Temporal and Regional Changes of T2* in the Repaired Meniscus

M. F. Koff[1], L. A. Fortier[2], S. A. Rodeo[3], A. Takahashi[4], S. Maher[5], D. Delos[3], P. Shah[1], and H. G. Potter[1]

[1]Department of Radiology and Imaging - MRI, Hospital for Special Surgery, New York, NY, United States, [2]College of Veterinary Medicine, Cornell University, Ithaca, NY, United States, [3]Department of Orthopaedic Surgery, Hospital for Special Surgery, New York, NY, United States, [4]Global Applied Science Laboratory, General Electric Healthcare, Menlo Park, CA, United States, [5]Department of Biomechanics, Hospital for Special Surgery, New York, NY, United States

Introduction. The menisci of the knee function to increase the contact area between the incongruent articular surfaces of the distal femoral and proximal tibial, joint lubrication, chondrocyte nutrition and joint stability [1]. Aggressive attempts at meniscal repair should be made to preserve meniscus function and subsequent joint health since meniscal tears lead to degenerative osteoarthritis [2]. A meniscus that is only partially healed may be clinically asymptomatic [3], and a patient may return prematurely to activities that can put the repair at risk. The current *poor sensitivity* and *qualitative* nature of clinical meniscal healing evaluation precludes accurate decisions about return to activities of daily living.

Magnetic resonance imaging (MRI) is used for non-invasive evaluation of meniscal repairs, but visualization of the meniscus is difficult due to limited signal intensity during standardized imaging due to short transverse relaxation times (T_2). Recently developed ultra-short echo (UTE) sequences display image contrast within the meniscus as well as producing multi-echo images for quantitative T_2* calculation [4]. It would be beneficial to have a validated qMRI technique for physicians to *objectively* and *quantitatively* assess meniscal healing and to provide accurate rehabilitation protocols and prognostic information for the patient. The goal of this study is to evaluate the qMRI technique of T2* mapping using UTE imaging as a biomarker of meniscal integrity. This goal was achieved by measuring the regional and temporal variation in T2* values in an ovine meniscal model.

Methods. This study has IACUC approval. A vertical, longitudinally oriented tear, 15-20 mm in length, was created in the anterior horn of the medial meniscus in 28 sheep under general anesthesia, and was repaired with vertical mattress sutures. A femoral condylar osteotomy procedure was performed to gain sufficient access to the medial compartment. A sham operation in the contralateral limb of the pilot animals confirmed meniscal T2* values similar to previously evaluated non-operative limbs. The animals were euthanized at 4 time points (8 each at 0, 4, 8 mo. and 4 pilot animals at 6 wks.) and MR imaging (GE Healthcare, Waukesha, WI) was performed on both surgical and contralateral limbs : *2D-FSE*: TE:20ms, TR:5000ms, FOV:12cm, Matrix:512x480, 1.3mm thick, BW: ±62.5kHz , NEX:2; *3D SPGR*: TE:3ms, TR:15ms, FOV:12cm, Matrix:512x512, 0.7mm thick, BW: ±62.5kHz; *2D-UTE*: TE:0.3,5.4,10.6,16.4ms, TR:350ms, Flip Angle:45°, FOV:12cm, Matrix:512x512, Radial Spokes: 1001, 2mm thick, BW: ±100kHz, NEX:2. Custom written MATLAB programs (Mathworks, Natick, MA) were used to calculate meniscal T2* values on a pixel-by-pixel basis by fitting the TE data and the corresponding signal intensity (SI) to the equation: $SI(TE)=M_o \cdot exp(-TE/T_2*)+C$, where M_o is proportional to proton density, T_2* is the time constant, and C is a constant and proportional to the image noise. A semi-automated segmentation program divided each meniscus into peripheral (R1), central (R2) and internal (R3) zones. *Statistics*: A three-way ANOVA (Factors: Treatment – Non-Op or Tear Limb, Region – R1, R2, R3, and Time – 0, 6wk, 4mo, 8mo) was used to detect differences of T2* across all factors separately for the anterior and posterior meniscal horns. Statistical significance was set at $p< 0.05$. Appropriate post-hoc Student-Neuman-Keuls (SNK) tests were performed when statistical significant was found.

Results. The groups of time zero, 6 wk pilot animals and 4 month animals have been analyzed to date. *Anterior Horn*: The factor of Type significantly affected T2* values, $p<0.0001$. Tear limbs had significantly longer T2* values than Non-Op limbs (Figs.1&2). T2* values at 6 wk and 4 mo were shorter than T2* at time zero, but the differences were not significant ($p=0.22$). Regional differences of T2* were not detected, $p=0.41$ (Fig.3). *Posterior Horn*: The factors of Type and Time significantly affected T2* values ($p=0.0001$ and $p=0.0011$ respectively). Tear limbs had significantly longer T2* values than Non-Op limbs (Fig.2). T2* values at 6wk were similar to time zero, but significantly shorter than T2* at 4 mo. (Fig.3). Differences of T2* across all regions were also detected, $p=0.004$, with shortening of T2* values from the peripheral to internal zones (Fig.3).

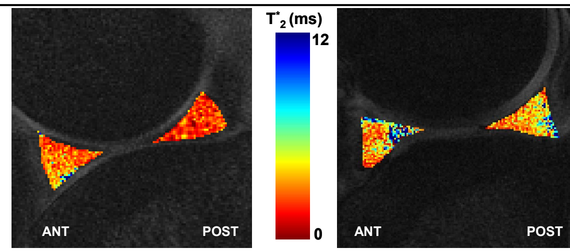

Figure 1. Sagittal T2* maps of the anterior and posterior horns of a non-operative (Left) and a tear (Right) limb of 4 mo animals. An increase of T2* values and greater homogeneity of the T2* values is seen in the anterior horn of the limb with a tear present.

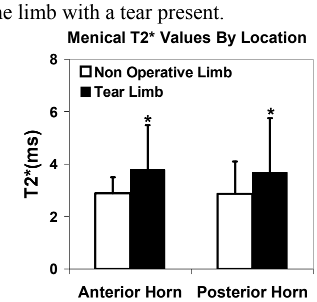

Figure 2. Meniscal T2* values of the anterior and posterior horns of limbs with meniscal tears were significantly longer than the corresponding T2* values of non-operative limbs.

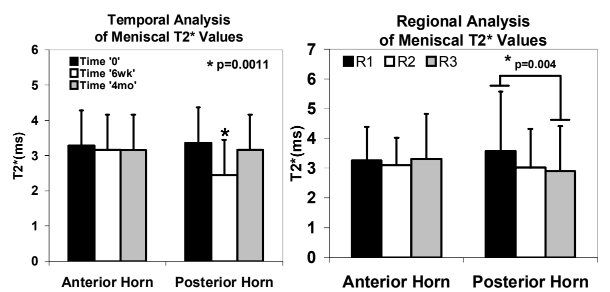

Figure 3. Left –Meniscal anterior horn T2* values are maintained over time and posterior horn T2* values initially decreased, then increased. Right – T2* values of the meniscal posterior horn significantly decreased in magnitude from peripheral (R1) to internal (R3) regions and T2* values of the meniscal anterior horn were heterogeneous due to the tear present.

Discussion. This study evaluated quantitative T2* values as an imaging biomarker. The results to date indicate that temporal and zonal variations of ovine meniscal T2* values are detected by the qMRI UTE imaging analysis. The finding of longer T2* values in the peripheral red-zone and shorter T2* values in the internal white-zone, likely due to the presence and the lack of vascularity, respectively, is similar to a previous human study [4]. Furthermore, a tear in the meniscus not only increases the bulk and zonal T2* values of the meniscus at the zero time point, but also creates greater homogeneity of the T2* values across the regions, likely due to the fibrovascular repair process in the immediate postoperative period. The prolongation of T2* values in the posterior horn at the 4 month time point is likely due to an altered loading pattern as a result of the meniscal surgery which was manifested by the 6 week time point. Planned histological and biomechanical assessment of the repaired menisci will provide information about the composition and strength of the reparative tissue, which will be correlated with meniscal T2* values. A statistically significant correlation will indicate that UTE imaging provides a quantitative and objective measure of in vivo meniscal integrity using T2* mapping.

References. 1.Fithian DC, et al. *Clin Orthop Relat Res* (252), 1990. 2. Turman KA, et al. *J Knee Surg* 21(2), 2008. 3.Steenbrugge F, et al. *Acta Orthop Scand* 75(3), 2004. 4.Gatehouse PD, et al. *Br J Radiol* 77(920), 2004. **Acknowledgements.** This project was supported by NIH/NIAMS grant RC1-AR058255. Institutional research support was provided by General Electric Healthcare. The authors thank Drs. Saadiq El-Amin and Sarah Pownder, and Dan Chen for their assistance with the study.