Fitting DCE-MRI data in the liver with a dual-inlet model: choice of venous and arterial delay parameters

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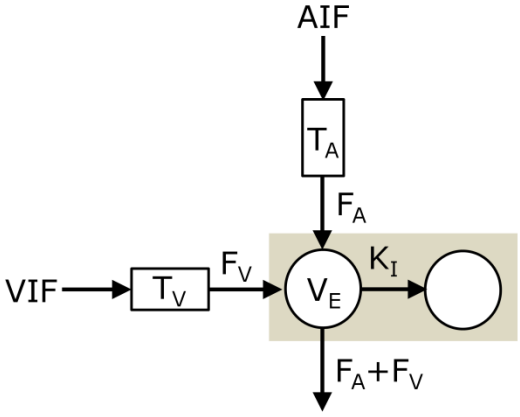

Figure 1. A diagram of the dual-inlet two-compartment uptake model for Gd-EOB-DTPA in the liver. The grey rectangle represents the ROI with extracellular (left circle) and intracellular (right circle) compartments. The tissue model is defined by 4 free parameters: the arterial (F_A) and venous (F_V) plasma flow, the extracellular volume (V_E) and the intracellular uptake rate (K_I). The AIF and VIF are sampled upstream and shifted by delay times T_A and T_V, respectively.

PURPOSE: Arterial and venous components of liver perfusion can be quantified from DCE-MRI with a dual-inlet model [1,2,3], using arterial- and venous input functions (AIF and VIF) sampled in the aorta and the portal vein. The transit from these sites to the tissue can be modelled using arterial and venous delay times, but the choice of these parameters has a strong effect on the results. A number of alternative approaches exist [1-4], but it is currently unclear which is most suitable. In this study the alternatives are applied to patient data and compared on the basis of the values they produce, and the best fit to the data.

METHODS: DCE-MRI data were acquired at 3T (Verio, Siemens) in 26 patients using the 3D gradient-echo sequence TWIST (48 coronal slices, 4mm thickness, 192x192 matrix, 2.1sec temporal resolution, 5min acquisition). A standard dose of Gd-EOB-DTPA (Primovist, Bayer) was injected 10 sec after the start of the acquisition at 2ml/s. Data were post-processed using the software PMI 0.4 [7]. ROIs were drawn on parametric maps in the abdominal aorta and the portal vein to measure AIF and VIF. In each patient, 5 circular ROIs were drawn on different slices in normal-appearing liver tissue. The tissue was modelled with a dual-inlet two-compartment uptake model (fig 1) to account for the intracellular uptake of Gd-EOB-DTPA [5,6]. Arterial and venous delays were simulated by shifting AIF and VIF over a time T_A and T_V, respectively (fig 1). Four different methods for choosing T_A and T_V were compared: (1) no delay (T_A=T_V=0); (2) only the AIF delayed (T_A fitted, T_V=0); (3) only the VIF delayed (T_A=0, T_V fitted); (4) both AIF and VIF delayed (T_A and T_V fitted). For each method, mean and standard deviation over all ROIs were calculated for each parameter. An expert in kinetic modeling (SS) performed a visual assessment of the quality of the fit.

Mean ± Stddev	None	AIF	VIF	AIF & VIF
Total Plasma Flow (ml/min/100ml)	66 ± 31	57 ± 27	113 ± 389	110 ± 373
Arterial Flow Fraction (%)	12 ± 19	23 ± 27	12 ± 19	25 ± 24
Extracellular Volume (ml/100ml)	15 ± 5.5	15 ± 5.4	15 ± 5.1	14 ± 4.9
Uptake Rate (/100/min)	3.4 ± 1.9	3.3 ± 1.9	3.5 ± 1.9	3.4 ± 1.8
Arterial Delay (sec)	N/A	5.2 ± 3.5	N/A	6.2 ± 3.3
Venous Delay (sec)	N/A	N/A	1.4 ± 2.0	3.3 ± 2.9

Table 1. Summary of the independent parameters calculated with the four alternative delay options: no delay fitted, only the AIF delayed, only the VIF delayed, both AIF and VIF delayed independently.

RESULTS: Table 1 summarises the results, and shows that: (i) Intracellular uptake rate K_I and extracellullar volume V_E are insensitive to the choice of the delay model; (ii) There are strong differences in mean and standard deviation of total plasma flow F_A+F_V between models that allow for venous delay and those that don't; (iii) There are strong differences in mean arterial flow fraction $F_A/(F_A+F_V)$ between methods that allow for AIF delay and those that don't. Relative to the mean, the standard deviations in the arterial flow fraction are comparable. Without a delay parameter, the best fit to the data systematically shows a mismatch in the initial slope of the curve. The upslope is always accurately fitted when an arterial delay parameter is added, but adding a venous delay alone is not sufficient.

CONCLUSION: Previous studies in healthy humans produced total plasma flow values (ml/min/100ml) of 65 ± 25 [2] and 75 ± 38 [3]. Hence both methods that allow for a venous delay produce unstable and overestimated values and can be excluded (Table 1). This is also consistent with the observation that venous delays T_V are small (1.4-3.3 s). The remaining two methods produce realistic plasma flow values, but they differ in the mean values of the arterial flow fraction. The value measured without a delay (12 ± 19 %) appears most consistent with the literature: 18 ± 15 % [2] and 7.5 ± 7.9 % [3]. One the other hand, the addition of an arterial delay is necessary to obtain a good fit to the data, which provides a strong argument for this method. Also, the measured value of T_A (5.2 ± 3.5 s) is more than twice the sampling time. which does indicate that the effect is significant. The arterial flow fraction calculated with AIF delay alone (23 ± 27 %) is higher than in [2,3], but this is not unlikely in tumor patients. We conclude that DCE-MRI data in the liver are best analysed by fitting an arterial delay alone, and assuming that the venous delay is zero - as in [3]. These results are likely to remain valid for standard extracellular tracers, which have the same behaviour as Gd-EOB-DTPA in large vessels.

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