Human Liver Transplant Graft Steatosis: Evaluation with MRI

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Introduction

There is a worldwide shortage of donor organs for liver transplantation and although the indications for this procedure have widened the availability of donor organs has not increased to match this demand. As a result the criteria for accepting organs for transplantation have been progressively relaxed in terms of age and other donor criteria which may influence the outcome. Donor graft steatosis is known to be an important factor influencing early graft performance and outcome [1]. In the general population the prevalence of hepatic steatosis is increasing which is being reflected in the grafts made available for transplantation although overall outcomes have in practice improved [2]. Partly owing to the limited time available in most centres there is no routine histological assessment of hepatic steatosis before transplantation and only a visual external assessment is made by the operating surgeon. Despite work demonstrating the subjectivity of this approach [3] this assessment has been shown to correlate with graft outcome [4].

Validated MRS and rapid MRI methods have been developed for quantifying liver fat [5] and are being widely used for evaluating hepatic steatosis "in vivo". A pilot study [6] on donor liver grafts "ex-vivo" using an MRI technique has demonstrated that this approach is feasible for rapid assessment of liver fat immediately prior to transplantation and suggested a correlation between steatosis levels and early graft function. The aim of this study is to use rapid MRI based hepatic steatosis quantification in a larger cohort of "ex-vivo" grafts and to investigate firstly whether the degree of steatosis correlates with surgical and pathological assessment and secondly if there is any relationship with early graft performance and early graft outcome following transplantation.

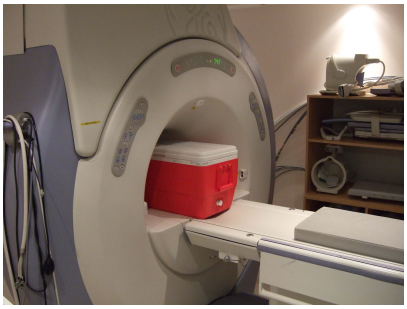

Figure 1: The liver graft undisturbed in its transport coolbox being positioned for MR examination

Methods

The study was Ethical Committee approved and informed consent obtained from potential graft recipients. When an organ became available for a consented recipient then MRI was performed if practical. This was not possible on all occasions owing to the urgency of transplantation, staff availability, and technical MR system failure.

MRI protocol: Examinations were performed after completion of surgical benchwork during the time when recipient was being anaesthetised and prepared for transplantation. The liver graft was examined undisturbed in a coolbox surrounded by preservation fluid and crushed ice. Time from collection of the graft to return to the operating theatre was approximately 20 minutes. All examinations used a 1.5T whole body MRI (Excite, GEHC, Waukesha, USA) and the standard body coil. In and out of phase gradient echo images were acquired in the coronal plane during 20 second acquisitions (matrix 256 x 128, 6 sections, section thickness 10mm, gap 1.5mm, TR/TE/NEX = 180/2.2 (out of phase), 4.4 (in phase)/1, flip angles 20° and 70°. An R2* map of the liver was derived from 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 I/O phase images for $T2^*$ relaxation [5]. The four most central sections were analysed and up to 3 ROIs were selected within each slice from which the mean percentage fat and s.d. were calculated.

Reference Data: At the time of benchwork the surgeon recorded a visual assessment of the severity of graft steatosis and a "time zero" biopsy was performed that was evaluated later by an experienced histopathologist using the same scale – none/mild/moderate/severe. Following transplantation biochemical data for each patient was recorded along with any defined subsequent graft events including graft failure. The assessments of graft steatosis were all made independently of one another with no knowledge of the other results. The different evaluations of graft steatosis were analysed for correlations with each other and with the recipient peak prothrombin (PT) time, alanine transaminase (ALT), and bilirubin (BILI) during the first week following transplantation (these are measured daily for at least 10 days). Analysis was performed using rank correlations on the data uncorrected for any other factors.

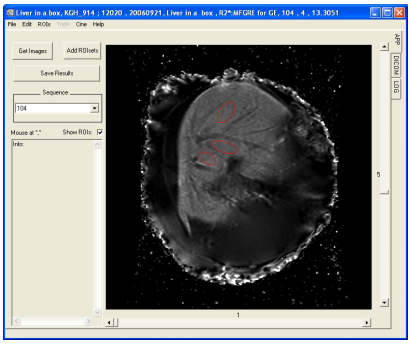

Figure 2: R2* map with (red) sample ROIs which are matched onto the 20flip I/O phase images

Results

39 consecutive grafts were examined with MRI prior to transplantation during the period 1 August 2005 to 31 August 2007. There were 23 male and 16 female corresponding recipients with a mean age of 52.6 yrs. Liver graft steatosis ranged from 0 to 7.3% over the 39 grafts. There were 3 graft failures within the first 3 months post transplantation, insufficient for meaningful analysis. The correlations between the three evaluations of graft steatosis and the first week peak blood tests post transplantation are summarised in Table 1.

Conclusion

This work demonstrates that the three assessments of hepatic steatosis are correlated, although the weakest correlation was between the MRI and Surgical assessments. Initial analysis indicates that only the MRI assessment correlated significantly with any of the early serum performance indicators. Further analysis will investigate the effects of data correction for other factors known to influence outcome and evaluate longer term outcome of the studied grafts.

Table 1

	Correlations & (p value) ***significant**	Graft Steatosis Estimates			Peak 1st Week Biochem		
		SURG	PATH	MRI	ALT	BILI	PT
Graft Steatosis Estimate	SURG	1	**0.5* (0.001)**	**0.36* (0.026)**	0.14 (0.4)	0.21 (0.2)	-0.049 (0.77)
	PATH	0.5* (0.001)	1	**0.51* (0.001)**	0.25 (0.12)	0.21 (0.21)	0.18 (0.28)
	MRI	0.36* (0.026)	0.51* (0.001)	1	0.21 (0.21)	**0.39* (0.014)**	0.26 (0.11)
Peak 1st Week Biochem	ALT	0.14 (0.4)	0.25 (0.12)	0.21 (0.21)	1	0.28 (0.086)	0.41 (0.011)
	BILI	0.21 (0.2)	0.21 (0.21)	0.39* (0.014	0.28 (0.086)	1	**0.44* (0.005)**
	PT	-0.049 (0.77)	0.18 (0.28)	0.26 (0.11)	0.41 (0.011)	0.44* (0.005)	1

References

[1] Ploeg et al., *Transplantation* **55**:807-813 (1993).
[2] van der Meulen et al., *Transplantation* **84**(5):572-9.(2007)
[3] Fiorini et al., *Clin. Trans.* **18**, 700 (2004)
[4] Marsman et al., *Transplantation* **62**, 1246 (1996)
[5] Hussein HK et al., *Radiology* **235** :1048-1055 (2005)
[6] Hollingsworth *et al., Proc ISMRM* 2297 (2006)

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ACT, MRIS Unit