Feasibility and reproducibility of $T_{1\rho}$ MRI examining osteoarthritis in a guinea pig model

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Background

Osteoarthritis (OA) is a degenerative joint disease which causes severe pain and is associated with tremendous burden and health care costs. Knee and hip OA are especially important because they are primarily the OA cases contributing to chronic disability amongst the older population (1). More than 50% of U.S. residents over 65 years of age experience pain and limitation in mobility due to knee OA (2). Currently there is no cure for the disease and therapeutic interventions are primarily targeted to symptomatic relief. Different kind of animals have been shown to spontaneously develop OA (3). Guinea pigs are unique in that OA progression occurs much quicker than other animals. The purpose of this study is to demonstrate the feasibility of using the Dunkin-Hartley guinea pig model as a reliable and practical system for the study of OA progression in longitudinal studies.

Materials and Methods:

All experiments were performed with approval from the Institutional Animal Care and Use Committee. Images were obtained from the guinea pig stifle joint using a $T_{1\rho}$-prepared 3D balanced Gradient Echo (bGRE) sequence at 9.4T (Varian horizontal bore magnet with a custom coil). While previous studies utilized $T_{1\rho}$ -weighted Fast Spin Echo sequences, a bGRE readout allows for significantly shorter scan duration compared to the FSE. Reproducibility was assessed using 4 month old guinea pigs (n=3) and was determined by coefficient of variation analysis. Two age cohorts, 3 (n=3) and 12 months (n=3), were used to confirm age variation of $T_{1\rho}$ values. $T_{1\rho}$ MRI was performed with the following parameters: FoV=40mm x 40mm, slab thickness=16mm, acquisition matrix=512x256x16 – interpolated to 512x512x32, for a voxel size of 78µm x 78µm x 500µm, α=20°, centric k-space encoding, TE=9ms, TR=14ms, T_1 magnetization recovery delay = 2 seconds. Total imaging time was 24 minutes per acquisition using 16 signal averages. The spin-lock amplitude was fixed at 1500Hz. Four $T_{1\rho}$-weighted images (spin-lock duration 5,10,20,30 ms) were acquired. Images were then fitted on a pixel by pixel analysis to the $T_{1\rho}$ exponentially decaying function to generate $T_{1\rho}$ relaxation maps as described previously ( ).

Results and Discussion:

Figure 1 shows the representative images obtained with different spin lock duration with a fixed spin lock amplitude. Table 1 shows the inter- and intra- animal coefficient of variation from the three repeated measurements of $T_{1\rho}$ relaxation maps from three animals. The mean coefficient of variation of $T_{1\rho}$ measurement from all the animals was 6.6%, indicating a high degree of reproducibility of the measurement. Figure 2 shows representative $T_{1\rho}$ maps from a 3 month and a 12 month old animal. These maps show significantly elevated $T_{1\rho}$ values in 12 month old (50-70 ms) animal compared to that of 3 month old (30-40 ms). Further, we observed a consistent lower $T_{1\rho}$ relaxation number from medial compartment of all the animals studied.

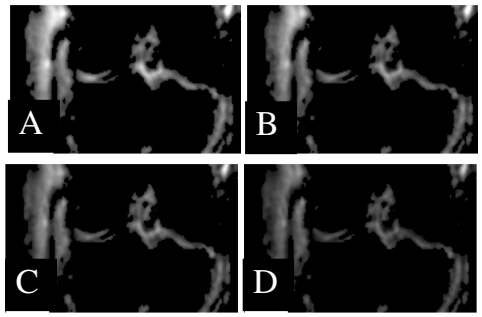

Figure 1 - Four same-slice $T_{1\rho}$-weighted images at spin-lock durations of 5ms (A), 10ms (B), 20ms (C), and 30ms (D). Windowing threshold is same for all images.

	Animal 1	Animal 2	Animal 3
Medial CoV	3.47%	2.91%	9.21%
Lateral CoV	9.54%	4.90%	9.36%
Mean Animal CoV	6.51%	3.90%	9.29%
Mean Total CoV	6.57%		

Table 1 - Coefficient of variance results demonstrating reproducibility of the $T_{1\rho}$ -prepared bGRE sequence. Values are calculated by taking a medial and lateral mean $T_{1\rho}$ value and standard deviation of the ROI to calculate the CoV with inter-animal and intra-animal scanning.

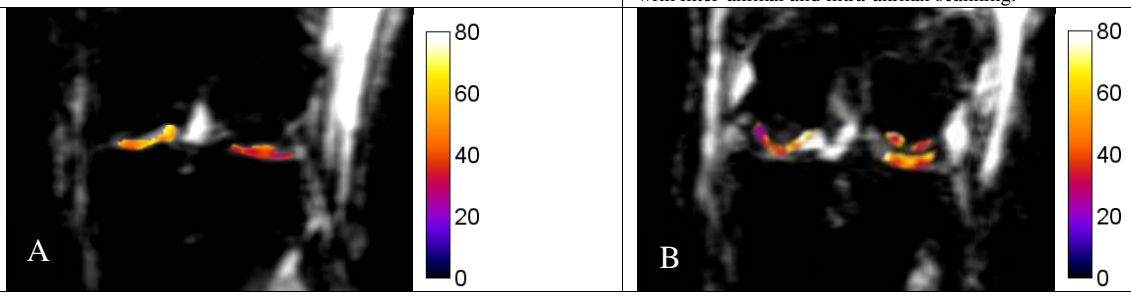

Figure 2 - Representative $T_{1\rho}$ maps overlaid on 3 (A) and 12 (B) month old animals. Color bar is $T_{1\rho}$ values in ms. ROI analysis shows a 40% lateral mean $T_{1\rho}$ increase and 15% medial mean $T_{1\rho}$ increase in 12 month old compared to 3 month old guinea pigs. Additionally, 12 month old cartilage shows significant heterogeneity as opposed to 3 month old animals as shown from mean $T_{1\rho}$ standard deviation measurements from our ROIs – 11ms for 3 month and 25ms for 12 month animals. Initial findings have shown non-uniform cartilage degeneration among medial and lateral compartments. With both young and old animals, lateral cartilage suffers greater degeneration and deterioration than of cartilage in the medial compartment. Accumulation of fluid in the joint space in older guinea pigs causes artificially high $T_{1\rho}$ values and will have to be suppressed to accurately quantify $T_{1\rho}$ in late stage osteoarthritis.

Conclusions:

It is demonstrated that $T_{1\rho}$-mapping can be performed on guinea pig stifle joint with high degree of intra- and inter animal reproducibility. Up to 40% higher $T_{1\rho}$ relaxation times were observed in 12 month old animals compared to that of 3 month old, indicating the feasibility of studying the age dependent disease progression. These preliminary data will form the basis to monitor and track the progression of OA *in vivo* by monitoring the $T_{1\rho}$ relaxation parameter in the guinea pig model.

References:

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