The use of slope-ratio methods to quantify liver perfusion from dynamic contrast-enhanced MR data: comparison with perfusion quantification using a dual-input single compartment model

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Introduction: The normal liver has a dual vascular supply mainly derived from the portal vein, with a smaller contribution from the hepatic artery. The relative vascular contribution is altered in the presence of disease. Dynamic contrast-enhanced (DCE-) MRI is a technique that enables non-invasive interrogation of tissue microvascular environment. Different analysis approaches can be taken to quantify arterial and portal-venous hepatic perfusion from liver DCE-MRI data. In this study, the slope-ratio methods proposed by Miles *et al* [1] and Tsushima *et al* [2] in dynamic CT studies were used to quantify arterial and portal-venous perfusion from clinical MR data. Comparisons were made with perfusion quantified using a dual-input single compartment model [3].

Materials and methods: 30 DCE-MRI data acquired from patients with neuroendocrine tumour liver metastases were analysed. Imaging was performed on Siemens Avanto 1.5T using a phased array body coil and a 3D FFE sequence. Coronal dynamic images were acquired in pairs during breath-holds on expiration with 5s gap between successive breath-holds. 40 volumes were acquired over a 4 minute period. Gd-DTPA was injected at the start of the third breath-hold (iv. Magnevist® 0.1mmol/kg body weight). The imaging parameters were TR/TE = 3.28/1.10 ms, FA = 18°, 12×5 mm partitions, NSA = 1, iPAT = 2, FOV = 350 mm^2, 256×256 matrix. The dynamic scan was preceded by a single scan with the same parameters except with FA = 2° and NSA = 3 to allow conversion of dynamic signal intensities to gadolinium concentration. Data analysis was performed using in-house software, MRIW [4]. Dynamic images were registered using a simple rigid body algorithm. Regions-of-interest (ROIs) were drawn around the tumour (T) and whole liver (WL) in the three central partitions. DCE-MRI parameters were evaluated on a voxel-by-voxel basis within the ROI. With the *dual-input single compartment model*, tissue contrast agent concentration is described by the following expression: $c_t(t) = [\gamma c_A(t) + (1-\gamma)c_V(t\text{-}t_p)]\otimes F.\exp(-(t\text{-}\tau_0)F/DV)$, where $c_A(t)$ and $c_V(t)$ are the arterial and portal-venous curves, F, DV and γ are total hepatic pefusion, distribution volume and the ratio of arterial to total hepatic perfusions, respectively. F_a and F_p were calculated using the following expressions: $F_a = \gamma.F$ and $F_p = (1\text{-}\gamma).F$. τ_0 and t_p are the onset and portal delay times, respectively. A population-averaged arterial curve based on that published in the literature and a study-specific portal-venous curve estimated using a dispersion model were used in the analysis [5,6,7]. The two *slope-ratio methods* are summarised in figure 1. Peak vascular concentrations, I_a and I_p, were obtained from the same vascular input functions used in the dual-input modelling procedure. The total hepatic perfusion, F, and arterial fraction, γ, were calculated using the following expressions: $F = F_a+F_p$ and $\gamma = F_a/(F_a+F_p)$. Correlations between median values of perfusion parameters quantified using the slope-ratio methods versus the dual-input model were analysed using the Pearson's correlation coefficient R^2 and via linear regression.

Results: Example sets of parametric maps quantified using the slope-ratio, Tsushima method *(top)* and the dual-input model *(bottom)* are shown in figure 2. In general, high spatial correlations were observed visually between the parametric maps quantified using the two approaches. The slope and intercept of the linear regressions and the Pearson's correlation coefficient R^2 between the slope-ratio (Mile and Tsushima) vs dual-input model perfusion parameters are summarised in table 1. Correlation plots of slope-ratio vs dual-input model derived F_a are shown in figure 3. Significant linear correlations were found between the two quantification approaches ($p<0.001$).

	Miles	Tsushima
Arterial perfusion	g_a/I_a	g_p/I_a
Portal perfusion	g_a/I_a	g_p/I_p

where
g_a = max. gradient of liver curve before t_s
g_p = max. gradient of liver curve after t_s
I_a = peak aortic concentration
I_p = peak portal-venous concentration

Schematic tissue concentration-time curves

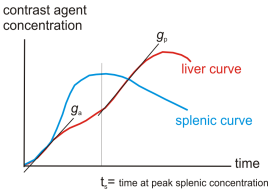

Figure 1: Perfusion quantification using the slope-ratio methods

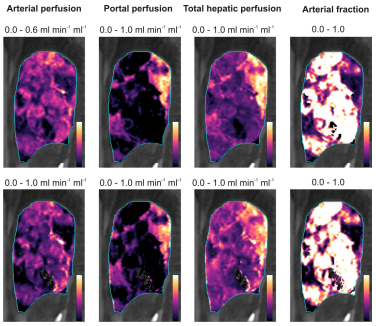

Figure 2: Parametric maps of perfusion quantified using the slope-ratio, Tsushima method (*top*) and the dual-input model (*bottom*). *Black* = low parameter value, *white* = high parameter value.

	Whole liver		Tumour	
	Miles	Tsushima	Miles	Tsushima
F_a	0.62, -0.01 **(R^2=0.764)**		0.60, -0.01 **(R^2=0.937)**	
F_p	0.33, -0.01 **(R^2=0.540)**	0.55, 0.02 **(R^2=0.719)**	0.20, 0.01 **(R^2=0.322)**	0.44, 0.03 **(R^2=0.282)**
F	0.36, 0.02 **(R^2=0.515)**	0.56, 0.03 **(R^2=0.811)**	0.52, -0.00 **(R^2=0.894)**	0.58, 0.02 **(R^2=0.886)**
γ	1.00, 0.13 **(R^2=0.616)**	0.93, 0.01 **(R^2=0.652)**	0.83, 0.12 **(R^2=0.473)**	0.97, -0.10 **(R^2=0.417)**

Table 1:. Summary of the linear regression estimates (slope, intercept) and the Pearson's correlation coefficient (R^2) between slope-ratio (Miles and Tsushima) versus dual-input model perfusion parameters for the whole liver and tumours.

Discussion: For the three perfusion parameters, F_a, F_p and F, the slope-ratio methods result in lower perfusion estimates compared with the dual-input model derived parameters (slopes of the linear regressions < 1.0). This underestimation is largely due to the assumption made in any slope-ratio methods that there is no venous outflow at times of maximal arterial and portal-venous gradients. Correlations between the slope-ratio and the dual-input model derived parameters are comparable between the two slope-ratio methods for all parameters except whole liver F_p and F, for which the Tsushima method is preferable to the Miles method. The following discussion will focus on comparisons between the Tsushima method and the dual-input model. Correlations of F_a quantified using the two approaches are high, especially in tumours. Tumours are characterised by regions with rapid arterial phase contrast (e.g. tumour rim). In these regions, maximal arterial gradients can be more precisely quantified and are less corrupted by noise in the data compared with surrounding liver tissues where enhancement is more gradual. Correlations of F_p quantified using the two approaches are high in the whole liver but low in the tumours which are known to have markedly lowered portal-venous perfusion. The poor correlation observed in the tumours may reflect the uncertainties associated with quantifying the maximal gradients in this later phase which has relatively small changes in tumour contrast agent concentration. Correlations of F quantified using the two approaches are high (R^2>0.80). In order to enable a fair comparison between the two methods, the same input functions were used for the two methods. Further works on input function determination are needed.

Conclusions: Arterial and portal hepatic perfusion were separately quantified using two slope-ratio methods. The slope-ratio methods used in this study are conceptually simple and can be easily implemented in the data analysis software. Additionally, these methods are computationally efficient which is especially attractive when analysing a large number of datasets, for example in large-scale clinical trial settings. In terms of data acquisition, since only first-pass data are used in the analysis, the DCE-MRI protocol could be shortened. In general, perfusion quantified using the slope-ratio methods were lower than those quantified using the dual-input model. High correlations were observed between the two approaches, especially in the estimates of arterial perfusion.

References: [1] Miles KA et al. Radiology 1993, 188:405-411, [2] Blomley MJ et al. J Comput Assist Tomogr 1995, 19:424-433, [3] d'Arcy JA et al. Radiographics 2006, 26, 621-632, [4] Materne R et al. MRM 2002, 47, 135-142 [5] Parker GJM et al. MRM 2006, 56, 993-1000, [6] Orton MR et al. PMB 2008, 53, 1225-1239 [7] Orton MR et al. In proc ISMRM 2009, 3615

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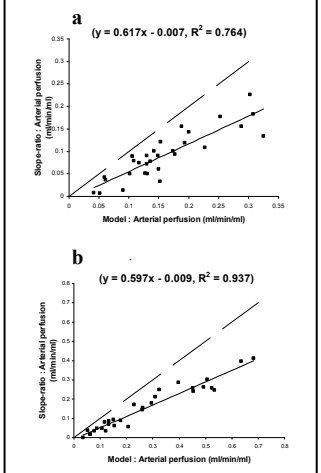

Figure 3:. Correlation plots of arterial perfusion quantified using the slope-ratio versus the dual-input single compartment model for the **(a)** whole liver and **(b)** tumours.