A study on T1ρ mapping of Healthy and Fibrotic Human Liver

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Introduction: Most types of chronic liver diseases lead to fibrosis, which is an excessive accumulation of anomalous extracellular matrix (ECM) proteins (scar). Currently, invasive biopsy of the liver tissue is the gold standard for staging liver fibrosis. Although Elastography combined with MRI is an excellent noninvasive technique for staging liver fibrosis, it requires separate device. There is a clearly unmet need for specific noninvasive techniques for diagnosis of liver fibrosis. Spin lock relaxation in rotating frames (T1ρ) MRI (1) is an emerging technique for exploring changes in ECM in different pathologies (2-6). Objective of the current study was to use $T_{1\rho}$ technique for detecting liver fibrosis. We used T1ρ MRI technique for studying human subjects with liver fibrosis and compared the results with data from healthy livers.

Materials and Methods: All the studies were performed under an approved Institutional Review Board protocol of the University of Pennsylvania. Following informed consent, ten healthy volunteers (27-61 Y) and ten patients (40-60Y) with liver fibrosis as confirmed with biopsy underwent the T1ρ MRI on 1.5T clinical scanner (Siemens, Malvern, PA).

T1ρ Pulse Sequence Design: T1ρ pulse sequence consists of two parts, a B_1 and B_0 compensated T1ρ pulse cluster 90^o(+x)-SL(+y)-180^o(+y)-SL(-y)-90^o(-x) (6, 7, 8) and a segmented turbo FLASH readout and spoiler for each shot. The flash readout sequence uses 1 shot and centric encoding to preserve the maximum T1ρ weighting.

***Imaging parameters*:** T1ρ imaging was performed with time of spin lock (TSL) =0, 10, 20, 30ms, spin lock pulse amplitude B_1 =500Hz, FLASH readout TR/TE =5.1/2.4ms, flip angle =10^o, FOV=300*300mm^2, matrix size =128*128, slice thickness =10mm, number of slices =8, number of shots =1 and a shot TR of 2.5s. The T1ρ weighted data corresponding to a single slice and four TSL's was acquired in a single breath-hold period (scan time =10s).

Image Processing and Data Analysis: The T1ρ-W data corresponding to different spin-lock pulse duration were fitted voxel-wise to mono-exponential decay expression S(TSL) = S(0)*exp(-TSL/T1ρ) for computing T1ρ values. T1ρ values greater than 150ms were set to zero. Average values and standard deviations were also computed from entire segmented liver as well as multiple ROI's drawn on liver tissues (excluding blood vessels). Normalized histogram for each patient was generated from entire liver data. Normalization was carried with respect to peak value in histogram corresponding to liver tissue T1ρ values. Full-width-at-half-maximum (FWHM) values and mode value of normalized histogram of T1ρ were also computed. T-test was used to compare the mean T1ρ values of two groups.

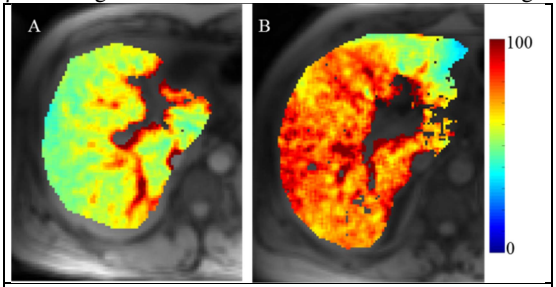

Fig. 1: T1ρ maps of segmented liver overlaid on anatomical image from a health (A) and fibrotic (B) human liver. Color scale is in milliseconds.

Results and Discussion: T1ρ maps of fibrotic liver showed a high T1ρ values (excluding blood vessels) compared to healthy liver as shown in **Fig 1**. Gray values inside liver correspond to pixels either with poor fit (R2<0.8) or T1ρ>150ms and were discarded from analysis. Figure 2 clearly shows higher T1ρ values in subjects with fibrotic livers compared to healthy livers and this difference was significant (p value = 0.001). Due to a small sample size we have included data from all subjects with different grades of fibrosis into single group. As such excessive accumulation of abnormal ECM should lower the T1ρ values; however, this preliminary data show a clear elevation of T1ρ values. This could be due to several factors like inflammation mediated fluid accumulation, change in matrix arrangements in the liver, etc.

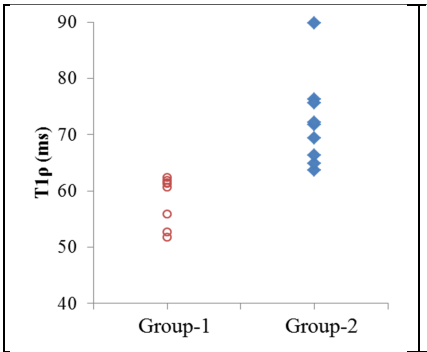

Fig. 2: T1ρ values of human subjects with healthy (Group-1) and fibrotic (Group-2) liver.

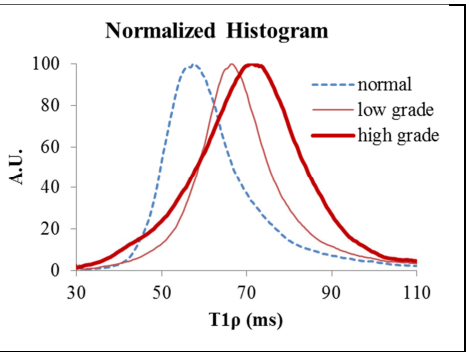

Fig. 3: Normalized histograms of T1ρ values from healthy liver and low grade and high grade fibrosis livers of human subjects.

Interestingly, FWHM parameter, a measure of heterogeneity, for some of the patients was also high. However, there was not a clear separation of FWHM for data from healthy and fibrotic livers. Two data sets of low-grade fibrosis showed a high T1ρ values, but FWHM values similar to healthy livers. Representative histograms from low and high grade fibrosis along with healthy liver are shown in Fig.3. Width of histogram for high grade is greater compared to lower grade fibrosis. Note that for this representative data (Fig.3), T1ρ values for low and high grade fibrosis were similar. We expect that that use of FWHM along with T1ρ values may provide better staging of different grades of liver fibrosis, which need to be tested on large data sets with different grades of fibrosis. Similar to mean T1ρ values, mode value derived from histogram also showed statistically significant (p=0.002) difference between two groups of data. Results of this preliminary study suggest that T1ρ values along with parameter FWHM may be useful in staging liver fibrosis.

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