Practical T2 Mapping of Cartilage in a Rabbit Model of Hemophilic Arthropathy

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Introduction:

Hemophilia is an inherited bleeding disorder caused by deficiencies of clotting factors VIII and IX, respectively. Cartilage degeneration contributes to most of the disease morbidity. Early treatment of hemophilia has been shown to reduce long-term joint morbidity [1]. Novel functional MR imaging techniques hold the potential for being ideal diagnostic and prognostic tools for assessment of early cartilaginous changes in hemophilic arthropathy, prior to the development of cartilaginous abnormalities. Specifically, T2 mapping is known to be sensitive to alterations in collagen structure that result from ingrowth of reparative fibrocartilage and/or fibrous tissue [2]. The mapping could therefore be used as a proxy of collagen organization in the articular cartilage of hemophilic arthritis. Unfortunately, conventional T2 mapping techniques using multiecho spin-echo pulse sequences can be very time consuming and non-feasible in clinical practice. To address this problem, we employed a new short-TR spin echo T2 mapping technique. In this technique by keeping TR-TE constant, undesired T1 weighting is eliminated from the T2 weighting. This maintains the accuracy of the T2 measurement [3]. In addition to cartilage alterations, another important characteristic of hemophilia is the presence of active macrophages in the joint synovium. To detect this activity, the use of ultrasmall paramagnetic iron oxide contrast-enhanced MRI (USPIO CE MRI) has been proposed. However, the presence of USPIO may alter the T2 maps. The objectives of this study were therefore: 1) to validate the use of a new short-TR T2 map technique (constant TR-TE values) for assessment of early cartilaginous changes over time in knees of a rabbit model of hemophilic arthritis, and 2) to determine whether the use of USPIO CE MRI prior to acquisition of T2 maps alter the T2 values**.**

Material and Methods:

Unilateral hemophilic arthritis was induced by intraarticular injection of whole blood in one of the knees of 9 juvenile rabbits. Four knees of non-injected rabbits served as controls. Imaging was acquired on a 1.5T GE Signa system (GE Healthcare, Milwaukee, WI) using a dualflex surface 3 inch coil. Intraarticular blood injections were performed on weeks 1, 5 and 10 of the experiment. The rabbit knees were scanned at baseline (prior to any injections) and after arthritis induction on weeks 1, 5 and 10. At each of the four time points, scans were performed before and 48h following intravenous administration of USPIO contrast agent. T2 maps were acquired with conventional (TR=2000ms, scan time, 13.12min per echo) and short-TR T2 (TR-TE=500ms, scan time, 3.24min per echo) spin echo techniques. In both cases, TE=13, 19, 28 and 41ms were used. The weight bearing part of the knee cartilage was selected as the region of interest (ROI) (Fig. 1). T2 maps of each ROI were calculated on a pixel by pixel basis with Matlab (indirectMatlab, Natick, Mass). All rabbits were sacrificed at week 10 after the last imaging session and the medial condyle of the femur underwent histologic analysis (picrosirius red staining by means of polarized light microscopy).

Results:

Five out of 9 (56%) arthritic knees developed erosions visible macroscopically on week 10 of the experiment. Figure 2 shows the T2 values of the ROIs over time (with and without prior administration of USPIO contrast agent) using the two T2 mapping (conventional and short-TR) sequences. There was an overall decrease in average T2 values in arthritic knees over time for both cases of with and without USPIO contrast agent. This result was true for both the conventional T2 map sequence ($P<0.0001$, generalized estimation equation method) and the short-TR sequence ($P<0.0001$). No such decrease in T2 map values was noted in control knees (with use of USPIO, $P=0.97$ for conventional T2 map; and $P=0.74$ for short-TR T2 map). Quantitative assessment of the ROIs showed mean T2 values of 36.3, 30.0, 20.83, 21.28 for the conventional T2 map sequence, and mean T2 values of 39.67, 27.22, 26.21, 15.47 for short-TR T2 map, respectively at baseline, weeks 1, 5 and 10 of the experiment. Signal to noise ratios (SNR) measured for both methods showed lower (50%) SNR for short-TR T2 maps while the scan time of the short-TR scan was only 25% that of the long-TR scan. A significant difference was noted for T2 values obtained before and after the administration of USPIO contrast agent over time both for conventional ($P=0.0079$) and short-TR ($P=0.0147$) sequences. Status of organization of T2 maps (transition of high-to-low T2 signal) at week 10 of the experiment was well correlated with corresponding histological specimens.

Conclusion:

Both conventional and short-TR T2-mapping analyses are sensitive markers to detection of organizational changes in articular cartilage composition over time in knees of a rabbit model of hemophilic arthropathy. T2 maps with short-TR provide similar T2 values for cartilage in shorter scan time (one-quarter) with the price of lower SNR. Reduced SNR is caused by less longitudinal signal recovery. Therefore, quantitative short-TR T2 map seems to be valid as a marker of cartilage hydration and degeneration. The concomitant use of USPIO contrast material overestimates the decrease in T2 map values, either using the conventional or the short-TR technique.

Acknowledgements: The authors would like to acknowledge the generous support of Bayer Healthcare Inc

References: (1) Nuss R. et al. Pediatric Issues in Haemophilia (1997); (2) White LM et al. Radiology (2006); (3) Vidarsson L. et al. Magn Reson Med (2005)

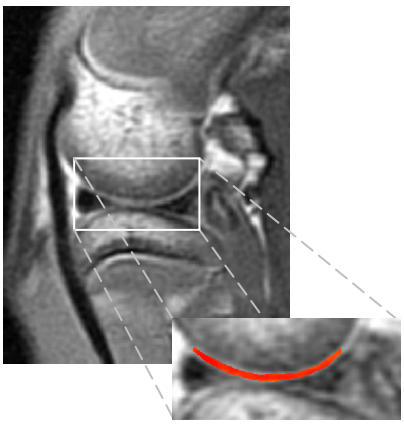

Figure 1. Sagital knee spin echo image. The inset demonstrates the ROI used for T2 mapping

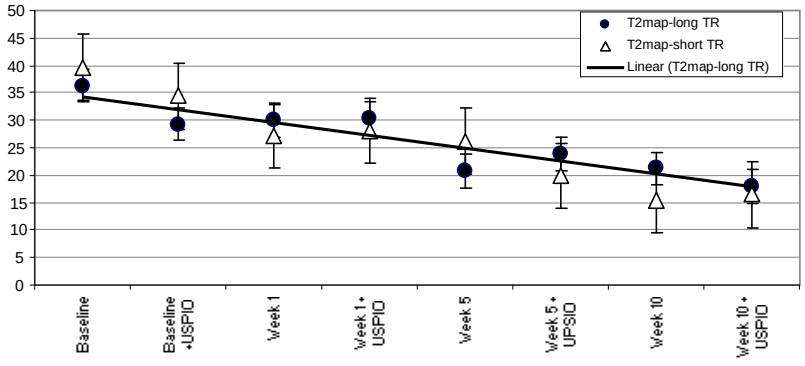

Figure 2. T2 map for short and long TR over time with and without USPIO