Clinical ultra-short TE-enhanced T2* mapping of meniscus

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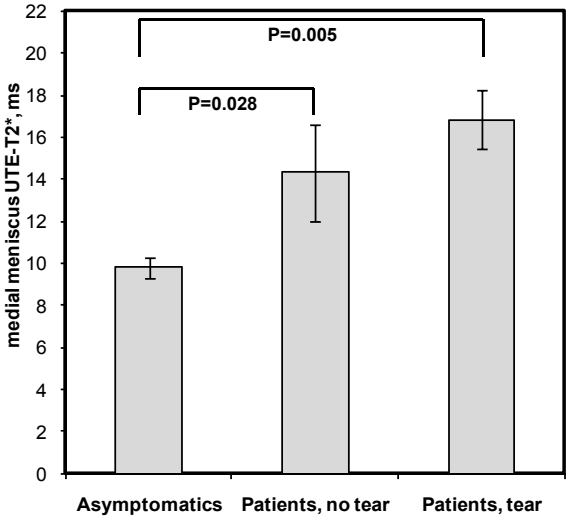
Introduction Ultra-short TE-enhanced T2* (UTE-T2*) mapping is sensitive to short transverse relaxations (T2 <10ms) [1,2]. In articular cartilage tissue, UTE-T2* mapping has been shown to reflect *in vitro* collagen matrix structural integrity, as determined by polarized light microscopy[3], as wells as *in vivo* subsurface cartilage damage, as assessed by arthroscopy[4]. UTE-T2* mapping of meniscus has the potential to reveal subtle structural pathologies not well captured by standardized MRI sequences because the highly organized ultrastructure of meniscus tissue restricts proton mobility and causes rapid T2 relaxation[5]. This work applies clinical UTE-T2* mapping to meniscus to test the hypothesis that it can be used for early detection of meniscus degeneration.

Methods UTE-T2* were acquired on the knees of 32 human subjects on a clinical 3T MRI scanner (MAGNETOM Trio TIM 3T, Siemens Medical Solutions, Erlangen, Germany) using an 8-channel knee coil (In vivo Inc., Gainesville, Florida, USA). Ten asymptomatic subjects, with no known or suspected knee injury or disease (mean age = 26.8 yrs, 5 females), 9 patients with ACL injury but *no* clinically detectable medial meniscus tear (mean age = 28.7yrs, 3 females), and 13 patients *with* a clinically diagnosed (MRI and/or arthroscopy) tear to the medial meniscus (mean age 31.6yrs, 9 females) were included. All subjects provided informed consent; all studies were IRB approved. UTE-T_2* maps in the sagittal plane centered on the femorotibial joint were acquired with an AWSOS sequence (acquisition-weighted stack of spirals)[6]. Eleven echo images, TE ranging 0.6 – 40ms, were collected with 140mm FOV and 256 matrix for 547µm resolution in-plane, and 2mm section thickness. Other acquisition parameters were: 60 slices, 24 in-plane spirals, 11.52ms spiral readout time, 5µs data sampling interval, and FA/TR 30º/80ms. Scan time was 1.92 minutes per TE-image. UTE-T_2* maps were generated with a mono-exponential fitting routine using MRIMapper software (© Beth Israel Deaconess and MIT 2006). Regions of interest (ROIs) were manually segmented from a single section from each knee to include the posterior horn of the medial meniscus as viewed on an AWSOS images with an echo time of 7ms. Mean UTE-T2* values were calculated. Non-parametric Kruskal-Wallis statistics examined differences across all groups and Wilcoxin Signed Rank Sum tests were used to assess pairwise differences. Intersession UTE-T2* repeatability was assessed in 6 of the asymptomatic subjects who underwent MR imaging for UTE-T2* mapping of the left knee, one time daily for 3 consecutive days. To reduce variability due to diurnal variations, subjects were scanned at the same time each day ± 1 hour[7]. To calculate UTE-T2* value repeatability, intra-study-subject average UTE-T2* value (mean ±standard deviation (SD)) was calculated across the 3 study-days for each ROI. Relative inter-subject intersession reproducibility across study subjects was expressed by the root-mean-square average coefficient of variation (RMSA-CV) for each ROI. RMSA-CV was determined by $\sqrt{((\sum CV^2)/n)}$ where intra-subject CV was calculated by dividing the SD of a subjects' UTE-T2* values from Day1, Day2 and Day3 by the mean of the subjects'UTE-T2* values from Day1, Day2 and Day3 for each ROI, and where n was the number of subjects. All statistical analyses were performed using SPSS (SPSS Inc) and Excel (Microsoft).

Results The intersession precision error of UTE-T2* values in meniscus of asympotomatic subjects (n=6) was found to be 1.00ms or under 10% (RMSA-CV). UTE-T2* values observed in menisci of asymptomatic subjects ranged approximately 4-20ms. Qualitatively, UTE-T2* maps of subjects with medial meniscus tear appeared higher and more heterogeneous compared to asymptomatic subjects. Quantitatively, meniscus UTE-T2* values varied significantly with degree of joint pathology (Kruskal-Wallis, P=0.001), Figure 1. UTE-T2* menisci values in subjects with clinically diagnosed medial meniscus tear (n=13, mean±SD 16.8±5.0 ms) were 42% higher (Wilcoxin Rank Sum, P=0.005) than in the menisci of asymptomatic subjects (n=10, mean±SD 9.8±1.5 ms). The difference in UTE-T2* values between asymptomatics and subjects with ACL injury but *without* meniscus tear (n=9, mean±SD 14.3±6.9 ms) was also found to be significant: menisci UTE-T2* values of subjects with joint injury *not* including meniscal tear were 32% higher (Wilcoxin Rank Sum, P=0.028) than menisci UTE-T2* values of asymptomatic subjects.

Conclusion Clinical evaluation of human meniscus in vivo through UTE-T2* mapping is feasible and repeatable with intersession precision error of less than 10%. Moreover, clinical evaluation of 22 subjects with knee pathology suggests that this degree of repeatability is sufficient for non-invasive identification of meniscal tear, and potentially acute subsurface meniscus injury that is not well appreciated by standard MRI. The 40% increase in UTE-T2* values between asymptomatics and subjects with torn menisci seen in this pilot cohort indicate that UTE-T2* mapping of meniscus provides ample dynamic range in which to detect meniscus tear. More significantly, the increase in UTE-T2* values of morphologically intact menisci in subjects with ACL tears suggest that UTE-T2* mapping may be sensitive to subclinical meniscus injury following significant joint trauma. Longitudinal evaluation is needed to determine the ability of UTE-T2* mapping of meniscus to predict progression of meniscal degeneration and the development of future osteoarthritis.



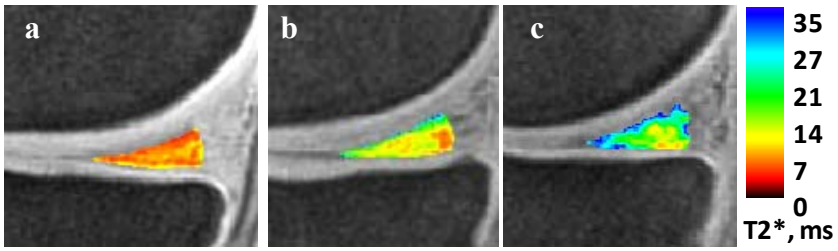


Figure 1 (Left) – UTE-T2* *in vivo* vary significantly with knee-injury status, P=0.001. Subjects with no known or suspected knee injury or disease have significantly lower posterior medial meniscus UTE-T2* values compared to patient subjects with clinically diagnosed medial meniscus tears (P=0.005) and subjects with knee injury but *without* medial meniscal tear (P=0.028). Error bars represent ± SEM.

Figure 2 (Above) - Example clinical 3T MRI UTE-T2* maps. The UTE-T2* value of (a) asymptomatic subject is lower and more homogeneous (top row; 8±2 ms, b) than that observed in (b) a patient subject *without* (middle row; 13±5 ms, c) or (c) *with* tear to the medial meniscus (bottom row; 21±7 ms, f). UTE-T2* values are reported as mean ± SD.

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