Simulation studies of impulse response functions for DCEMRI: Comparing a new mathematical model with a single exponential decay function in the two-compartment model.

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Introduction: Dynamic contrast enhanced MRI (DCEMRI) involves measurement and analysis of contrast media uptake and washout following bolus injection. These studies are critical for detecting and evaluating tumor vasculature and changes during therapy. However, there is no accepted method for analyzing contrast media uptake and washout. The two-compartment model (TCM) [1], though widely used, is not ideal for tumors because of their microscopically heterogeneous anatomy. The TCM treats the contrast concentration curve C(t) as the result of a convolution between the arterial input function (AIF) and the impulse response function (IRF) with a single exponential decay. In this research we introduce a bi-exponentially decaying IRF; results of fitted DCEMRI data were compared with the TCM.

Material and Methods: For a causal, linear time-invariant system, C(t) can be considered as convolution between the IRF and the AIF, i.e., C(t) = AIF⊗IRF. The IRF in the TCM has the form: $K^{trans}\exp(-t\cdot K^{trans}/v_e)$, where K^{trans}(min^{-1}) is the volume transfer constant between blood plasma and extravascular, extracellular space (EES), and v_e is the volume of the EES per unit volume of tissue. Our new IRF was developed based on the results of a recursive deconvolution algorithm and has the following form: $K\left(1-e^{-\lambda t}\right)^{\rho}\cdot\left(e^{-\kappa_1 t}+\varepsilon e^{-\kappa_2 t}\right)$, where K(min^{-1}) is the transfer constant of the tissue, κ_i (i=1,2) is the decay constant, λ is a uptake rate, ρ is a constant related the slope of uptake, and ε is a scaling factor. Simulated tumors and muscle C(t)'s were generated by varying the empirical mathematical model [2] parameters within reasonable ranges based on a previous experimental study. The AIF was calculated from the C(t) of a reference tissue (muscle) under the assumption that it is well approximated by the TCM. The two IRFs under the same AIF were compared via 14 simulations (covering a variety of tumors) and with one animal dataset.

Results: Table 1 shows the simulated results for both muscle and tumors by convolution fitting C(t) = AIF⊗IRF with the fixed AIF. It can be seen that when $\lambda >> \mathbf{1}$ and $\varepsilon \sim \mathbf{0}$ (as is seen in muscle), our new IRF is equivalent to the single exponential decay, with $K = K^{trans}$ and $\kappa_1 = K^{trans}/v_e$. Generally, the TCM requires a much higher v_e than is realistic for a tumor. The fits provided by convolution with our new IRF were much better than the TCM and had higher "goodness of fit", R^2 ($p < 0.14$). Therefore, tumors require a multi-exponential decay IRF for accurate fitting. Fig. 1 (a) shows a typical Gd-DTPA C(t) (open circles – normalized by dose) obtained from a typical non-metastatic rodent prostate tumor convolution fitted with the TCM's IRF (black line) and our new IRF (green line). The corresponding IRF for our model is shown in Fig. 1(b) (red line) with the AIF in Fig. 1(c) (red line). Our new IRF generally included a rapid enhancement phase; this is likely due to the fact that the AIF is derived from a reference tissue near the tumor, i.e., a regional AIF. The contrast bolus is likely to experience additional delay and dispersion on the way to specific voxels or regions within the tumor. Thus, we modified the derived AIF (Fig. 1(c) blue line) by introducing additional delay and dispersion to produce a truly local AIF. By using this modified AIF, we obtained a monotonically decaying IRF (Fig. 1 (b) blue line).

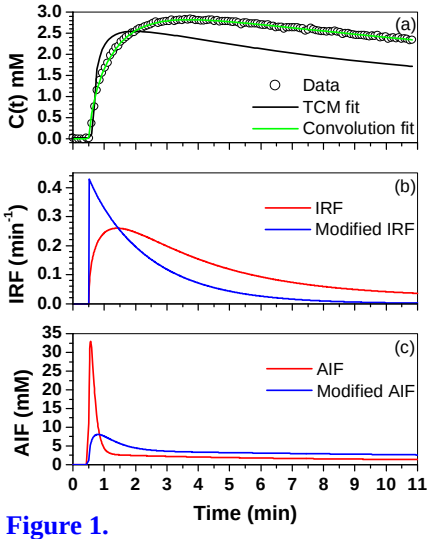

Figure 1.

Discussion: The present work demonstrates that our new IRF has potential advantages compared to the more widely used IRF in the TCM. A monotonically decaying IRF requires a modified the AIF. An extension of the method allows calculation of a local AIF and provides new parameters that describe the delay and dispersion of the contrast media bolus in tumor vasculature, and these parameters may have diagnostic utility. Future work will evaluate the use of this approach to distinguish between benign and malignant cancers, and detect tumor response to therapy.

Table 1.	K^{trans}	v_e	R^2	K	λ	ρ	κ_1	ε	κ_2	R^2
Muscle (1 case)	0.11	0.20	0.99	0.11	20.5	0.12	0.54	0.003	0.12	0.99
Tumor (13 cases)	0.27	0.83	0.69	0.27	12.4	0.28	0.42	0.13	0.06	0.99

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Reference:

[1] Tofts et al., JMRI 1999
[2] Fan et al., MRM 2004