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# Whole Knee Joint T<sub>1</sub> Values Measured *In Vivo* at 3T by Combined 3D Ultrashort Echo Time Cones Actual Flip Angle and Variable Flip Angle Methods

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# Abstract

**Purpose:** To measure  $T_1$  relaxations for the major tissues in whole knee joints on a clinical 3T scanner.

**Methods:** The 3D UTE-Cones actual flip angle imaging (AFI) method was used to map the transmission radiofrequency field ( $B_1$ ) in both short and long  $T_2$  tissues, which was then used to correct the 3D UTE-Cones variable flip angle (VFA) fitting to generate accurate  $T_1$  maps. Numerical simulation was carried out to investigate the accuracy of  $T_1$  measurement for a range of  $T_2$  values, excitation pulse durations, and  $B_1$  errors. Then, the 3D UTE-Cones AFI-VFA method was applied to healthy volunteers (n=16) to quantify the  $T_1$  of knee tissues including cartilage, meniscus, quadriceps tendon, patellar tendon, anterior cruciate ligament (ACL), posterior cruciate ligament (PCL), marrow and muscles at 3T.

**Results:** Numerical simulation showed that the 3D UTE-Cones AFI-VFA technique can provide accurate  $T_1$  measurements (error less than 1%) when the tissue  $T_2$  is longer than 1 ms and a 150 µs excitation RF pulse is used, and thus is suitable for most knee joint tissues. The proposed 3D UTE-Cones AFI-VFA method showed an average  $T_1$  of 1098±67 ms for cartilage, 833±47 ms for meniscus, 800±66 ms for quadriceps tendon, 656±43 ms for patellar tendon, 873±38 ms for ACL, 832±49 ms for PCL, 379±18 ms for marrow and 1393±46 ms for muscles.

**Conclusion:** The 3D UTE-Cones AFI-VFA method allows volumetric  $T_1$  measurement of the major tissues in whole knee joints on a clinical 3T scanner.

### Keywords

ultrashort echo time; actual flip angle imaging; variable flip angle; knee joint

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#### INTRODUCTION

Human knee joints are composed of many soft tissues including articular cartilage, menisci, ligaments, tendons and muscles, all of which are important to the health of the joint (1–3). Accurate  $T_1$  measurements of the major knee joint tissues can be used for optimization of signal intensity and image contrast (4). Additionally,  $T_1$  relaxation is a fundamental property of a tissue and may be directly useful as a biomarker of disease or degeneration (5, 6), or used to measure other quantitative MRI biomarkers, such as the macromolecular proton fraction from magnetization transfer modeling or low frequency exchange information from  $T_{1,a}$  imaging (7–9).

Many  $T_1$  measurement techniques have been proposed including inversion recovery (IR) and saturation recovery (SR) methods, as well as spoiled gradient recalled echo (SPGR)-based variable flip angle (VFA) and variable repetition time (VTR) methods (10–13). However, conventional MRI pulse sequences (such as SPGR and fast spin echo sequences) are of limited value for imaging deep radial and calcified cartilage, menisci, ligaments, bone and tendons because these tissues typically have  $T_2$  values ranging from sub-milliseconds to several milliseconds and thus provide little or no detectable signal (14–16). In contrast, all of the major knee joint components, including both short and long  $T_2$  tissues, can be imaged using ultrashort echo time (UTE) sequences with TEs less than 100 µs (6, 14–16). Thus, combining  $T_1$  measurement techniques with UTE acquisitions has the potential for simultaneous  $T_1$  mapping of the whole knee joint.

However, the IR based UTE (IR-UTE) method is inaccurate for  $T_1$  measurement of short  $T_2$  tissues because the required inversion pulse is too long (typically on the order of several milliseconds) on currently available clinical scanners to provide complete inversion of the short  $T_2$  magnetization (17). The SR based UTE (SR-UTE) method provides more accurate  $T_1$  measurements for short  $T_2$  tissues (13) but would require long scan times for volumetric  $T_1$  mapping. UTE-based VFA or VTR methods can provide volumetric  $T_1$  mapping (17–22), but they suffer from high sensitivity to  $B_1$  inhomogeneity (23–26). Obtaining an accurate  $B_1$  map is crucial with VFA and VTR  $T_1$  measurement approaches. Actual flip angle imaging (AFI) is a fast 3D  $B_1$  mapping technique which has been successfully used for correction of VFA and VTR based  $T_1$  measurements (23, 25).

UTE-AFI has been recently developed to map flip angles for both short and long  $T_2$  tissues (22, 26). However, with conventional peak power limitations on the radiofrequency (RF) amplifiers of clinical scanners, the RF pulse duration must be increased in order to produce the large flip angle excitation (>40°) required for AFI. This longer RF pulse has reduced excitation efficiency (i.e.  $T_2$  relaxation during the RF pulse) for short  $T_2$  tissues, resulting in noticeable errors in the derived  $B_1$  map when the tissue  $T_2$  value is less than 0.5 ms (22).  $T_2$  relaxation during the RF pulse results in smaller actual flip angles for short/ultrashort  $T_2$  components than the nominal flip angle.

Previously, we have proposed using a UTE AFI-VTR method for accurate  $T_1$  mapping of both short and long  $T_2$  tissues of the knee (22). The effects of variable excitation efficiency were overcome by using an identical excitation pulse for the UTE-AFI and UTE-VTR

sequences (22). However, UTE AFI-VTR would require a long scan time for 3D high resolution knee imaging, making it unacceptable for clinical use (22). Since all major knee tissues other than bone have a  $T_2$  value longer than 1 ms (11, 27–33), the  $B_1$  map generated by the UTE-AFI method can still be used for  $B_1$  correction of the faster VFA-based  $T_1$  measurement for these tissues. Therefore, the UTE AFI-VFA method would be expected to provide accurate  $T_1$  measurements of the soft tissues of the whole knee joint with much less scan time than the UTE AFI-VTR method.

In this study, numerical simulations were carried out to investigate the  $T_1$  measurement accuracy of the UTE AFI-VFA method for the knee joint tissues with a variety of  $T_2$  values on a clinical scanner. Then we applied the 3D UTE-Cones AFI-VFA method for *in vivo* whole knee imaging to measure  $T_1$  values of cartilage, meniscus, quadriceps tendon, patellar tendon, anterior cruciate ligament (ACL), posterior cruciate ligament (PCL), marrow and muscles at 3T.

### THEORY

Features of the 3D UTE-Cones pulse sequence with a single TR (Fig. 1a) have been described before (33–35). A series of 3D UTE-Cones acquisitions with variable flip angles are used for T<sub>1</sub> measurement. UTE-AFI can be achieved with the 3D dual TR UTE-Cones sequence (Fig. 1b) (22). Both the UTE-Cones AFI and the UTE-Cones VFA sequences use a short rectangular pulse (e.g. RF duration  $\tau = 150 \ \mu s$ ) for non-selective signal excitation (Fig. 1c), followed by spiral trajectory data acquisition with conical view ordering (Fig. 1d).

The generalized signal expressions of  $S_1$  and  $S_2$  for  $TR_1$  and  $TR_2$  of the AFI sequence (Fig. 1b) for both short and long  $T_2$  tissues are expressed as follows (22):

$$S_1 = M_0 f_{xy}(\alpha, \tau, T_2) \frac{1 - E_2 + (1 - E_1)E_2 f_Z(\alpha, \tau, T_2)}{1 - E_1 E_2 f_Z^2(\alpha, \tau, T_2)}$$
[1]

$$S_{2} = M_{0}f_{xy}(\alpha, \tau, T_{2})\frac{1 - E_{1} + (1 - E_{2})E_{1}f_{Z}(\alpha, \tau, T_{2})}{1 - E_{1}E_{2}f_{Z}^{2}(\alpha, \tau, T_{2})}$$
[2]

with

$$E_1 = \exp\left(-TR_1/T_1\right),$$

$$E_2 = \exp\left(-TR_2/T_1\right).$$

 $M_0$  is the equilibrium magnetization.  $f_{xy}(\alpha, \tau, T_2)$  and  $f_Z(\alpha, \tau, T_2)$  are the respective transverse and longitudinal magnetization mapping functions, which are described as follows (22, 37):

$$f_{xy}(\alpha,\tau,T_2) = e^{-\frac{\tau}{2T_2}} \alpha \operatorname{sinc}\left(\sqrt{\alpha^2 - \left(\frac{\tau}{2T_2}\right)^2}\right) \quad [3]$$

$$f_z(\alpha,\tau,T_2) = e^{-\frac{\tau}{2T_2}} \left( \cos\left(\sqrt{\alpha^2 - \left(\frac{\tau}{2T_2}\right)^2}\right) + \frac{\tau}{2T_2} \operatorname{sinc}\left(\sqrt{\alpha^2 - \left(\frac{\tau}{2T_2}\right)^2}\right) \right) \quad [4]$$

 $\alpha$  is the nominal flip angle and  $\tau$  is the duration of the rectangular excitation pulse.

With TR<sub>1</sub> and TR<sub>2</sub> that are short relative to T<sub>1</sub>, the signal ratio r of  $S_1$  and  $S_2$  can be simplified using a first-order approximation for the exponential terms such that (23):

$$r = S_2/S_1 \approx \frac{1 + nf_Z(\alpha, \tau, T_2)}{n + f_Z(\alpha, \tau, T_2)} \quad [5]$$

where  $n = \text{TR}_2/\text{TR}_1$ . The ratio *r* can then be used as a T<sub>1</sub>-independent measure of  $f_Z(\alpha, \tau, T_2)$ :

$$f_z(\alpha, \tau, T_2) \approx \frac{rn-1}{n-r}$$
. [6]

For a tissue with  $T_2 \gg \tau$ ,  $f_{xy}(\alpha, \tau, T_2)$  and  $f_Z(\alpha, \tau, T_2)$  simplify to  $\sin(\alpha)$  and  $\cos(\alpha)$ , respectively.

Thus, the actual flip angle  $\alpha$  can be accurately estimated with the following equation (22, 23):

$$\alpha \approx \arccos\left(\frac{rn-1}{n-r}\right).$$
 [7]

Then, the B<sub>1</sub> scaling factor (B<sub>1s</sub>) is obtained by dividing the measured  $\alpha$  by the nominal flip angle  $\alpha_{nom}$ :

$$B_{1s} = \alpha / \alpha_{nom}.$$
 [8]

 $B_{1s}$  is used to quantify the RF inhomogeneity, with  $B_{1s} = 1$  corresponding to an unaltered RF field.

The signal equation of VFA based  $T_1$  measurement with  $B_1$  correction is expressed as follows (37):

$$S_{spgr} = M_0 sin(B_{1s}\theta) \frac{1 - E_s}{1 - E_s cos(B_{1s}\theta)}$$
[9]

with  $E_s = exp(-TR_s/T_1)$ .

 $\theta$  is the nominal flip angle and  $TR_s$  is the repetition time of the UTE-Cones sequence.

For tissues with T<sub>2</sub> values comparable to the RF duration  $\tau$ , the excitation efficiency of the RF pulse decreases with T<sub>2</sub>. The high dependency on tissue T<sub>2</sub> in  $f_Z(\alpha, \tau, T_2)$  means that Eq.

[7] is no longer accurate for the calculation of  $\alpha$ , resulting in inaccurate B<sub>1s</sub> estimates (22). This can result in estimation errors for VFA-based T<sub>1</sub> measurements because the method is sensitive to B<sub>1</sub> errors.

To investigate the accuracy of VFA  $T_1$  measurement with AFI  $B_1$  correction (UTE AFI-VFA) for tissues with a variety of  $T_2$  values on a clinical scanner, numerical simulations were carried out as described below.

#### METHODS

The 3D UTE-Cones and 3D UTE-Cones AFI sequences (see Figure 1) were implemented on a 3T MR750 scanner (GE Healthcare Technologies, Milwaukee, WI). An 8-channel transmit/receive knee coil was used for both RF transmission and signal reception. Unique k-space trajectories were used in the UTE-Cones sequences that sampled data along evenly spaced twisted paths in the form of multiple cones (29–31). Data sampling began from the center of k-space and continued outwards. It began as soon as practical after the RF excitation with a minimal nominal delay time of 32 µs. Both RF and gradient spoiling were used to crush the remaining transverse magnetizations. In VFA UTE-Cones, the area of the gradient crushers was 180 mT·ms/m and the RF phase increment was 169°. In UTE-Cones AFI, the areas of gradient crushers in TR<sub>1</sub> and TR<sub>2</sub> were 180 and 900 mT·ms/m respectively, and the RF phase increment was 39° (22). The UTE-Cones sequence allowed anisotropic resolution (e.g., higher in-plane resolution and thicker slices) to provide an improved signal to noise ratio (SNR) and a reduced scan time relative to isotropic imaging (30, 31).

#### Simulation

Numerical simulation was performed to investigate the accuracy of the proposed UTE AFI-VFA T<sub>1</sub> measurement for relatively short T<sub>2</sub> tissues. The UTE AFI-VFA technique is expected to accurately measure T<sub>1</sub> for long T<sub>2</sub> tissues. Simulated rectangular RF pulses used for signal excitation in both the 3D UTE AFI and VFA sequences had identical durations and ranged from 0.1 to 300  $\mu$ s. T<sub>2</sub> values of simulated tissues ranged from 0 to 5 ms. The B<sub>1</sub> scaling factors and the ratio between f<sub>xy</sub> and sin (B<sub>1s</sub> $\theta$ ) measured with different nominal flip angles (range from 0° to 90°) for short T<sub>2</sub>s were also investigated with a pulse duration of

150 µs. This ratio was calculated to investigate whether the obtained  $B_{1s}$  could correct the transverse part of the excitation. The  $T_1$  measurement accuracy with the VFA method depends on the accurate correction of both transverse and longitudinal magnetizations after excitation. The  $T_1$  value was set to a constant of 800 ms and  $M_0$  was set to 1. The sequence parameters for UTE AFI and VFA sequences were adjusted as follows: 1) UTE-AFI:  $TR_1/TR_2 = 20/100$  ms and flip angle = 45°; 2) UTE-VFA: TR = 20 ms, and flip angle = 5°, 10°, 20° and 30°. B<sub>1</sub> scaling factors and  $T_1$  values with and without B<sub>1</sub> correction were calculated for three nominal B<sub>1</sub> scaling factors (B<sub>1n</sub>): 0.8, 1 and 1.2.

*In Vivo* Study—*In vivo* whole knee imaging was carried out on 16 healthy volunteers (aged 20–49 years, mean age 34 years; 7 males, 9 females). Informed consent was obtained from all subjects in accordance with guidelines of the institutional review board. The 3D UTE-Cones AFI and VFA sequences were used to scan these knee joints using the same field of view (FOV) of  $15\times15\times10.8$  cm<sup>3</sup> and receiver bandwidth of 166 kHz. Other sequence parameters were: 1) 3D UTE-Cones AFI:  $TR_1/TR_2 = 20/100$  ms, flip angle =  $45^{\circ}$ , acquisition matrices of  $128\times128\times18$ , readout duration =  $924 \ \mu$ s and a total scan time of 4 min 57 sec; 2) 3D VFA UTE-Cones:  $TR = 20 \ ms$ , flip angle =  $5^{\circ}$ ,  $10^{\circ}$ ,  $20^{\circ}$  and  $30^{\circ}$ , acquisition matrices of  $256\times256\times36$ , undersampling factor of 0.9, readout duration =  $1644 \ \mu$ s and a total scan time of 9 min 28 sec.

#### **Data Analysis**

Before  $T_1$  calculation, motion registration was performed for all datasets using the Elastix open source software (38). Rigid registration was carried out first to correct for tissue translations and rotations, and then non-rigid registration was applied for further fine adjustment (such as scaling and shearing), which is particularly important for soft tissues. The Levenberg-Marquardt algorithm was used to solve the non-linear fitting of Eq. [9] for VFA T<sub>1</sub> measurement. The analysis algorithms written in Matlab (The Mathworks, Inc., Natick, MA) were applied to the DICOM images obtained from the 3D UTE-Cones AFI and VFA UTE-Cones protocols described above. Both T<sub>1</sub> values and fitting errors were calculated. Manually drawn regions-of-interest for the 16 *in vivo* knees were used to measure the mean and standard deviation T<sub>1</sub> values of various tissues including the articular cartilage, meniscus, quadriceps tendon, patellar tendon, ACL, PCL, marrow and muscles.

# RESULTS

The simulation results with variable pulse durations for a range of T<sub>2</sub>s are shown in Figure 2. The top two rows show the theoretical longitudinal  $(M_z \text{ or } f_z(\alpha, \tau, T_2))$  and transverse  $(M_{xy} \text{ or } f_{xy}(\alpha, \tau, T_2))$  magnetizations calculated by Eqs. [3] and [4]. Longer RF pulses were shown to be less effective than shorter ones in generating  $M_{xy}$  for shorter T<sub>2</sub> tissues.  $M_z$  and  $M_{xy}$  approached  $\cos(\alpha)$  and  $\sin(\alpha)$ , respectively, as T<sub>2</sub> increased. The third row in Figure 2 shows the estimated B<sub>1</sub> scaling factors B<sub>1s</sub> computed using the AFI method with Eqs. [7] and [8]. As expected, the measured B<sub>1s</sub> were more accurate when using shorter RF pulses and when imaging longer T<sub>2</sub> species. Otherwise, the estimated B<sub>1s</sub> were smaller than the nominal values.

The bottom two rows show the simulation results of  $T_1$  measurements using the VFA method without and with  $B_1$  correction. The  $B_1$ -uncorrected  $T_1$  values show significant estimation errors and increased with larger values of the nominal  $B_1$  scaling factor  $B_{1n}$ . Overall, the  $T_1$  values generated by the  $B_1$ -corrected VFA method were much more accurate than the  $T_1$  values measured by the  $B_1$ -uncorrected VFA method. However,  $T_1$  estimation errors still existed in the  $B_1$ -corrected  $T_1$  values when  $T_2$  values were shorter than 0.5 ms, and the errors became larger with increased  $B_{1n}$ . All three of the  $B_1$ -corrected  $T_1$  maps were separated into two regions by dashed black lines: the  $T_1$  estimation errors in the other portions (triangular shaped area) and the  $T_1$  estimation errors in the other portions were lower than 1%. Thus, we found that when an excitation pulse with a duration of 150 µs is used for imaging tissues with  $T_2$  values greater than 1 ms, the  $B_1$ -corrected  $T_1$  value measured by the AFI-VFA method is accurate with less than 1% estimation error in the setting of up to 20%  $B_1$  inhomogeneity.

The simulation curves with a range of nominal flip angles for the four short T<sub>2</sub>s (i.e. 0.2 ms, 0.3 ms, 0.5 ms and 1 ms) are shown in Figure 3. Both B<sub>1</sub> scaling factors and the ratio between  $f_{xy}$  and  $\sin (B_{1s}\theta)$  slightly changed with different nominal flip angles. More changes

can be found when tissue  $T_2$  is shorter. So for shorter  $T_2s$ , a single correction factor is not good enough to correct the excitation errors in different flip angles for VFA  $T_1$  measurement as shown in the last row of Figure 2. However, both  $B_{1s}$  and the ratio almost stay constant for flip angles lower than 50° when  $T_2$  is 1 ms or longer, which demonstrate the accuracy of the proposed AFI-VFA  $T_1$  measurement method for tissues with  $T_{2s}$  longer than 1 ms.

Since the articular cartilage, meniscus, quadriceps tendon, patellar tendon, ACL, PCL, marrow and muscles all have  $T_2$  values longer than 1 ms, the B<sub>1</sub>-corrected VFA method with a 150 µs long excitation pulse should be suitable for the measurement of  $T_1$  values of these tissues. The signal intensities of the tissues have been measured before and after registration. There were almost no signal intensity changes due to the motion registration. Figure 4 shows  $T_1$  fitting results for various knee joint tissues of a representative healthy volunteer (age 35, male). All the data show excellent fittings. The proposed 3D UTE-Cones AFI-VFA method showed a  $T_1$  value of  $832\pm18$  ms for meniscus,  $779\pm7$  ms for quadriceps tendon,  $637\pm16$  ms for patellar tendon,  $870\pm13$  ms for ACL,  $819\pm17$  ms for PCL,  $1133\pm40$  ms for cartilage,  $386\pm2$  ms for marrow and  $1406\pm63$  ms for muscles of this volunteer.

Figure 5 shows  $T_1$  mapping results of the knee of the same healthy volunteer as above.  $T_1$  maps generated by the proposed 3D UTE-Cones AFI-VFA method are shown in Figs. 5d to 5f. For comparison, the  $T_1$  maps generated by the 3D UTE-Cones VFA method without  $B_1$  correction are shown in Figs. 5g to 5i.  $T_1$  estimation errors induced by  $B_1$  inhomogeneity, which are more severe in regions close to the coil boundary, have been corrected by the proposed 3D UTE-Cones AFI-VFA method. Corresponding  $B_{1s}$  maps are shown in Figs. 5j to 51. As expected, lower  $B_{1s}$  values can be found in cortical bone regions due to lower excitation efficiency.

Table 1 summarizes  $T_1$  measurements by the proposed 3D UTE-Cones AFI-VFA method for the principal knee joint tissues of healthy volunteers (n = 16). The proposed 3D UTE-Cones AFI-VFA method showed a mean  $T_1$  value and standard deviation of 833 ± 47 ms for

meniscus,  $800 \pm 66$  ms for quadriceps tendon,  $656 \pm 43$  ms for patellar tendon,  $873 \pm 38$  ms for ACL,  $832 \pm 49$  ms for PCL,  $1098 \pm 67$  ms for cartilage,  $379 \pm 18$  ms for marrow and  $1393 \pm 46$  ms for muscles.

# DICUSSION

We have demonstrated that the proposed 3D UTE-Cones AFI-VFA method can accurately measure  $T_1$  values for most major tissues of the whole knee joint. Simulation shows that the proposed 3D UTE-Cones AFI-VFA method provides accurate  $T_1$  measurements for tissues with  $T_2$  values longer than 1 ms. Since most knee tissues have  $T_2$ s longer than 1 ms (meniscus: 5–8 ms, ligament and tendon: 4–10 ms, cartilage: 27–43 ms, muscle: 32–50 ms and fat: ~133 ms) (11, 27–33), accurate  $T_1$  maps were obtained using the proposed method to provide *in vivo* knee measurements in 16 healthy volunteers.

Due to the high sensitivity in VFA  $T_1$  measurements to  $B_1$  errors, obtaining an accurate  $B_1$  map is crucial. AFI is a fast 3D  $B_1$  mapping technique which fits very well with VFA based  $T_1$  corrections. It has been used for volumetric  $B_1$  mapping of brain, body, and musculoskeletal tissues (23, 40, 41). UTE-AFI techniques using radial trajectories have been implemented for  $B_1$  mapping of short  $T_2$  tissues on both clinical 3T and 9.4T MRI systems (20, 26). Most recently, we have implemented the 3D UTE-Cones based AFI sequence on a clinical 3T scanner (22). 3D UTE-Cones employs a spiral trajectory data acquisition with conical view ordering, which provide the flexibility to stretch each spiral interleave to vastly reduce the total number of interleaves. Thus, combined with the ability for anisotropic resolution, the 3D UTE-Cones data acquisition is much more efficient than the radial UTE acquisition (33, 34).

As shown in the simulation study and a previous cortical bone study (22), the VFA  $T_1$  maps did not show much improvement after  $B_1$  correction for very short  $T_2$  tissues such as cortical bone. However, for tissues with  $T_2$  values longer than 1 ms (much longer than pulse duration of 150 µs), the obtained  $B_{1s}$  is almost accurate and AFI-VFA can provide accurate  $T_1$ measurement. The coverage of the simulated nominal  $B_1$  scaling factors  $B_{1n}$  from 0.8 to 1.2 should be wide enough for most cases of *in vivo* knee imaging. Thus, the proposed 3D UTE-Cones AFI-VFA method was able to accurately measure  $T_1$  of all the major knee tissues except for bone.

To our best knowledge, this study is the first to report the  $T_1$  values for all the soft tissues in the human knee joint *in vivo*. Most of previous  $T_1$  measurement studies focused on the articular cartilage, meniscus and muscle. The  $T_1$  values of the ligaments including quadriceps tendon, patellar tendon, ACL and PCL have been barely studied since they are not detected by clinical sequences due to their relatively short  $T_2$  values. Our measured  $T_1$ values for cartilage (~1098 ms), muscle (~1393 ms) and marrow (~379 ms) at 3T are comparable with previous 3T studies. For example, Stanisz et. al. reported  $T_1$  values of 1156 ms for cartilage and 1412 ms for skeletal muscle (11); Gold et. al. reported  $T_1$  values of 1240 ms for cartilage, 1420 ms for skeletal muscle and 365 ms for marrow (33); and Jordan et. al. reported  $T_1$  values of 1016 ms for cartilage, 1256 ms for muscle and 381 ms for

marrow (42). We recently measured *in vivo* cortical bone  $T_1$  values of around 220 ms using a related 3D UTE-Cones AFI-VTR method (22).

Magnetization transfer (MT) effects were not considered for both the AFI  $B_1$  scaling factor and VFA  $T_1$  quantification in this study. Since most tissues in our study such as cartilage and menisci have high macromolecular contents, MT effects can lead to  $T_1$  measurement errors for the AFI-VFA method (43–45). Further work should consider and correct MT effects for more accurate  $T_1$  measurement. In addition, an interesting finding is that the  $B_{1s}$  maps in Figure 5 show contrast between fat and other tissues. This may be a result from the MT effect since fat has negligible MT effect in comparison to other tissues. Another possible explanation for the contrast is the different dielectric properties of fat and other tissues (46). Secondary  $B_1$  field components can be generated by tissue-specific induced current densities. Thus, the higher  $B_{1s}$  values observed in cartilage, menisci, and muscle may also result from greater induced current densities, since their conductivity and permittivity values are much greater than those of fat (47). Previous authors have investigated tissue dielectric properties based on the transmit  $B_1$  maps (48, 49).

There are also several limitations of this study. First, the total data acquisition time is relatively long, in part due to the parameters selected for high accuracy, high image resolution and broad spatial coverage. A number of strategies can be employed to reduce the total scan time, including decreasing the total number of FAs for VFA (10), using lower resolution for  $B_1$  mapping and advanced techniques for image reconstruction such as parallel imaging and compressed sensing reconstruction (50). Second, fat and chemical shift artifacts (which produce ring artifacts in 3D UTE-Cones imaging) may lead to errors in  $T_1$  estimation, necessitating some form of fat-water signal separation to improve accuracy (51).

# CONCLUSION

The 3D UTE-Cones AFI-VFA method provides a robust technique for volumetric  $T_1$  mapping of all the soft tissues in knee joints *in vivo* with a clinical 3T scanner, including the articular cartilage, meniscus, quadriceps tendon, patellar tendon, ACL, PCL, marrow and muscles.

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#### Figure 1.

The 3D UTE-Cones sequence with a single TR is used for  $T_1$  measurement with the variable flip angle (VFA) method (a). The 3D UTE-Cones actual flip angle imaging (AFI) sequence employs a pair of interleaved TRs for accurate  $B_1$  mapping (b), which together with the VFA method provides accurate  $T_1$  measurements. In these two UTE-Cones sequences, a short rectangular pulse is used for signal excitation followed by 3D spiral sampling with a very short TE of 32 µs (c). The spiral trajectories are arranged with conical view ordering (d).



#### Figure 2.

Simulation results for different T<sub>2</sub> tissues (T<sub>2</sub> values from 0 to 5 ms) with rectangular RF pulse excitation (durations from 0.1 to 300 µs). The top two rows show color maps corresponding to the longitudinal ( $M_Z$  or  $f_Z(\alpha, \tau, T_2)$ ) and transverse ( $M_{xy}$  or  $f_{xy}(\alpha, \tau, T_2)$ )

magnetizations calculated from Eqs. [3] and [4]. The third row shows the resulting  $B_{1s}$  scaling factors obtained by the AFI method (i.e. Eqs. [7] and [8]).  $T_1$  values (units of ms) generated by the VFA method are shown without (fourth row) and with  $B_{1s}$  correction (fifth row). For the  $B_1$ -corrected  $T_1$  results, a dashed black line was drawn such that the region to the left of the line had a  $T_1$  estimation error greater than 1% and the region to the right had an estimation error less than 1%. The columns represent simulation results with nominal  $B_1$  scaling factors  $B_{1n}$  of 0.8, 1, and 1.2, respectively.

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#### Figure 3.

Simulation curves for different T<sub>2</sub> tissues (green: 0.2 ms, blue: 0.3 ms, red: 0.5 ms and black: 1 ms) with rectangular RF pulse excitation (nominal FA from 0° to 90°; pulse duration  $\tau = 150 \,\mu$ s). The first row shows the resulting B<sub>1</sub> scaling factors obtained by the AFI method (i.e. Eqs. [7] and [8]). The second row shows the ratio between f<sub>xy</sub> in Eq. [3] and sin( $B_{1s}\theta$ ) in Eq. [9]. The columns represent simulation results with nominal B<sub>1</sub> scaling factors B<sub>1n</sub> of 0.8, 1, and 1.2, respectively.



#### Figure 4.

T<sub>1</sub> fitting results in knee tissues from a representative healthy volunteer (age 35, male) using the proposed 3D UTE-Cones AFI-VFA method. The measured T<sub>1</sub> values for this volunteer were  $832\pm18$  ms for meniscus, 779±7 ms for quadriceps tendon,  $637\pm16$  ms for patellar tendon,  $870\pm13$  ms for ACL,  $819\pm17$  ms for PCL,  $1133\pm40$  ms for cartilage,  $386\pm2$  ms for marrow and  $1406\pm63$  ms for muscles.



#### Figure 5.

Results in knee tissues from a healthy 35-year old male volunteer (a–l). (a–c) are the selected VFA images with FA = 5°. T<sub>1</sub> mapping using both the proposed 3D UTE-Cones AFI-VFA (d–f) and B<sub>1</sub>-uncorrected VFA (g–i) methods are shown. The B<sub>1s</sub> maps generated by the AFI technique (j–l) are shown. B<sub>1</sub> inhomogeneity induced T<sub>1</sub> estimation errors in the images of g–i have been corrected by the proposed 3D UTE-Cones AFI-VFA method, especially in regions close to the coil boundary.

#### Table 1

Mean and standard deviations of  $T_1$  values of knee tissues of 16 healthy volunteers measured by the proposed 3D UTE-Cones AFI-VFA method.

Meniscus	Quadriceps tendon	Patellar tendon	ACL
$833\pm47\ ms$	$800 \pm 66 \text{ ms}$	$656 \pm 43 \text{ ms}$	$873\pm38\ ms$
PCL	Cartilage	Marrow	Muscle
922 ± 40 mg	1008 + 67	270 + 18	$1202 \pm 46$ mg