Assessment of perfused *ex vivo* human livers by MRS and MRI

Liam Young[1], Carlo Ceresa[2], Daniel Voyce[3], Jane Ellis[1], Ferenc Mozes[1], Justin Lau[4], Jack Miller[4], Ladislav Valkovič[1], Damian Tyler[4], Peter Friend[2], Constantin Coussios[5], Christopher Rodgers[1,6]

[1]OCMR, Univ Oxford, [2]Nuffield Dept Surgical Sciences, Univ Oxford [3]OrganOx Ltd, Oxford, [4]Dept Physiology, Anatomy and Genetics, Univ Oxford, [5]Inst Biomedical Engineering, Univ Oxford, [6]Wolfson Brain Imaging Centre, Univ Cambridge

Introduction

Liver transplantation is the only cure for end-stage liver disease. However, rapidly increasing waiting lists require the use of more "marginal" donated livers that are currently discarded due to increased risk of graft failure. Recent advances in organ preservation techniques have shown that normothermic machine perfusion (NMP) of donated livers – supplying oxygenated blood and nutrition at body temperature during preservation– improves transplant outcomes.[1] Currently, viability assessment relies heavily on visual inspection of the graft which is a crude marker of the viability, especially in marginal cases. In previous work we have demonstrated the feasibility of combining a CE-marked NMP device with a 3T MRI scanner to scan perfused pig livers.[2] Here we present the first cases of discarded human livers assessed using our NMP-MRI system.

Table 1: *Donor characteristics. DBD, donor after brain death; CIT, cold ischemia time.*

Donor	A	B
Donor type	DBD	DBD
Sex	Male	Female
Donor age	52	72
CIT	10 hr 8 min	21 hrs 22 min
Discard reason	Severe steatosis	Severe steatosis

Methods

Donated human livers deemed unsuitable for transplantation, with consent for research, were retrieved according to the standard protocol and perfused using an adapted version of the Metra (OrganOx Ltd, UK) as described previously.[2] Perfusate blood gas analysis was performed every 4 hrs. MRI protocol: Scans were performed on a 3T TIM-Trio (Siemens) for 12 hrs. ^{31}P-MRS: a 10 cm loop coil (PulseTeq, UK) was used to acquire non-localised spectra every 2 hrs (TR/TE=3000/0.85 ms, FA=90°, bandwidth=4 kHz, averages=1000). ^{1}H: A 32-channel receiver array (InVivo Inc, USA) was used to acquire single-voxel MRS spectra using a stimulated echo acquisition mode (STEAM) sequence with TR/TE=760/10.0 ms, voxel size=20×20×20 mm^3, measurements=5, averages=16 and water suppression. Measurements were repeated without water suppression and a proton density fat fraction (PDFF) calculated. Shortened modified Look-Locker inversion recovery (ShMOLLI) T1 maps were acquired every 2 hrs (TR/TE=2.5/1.02 ms, TI_1=130 ms, TI increment=80 ms, simulated R-R interval=800 ms). Mean values of 3 regions of interest in the right lobe were analysed.

Results

Both livers showed ATP regeneration and evidence of glucose metabolism. However, only liver A showed a decreasing perfusate lactate concentration (Fig. 1). The mean PDFF was 23.1% in liver A and 18.7% in liver B with no significant changes seen during perfusion. ShMOLLI T_1 remained stable at 873 ± 20 ms and 1281 ± 44 ms for livers A and B respectively.

Discussion

High PDFF values confirm the diagnosis of severe steatosis made visually during retrieval of the livers. A very high initial T_1 in liver B suggests a significant amount of fibrosis or inflammation, although the stability of T_1 measurements suggests no further insult during perfusion. Both livers showed ATP recovery, indicating that even though liver B was heavily damaged, it managed to recover energetically with ATP reserves known to be a predictor of transplant outcome.[3]

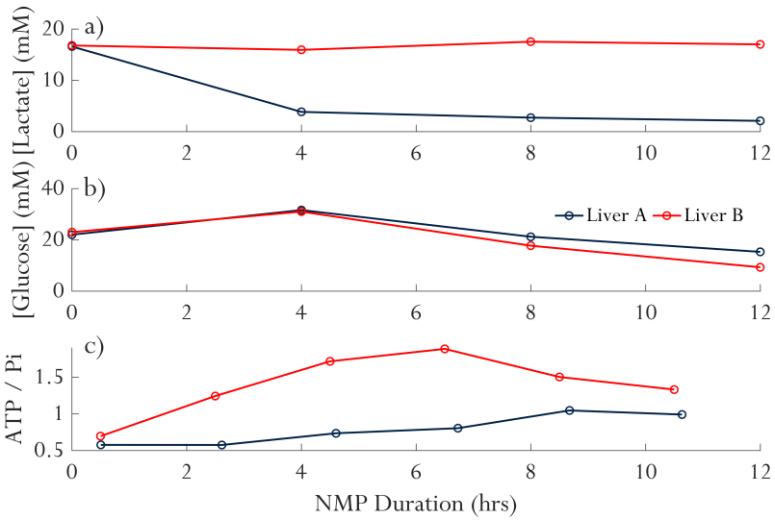

Figure 1. Variation in lactate (a) and glucose (b) concentration during perfusion. (c) Changes in ATP / Pi ratio during perfusion.

Conclusion

This study demonstrates the practicality of using our NMP-MRI system on discarded human livers and suggests that no single parameter can completely characterise a liver's metabolic state.

References

[1] Nasralla et al. Nature 2018

[2] Young et al. ISMRM2018 #0446

[3] Vajdová et al. Hepatology 2002

Acknowledgements This work was funded by the NIHR Oxford Biomedical Research Centre (BRC).