Liver $T_1$ increases with fibrosis and is correlated with liver stiffness and ELF score

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TARGET AUDIENCE
The ability to stratify cirrhosis (scarring) of the liver is important for clinicians and patients to assess disease severity and ascertain prognosis. The current reference tests to assess cirrhosis are either inadequate for stratification (liver biopsy) or invasive (hepatic venous pressure gradient). The ability to assess cirrhosis using a continuous and non-invasive diagnostic tool, which provides detail of the entire liver, is attractive to healthcare professionals, patients and industry.

BACKGROUND
Liver disease is now the 5th largest cause of death in the UK, with a recent study reporting a 68% increase in the prevalence of liver cirrhosis between 1992 and 2001. The gold standard for evaluating the severity of liver disease is a biopsy. However, this procedure is invasive, affected by inter- and intra-observer variations and sampling errors. In the context of significant liver scarring (cirrhosis), liver biopsy provides limited stratification as there can be a spectrum of severity across one categorical stage of disease (e.g. stage 4 in the Metavir classification). The stratification of cirrhosis is imperative for decisions on prognosis and assessing novel compounds in therapies. Two alternative non-invasive methods to stratify cirrhosis use physical or biological approaches. FibroScan® is a recent, physical method to measure liver stiffness [1]; a mechanical pulse is applied, and ultrasound used to measure the resulting wave velocity from which stiffness can be measured and related to fibrosis severity, with a prior study showing a correlation with histopathology [2]. The enhanced liver fibrosis (ELF) test is a biological technique using an algorithm based on serum markers to generate an ELF score [3]. Recently, it has been reported that the MR longitudinal relaxation time ($T_1$) is elevated in the liver of patients with cirrhosis compared with healthy volunteers [4], using a saturation recovery technique in a single axial slice through the liver. We have recently developed a respiratory-triggered inversion recovery method for multi-slice measures of $T_1$ in the abdomen, without the need for complicated motion correction methods [5].

AIM
To compare the MR longitudinal $T_1$ relaxation time parameter in the liver with the non-invasive techniques of ELF and Fibroscan® to stratify liver cirrhosis.

METHODS
The study was approved by the NHS ethics committee, and all volunteers gave informed, written consent. Patients were studied from a prospective, longitudinal study of compensated cirrhosis (CC) (Child Pugh A). 29 CC patients (18M/11F, age 59 ± 1 yrs (mean±SEM), aetiology: 9 ALD/ 8 HCV/ 6 NAFLD/ 2 Haemochrom./ 1 PBC/ 1 HBY/ 1 Autoimmune, MELD score: -0.04 - 10.79). In addition 19 healthy volunteers (HV) were recruited: 12M/7F, age 57 ± 2 yrs. Patients attended on a single day following an overnight fast for a blood test (to evaluate ELF score), FibroScan® and MRI scan. The HV group had only the blood test and MRI scan. FibroScan® measurements were repeated 10 times and a median calculated. MRI was performed using a 1.5T Philips Achieva scanner (body transmit coil, 16-channel SENSE torso receive coil). A modified respiratory-triggered inversion recovery method for multi-slice measures of $T_1$ was used to a 2 parameter model to generate $T_1$ maps using a least squares non-linear curve fit in Matlab®. A binary mask of the liver, excluding major vessels, was used to obtain a mean $T_1$ value across the 3 slices of the liver. $T_1$ values were plotted against stiffness as measured from Fibroscan® and ELF score, and the Pearson correlation coefficient (R) calculated using SPSS 18.

RESULTS AND DISCUSSION
The stiffness and ELF score were highly correlated (Figure 1, R=0.71, p=0.001). The stiffness $T_1$, was 781 ± 31 ms for CC patients and 645 ± 8 ms for the HV group (p<0.0001) whilst the mean ELF score was 10.8 ± 0.3 for CC and 8.3 ± 0.1 for HV (p<0.0001). Figure 3 shows the correlation of $T_1$ with the ELF score. For all subjects, there is a highly significant Pearson correlation coefficient of R=0.723 (p<0.0001). A clear distinction is seen between CC and HV, with a mean R=0.617 for CC (p=0.006) and no significant correlation for HV. Figure 4 shows $T_1$ maps from a single HV and example CC patients with the histogram of $T_1$, mean $T_1$, ELF score and stiffness. Heterogeneity of $T_1$ across the liver is clearly seen, as indicated by the increased FWHM with disease severity, a factor which cannot be assessed using either ELF or Fibroscan® measurements.

REFERENCES: