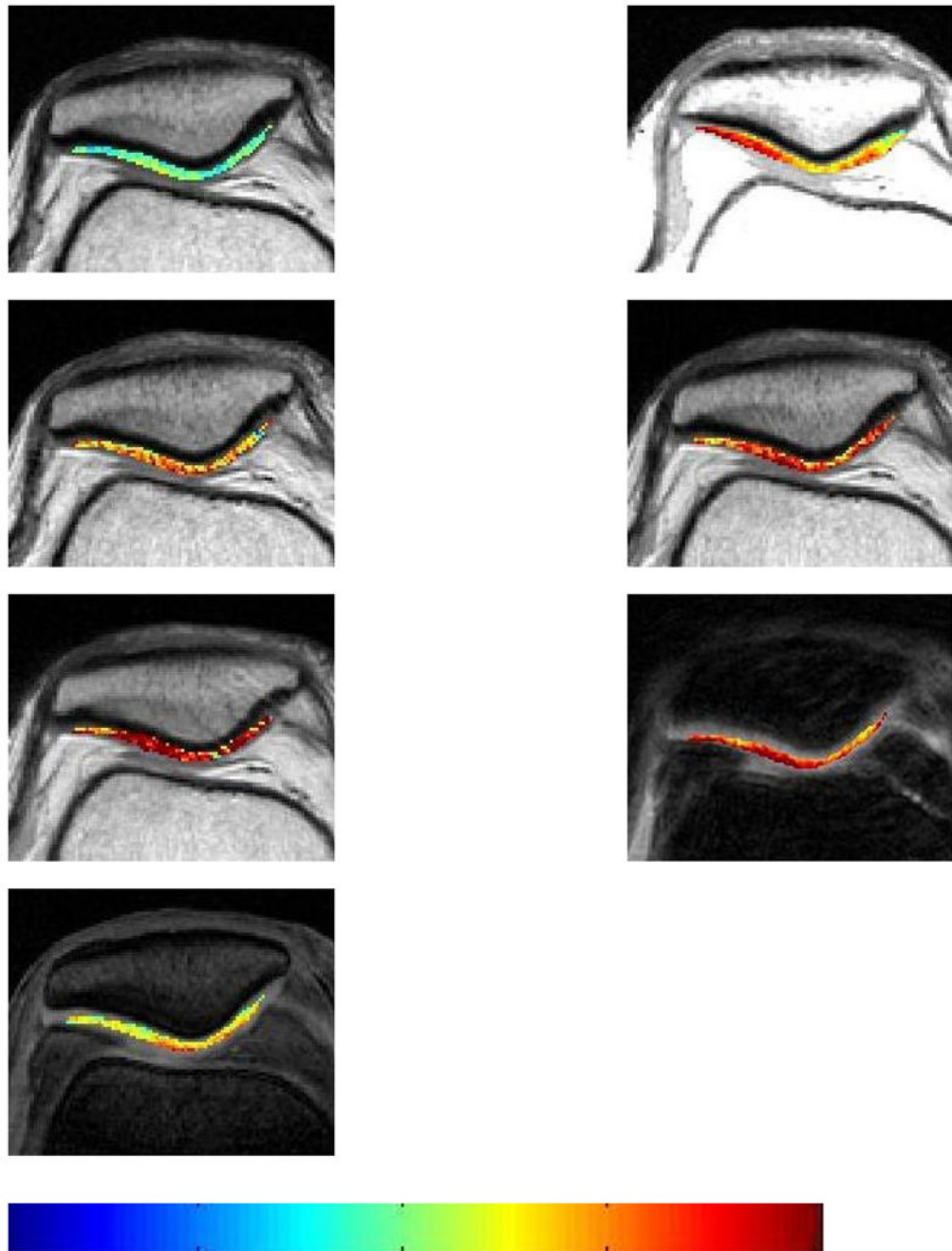


Figure 5. T2 maps of patellar cartilage in one subject for each sequence. From left to right, then top to bottom, the sequences are SE, MESE, FSE ETL=4, FSE ETL=8, FSE ETL=16, spiral, and SPGR.

Table 1

Coefficients of Variation in (a) phantoms and (b) in vivo.

(a)										
	SE	MESE	FSE 4	FSE 8	FSE 16	Spiral	SPGR	Average		
Phantom 1	0.066	0.008	0.036	0.019	0.026	0.037	0.003	0.028		
Phantom 2	0.038	0.001	0.027	0.026	0.026	0.039	0.051	0.030		
Phantom 3	0.068	0.028	0.061	0.045	0.075	0.016	0.006	0.043		
Average	0.057	0.012	0.041	0.030	0.042	0.031	0.020	0.033		

(b)										
	SE	MESE	FSE 4	FSE 8	FSE 16	Spiral	SPGR			
Cartilage	0.053	0.054	0.071	0.073	0.070	0.051	0.042			
Muscle	0.044	0.025	0.030	0.033	0.028	0.018	0.011			
Sub Fat	0.024	0.025	0.123	0.053	0.032					
Marrow	0.012	0.007	0.052	0.046	0.038					