Liver Fibrosis Grading based on MR Elastography and 31P Spectroscopy
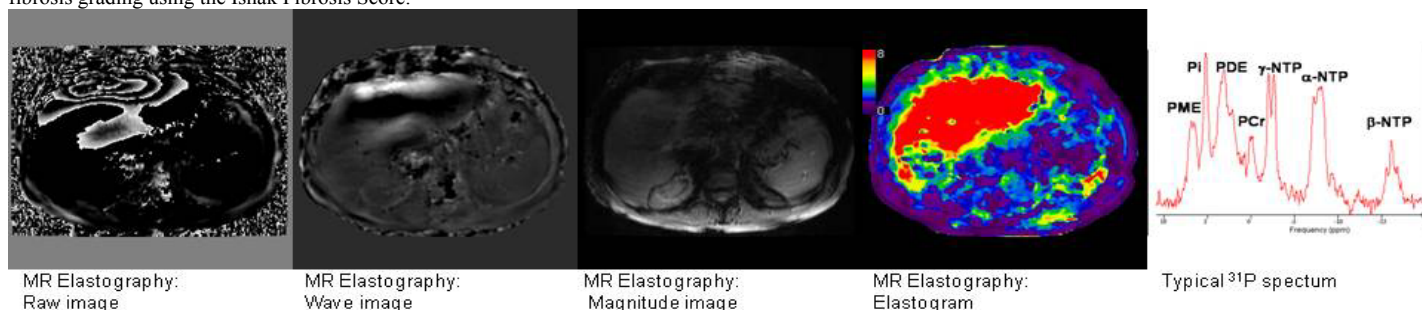
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Liver Fibrosis Grading based on [31]P Spectroscopy

Introduction - The diagnosis of early liver fibrosis currently requires a liver biopsy which risks complications and sampling error. The invasive nature of liver biopsy also makes serial monitoring of fibrosis progression/regression difficult to undertake in patients on treatment for infective hepatitis. Virtually all conventional imaging techniques are insensitive to early liver fibrosis, but recently several MR techniques have been developed that have demonstrated a correlation with histological grades of fibrosis. Magnetic resonance elastography (MRE) has been used to measure the stiffness of the liver *in vivo* as a surrogate marker for hepatic fibrosis[1]. To date it is the only imaging technique reported to be able to diagnose early fibrosis[2]. Animal work suggests it may also distinguish simple steatosis from steatohepatitis[3]. While ultrasound techniques for elastography are sensitive to cirrhosis, they are relatively insensitive to mild and moderate fibrosis[4]. Serum markers for liver fibrosis, such as the aspartate aminotransferase to platelet ratio index, have also been found to be insensitive to fibrosis[5]. [31]Phosphorus MR spectroscopy has also shown promise as a method of assessing the degree of hepatic fibrosis in particular the PDE/PME ratio[6]. The aim of this work was to evaluate both MRE and ^{31}P spectroscopy in a cohort of patients with suspected liver fibrosis undergoing subsequent same day liver biopsy.

Methods - Consecutive patients with clinically suspected hepatic fibrosis referred for liver biopsy were recruited. Each patient underwent an MR examination including: Multishot T2w RARE, MRE and [31]P Spectroscopy. The patients underwent a liver biopsy later the same day. Each examination was independently evaluated for liver stiffness (KPa) and PME/PDE Ratio. All examinations were performed with a 1.5T GE whole body MR system (HDx, GEHT, Waukesha, WI). For the MRE sequence, a passive pneumatic driver was placed over the ribs superficial to the right lobe of the liver. The passive driver was connected to an active drive unit which produces low frequency longitudinal pressure waves at 60Hz. Using a previously described phase contrast gradient echo sequence and an inversion algorithm[7], elastograms were generated at two transaxial levels through the liver. These were analysed, using an ROI that defined the margins of the liver based on the matching magnitude images, by two independent observers. The ^{31}P spectra were acquired during free breathing, in a right decubitus position to minimise respiratory artefacts. A 12cm loop dual tuned transmit/receive coil was used along with a slice-selective spin-echo acquisition (TE = 2.5 ms, TR = 2 s, 40 mm slab) to acquire signal from liver, and manual shimming was performed using the water signal. Data were analysed using the AMARES algorithm[8] within the jMRUI 3.0 software package[9]. Both the PME and PDE peaks were fitted as the sum of two decaying exponentials and a ratio derived. Based on the original liver biopsy report a pathologist provided an initial fibrosis grading using the Ishak Fibrosis Score.

MR Elastography: Raw image | MR Elastography: Wave image | MR Elastography: Magnitude image | MR Elastography: Elastogram | Typical ^{31}P spectum

Results - The inter observer agreement in MRE was computed using the intra class correlation (ICC) coefficient. Both the distribution of MRE and the distribution of the PME/PDE ratios failed a formal Shapiro Wilks W test. Hence both distributions are not normally distributed. The non-parametric Spearman's rank correlation method was used to investigate if there was an association between either MRE stiffness or the PME/PDE ratio and Ishak's score. There was a high level of inter-observer agreement ($r = 0.99$). The association between MRE stiffness and Ishak's score was statistically significant ($r = 0.561$, p-value<0.001). No association was observed between the PME/PDE ratio and Ishak's score ($r = 0.11$, p-value$=0.403$).
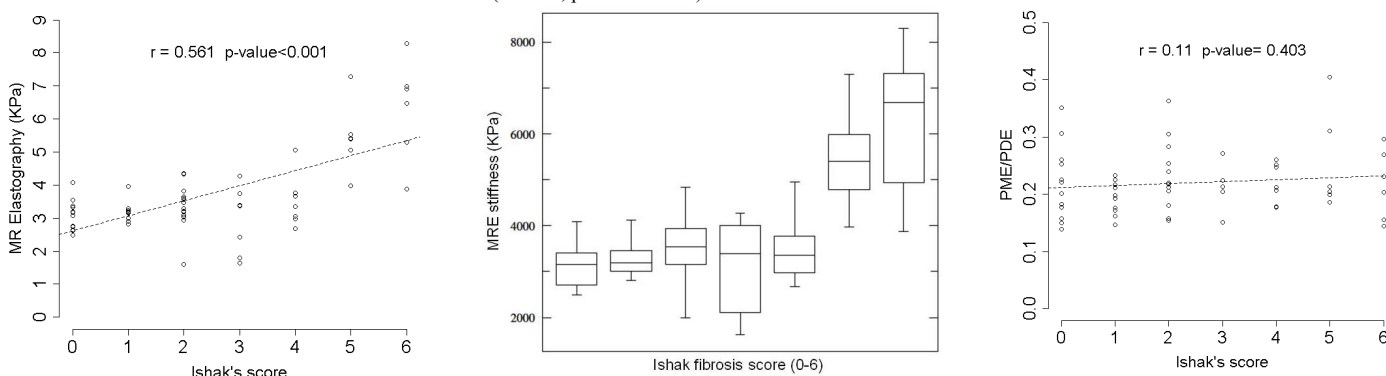
Conclusion - Our results show a correlation between MRE stiffness and Ishak fibrosis score but achieved poor discrimination between the early and moderate fibrosis grades (Ishak scores 0, 1-2 and 3-4) which is not in keeping with previous reports[2]. There was no correlation between PME/PDE ratio and Ishak fibrosis score, also different from previous reports[6]. A possible explanation for our findings is that the histological grading was based on the report, rather than the original biopsy material and a blinded review of the histology fibrosis scores based on the original material is planned. We plan to repeat the analysis of our results with this data and to investigate any relationship with the underlying aetiology.

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