Robust measurement of hepatic perfusion using an interleaved saturation prepared double echo sequence: comparison of dual-input and gradient models.

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Introduction Hepatic perfusion can be altered by the development of fibrosis and cirrhosis or lesions, and the ability to accurately quantify perfusion may be clinically significant [1]. In addition, assessment of liver perfusion (and perfusion heterogeneity) after orthotopic liver transplantation may indicate graft impairment. Perfusion measurements have been made with nuclear isotopes [2] or by the use of multi-phase CT acquisition and contrast agent [2,3]: such methods involve the use of ionising radiation. MRI (with Gd-DTPA) can be used in a similar way, but unlike CT, there is no linear relationship between the image intensity and contrast agent concentration. Since the liver is supplied by the hepatic artery and the portal vein, it is necessary to image contrast uptake in the aorta (as a substitute for hepatic artery), portal vein and liver parenchyma. MR images have a limited range of sensitivity to T1: imaging parameters which will be sensitive for uptake in the liver are not optimal for measuring the high concentrations in the aorta. This paper demonstrates a method of addressing this problem.

Methods The study was approved by the local ethics review board and informed consent was obtained from the volunteers (3 male, 3 female, age 29-53). The volunteers fasted for 8 hours before the examination to ensure a basal portal vein flow. Examinations were performed on a 1.5T whole body MRI (Excite, GEHT, Milwaukee) using an 8 channel torso array. Pre-contrast measurements of T1 in the aorta, portal vein and liver parenchyma were made using a custom non-selective, saturation-prepared, ECG-gated fast spoiled gradient echo with different saturation recovery times (11 points, TS = 200-5000ms) acquired in diastole. The dynamic uptake curves were acquired with a custom pulse sequence [4] (figure 1) in the axial plane for 200 heartbeats (matrix 256 x 128, 1 section, thickness 15mm, TR/TE/NEX = 3.3ms/1.0ms/1, bandwidth 62.5 kHz, ASSET factor 2, centric phase ordering). The pulse sequence is triggered by the ECG signal: a low-resolution image (32 phase encodes) is collected after a saturation recovery time of 50ms to prevent saturation of aorta signal and within the same heartbeat a second, high-resolution image (64 phase encodes) is collected to measure lower concentration signals. Gd-DTPA was injected into the median antecubital vein (0.1 mmol/kg followed by 25ml saline at 3ml/s) and the pulse sequence started simultaneously.

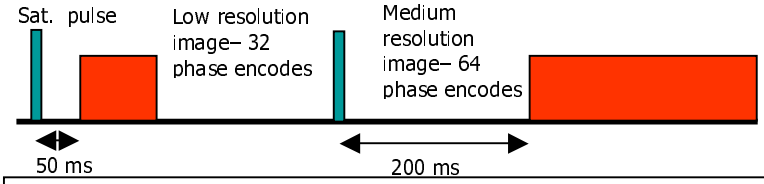

Figure 1 : Dual acquisition sequence for liver perfusion measurement. The sequence is triggered by the ECG.

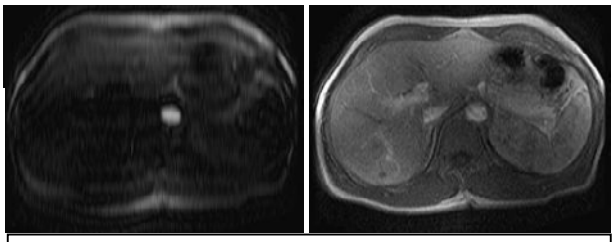

Figure 2: Example images from the dynamic run for (*left*) the low-resolution image at TS = 50 ms for the uptake in the aorta and (*right*) the high resolution image at TS = 200 ms for uptake in the portal vein, spleen and liver parenchyma.

The pre-contrast T1 values and ROI intensities were extracted using Cinetools (GEHT, version 4.1.2) for the aorta, the portal vein and right lobe parenchyma: these time courses were then converted to gadolinium concentrations using the pre-contrast T1 map. The time series were analysed by the following methods (i) an estimate of the perfusion made by evaluating the maximum gradient of the liver concentration curve and dividing by the peak arterial concentration, an estimate used in CT studies (ii) a dual-input model:

$$\frac{dc_L}{dt} = k_{1a}c_a(t-\delta) + k_{1p}c_p(t-\delta) - k_2 c_L(t)$$

Where c_L, c_P and c_A are Gd concentrations in the liver, portal vein and aorta respectively. k_{1a}, is the first-order transfer constant from the aortic plasma to the liver, k_{1p}, the first order transfer constant from the portal plasma to the liver, and k_2, the first-order transfer constant from the liver to the hepatic veins: δ is the delay between uptake in the aorta and parenchyma The arterial fraction of the perfusion was calculated by $100k_{1p}/(k_{1a}+k_{1p})$, the distribution volume of the contrast agent as $100(k_{1a}+k_{1p})/k_2$ and the mean transit time as $1/k_2$. The fitting was made by estimating dc_L/dt from the experimental data by a seven-point regression and fitting the above model.

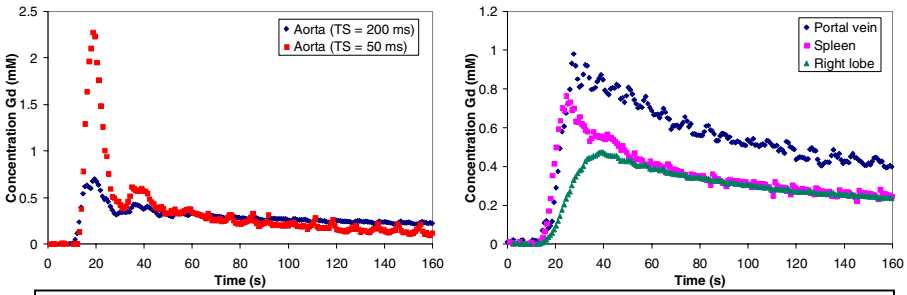

Figure 3: Gadolinium concentrations against time for subject 1. (*Left*) comparison of Gd conc estimated for the aorta from the short saturation time acquisition (red) and the long saturation time acquisition. (*Right*) time course for the portal vein, spleen and right lobe

Table 1: Results of perfusion modelling for 6 healthy volunteers

Subject	*$(dc_L/dt)_{MAX}$/ C_{aMAX} (x 10^{-3}s) Method (i)*	*Arterial fraction (%) Method (ii)*	*Total perfusion (mL min^{-1} 100 mL^{-1}) Method (ii)*	*Mean Transit Time (s) Method (ii)*	*Distribution Volume (%) Method (ii)*
1	5.7	27	213	8.9	32
2	4.1	10	213	7.5	27
3	10.1	6	331	5.2	29
4	2.7	5	146	14.1	35
5	12.9	20	192	23.0	75
6	7	5	238	9.0	36
Mean ± s.d.	**7.1 ± 3.8 (CoV 54%)**	**12 ± 9**	**222 ± 61 (CoV 27%)**	**11.3 ± 6.4**	**39± 18.0**

Results Table 1 shows the results from the 6 volunteers in the study, together with the average parameters for the cohort. The initial T1's measured were 1213 ± 79 ms (aorta), 1084 ± 124 ms (portal vein) and 676 ± 59 ms.(right lobe). These figures (means and s.d.'s) compare favourably with other studies on healthy volunteers performed using MRI and CT [2,5]. Comparing the heuristic gradient method with the total perfusion estimated by the dual-input model shows a moderate correlation (κ = 0.44), though the coefficient of variance was much smaller for the dual-input method. The hardest signal to extract robustly is that of the portal vein, which varies widely in presentation in the axial plane: refining this estimate will be the subject of future work.

Conclusions It has been shown that it is feasible to measure liver perfusion in healthy volunteers using a custom double echo dual resolution pulse sequence with parallel imaging to accurately record the gadolinium concentration in the aorta, portal vein, spleen and liver parenchyma with each pair of images captured within a heartbeat: in particular, it is possible to measure the arterial input function. The method shows potential for assessing diffuse liver diseases and post-transplantation outcome.

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References [1] Pandharipande *et al.*, *Radiology* **234**, 661 (2005) [2] Van Beers *et al.*, *AJR* **176**, 667 (2001) [3] Miles *et al.*, *Radiology* **188**, 405 (1993) [4] Gatehouse *et al.*, *JMRI* **20**, 39 (2004) [5] Annet *et al.*, *Radiology* **229**, 409 (2003)