Noninvasive ultrashort echo time magnetic resonance imaging assessment of anterior cruciate ligament graft strain

Sarah L. Pownder[1], Michael O. Schaer[2], Richard Ma[2,3], Xiang-Hua Deng[2], Matthew F. Koff[1], Scott A. Rodeo[2,3], and Hollis G. Potter[1]

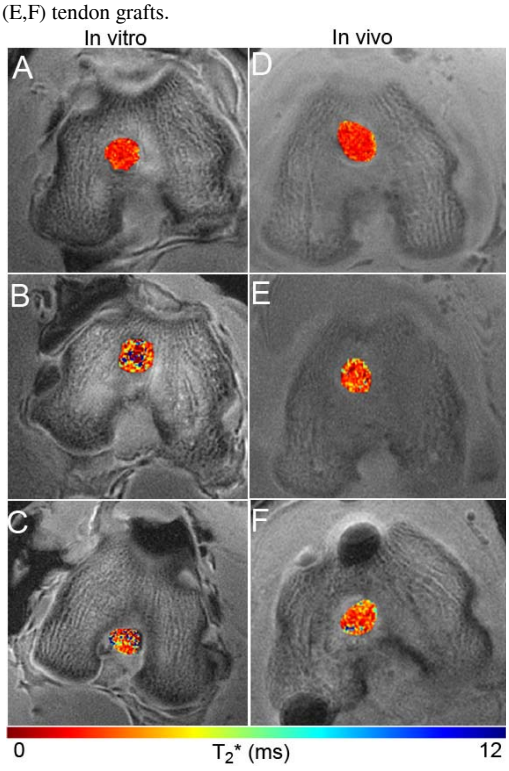
[1]MRI Research Laboratory, Hospital for Special Surgery, New York, NY, United States, [2]Laboratory for Soft Tissue Research, Hospital for Special Surgery, New York, NY, United States, [3]Department of Orthopaedic Surgery, Hospital for Special Surgery, New York, NY, United States

Target Audience: Clinician scientists, radiologists, and orthopaedic surgeons with an interest in non-invasive evaluation of graft strain in anterior cruciate ligament reconstruction (ACLR) using magnetic resonance imaging (MRI)

Purpose: Knee motion is initiated soon after ACLR surgery to prevent knee stiffness; however, studies have shown that early or excessive knee motion resulting in increased graft strain may adversely affect graft-to-bone healing.[1-3] Currently, no validated non-invasive methods exist to directly evaluate the tendon graft and its developing bone attachment following surgery. Fast spin echo (FSE) MRI is commonly used to assess joint structure morphology post-operatively; however, direct assessment of tendon grafts is difficult due to the short transverse relaxation time constant (T2) of the tissue. Tendon grafts are only visible when substantial pathology and disruption of the highly organized collagen fibers has created sufficient proton mobility, resulting in increased signal intensity.[4] Ultrashort Echo Time (UTE) images can be used to visualize changes in short T2 species such as tendon grafts and images acquired at different echo times may be used to calculate the corresponding decay constant (T2*). The goal of this study was to establish UTE as a biomarker of graft strain, using a rabbit ACLR model at the clinically-relevant field strength of 3T. We hypothesized that UTE MRI would provide a quantitative, non-invasive, diagnostic means to assess graft strain.

Methods: *Cadaveric in vitro Study:* A pilot experiment was performed using 3 cadaveric pelvic limbs from 3 individual rabbits. An ACLR was performed on each limb using an ipsilateral flexor tendon graft. Two grafts were pre-loaded to 30N and no preload was placed on the third limb prior to reconstruction. *In vivo Study:* Following IACUC approval, an ACLR was performed on 3 rabbits. Two rabbits were allowed normal cage activity and one was immobilized with an external fixation device. Animals were euthanized at 3 weeks. *MR Imaging*: All MR imaging was performed post-mortem with pelvic limbs disarticulated at the hip. Stainless steel suture used to anchor the tendon graft was present on the cadaveric limbs; stainless steel suture and transfemoral/transtibial bone pins were present in the in vivo limbs. MRI was performed on all limbs using an 8-channel T/R wrist coil on a 3T clinical field strength MRI (14.0 HDx and DV 22.0, GE Healthcare, Milwaukee WI). Limbs were positioned in the coil avoiding placement of the graft at the magic angle. Morphologic axial, coronal, and sagittal FSE images were acquired with the parameters: TE: 25 ms, TR: 6000 ms, ETL: 12, RBW: 195-244Hz/pixel, acquisition matrix: 512x(416-512), FOV: 5-6 cm, slice thickness: 1 mm, slice spacing: 0 mm. 2D UTE imaging was performed in the oblique sagittal and axial planes aligned with ACL using the parameters: TE: 0.3, 5.4, 10.6, 16.4 ms, TR: 350 ms, flip angle: 45°, FOV: 6 cm, acquisition matrix: 512x512, radial spokes: 1001, slice thickness: 2 mm, RBW: 244Hz/pixel, NEX: 2. Image Analysis: Morphologic images were evaluated at all levels of the graft. Axial FSE images were assessed for signal intensity (SI) by drawing a 2 mm^2 circular region of interest (ROI) using a dedicated workstation. Custom written software (Matlab, Natick, MA) was used to calculate tendon graft T2* values at the matching axial slices to those used for SI measurements. Statistical Analysis: A paired t-test was performed for morphologic measurements and T2* values to detect differences between the unloaded and preloaded grafts and between the immobilized and mobilized tendons in the cadaveric and in vivo studies, respectively. Statistical significance was set at $p<0.05$.

Figure 1: Axial UTE MRI of rabbit knees with unloaded (A), preloaded (B,C), immobilized (D), and mobilized (E,F) tendon grafts.



Results: Stainless steel transcortical pins in the in vivo group created susceptibility artifact limiting the number of axial images/ROIs that could be assessed. *Morphologic Evaluation:* No visible morphologic differences were detected on the cadaveric unloaded or preloaded tendon grafts. No differences of SI were detected between unloaded and preloaded tendon grafts on the FSE images, 686.2±222.5 and 571.3±225.3, respectively, p=0.14. Subjective differences were seen on the in vivo mobilized and immobilized tendon grafts. No differences of SI were detected between immobilized and mobilized tendon grafts on the FSE images, 593.7±587.3 and 606.8±414.0, respectively, p=0.96. *Quantitative Evaluation:* Significant differences of T2* values were found between unloaded (2.1±0.3 ms) and preloaded (3.4 ±0.8 ms) tendon grafts (p=0.0024, Figure 1[A,B,C]). Differences were also found between immobilized (2.1±0.2) and mobilized (3.4±1.2) in vivo tendon grafts (Figure 1[D,E,F]), however, these differences were not statistically significant, p=0.2.

Discussion: Visual assessment and SI measurements were poor at detecting differences in the unloaded and loaded or immobilized and mobilized tendon grafts in the cadaveric or in vivo studies, respectively. This is attributed to the rapid T2 decay of tendons, ligaments, and other highly ordered collagen and the comparatively long echo times of FSE pulse sequences. In contrast, quantitative UTE MRI was able to detect differences in grafts experiencing different loads. Preloaded tendon grafts in cadaveric limbs demonstrated a prolongation of T2* suggestive of disruption of the highly ordered collagen environment. Prolongation of T2* likely reflects collagen disruption due to differences in graft strain, noted in the absence of the physiologic remodeling that occurs in vivo. Additionally, mobilized in vivo grafts demonstrated prolongation of T2* values compared to the immobilized limb, indicating a further response due to early graft motion. Prolongation of T2* is attributable to collagen disruption and remodeling of the tendon graft ("ligamentization") as a reflection of physiologic responses. The T2* differences in the in vivo group likely did not reach statistical significance due to the small number of axial slices evaluated as a consequence of susceptibility artifact secondary to metal implants.

Conclusion: UTE MRI has been shown to detect differences in ACLR tendon grafts with different levels of loading. These pilot data demonstrate the utility of using non-invasive UTE MRI to evaluate ACLR tendon grafts. Further studies using controlled loading are needed to correlate T2* values with the degree of tendon strain. Additionally, T2* values need to be correlated with degree of healing to account for the process of ligamentization which may alter T2* values. T2* may be a valuable tool to identify tendon graft strain prior to any detectable changes in standard-of-care FSE images and may help direct patient care including modification of rehabilitation protocols.

References. 1. Al-Nasser, B., et al Arch Phys Med Rehabil 85(2), 2004. 2. Brophy, R.H., et al., J Bone Joint Surg Am, 93(4), 2011 3. Stasiak, M., et al., J Med Device, 4(1), 2010. 4. Gold, G.E., et al., Magn Reson Med 34(5), 1995. **Acknowledgements:** Institutional research support was provided by General Electric Healthcare.