The effect of onset time detection on reproducibility of vascular parameters derived from DCE-MRI

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Introduction: Dynamic contrast enhanced MRI (DCE-MRI) has been successfully used as biomarker of angiogenic activity in preclinical and clinical trials[1]. However, the variability of the analysis methods employed can affect the quantification of the derived parameters and thus reduce their value as potential biomarkers and/or surrogate end points. For dynamic serial imaging with finite temporal resolution, the true peak value and the rise time of the tracer concentration-time curve during the bolus injection may be inaccurately measured because of a wide sampling interval. In addition, definition of the time of arrival of the bolus (onset time) also can critically affect parameter estimates [2]. Several automated methods for onset time detection have been described[2-5] but in our experience automated methods can fail to detect an accurate onset time particularly when tumors show low contrast uptake making manual adjustment essential. This study compares the reproducibility of vascular parameters derived from DCE-MRI using four different methods for defining onset time.

Methods: 10 patients with metastatic liver disease referred for a phase I trial were scanned twice, 1-7 days apart, on an 1.5T Avanto (Siemens, Erlangen, Germany) using Gadopentate dimeglumine (Magnevist, 0.5M solution Schering) 0.1 mmol /kg injected at 3mls/s followed by 20mls saline at 2mls/s. The images were acquired coronally in sequential breath-hold at expiration using a 3D fast field echo (FFE) sequence, TR/TE = 3.05/0.89 ms, FA = 16^0, 14×5mm slices NSA = 1, IPAT = 2, FOV = 308x320mm, 208x256 matrix. Two image volumes were acquired during each 6 s breath-hold, followed by a 6 sec breathing gap with 40 volumes acquired over a 4 minute period. The dynamic scan was preceded by a calibration scan with the same parameters except FA = 3^0 and NSA = 8. All the analysed liver metastases (n=20) had variable degrees of central necrosis and demonstrated rim enhancement on the late subtraction images. An experienced radiologist drew regions of interest (ROI) through the central slice with (Outer) and without (Inner) inclusion of the rim enhancement, resulting in 40 ROIs. The onset time was calculated from the concentration–time curve for the whole ROI, using the following methods: visual assessment of the onset time at the point at which the curve intersected the time axis taking into consideration the slope of the curve (M); drawing a small ROI through the closest visualised hepatic artery and recording an automated onset time (H), drawing a ROI through the ascending thoracic aorta and recording the time of the peak intensity enhancement (Ao) and finally an automated method using a Bayesian onset estimator (A).
The analysis was repeated 7-14 days later for all 20 lesions. All results were compared to those obtained using the manual method (the best available "gold standard"). Data were analysed using MRIW (in house DCE analysis platform) using extended Tofts model[6]. Median values were calculated for the following parameters: volume transfer constant between plasma and extracellular space (K_{trans} min^{-1}), volume of extracellular-extravascular space per unit volume of tissue (V_e ml/ml), flux rate constant between extracellular space and plasma (K_{ep} min^{-1}) and Initial Area Under the Gadolinium Curve for the first 60 seconds (IAUGC60 mMol.sec). Median DCE parameters values were used to summarise the distribution. Bland–Altman analysis was performed to test reproducibility.

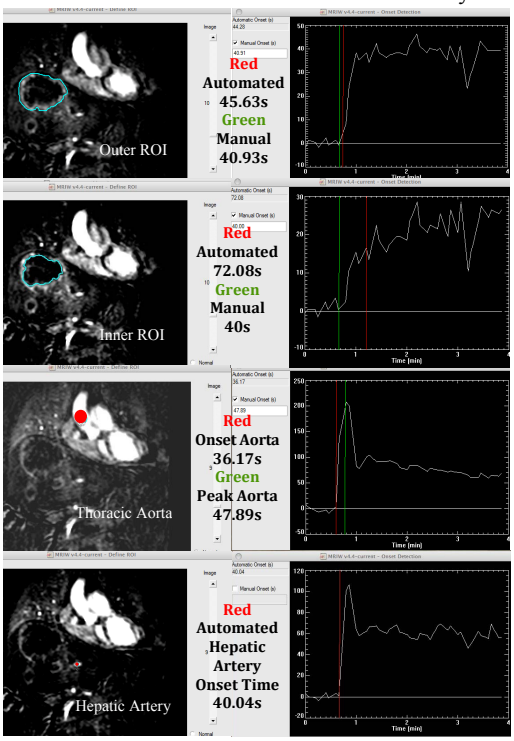

Fig.2 Onset time for different types of ROI in the same study

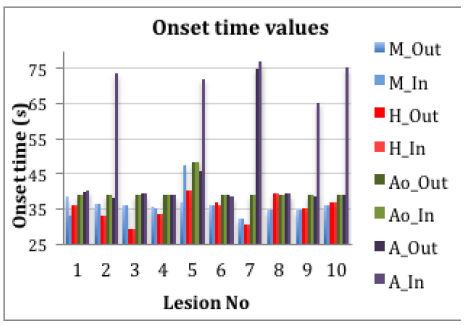

Fig.1 Onset times values for different types of ROI

ROI	Inner				Outer			
Parameter / Method	K_{trans}	V_e	K_{ep}	IAUGC 60	K_{trans}	Ve	K_{ep}	IAUGC 60
M	28.45	43.39	43.38	36.43	25.94	30.52	28.60	34.01
H	28.10	41.76	44.17	37.03	28.90	28.17	28.83	32.37
Ao	29.28	43.92	40.49	30.73	30.05	29.82	29.40	28.26
A	44.60	34.45	37.87	38.32	40.11	32.13	33.00	33.98

Table 1. Values of the reproducibility coefficient r% for DCE-MRI parameters for the 4 methods calculated using Bland Altman

Results: Onset times and vascular parameters generated by using the manual (M) and hepatic artery (H) methods were not significantly different ($p>0.05$, Table 1, Fig 1). Compared to the manual selected onset times, the peak aortic enhancement and automated methods generated statistically different times ($p<0.05$) for Inner and Outer ROI types, although the latter showed a smaller difference. The hepatic artery method had a good intra-observer reproducibility of the onset times values: r = 2.56 – 2.91 % compared to an r = 8.5-16.8% for the manual method.

Discussion and Conclusion: The hepatic artery contrast arrival automated onset time method had lower intra-observer variability equivalent to a manual method and can be used across the entire analysed tumour (3-6 slices). As it reflects the time of contrast arrival in the relevant segment of the liver it results in improved reproducibility of the DCE estimates, despite the fact that hepatic arterial has a small calibre resulting in an ROI of 3-12 pixels. The small ROI has the advantage of reducing the variability of ROI placement and therefore potentially less inter-observer variability. Fully automated methods or those using aortic enhancement can cause larger variability and poorer reproducibility.

References: [1]Leach et al (2005) BJC 92(1599-1610); [2]Orton et al Phys Med Biol (2007) 52(2393-408); [3]Galbraith et al (2002) NMR Biomed 15 132–42; [4]Cheong et al (2003) Phys. Med. Biol. 48 N83–8; [5]Huisman et al (2001) J. MRI 13 607–14; [6]dArcy et al (2006) Radiographics 26(2) 621-32.

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