Comparison of MRI and Histopathologic Methods of Quantifying Hepatic Fat Fraction

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Introduction: Quantification of hepatic fat fraction is useful for the diagnosis of non-alcoholic fatty liver disease (NAFLD), investigations into donor suitability for live liver transplantation and monitoring of hepatic fatty change in the patients with liver tumours. Histopathologic evaluation of fat from liver biopsy is the gold-standard for fat quantification but is an invasive procedure with significant morbidity and only samples a small portion of the liver. In- and opposed-phase MRI provides a non-invasive fat quantification method that is quick and simple to implement and enables whole liver analysis of steatosis. The purpose of this study was to compare qualitative and quantitative methods of estimating fat fraction from MR imaging with histological measurement. Previous studies [1] have used qualitative histopathogical analysis, which has limited accuracy because it is a subjective measure based on the pathologist's visual estimation of the total percentage of fat relative to non-fatty tissue. This study used a robust, semi-automated computer algorithm to measure the percentage area of fat in resected liver specimens quantitatively.

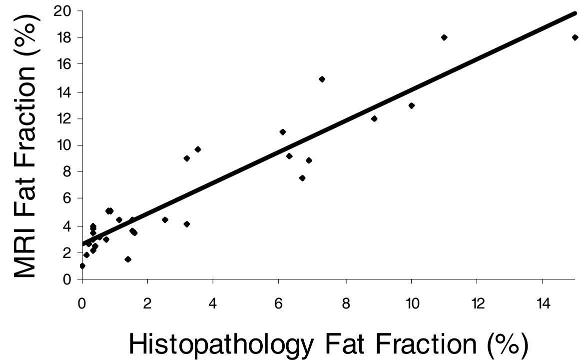

Figure 1 – Histopathology vs. quantitative MRI fat fraction data.

Methods: 32 patients with colorectal liver metastases, and who subsequently underwent hepatic resection and/or non-anatomic metastatectomy, were included into this study with local ethical approval. Histological samples were taken of the metastases and surrounding, non-neoplastic liver. The entire slides, stained with the standard histological stain hematoxylin & eosin, were scanned at 20x magnification using an Aperio slide scanner to create "virtual slides". Images of approximately 0.3mm x 0.3mm were taken from regions of the virtual slides showing non-neoplastic liver and quantitatively analysed using the NIS-elements, Nikon software. Each image underwent white balance normalization followed by histogram analysis, which detected the white areas likely to be fat. An object detection step then identified the fat. To distinguish between the round, fat lobules and other features, such as blood vessels, limits were placed on the circularity and size of objects classed as fat.

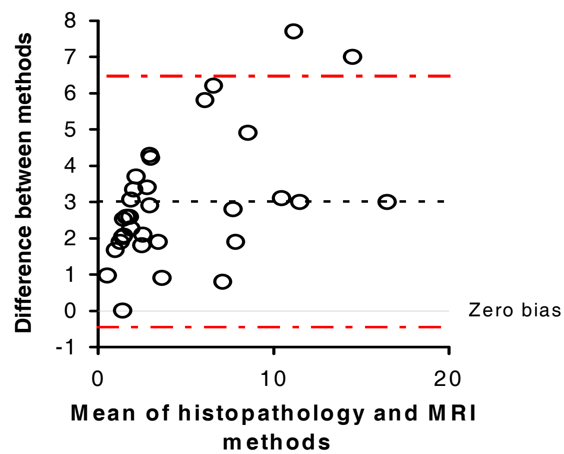

Figure 2 – Bland-Altmann analysis of histopathology and quantitative MRI data showing 3% positive bias in MRI data.

Patients underwent MRI an average of 66 days before surgery Imaging was performed on a 1.5T Siemens Symphony scanner with a body phased-array coil. For qualitative analysis of fat fraction in- and opposed-phase T1-weighted spoiled gradient echo, breath-hold images of the liver were acquired with TE/TR of 2.38ms/144ms and 4.76ms/174ms respectively and a flip angle of 75°. The fat content of the liver parenchyma was assessed by consensus between two experienced observers as: none, mild, moderate or severe, taking into account vessel contrast in the liver and the relative signal intensity of the liver and spleen. For quantitative analysis axial, dual-echo, gradient echo, breath-hold images of the liver were acquired with TE = 2.38ms and 4.76ms, flip angle = 10°, and TR = 112ms. A further, TE=9.5ms, image was acquired in order to correct for T2* decay between the in- and opposed-phase images. Signal intensities were measured from regions of interest placed in three non-cancerous regions of the liver avoiding vessels. The fat fraction was calculated in terms of in-phase signal (S_{ip}) and out-of-phase signal (S_{op}) according to:

$$\text{Fat fraction} = \frac{S_{ip} - S_{op}}{2.S_{ip}} \quad .[2]$$

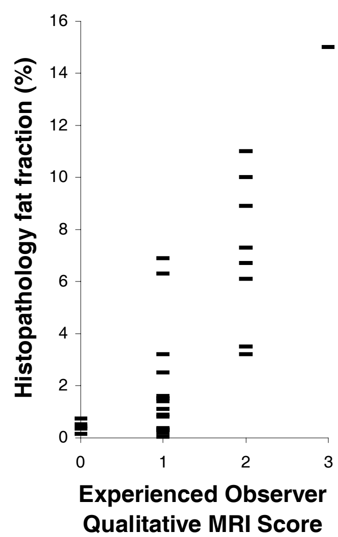

Figure 3 – Experienced observer scores vs. histopathology fat fraction

Results: The quantitative MRI and histology data correlate with an R^2 value of 0.88 (figure 1). MRI overestimated the fat fraction by approximately 3% (figure2). 95% of the MRI results fall within $\pm$3.5% percentage points of this mean positive bias. Figure 3 shows the distribution of histopathological fat fraction values for each qualitative MR fat fraction score, showing a significant overlap between scores.

Discussion: The 3% overestimate in the MRI fat fraction may be due to an underestimation in the histological quantification algorithm, which discounts micro-vesicular fat, and/or an overestimation in the MRI quantification due to T1 effects. The most severely fatty case in this study had a histologically assessed fat fraction of 15%, implying that the consideration of fat-water dominance issues around the 50% fat fraction mark may be irrelevant in measuring hepatic fat fraction. The weaknesses of the study were the long MRI to surgery interval, during which fat fraction may have changed, and the fact that samples were necessarily taken close to the metastasis, which could lead to the results being affected by fatty sparing near the metastasis.

References:

1. Kim S.H. Radiology, 240:116-129 (2006).
2. Glover. JMRI, 1:521-530 (1991).