

# DCE-MRI at 3T in patients with hepatocellular carcinoma using a saturation-prepared dual-acquisition pulse sequence

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## Introduction

A method addressing the considerable challenges involved in acquiring DCE-MRI data at 3T from the liver, aorta and portal vein of human volunteers has been previously described [1]. The pilot study reported here applies these techniques to a sample of patients with hepatocellular carcinoma with a view to distinguishing tumour tissue from normal background tissue on the basis of DCE parameter index values. This would be a preparation for investigation of possible biomarkers of treatment response.

## Methods

The study was approved by the local ethics review board and 8 patients were imaged after giving written consent. Each received an intravenous bolus injection of 0.1 ml/kg of gadobutrol (Gadovist, Schering AG, Germany), into an antecubital vein, administered at 6 ml/s using a power injector (Spectris; Medrad, Indianola, PA). The injection was given after approximately 20 seconds of baseline imaging. The pulse sequence has been previously described [1] and is summarised in Figure 1. Two slices with independent orientation were imaged in each heart-beat [2], with free-breathing, using a relatively B<sub>1</sub>-insensitive saturation-recovery preparation implementation [3]. One slice was positioned sagittally through the tumour under study, the other in an oblique plane providing a cross section through the portal vein and aorta. Each image pair shared the following parameters (matrix 128x128, parallel imaging acceleration (ASSET) factor 2, slice thickness 10mm, TR/TE = 3.4ms/1.1ms, NEX = 1, flip angle 10°, BW ±31.2 kHz and centric phase ordering) but had individually specified saturation times. Optimal saturation recovery times for each slice were estimated by imaging vials containing differing dilutions of gadobutrol representative of the concentrations to be found in vivo (1 – 20 mM), and values of 20 ms and 200 ms were used for the blood vessels and liver respectively. T<sub>1</sub> imaging was achieved through a modified Look-Locker inversion prepared sequence (MOLLI) [4]. The images were analysed using custom software. Regions of interest were placed around the aorta and portal vein on the oblique slice and the tumour/background parenchyma on the sagittal slice. Post-processing 2-D motion correction was applied to the vessel ROIs using an algorithm tracking high signal intensity. 1-D motion correction was applied to the liver ROIs by tracking the motion of the diaphragm. Signal to [Gd] conversion was achieved using the standard saturation-recovery and relaxivity equations, after applying a correction (previously described [5]) to the liver signal data for the residual magnetisation remaining after any non-perfect 90° saturation pulses. A dual-input single compartment pharmacokinetic model (Equation 1) [6] was fitted to mean ROI signal data, employing a range of circulation delay times (τ<sub>a</sub> and τ<sub>p</sub>) and selecting the delay times giving the best curve fit. Standard perfusion parameters were derived from the fitted DCE parameters k<sub>1a</sub>, k<sub>1p</sub> and k<sub>2</sub> for both tumour and background parenchyma for each patient. 'Normal' liver parenchyma data from 9 healthy volunteers had been previously collected and analysed in a similar way [5].

## Results

Two patients' examinations failed for technical reasons. The remaining results are summarised in Figure 3. It can be seen that the median (and range of) the arterial fraction (A%) is higher in tumour tissue than in background liver tissue. When quantified using a Wilcoxon signed rank test, this difference is significant (p=0.031). Surprisingly, total perfusion (F ml/min/100ml) in both tumour tissue and background liver tissue is lower than in 'normal' volunteer liver tissue (p=0.020 & p=0.007: Mann-Whitney U test). The mean transit times (MTT s) show a significant increase from 'normal volunteer' to tumour tissue (p=0.020). There are no significant differences in distribution volume (D%) between the three categories.

## Discussion

It was clear from visual inspection of the images that the majority of these tumours had non-enhancing central regions (see Figure 2). Histological reports from biopsy and post-mortem examinations showed corresponding necrosis in each case. In the absence of voxel-by-voxel parameter mapping (low image quality and registration inaccuracies as yet preclude this method of analysis), it might be expected that a ROI average of a largely necrotic tumour would yield a lower perfusion value and larger MTT than unaffected tissue. The perfusion that is present, however, would be expected to be largely arterial, as is observed in these results. The low perfusion and long MTT of the background (non-tumour) liver tissue regions is almost certainly due to background liver disease.

## Conclusion

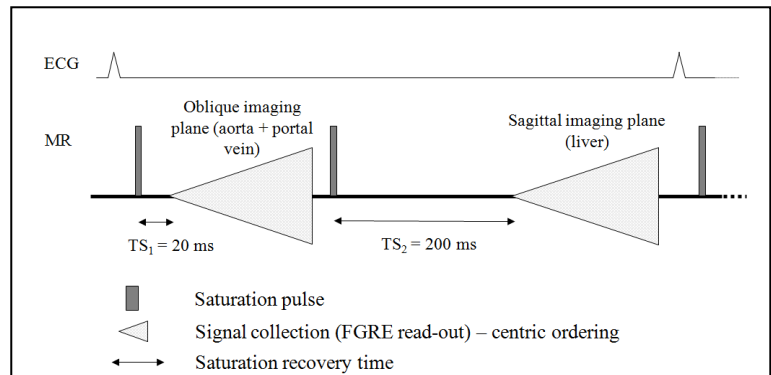
This study shows that 3T DCE imaging using a saturation-recovery method can successfully distinguish HCC tumour tissue from background 'non-tumour' liver tissue (and from liver tissue in healthy volunteers) on the basis of the arterial fraction, derived using a dual-input pharmacokinetic model. In view of the heterogeneity of the studied tumours, further work will focus on developing capabilities for mapping DCE index values on a pixel-by-pixel basis.

## References

- [1] Black RT et al, Proc ISMRM 3562 (2007)
- [2] Gatehouse PD et al, jMRI 20:39-45 (2004)
- [3] Kim D et al, Magn Reson Med 59:209-215 (2008)
- [4] Messroghli DR et al, Magn Reson Med 52:141-146 (2004)
- [5] Gill AB et al, Proc ISMRM 1806 (2011)
- [6] Materne R et al, Magn Reson Med 47:135-142 (2002)

## Acknowledgements

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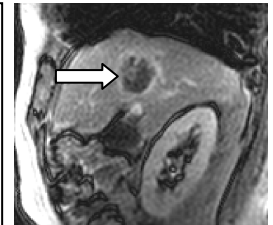
**Fig. 1:** Schematic diagram of dual-acquisition pulse sequence used

## Equ. 1:

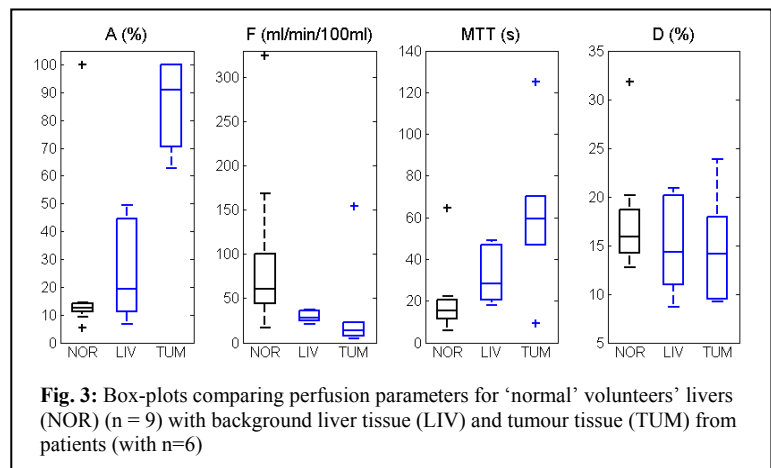
Dual-input kinetic model equation:-

$$\frac{dC_L}{dt} = k_{1a}C_a(t - \tau_a) + k_{1p}C_p(t - \tau_p) - k_2C_L(t)$$

- $C_L(t)$  :- [Gd] in tissue
- $C_a(t)$  :- [Gd] in feeding artery
- $C_p(t)$  :- [Gd] in portal vein
- $\tau_a, \tau_p$  :- circulation delays
- $k_{1a}, k_{1p}, k_2$  :- parameters to fit



**Fig. 2:** Tumour with non-enhancing centre



**Fig. 3:** Box-plots comparing perfusion parameters for 'normal' volunteers' livers (NOR) (n = 9) with background liver tissue (LIV) and tumour tissue (TUM) from patients (with n=6)