Commonest cause of death was cardiac related events (24%), followed by sepsis (23%) or liver related complications (14%). Disease duration prior to transplantation, initial presentation with autonomic rather than peripheral neuropathy, TTR mutation, and modified body mass index (mBMI) of <600, indicating poor nutritional status, were identified as significant factors influencing survival after LT (p<0.01).

**Conclusion**
Liver transplantation is rational and effective treatment for FAP with excellent long-term outcomes and 10-year survival >70%. Type of mutation, nutritional status, disease duration and degree of autonomic involvement are significant prognostic factors.

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**HEPATO CYTE TRANSPLANTATION IN RATS WITH ACUTE LIVER FAILURE USING CELLS LABELLED WITH A CLINICAL GRADE MRI CONTRAST AGENT**

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**Introduction**

Hepatocyte transplantation is being evaluated as an alternative to orthotopic liver transplant. However, the fate of hepatocytes after transplantation is not well defined.

**Aim**

The aims of the study were to: (1) investigate the possibility of labelling hepatocytes in vitro using superparamagnetic iron oxide nanoparticles (SPIOs), (2) determine the effects of labelling on cell viability and function, and (3) perform in vivo experiments on tracking labelled cells by MRI.

**Method**

Human and rat hepatocytes were labelled in culture for 16 h with clinical SPIOs (12.5 μg Fe/ml) and protamine sulphate (5 μg/ml) as a transfection agent. Cellular iron uptake was determined using Prussian blue staining, and quantified by a ferrozine-based assay. Cell viability and function were assessed using MTT assay, mitochondrial dehydrogenase activity, [14C]-leucine incorporation, albumin and urea assays. Effects of labelled cells on T2-weighted images were assessed in vitro using a 7-T MR scanner. Intrasplenic transplantation of 2×10^7 male rat hepatocytes labelled with SPIOs (n=4) or non-labelled (n=4) was performed in female recipients 28–30 h after acute liver failure induction by intraperitoneal injection of D-galactosamine. Hepatocytes were also marked with the fluorescent dye CM-Dil. A control group (n=4) received medium injection only. T2*-weighted gradient-echo images at 7-T MRI were acquired at days 7 post-acute liver failure induction. Transplanted cells were detected in the liver by PCR for the Y-chromosome (Sny-2 gene) and histological analysis.

**Results**

Mean intracellular iron concentrations were 11.4±SE1.1 pg/cell in human and 8.6±0.3 pg/cell in rat hepatocytes. Cell viability and metabolic function were not significantly affected at these SPIO concentrations. In vitro MRI of SPIO-labelled cells (2000 cells/μl) induced a 50% change in T2 relaxivity compared to non-labelled cells. SPIOs were detected in rat liver as a decrease in the MRI signal intensity 6 days after transplantation in the three survivors. On histology most of the SPIO particles were located in Kupffer cells, indicating the loss of iron oxide particles from hepatocytes. In keeping with this, labelled cells could not be detected in the liver by the fluorescent dye or by PCR for Sny-2 gene.

**Conclusion**

Optimum conditions to label human and rat hepatocytes with SPIOs were determined, which did not affect cell viability or metabolic function, and were sufficient for in vitro MRI detection. However, the clearance of hepatocytes after transplantation limits the value of MRI for assessing long-term hepatocyte engraftment.