Ultrashort TE (UTE) Imaging of the Knee Cartilage at 3T

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Abstract

While MR imaging has emerged as the imaging method of choice for diagnosis of cartilage disease, the deep radial and calcified layers of cartilage are difficult to image with conventional MRI because of their short T2 relaxation times. The imaging of cartilage injury and osteoarthritis (OA) has therefore focused on the superficial layers of cartilage. We describe herein the implementation of Ultrashort Echo Time (UTE) pulse sequences with Echo Times (TEs) as low as 8 μs on a clinical 3T scanner. Various adaptations were made to the regular UTE acquisition in order to optimize image contrast between the deep layers and superficial layers of cartilage. These modifications included multiple gradient echo UTE acquisition with and without fat saturation, and multiple spin echo UTE acquisition. The efficacy of these techniques in depicting the targeted tissues was demonstrated through imaging of cadaveric samples and healthy volunteers. Excellent depiction of these different regions was obtained, enhanced particularly with fat suppression and later echo subtraction methods. Quantitative measurements showed that while UTE Free Induction Decay (FID) acquisition provided the highest signal-to-noise ratio, both fat suppression and later echo subtraction enhanced the contrast between the deep and superficial layers of cartilage.

Keywords: Ultrashort TE; Short T2; Deep radial and calcified layers; Cartilage; Osteoarthritis

Introduction

Noninvasive radiologic techniques are required to assess and characterize cartilage lesions in the setting of injury and degenerative joint disease. Their high prevalence is a major cause of morbidity and diminished quality of life [1]. Due to its excellent soft tissue contrast, Magnetic Resonance (MR) imaging has emerged as the imaging method of choice for diagnosis of cartilage disease [2]. However, articular cartilage imaging is challenging due to its small geometric dimensions, variation of T2 values from subchondral bone to surface, relative short T2 in the deepest layers and susceptibility at the bone cartilage interface [3].

Articular cartilage can be divided into four zones, namely the superficial zone, the transitional or middle zone, the radial zone and the calcified zone, which have variable structural organization reflected by the variation in T2 ranging from ~20 to 40 ms for superficial layer to sub-millisecond for calcified cartilage [4-9]. Most of the currently available clinical and research MR imaging techniques, including proton-density weighted Fast Spin Echo (FSE) [10], T2-weighted FSE [11], gradient echo imaging [12], magnetization transfer [13], T2 mapping [14], delayed Gadolinium enhanced MR imaging (dGEMRIC) [15], and steady State Free Precession (SSFP) imaging [16-18] have focused on the superficial layers of cartilage. The study of early and late alterations to the deeper layers of cartilage, including the deepest radial zone and calcified cartilage, has been overlooked due to technical limitations (i.e., the minimal achievable TEs are too long to detect signal from the deeper layers of cartilage because of their very short T2s).

There is growing interest in the deepest layers of articular cartilage, including the calcified and deep radial layers located just superficial to the subchondral bone. In the setting of osteoarthritis, it has been historically accepted that cartilage degeneration begins in its superficial region. More recently, however, the role of lesions in the deep radial and calcified layers of cartilage in the pathogenesis of OA has been emphasized [19-26]. Lesions in these layers may destabilize the foundation of cartilage and result in degeneration of more superficial layers [20-23]. Such lesions can result from a single impaction injury while leaving superficial cartilage intact [24]. In the setting of OA the calcified layer of cartilage has shown a spectrum of findings ranging from eburnated or absent, to extremely hypermineralized [25,26].

The deep layers of cartilage are also important in chondral repair. In the setting of osteochondral allograft and autologous chondrocyte implantation, there is evidence that graft incorporation and chondral healing occurs first in the deep layers of cartilage before progressing superficially (rather than proceeding in the reverse direction) [20-23,25]. In the setting of microfracture, a recent study suggests that complete removal of the pre-existing calcified layer of cartilage significantly improves the healing of chondral defects [27]. The study pointed out that removal of the calcified layer was not obvious using standard arthroscopic equipment. In this situation, a non-invasive means of evaluating the status of the deep layers of cartilage could ensure optimal repair.

The paucity of MR imaging studies exploring the deep layers of cartilage are due to the fact that they have very short T2 values and are typically undetectable with conventional MR sequences at all field strengths on all clinical MR systems. By using a novel form of slice selection, radial mapping of k-space and variable-rate selective excitation (VERSE), pulse sequences with TEs 100-1000 times shorter than those currently available on clinical MR systems can be achieved [28-36]. These Ultrashort TE (UTE) sequences can directly image the deep layers of cartilage with high spatial resolution [34,35].

While UTE imaging of articular cartilage has been investigated on clinical scanners at 1.5T [33], their implementation at higher...
fields, capitalizing on the considerably higher signal achievable, has not yet been investigated. In order to use the UTE imaging scheme in routine clinical setting at the higher field of 3T, several enhancements are essential. These include primarily, the detection of signals which decay very rapidly after the RF pulse with the concomitant problems of remnant RF energy and gradient eddy currents at these short TE values, suppression of tissues with longer T2s, and of fatty tissues. This paper describes the development and implementation of these features in UTE acquisition, and testing their relative efficacy in terms of Signal-to-Noise Ratio (SNR) and Contrast-to-Noise Ratio (CNR) in imaging the deep radial and calcified layers of articular cartilage.

Materials and Methods

All scans were performed on a 3T Signa TwinSpeed scanner (GE Healthcare Technologies, Milwaukee, WI) with a peak gradient amplitude of 40 mT/m and a maximum slew rate of 150 mT/m/s. A single channel receive-only 3-inch coil was used for imaging of cadaveric samples. A quadrature knee coil or an eight-channel knee coil was used for volunteer knee cartilage imaging. The standard UTE MR imaging sequence as well as several variations of this sequence were developed and subsequently applied to the deep radial and calcified layers of cartilage. The various components are listed as follows.

Standard 2D UTE pulse sequence

This 2D UTE sequence (Figure 1) was designed to profile tissues with predominantly short T2 components, in this case the deep radial and calcified layers of articular cartilage. A specially designed radiofrequency (RF) "half"-excitation pulse was combined with VERSE to synchronize RF excitation and gradient ramp-down [33]. Radial projection reconstruction combined with ramp sampling was used for UTE data acquisition. For each radial line of k-space, two acquisitions were performed by collecting data with the slice selection gradient in one direction and adding this data to that collected with the slice selection gradient reversed [31-34]. The radial projections were repeated through 360° to cover the whole k-space. The combination of VERSE and radial ramp sampling enables very short delay time between RF excitation and Free Induction Decay (FID) data acquisition. This delay time, referred to as TE though actually it is the time to start FID acquisition, is determined primarily by the time required to turn off the RF transmitter and to enable the receiver, and can be reduced to 8 µs by using a fast transmit/receive (T/R) switch [33-34]. Since there is no fast T/R switch available for the 8-channel phased-array knee coil, a longer minimal TE of 100 µs was used whenever images were acquired using this coil.

The 2D UTE sequence is sensitive to eddy currents, gradient anisotropy and timing errors [36]. Timing for slice selection gradients and readout gradients was manually tuned to within an error of ± 2 µs by monitoring of the image quality. Artifacts originating from these errors were further reduced by empirically shifting the radial k-space trajectories during on-line image reconstruction. Further, a hysteresis gradient was added after each readout gradient [37]. This reset pulse results in residual magnetization which is less dependent on the preceding waveform history and results in more consistent gradient errors which can be corrected through k-space trajectory shift.

Multi-echo gradient echo UTE pulse sequence

Multi-echo acquisition followed by later echo subtraction has been shown to be effective in suppressing long and medium T2 signals and provides high contrast imaging of short T2 components in brain, knee and cortical bone at 1.5T [31,32]. Therefore, a multi-echo gradient echo UTE acquisition was developed at 3T in an effort to increase the contrast by suppression of the long T2 components in the articular cartilage. This was achieved by subtracting the later echo image from the first one, equivalent to a band pass filtering. Short T2 signals decay to near zero in the second echo, thus minimally affected by the subtraction.

Gradient echo UTE pulse sequences with fat suppression

Signals from fat may reduce the conspicuity and dynamic range of the short T2 signals from the deep layers of cartilage. Fat suppression techniques were applied in an effort to increase the dynamic range of the deep layers of cartilage and thereby improve their contrast. However, conventional fat saturation may be problematic in imaging tissues with very short T2s, which have a broad spectrum which may overlap with that of fat. As a result, fat saturation pulses may degrade the short T2 signals either directly, or as a result of magnetization transfer [6,13]. Various fat suppression pulses with different excitation profiles and frequency positions were investigated. These included a long duration asymmetric SINC pulse (duration of 16 ms) and an adiabatic pulse (duration of 17 ms). The optimized fat saturation pulse was then combined with UTE FID acquisition and dual echo gradient echo UTE acquisition, respectively.

Multi-echo spin echo UTE pulse sequence

The later echoes in a multi-echo gradient echo UTE acquisition described in 2) above are sensitive to off-resonance effects due to B₀ inhomogeneity and susceptibility. Therefore a multi-echo spin echo UTE acquisition technique was developed where a spin echo image was generated by introducing a refocusing 180° pulse after the UTE FID acquisition as shown in (Figure 2). The 180° pulse refocuses the long T2 water and fat spins, and is therefore less sensitive to off-resonance effects. Subtraction of the spin echo image from the first FID image may result in better suppression of long T2 water and fat signals, thus improving the delineation of the deep layers of cartilage.

Ex vivo and In vivo imaging of knee cartilage

In the ex vivo study UTE imaging of knee cartilage was performed on 8 cadaveric specimens. In the in vivo study 6 healthy volunteers were recruited for UTE imaging after obtaining written informed consent approved by the investigational review board of our institute. Conventional UTE imaging was acquired in the axial plane for the patella cartilage, and oblique sagittal plane for the femoro-tibial
two-dimensional fast Fourier transformation to generate UTE images. During reconstruction the k-space data were first regridded onto a Cartesian grid using Kaiser-Bessel kernel, followed by inverse 512 × 512 half projections, 511 half projections, ± 62.5 kHz bandwidth, and 50% to 200% slice gap. The total scan time ranged from 4 to 10 minutes.

Image analysis

For quantitative assessment of the quality of subtracted and non-subtracted UTE images with and without fat saturation, both SNR and CNR measurements were performed. SNR was calculated as the ratio of the mean signal intensity inside a user-drawn Region of Interest (ROI) within the deep layers of cartilage to the standard deviation of the signal in an ROI placed in the background. Since the deep layers of cartilage are very thin, a small ROI containing 5 to 10 pixels was used. CNR between the deep layers of cartilage and superficial layers of cartilage (CNR_{DL,SL}) and fat (CNR_{DL,F}) were calculated as their signal difference over background noise.

Results

Figure 3 shows UTE imaging of a cadaveric knee sample using the basic UTE FID acquisition. A high signal line at the lateral facet (thin arrows) represents the deep radial and calcified layers of cartilage. A focal area of loss of the high signal line at the medial most portion of the medial facet (thick arrow) represents the loss of calcified layer cartilage.

Dual echo gradient echo UTE acquisition utilized an echo time of 8 to 100 μs for the first image and 6 to 16 ms for the second image. Echo subtraction suppressed signals from fat, muscle, and long T2 superficial layers of cartilage, thus selectively depicting the short T2 deep radial and calcified layers of cartilage as shown in figure 4. The femoral-tibial cartilage from the right knee of a 28-year-old healthy volunteer obtained through lateral femoral condyle shows high signal and excellent image contrast between the deep layers and superficial layers.

Image contrast between the deep layers of cartilage and fat is suboptimal in figures 3 and 4. A long duration fat saturation pulse was combined with the 2D UTE imaging sequence in order to suppress fat with minimal suppression of the short T2 deep layers of cartilage. It should be notified that long adiabatic pulse provides more uniform fat suppression and about 15% less attenuation of signal from the deep layers of cartilage than SINC pulse, and is used here. The center frequency for the fat saturation pulse was shifted from -440 Hz to -540 Hz, resulting in slightly less fat suppression but also less attenuation of the short T2 signal. Figure 5 shows fat suppressed UTE imaging of a cadaveric sample, which shows high contrast between fat and cartilage, but little contrast between the deep layers and superficial layers of cartilage. Figure 6 shows dual echo images of a cadaveric knee sample with fat saturation. Excellent image contrast was achieved for the deep layers of cartilage in the subtracted image (arrow), where the combination of fat saturation and dual echo gradient echo subtraction suppressed both fat and long T2 water signals simultaneously.
Dual echo spin echo acquisition employed an echo time of 8 to 100 µs for the first image and 16 ms or longer for the second image. Echo spacing is significantly longer than that used in dual echo gradient echo acquisition due to the requirement of a refocusing pulse (3.2 ms) and gradient lobes employed to suppress stimulated echoes. Figure 7 shows UTE imaging of a healthy volunteer using a dual echo spin echo acquisition (lower row) as compared to a dual echo gradient echo acquisition (upper row) using a quadrature knee coil for signal reception. More uniform signal was achieved for fat and muscle in the spin echo image, resulting in better image contrast between the deep layers of cartilage and fatty marrow in the subtracted image.

UTE imaging typically suffers from a poor slice profile due to half pulse excitation and VERSE. A slice gap of 50-100% was employed for multi-slice UTE imaging. Figure 8 shows dual echo gradient echo subtracted images of six of twenty sagittal slices which covered the whole left knee with 100% gap. The deep layers of cartilage and meniscus were highlighted with high SNR and high contrast for all slices. The superficial and middle layers of cartilage were well suppressed through echo subtraction. Figure 9 shows multi-slice UTE images of a cadaveric knee sample using a dual echo gradient echo acquisition combined with fat saturation. Excellent image contrast was achieved for the deep layers of cartilage for all slices (arrows).

Table 1: Mean SNR for the deep layers of cartilage (SNR_{DL}) and CNR between the deep layers of cartilage (CNR_{DL-FL}) and fat (CNR_{DL-F}) for five different approaches including: UTE free induction decay acquisition (UTE FID), UTE dual echo gradient echo acquisition and subtraction (UTE GES), UTE FID acquisition with fat saturation, UTE dual echo gradient echo acquisition with fat saturation, and UTE dual echo spin echo acquisition (UTE SE).

<table>
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<th>Protocol</th>
<th>UTE FID</th>
<th>UTE GES</th>
<th>UTE FID+ Fat Saturation</th>
<th>UTE GES+ Fat Saturation</th>
<th>UTE SE</th>
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<tr>
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<td>-1.3</td>
<td>16.4</td>
<td>7.8</td>
<td>3.7</td>
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Discussion

The lack of imaging evaluation of the deep layers of cartilage stems largely from the fact that it is technically difficult to image, very thin (<200 µm) and with a very short T2* (~1 ms at 3T), thus undetectable using conventional MR sequences [34,35]. It has been demonstrated here that 2D UTE acquisition provides high contrast images of short T2 species in the knee joint, including the previously undetectable deep radial and calcified layers of cartilage and meniscus (Figures 3-9). The high signal in the calcified layer of cartilage was probably due to calcification producing T1 shortening as described with some lesions in the brain with conventional sequences, and seen routinely in tissues such as cortical bone with UTE sequences [38]. Evidence that the high signal regions are from the deep radial and calcified layers was obtained by direct reference to cadaver specimens and observations in vivo of the short T2 components in this region. To optimize the image contrast for short T2 signals, quantitative measurement of T1 and T2* for these different layers of cartilage has been performed on cadaveric samples and volunteers. Preliminary results show that the calcified layer cartilage has short T2* in the order of 1 ms, and short T1 around
300 ms at 3T [9,33]. Details of T1 and T2 measurement at 3T and UTE imaging sequence optimization will be reported elsewhere.

Typical imaging of short T2 tissues requires long T2 suppression techniques to improve image contrast. These techniques include fat suppression, long T2 water signal saturation [39,40], and inversion recovery techniques [38]. Clinical fat saturation techniques employ a non-selective saturation pulse to selectively suppress fat signals. There might be significant overlap between the spectrum of the short T2 species and that of the fat saturation pulse, resulting in significant suppression of the short T2 signals [6,13]. An optimized fat saturation pulse should have enough spectral bandwidth to cover the dispersed fat resonance frequencies at 3T, but minimal spectral overlap with that of the short T2 signals and therefore has typically a relatively long duration. A long pulse duration also helps to reduce signal attenuation from the short T2 tissues, which may experience significant dephasing during the RF excitation and thus largely unaffected by the fat saturation pulse. Long T2 water signals from muscle and superficial layers of cartilage were suppressed through subtraction of a later echo image from the first one, as shown in figures 4 and 6. Echo subtraction is therefore a simple but robust method in improving contrast of the deep layers of cartilage. However, this approach leads to increased noise level. An alternative approach is to use linear combination filtering [41], where the addition of properly weighted multiple TE images results in good suppression of long T2 signals with less noise enhancement. Another approach for direct imaging of the short T2 tissues is to use long duration 90° pulse followed by gradient dephasing and UTE acquisition [39,40]. Recently a dual-band long-T2 suppression pulse was reported to suppress fat and long T2 water signals simultaneously, providing good contrast for short T2 tissues such as ligaments, tendon and meniscus [40]. The limitation of this approach is that long duration pulses typically have limited bandwidth coverage, and are sensitive to off-resonance and B1 inhomogeneity.

Among the five approaches investigated in this paper, the multi-echo gradient echo acquisition provides the best contrast between the deep layers and superficial layers of cartilage with a relatively high SNR, as shown in figures 4 and 8. UTE acquisition with fat saturation provides the highest CNR between the deep layers of cartilage and fat, but limited contrast between the deep and superficial layers of cartilage. The combination of dual echo gradient echo subtraction and fat saturation provides high contrast between the deep layers of cartilage and the superficial layers of cartilage and fat, simultaneously. The subtraction image from UTE spin echo acquisition significantly improved CNR over that from dual echo gradient echo acquisition. However, this technique requires a larger slice gap because a broader 180° pulse is required to more accurately refocus the broad slice profile resulted from half pulse excitation. A large flip angle close to 90° and longer TR is also helpful. All five approaches have been demonstrated to be successful in depicting the short T2 tissues in the knee, including the deep layers of cartilage and meniscus.

One disadvantage of the UTE sequence used here is that it is a 2D acquisition with a slice thickness of 1.7 to 2.5 mm and a gap of 50% to 200 % slice thickness. Partial volume effect may significantly degrade its depiction of lesions, which may be better depicted using three-dimensional UTE acquisition [42]. Another disadvantage of this technique is that the 2D acquisition is sensitive to eddy currents, field homogeneity and gradient non-linearity. Half pulse excitation requires the summation of two acquisitions with slice selection gradient polarity reversed, so that a conventional slice profile is formed. Gradient profile distortion may result in improper weighting of the excitation and mismatch between the two acquisitions with non-ideal cancellation of the imaginary parts of the complex signals and out-of-slice signal contamination. Corrections of the residual slice-select gradients and time-varying main field B0(t) caused by eddy currents are helpful in reducing out-of-slice signal contamination [36,43,44].

**Conclusion**

It has been shown that the 2D UTE sequence combined with multiple gradient echo or spin echo acquisition, with later-echo subtraction, with and without fat suppression, can depict the deep layers of cartilage on a 3T clinical scanner with a degree of delineation till now not possible. Among all the methods investigated in this study, dual spin echo UTE with fat suppression and echo subtraction seems to provide the best contrast for the deep layers of cartilage. Dual gradient echo UTE with fat suppression and echo subtraction is more time efficient in providing high contrast for the deep layers of cartilage. UTE imaging with these modification shows substantial potential of being a powerful radiologic modality for imaging of cartilage injury and osteoarthritic diseases.

**References**


