Introduction: Liver tissue NMR relaxation times have been shown to correlate well with histopathology of liver biopsies. \(T_1\) has been shown to correlate with advanced fibrosis and cirrhosis [1,2] and \(T_2/T_2^*\) with iron accumulation [1,3]. A recent application of respiratory triggered echo-planar imaging was used to determine \(T_1\), \(T_2\) and \(T_2^*\) from the whole liver to be acquired in under 10 minutes with excellent patient compliance [4]. However, the reproducibility and inter- and intra-observer variability of these parameters has yet to be determined. The reproducibility of these measurements is critical for assessing the power of the method and the intra- and inter-observer variability is critical to the transferability of the technique to other centres.

Aim: To investigate the reproducibility of \(T_1\), \(T_2\) and \(T_2^*\) measurements of liver tissue using respiratory-triggered EPI data, and assess the inter- and intra-observer variability of the data analysis.

Methods: Reproducibility Study: The study was approved by the local University Ethics Committee, and all volunteers gave written informed consent. Eight healthy volunteers (4 male, mean age 29 yrs, range 26-35 yrs) were scanned on 2 separate occasions after an overnight fast (Mean time between visits 21 days, range 7-81 days). (Healthy volunteers were used to minimise biological differences between visits, as the liver patients’ condition may alter over time). Volunteers were scanned on a 1.5 T Philips Achieva scanner, with a body transmit coil and 5-element SENSE cardiac receive coil. All relaxation maps were obtained 

Data from 20 chronic liver disease patients who were scanned once using the same protocol as the reproducibility study were used to determine inter- and intra-observer variability in the observer dependent components of the data analysis (patient data used to provide realistic biological variation). For the inter-observer measurements, two observers carried out the data analysis; for the intra-observer measurements, one observer carried out the data analysis on two separate occasions at least 3 months apart. Inter- and intra-observer variability was determined for \(T_1\), \(T_2\) and \(T_2^*\) using the 95% confidence intervals on a Bland-Altman (B-A) plot [5]. The reproducibility CV and the intra-class correlation coefficient (ICC) for both inter- and intra-observer measures were determined.

Results: Table 1 summarises the CV and correlation coefficient of the reproducibility data in healthy volunteers. Table 2 summarises the inter- and intra-observer variability results in the liver disease patients. The reproducibility data showed good agreement between visits, with a mean CV of 1.5%, 3.1% and 4.3% for \(T_1\), \(T_2\) and \(T_2^*\) measures respectively, and a statistically significant correlation coefficient. The inter- and intra-observer variability had similar CV and ICC, with a mean CV % of 0.3 % for \(T_1\), 1 % for \(T_2\) and 0.7 % for \(T_2^*\) (inter-observer data).

Discussion and Conclusions: The CVs for intra- and inter-observer repeatability data were much lower than the CV of the reproducibility data, suggesting that biological variability and scanner related noise (e.g. removal of volumes due to poor triggering) dominated the variability observed in the reproducibility data. In conclusion, the reproducibility of NMR relaxation measurements of the whole liver in healthy volunteers was extremely good, with the inter- and intra-observer variability being low. This suggests that measuring liver relaxation times from respiratory-triggered EPI at a single visit has the potential to be a robust non-invasive biomarker for liver fibrosis and iron accumulation.


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