

A physiological model for injected contrast agent concentration incorporating recirculation, extravasation and excretion

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Target audience:

Clinicians and researchers dealing with vascular concentration of contrast agent (CA) after intravenous bolus injection, typically known as arterial or vascular input function (AIF, VIF) measured at feeding artery or vein using DCE MRI.

Purpose:

In the analysis of dynamic contrast-enhanced (DCE) MRI using tracer kinetic model based deconvolution approaches, it is beneficial to have a functional or continuous curve to represent the VIF. Empirical formulations are dependent on the shape of the VIF, which is dependent on location and injection protocol, and its parameters provide little to no physiologic meaning [1,2]. Horsfield et al. [3] physiologically based model provides good fit to VIF measured from portal vein, but its application is limited to human DCE MRI study using Gd-DTPA as it requires some previously observed parameters. We have developed a physiologically based model without the above limitation for representing VIF.

Theory:

King et al. [4] vascular transport operator (VTO) can describe the delay and dispersion of a transiting bolus in vasculature. Each VTO curve can be defined by a bolus delay time (t_d), and a relative dispersion (RD) of the bolus during transit, and has unit area. We represent VIF with multiple VTO curves (MultiVTO). For the first VTO, its bolus delay time, t_{d1} corresponds to the actual bolus arrival time and RD_1 reflects the dispersion of the bolus between the points of injection and measurement. Subsequently, we assume all recirculation have the same t_{d_recirc} and RD_{recirc} reflecting the time taken to and the dispersion effects from circulating the body and back to the measurement point, respectively. We account for the reducing amount of CA in the vasculature, which are used to scale the area of each VTO, using a three compartment model (Fig. 1) with rate constants, K_{ij} , defined for each bolus transit period instead of per unit time.

Methods:

We tested the performance of this model on VIFs from different locations, acquired by different modalities, and compared with Horsfield's model. We fitted this model to different VIFs measured by DCE MRI at descending aorta (n=34), vertebral artery (n=8), hepatic artery (n=3), and portal vein (n=3). We also fitted DCE CT VIFs (n=43) measured at iliac artery.

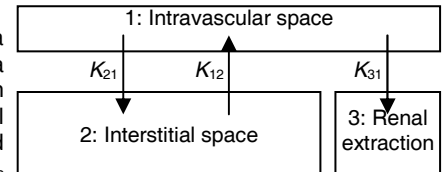


Fig. 1 Schematic diagram of a three-compartment model. K_{ij} are the fraction of contrast materials from compartment j moved into compartment i in each bolus transit period.

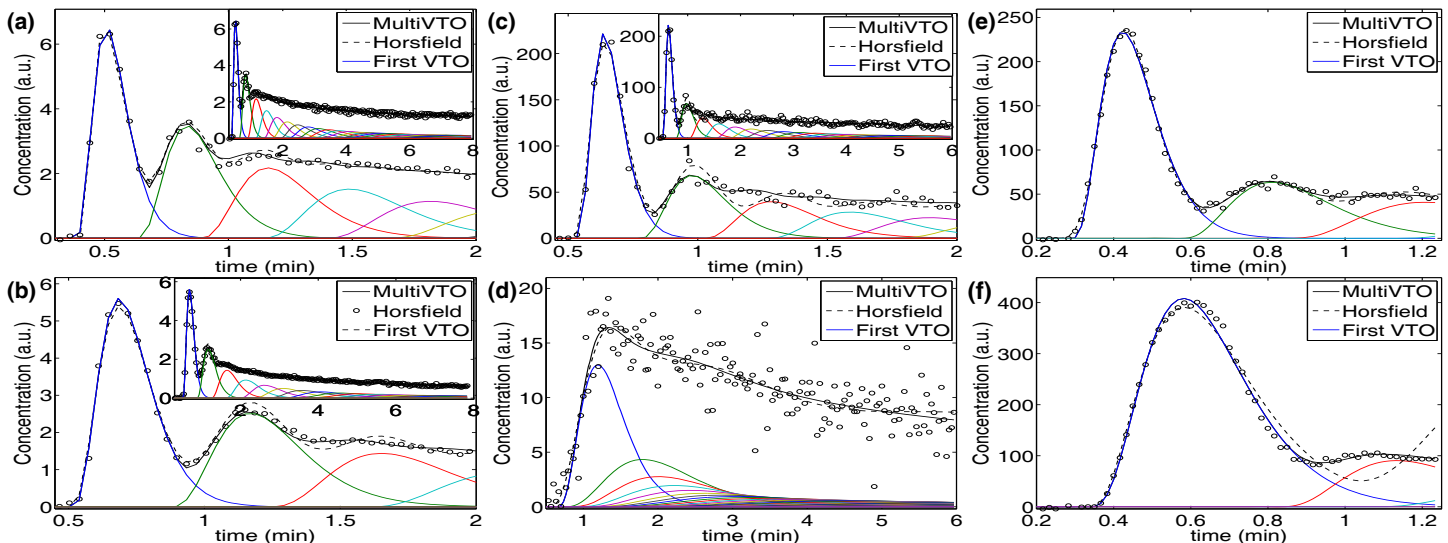


Fig. 2 Typical VIFs measured by DCE MRI at descending aorta (a), vertebral artery (b), hepatic artery (c), portal vein (d), and by DCE CT acquired at iliac artery (e,f) where (f) shows a case where the Horsfield model failed to fit the data. VIFs are fitted using MultiVTO (black solid line) and Horsfield model (black dashed line). Colored solid lines are the individual VTO curves. Insets in (a-c) show the full VIF to allow zoom-in view in the main plot.

Results:

Figure 2 shows typical fitting of various VIFs. Both models fitted to the data appropriately except Horsfield model visibly failed (Fig 2f) in 15 of the 43 DCE CT VIFs measured at the iliac artery. Horsfield model also tend to oscillate more than the data (Fig. 2a-c). Table 1 lists the mean±SD of the root mean squared errors (RMSE) of fittings. MultiVTO fit the data better than Horsfield model.

Discussion and Conclusion:

This physiological model for VIF is able to fit different VIFs measured by both DCE MRI and DCE CT, and at different blood vessel locations. Unlike Horsfield model, it is not limited to human data acquired from DCE MRI using Gd-DTPA. Thus, it should also be applicable to animal studies, using any measuring methods (DCE CT, PET, SPECT, blood sampling, etc.) that give a concentration-time curve of injected contrast agent at a blood vessel. In addition, its parameters have physiological meanings which may assist in the validating measured VIFs, especially in DCE MRI where quantification is problematic.

References:

	Descending aorta	Vertebral artery	Hepatic artery	Portal vein	Iliac artery
MultiVTO	0.0146 ± 0.0077	0.0036 ± 0.0015	0.343 ± 0.030	0.143 ± 0.015	1.649 ± 0.647
Horsfield	0.0180 ± 0.0116	0.0046 ± 0.0020	0.389 ± 0.054	0.189 ± 0.044	2.217 ± 1.255

1. Parker GJM et al. Magn Reson Med 2006 54:993–1000.
 2. Orton MR et al. Phys. Med. Biol. 2008 53:1225–1239
 3. Horsfield MA et al. Phys. Med. Biol. 2009 54:2933–2949
 4. King RB et al. Am. J. Physiol. 1993 265(6):H2196–H2208.