

MRI estimation of donor graft steatosis prior to orthotopic liver transplantation: Initial results with early serum outcome measures, surgical and histological correlation.

K. G. Hollingsworth¹, J. Smith², N. V. Jamieson², C. J. Watson², M. E. Allison³, G. J. Alexander⁴, D. J. Lomas¹

¹Radiology, University of Cambridge, Cambridge, Cambridgeshire, United Kingdom, ²Surgery, University of Cambridge, Cambridge, Cambridgeshire, United Kingdom, ³Hepatology, Addenbrookes Hospital, Cambridge, Cambridgeshire, United Kingdom, ⁴Medicine, University of Cambridge, Cambridge, Cambridgeshire, United Kingdom

Introduction

There is a worldwide shortage of donors for human liver transplantation with the result that age and other donor criteria have been relaxed in many countries and increasingly live donors are being used. Although donor graft quality has not been studied in depth it is well known that hepatic steatosis is associated with a worse outcome and an increased risk of primary non-function (early catastrophic graft failure)[1,2]. Graft assessment has to be made quickly and in most centres relies on the subjective visual evaluation of the transplanting surgeon. Rarely liver biopsy and histology is obtained (also subjective and prone to sampling errors) for evaluating the degree of fat infiltration pre-transplant. CT based quantification has been used in living donors but involves ionising radiation and relies on the presence of a spleen [3]. Rapid and robust MRI techniques for "in vivo" assessment of hepatic steatosis have been described [4,5]. This work reports the initial results of a study investigating the relationship between MRI quantification of deceased donor liver graft steatosis and serum markers used to indicate graft performance in the early post operative period following orthotopic human liver transplantation.

Methods

An initial feasibility study was performed to ensure that acceptable MRI quantification of donor liver graft steatosis could be performed rapidly and safely on graft organs within their sterile packaging and chilled transport container [6]. Local Ethical Committee approval was obtained and individual consent from potential liver transplant recipients on our institutional waiting list. On receipt of a graft at our institution initial surgical benchwork is performed and the repackaged graft is then available for MR examination during the period of recipient preparation. The graft is transferred to the MRI Unit and examined undisturbed inside its sterile wrappings and transport container using the standard body coil. Any metal fittings on the box (such as metal hinges) are removed prior to the exam and then replaced immediately afterwards. *MR protocol:* Exams were performed on a 1.5T whole body MRI (Excite, GEHT, Milwaukee). Coronal in and out of phase gradient echo scans were acquired during 20 second acquisitions (matrix 256 x 128, 8 sections, section thickness 10mm, gap 1.5mm, TR/TE/NEX = 180/2.2 (out of phase), 4.4 (in phase)/1, at both flip angles 20° and 70°). A T2* map of the liver was obtained using a location-matched, multi-slice, multi-echo gradient sequence (TR = 120, 16 equally spaced echoes, TE1 = 2.2 ms, TE2 = 4.4 ms) and used to correct the in and out of phase images for T2* relaxation [5]. 4 sections were analysed and 3 ROIs were selected within each slice, giving 12 ROIs for each graft. A mean percentage fat and s.d. were calculated from these ROIs. Other parameters recorded included: Surgical visual assessment of hepatic steatosis (blinded to the MR results), subsequent (several days later) histological steatosis assessment from the time-zero biopsy (both on a 4-point scale: none/mild/moderate/severe). The early performance of the liver was followed using standard clinical serum parameters: total bilirubin, ALT (a liver enzyme reflecting hepatocellular damage) and PT (prothrombin time, a marker of hepatic synthetic function) - recorded for the 14 days after the transplantation.

Results

Figure 1 shows sample MR images of the graft in its protective box. Table 1 shows the hepatic steatosis assessments made by different methods and selected blood test results. Figure 2 demonstrates the serial serum measures in the immediate post transplant period for each of the patients, with the MRI steatosis estimate % noted in the legend. For reference the normal serum total bilirubin is 17umol/l, ALT 50U/l, PT 14 seconds and the expectation is that these will be abnormally elevated in the immediate 48 hours post operatively but will then decrease towards normal as the graft starts to function. The same three patients (patients 1, 4 and 5) are found to have the highest peak total bilirubin measurements, the highest ALT score in the first three days following transplantation, and the highest prothrombin time over the first 7 days after transplantation, all of which are indicators of impaired graft performance of the graft. Of these patients 1 & 4 received grafts with above-median steatosis content (according to MR, >7%): the graft received by patient 5 was surgically assessed as having moderate steatosis but not confirmed histologically or by MRI: nevertheless early function is impaired. Although the numbers are too small at this stage for a full evaluation there are trends between the surgeon's assessment of graft steatosis and the histological assessment ($\kappa = 0.77$), and between the histological assessment and the MRI assessment of steatosis ($\kappa = 0.66$), though there was no correlation between the surgeon's assessment and the MRI measurement ($\kappa = 0.21$).

Table 1: Hepatic Steatosis Assessments (surgical, histological, MRI) & Serum Results

Patient	Surgeon's Assessment	Histological Assessment	MRI measurement	Peak Bilirubin	Peak ALT	Peak PT
1	Moderate	Moderate	12.4 ± 1.8	387	894	23.4
2	None	None	6.6 ± 3.5	22	393	18.5
3	None	None	0.8 ± 0.1	95	404	17.2
4	None	Mild	10.7 ± 2.3	173	2813	28.9
5	Moderate	Mild	4.1 ± 2.2	886	1888	20.6
6	Mild	Mild	2.9 ± 0.5	95	535	20.7

Conclusions

These initial results demonstrate that MRI quantification of donor liver graft steatosis correlates with the subsequently obtained histological fat assessment, though not with surgical assessment. Despite the many factors (pre-operative recipient status, peri-operative care, surgical technique) that may influence the early post-operative period the results indicate that of the 3 patients with the most impaired early graft performance two had the highest steatosis levels as determined by MRI. Larger numbers and 90 day follow up mortality data will allow a more detailed evaluation of the value of MRI quantification of hepatic steatosis prior to orthotopic liver transplantation.

Acknowledgements Fund and Friends of Addenbrookes, Jason Polzin, Celia Chan and theatre staff, transplant co-ordinators

[1] Fiorini *et al.*, *Clin. Trans.* **18**, 700 (2004) [2] Marsman *et al.*, *Transplantation* **62**, 1246 (1996)

[3] Iwasaki M. *et al.*, *Transplantation* **78**, 1501 (2004) [4] Hollingsworth *et al.*, *Proc. Int'l. Soc. Mag. Reson. Med.* **13**, 335 (2005)

[5] Fishbein *et al.*, *Magn. Reson. Imag.* **15**, 287 (1997) [6] submitted as separate abstract to ISMRM 2006

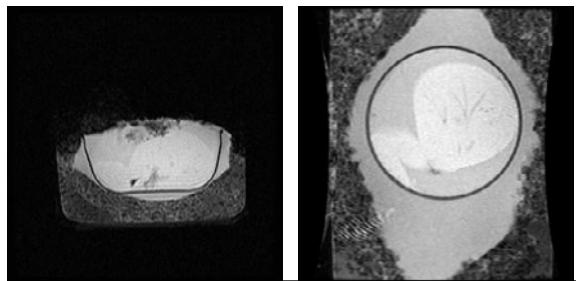


Figure 1: Gradient echo imaging of a donor liver graft in UW solution, plastic bowl (dark outline) in its protective box full of ice (left) axial view (right) coronal view.

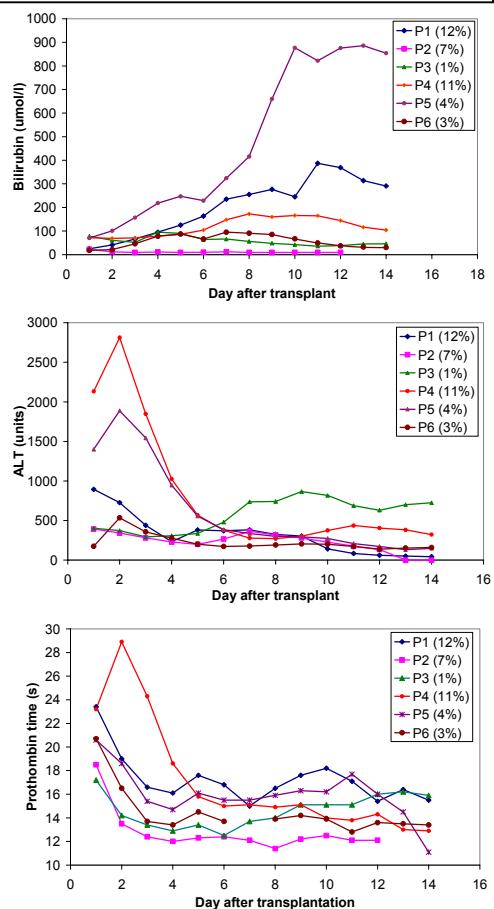


Figure 2: Blood test results for the 6 patients in the 14 days following transplantation: (top) total bilirubin (middle) ALT and (bottom) prothrombin time