T1_rho dispersion MR imaging for the Diagnosis and Characetrizaton of Different Liver Pathologies

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Introduction: Liver Disease is currently ranked as the fourth leading cause of death for individuals between the ages of 45 and 54 in the United States and as the ninth leading cause of death for all ages (1). Despite the prevalence of this condition, the gold standard to diagnose and monitor the progress of patients afflicted with liver conditions, particularly cirrhosis, remains limited to liver biopsy (2). Yet, liver biopsies are invasive, associated with high complication rates, poor reproducibility and inter- as well as intra- observer variability and has been reported to misclassify up to one third of conditions in cirrhosis alone (3). All of these shortcomings mandate a new reliable and non-invasive clinical tool, able to objectively diagnose different liver pathologies and quantify their extent. It has been previously shown that T1ρ weighted MR imaging has significant potential to provide for a quantitative and a non-invasive assessment of liver disease (4). In T1ρ weighted imaging, nuclear spins are locked with a radiofrequency locking field, yielding a longitudinal relaxation time (T1ρ) in the rotating frame. By varying the strength of the locking field (B_1), it is possible to make the $T_{1\rho}$ relaxation time changes sensitive to different contrast mechanisms in tissues. The dependence of T1ρ on spin lock field amplitude is called "T1ρ dispersion", a phenomena that has proven effective for tissue characterization (5). Here, we hypothesize that T1ρ dispersion MR imaging can further improve on T1ρ weighted MRI by providing more information to differentiate between different liver pathologies, as well as further characterize some of those pathologies, such as fibrosis.

Materials and Methods: In a preliminary study to evaluate the diagnostic potential of this technique, T1ρ-weighted MR spectroscopy of human liver explants with different liver pathologies as well as some exhibiting either early or advanced degrees of fibrosis were collected for different locking field amplitudes. The B_1 amplitude was incrementally increased from 100Hz to 2000Hz; Spin locking duration was varied from 50ms to 2 second. T1ρ relaxation time was fitted for each B_1 to determine T1ρ and the dispersion curve. Histopathologic diagnosis and fibrosis Metavir grading of samples from each of the imaged liver explants was performed by the collaborating pathologist. Correlation between the histopathalogic diagnosis or the Metavir grade as determined by the pathologist and the T1ρ MRI dispersion was done.

Results: Results demonstrate that consistent differences exist between the dispersion response of liver explants exhibiting different pathologies (Fig.1). Fibrotic livers tend to have persistently higher dispersion response than normal livers while livers with carcinomas show a lower dispersion response than normal livers. Similarly, consistent differences also exist between the dispersion response of samples with different degrees of fibrosis *in vitro* (Fig.2*)* The latter further demonstrates an ability to detect small changes in fibrosis within one histopathologic stage (F4).

Discussion: Different liver pathologies exhibited different dispersion responses, making T1ρ dispersion a potentially excellent technique for tissue characterization in different liver conditions. The lower T1ρ dispersion seen in carcinoma is consistent with less room for exchange between bulk water and macromolecules due to the increasing mass in the liver. The higher T1ρ dispersion response associated with increased fibrosis are thought to be due to increased water trapping associated with increased matrix deposition in the space of Disse in the liver. Our technique also showed an ability to detect small changes within one histopathological stage of fibrosis. T1ρ-based MR imaging of the liver can be sufficiently sensitive to measure early and small changes in hepatic ECM proteins and thus could be used to monitor the progress of patients through different disease stages over short periods.

Conclusion: In conclusion, the preliminary results presented here indicate that T1 ρ dispersion technique has significant potential to not only provide a reliable technique to differentiate between different liver pathologies but also offers a non-invasive quantification of some of those pathologies, such as in fibrosis. Once validated in a larger sample size and on human subjects, this technique can be useful both in the setting of improved patient diagnostics and in quantitative tracking of new treatments for liver disease.

References: (1)Wolf et al., eMedicine(2008). (2)Manning et al., Gatroenterol (2008). (3)Thampanitchawong et al., World J Gatroenterol (1999). (4)Daye et al. , ISMRM (2009), (5) Rommel et al., MRM (1989).

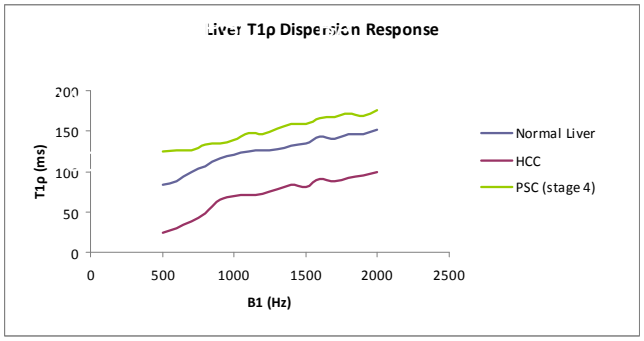

Figure 1: T1ρ dispersion response in different liver pathologies. Fibrotic livers shows a higher dispersion response than normal while a liver with carcinoma shows a lower dispersion response.

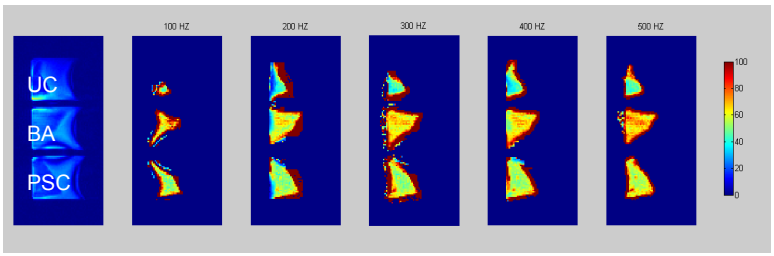

Figure2: T1ρ map of cirrhotic human liver explants at different spin-lock frequencies. Within the same stage of fibrosis (F4 on the Metavir scale), T1ρ MR imaging is able to distinguish smaller, more subtle changes with fibrosis. According to the collaborating pathologist, here, UC had the least fibrosis and BA had the most, with PSC being in the middle.

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