Clinical feasibility of a stimulated echo based diffusion sequence and correlation between T1rho and diffusion values

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Purpose: Research has shown that diffusion weighted imaging (DWI) has a strong potential for diagnosing early cartilage and meniscus damage and has clinical implications in joint disorders such as Osteoarthritis (OA) at high magnetic field strength (7T)[1,2]. In our previous work, we demonstrated a novel diffusion sequence using a stimulated echo (STE) diffusion preparation with magnetization prepared angle modulated partitioned k-space (MAPSS) acquisition for knee cartilage imaging at 3T[3]. In this current work, we have validated the sequence with a larger sample size and also analyzed the data to determine if any correlation exists with T1ρ. MR T1ρ relaxation time has been used as a non-invasive biomarker for cartilage degeneration since it is associated with proteoglycan content in the cartilage and increased T1ρ is seen in OA[4].

Methods: Forty-four subjects (22 healthy; Kellgren-Lawrence score[5],KL 0 and 1 and 22 OA; KL 2 and above) were recruited as a part of ongoing research study at our institution. Informed consent was obtained for each subject under an IRB approved protocol. All subjects were scanned at GE wide bore 3T scanner (MR750w) with an 8-channel phased array knee coil (Invivo Corp, Gainesville, FL). The STE-MAPSS acquisition is faster and more signal efficient than conventionally used spin eco EPI sequence at 3T. Our scan time (1:16 minute for 1 direction with a 2x phase acceleration, 1:52 minutes for 1 direction without acceleration, 20 slices) is significantly less than the acquisition time of the sequences that have been proposed in the past [2,6,7].The sequence parameters for the stimulated echo diffusion sequence were: image matrix:256x128, field of view:14cm, bandwidth:62.5kHz, slice thickness: 4mm, number of slices:22, number of directions: 6, δ:4.25ms, Tmix:150ms, b0-value:0.86sec/mm2, b-value:260.4sec/mm2, maximum gradient amplitude:$3.3x10^{-5}$ T/mm and scan time:7 minutes. To maintain stimulated echo behavior, the non-diffusion weighted image (b=0) has very small diffusion gradients (amplitude $0.25x10^{-5}$ T/mm). KL scores were assessed by an experienced radiologist. For calculating the MD and FA values, the articular cartilage was divided into six compartments namely, lateral femoral condyle (LFC), medial femoral condyle (MFC), patella, trochlea, lateral tibia (LT) and medial tibia (MT) during semi-automatic segmentation done using in house software in Matlab. A non-linear rigid registration of diffusion-weighted images was applied using Rview. Segmentation was performed on non-diffusion weighted image (b=0) of the diffusion sequence and superimposed on the diffusion weighted ones. The MD and FA values were calculated using a non-linear diffusion tensor-fitting algorithm in Matlab. The T1ρ sequences had the following parameters: FOV=14cm, 256x128 matrix, slice thickness=3mm, number of slices:30 slices, TSL=[0,2,4,8,12,20,40,60ms], spin lock frequency=500Hz, TE=[0 0,3.4,6.8,10.3,20.5,34.2,47.8,61.5ms], TR/TE=5.2/2.9ms. The composite tip-down and tip-up RF pulses were used to compensate for B0 and B1 inhomogeneities and the 3T exam used 2x phase ARC acceleration. The segmentations from diffusion images were superimposed over the T1ρ images and adjusted for using the same in house software. Lastly, the T1ρ values were correlated with MD and FA values using Pearson's correlation for ten subjects (5 healthy and 5 OA). The correlation was classified as low (<0.5), moderate (>0.5 but <0.7) and strong (>0.7).

Results and Discussion: The Mean Diffusivity (MD) and Fractional Anisotropy (FA) values are similar to previously reported values and show the expected trend of increasing and decreasing respectively with increasing KL score[2](Fig 1a). Some exceptions were seen in lateral tibia compartment for both MD and FA. In diffusion weighted sequences, patient motion introduces undesirable effects that may have resulted in variation in our diffusion values. Representative in-vivo images obtained using STE-MAPSS sequence are shown (Fig 1b). We were also able to correlate the high MD and low FA values with the damaged regions of the cartilage. A small correlation between the T1ρ and diffusion values in all six compartments except patella and lateral tibia for MD and a moderate correlation for medial femoral cartilage for FA was observed (Table 1). The small sample size and a higher number of subjects with medial OA (which is the most common type of OA[8]) may explain the small and moderate correlation we observe for MD and only medial femoral compartment for FA respectively.

Knee compartment	MD	FA
LFC	0.23	-0.19
MFC	0.35	-0.5
Patella	-0.03	-0.05
Tibia-Lateral	-0.27	-0.28
Tibia-Medial	0.21	-0.22
Trochlea	0.3	0.25

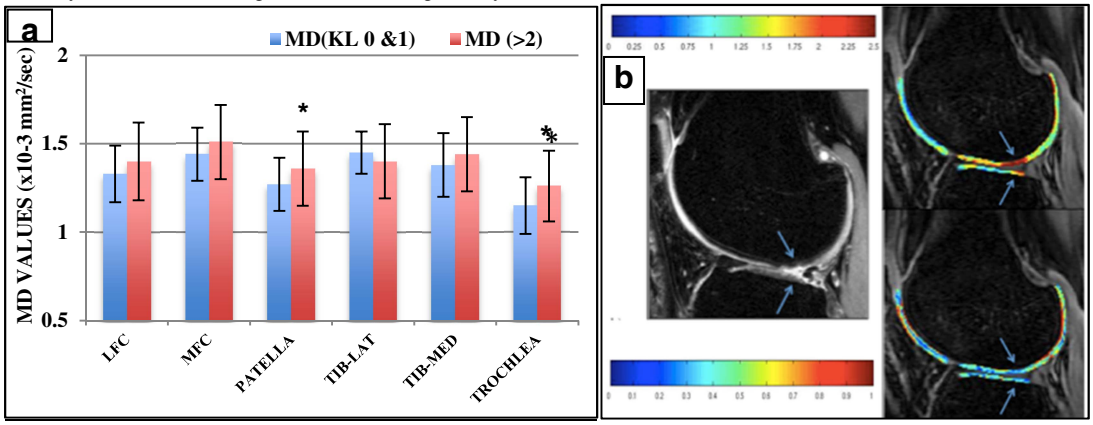

Fig. 1(a) Bar graph showing mean diffusivity (MD) values of healthy and OA for 44 subjects (denotes significance, error bar indicates std. deviation); (b) Knee MRI of a patient with OA (KL=3). The CUBE image (left) of Trochlea, LFC and LT regions and the corresponding STE-diffusion image with MD (top right) and FA (bottom right) colormap overlaid. The high MD and low FA diffusion values can be seen in regions of cartilage damage (shown with arrows). The diffusion gradient from low (blue) to mid (green) to high (yellow) MD values ($x10^{-3}mm^2/sec$) can also be seen within the cartilage layers in the trochlea (top right). (c) Table showing correlation between T1ρ and diffusion MD and FA values for ten subjects.*

Conclusion: In conclusion, the clinical feasibility of our STE-MAPSS sequence is validated in this work. Diffusion and T1ρ quantitative measurements have demonstrated potential to reflect biochemical composition of cartilage in early OA. These two non-invasive OA biomarkers when used complementarily with standard cartilage imaging may potentially increase a clinician's ability to detect subtle early cartilage matrix changes associated with early OA. Future work will include imaging of additional volunteers and subjects with knee osteoarthritis for further validation and correlation with T1ρ as well as T_2. Presently the main focus of this work is on imaging cartilage but in the future scope exists for imaging meniscus as well. In future it will be interesting to see the correlation results for diffusion and T1ρ and T_2 with bigger sample size.

References: [1] Filidoro et al., MRM 2005;53:993-998; [2] Raya et al.,Radiology 2012;262:550-559; [3] Guha et al; ISMRM 2013: 21,3543; [4] Li et al, Osteoarthritis and Cartilage 2007;15:789-797; [5] Kellgren et al.,Ann Rheum Dis 1957;16:494-501; [6] Miller et al, MRM 2004; 51:394-398; [7] Bieri et al, MRM 2012; 67:691-700; [8] Henriksen et al., Arthritis Care and Research 2010;62:501-509.