Novel procedures to derive the impulse response function and its mathematical model for DCEMRI

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Introduction: Analysis of contrast media uptake and washout kinetics would be more effective if the bias caused by using inappropriate physiologic models and incorrect arterial input function (AIF) could be avoided. This can be done if the tumor is treated as a system that gives a linear response to the AIF. The contrast concentration vs. time curve (C(t)) can be considered as the convolution between AIF and the impulse response function (IRF) - $C_\delta(t)$. The AIF can be deconvolved from the C(t), so that the IRF can be obtained. However, the deconvolution is an ill-posed problem and noise in the data is magnified in the common deconvolution procedures. The most commonly used deconvolution technique, singular value decomposition (SVD), introduces unwanted oscillations in the shape of IRF [1]. Some regularization methods have been used as an alternative to the deconvolution method to reduce the oscillations. The degree of complexity and potential for error involved in utilizing these techniques may outweigh their usefulness in analyzing clinical DCEMRI data. Therefore, a simple and robust technique to obtain accurate IRF's is desirable.

Material and Methods: To develop the new deconvolution technique, we utilized DCEMRI data acquired from rodent tumors at 4.7T. The C(t) curves from both tumor and muscle were fitted with an empirical mathematical model (EMM) that accurately fits a wide range of experimental data [2]. Subsequently, numerical C(t) curves with desired temporal resolution were calculated with the EMM. Under the assumption that the muscle was well approximated by the two-compartment model (TCM) [3], the AIF was calculated from the EMM-fitted muscle curves with the literature values of K^{trans} and v_e. We used two steps namely 'prediction' and 'correction' to obtain the IRF from calculated AIF and C(t). In the prediction step, a numerical IRF was calculated with the recursive formula: $C_\delta(t_j)=\left(C(t_j)-\sum_{i=1}^{j-1}AIF(t_j-t_i)C_\delta(t_i)\Delta t_i / A_0\Delta t_1\right)$, where j=1…N, A_0=AIF(0) or AIF(1) if AIF(0)=0. The rapid changes in the AIF(t) and C(t) at very early times cause oscillations in the initial few seconds of the numerical IRF. To eliminate these oscillations, the following mathematical equation was used to fit the numerical IRF: $C_\delta(t)=K\left(1-e^{-\lambda t}\right)^\rho\cdot\left(e^{-\kappa_1 t}+\varepsilon e^{-\kappa_2 t}\right)$, where the **K**($min^{-1}$) is the initial uptake rate constant, $\boldsymbol{\kappa}_i$ (i=1,2) is the washout rate constant, 1/**λ** is the time constant, **ρ** is related to the shape of the uptake portion of $C_\delta(t)$, and **ε** is a scaling factor. Finally in the correction step, the direct search technique was used to find the optimal parameters so that the $C_\delta(t)\otimes$AIF was as close as possible to the C(t).

Results: The numerical C(t) curves were produced by varying the EMM parameters to simulate for both muscle and tumors. The AIF and the $C_\delta(t)$ were calculated as described above. The numerical simulation results demonstrated that the $C_\delta(t)\otimes$AIF(t) fit the plots of C(t) with a goodness-of-fit R^2 = 0.98±0.02, which was significantly better than the R^2 = 0.88±0.15 obtained with the TCM approach. Fig. 1 shows a typical example of Gd-DTPA C(t) curves (open circles) for regions-of-interest in muscle and tumor (ROI1 and ROI2), from a non-metastatic rodent prostate tumor fitted with the TCM (red line), and $C_\delta\otimes$AIF (blue line). The results show that $C_\delta(t)\otimes$AIF(t) fits the data more accurately than the TCM. Fig. 2 shows the corresponding IRFs from muscle and two different tumor ROIs; and Table 1 shows the parameters for the IRFs. The IRF curves and parameters clearly demonstrate differences between normal tissue and tumor ROI's. For the ideal TCM case where the local AIF is known and there is a simple exponential washout, then the $C_\delta(t)$ is just the TCM kernel with $K = K^{trans}$, and $K^{trans}/v_e = k_{ep} = \kappa_1$, when $\lambda \to \infty$ and $\varepsilon \to 0$.

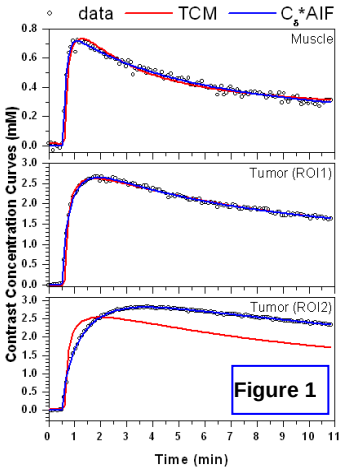

Figure 1

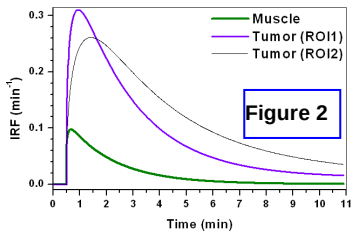

Figure 2

Discussion: The deconvolution method described here and the general mathematical model of IRF provided better fits to contrast media vs. time curves compared to the widely used TCM. The improved fits produced kinetic parameters that more accurately describe contrast media uptake and washout, without the bias and error associated with the use of physiologic models, such as the TCM. Common diagnostic parameters, including the 'area under the curve', 'signal enhancement ratio', 'maximum slope', and 'time to peak enhancement', can be easily calculated from the IRF. This could facilitate accurate classification of suspicious lesions. This IRF method is promising since it allows one to explore possible new parameters that have diagnostic utility not found in other models.

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[**1**] Calamante et al. MRM 2003; [**2**] Fan et al. MRM 2004; [**3**] Tofts JMRI 1997.

Table 1.	K	λ	ρ	κ_1	ε	κ_2
Muscle	0.11	9.93	0.25	0.57	0.003	0.009
Tumor(ROI1)	0.42	2.67	0.36	0.45	0.030	0.004
Tumor(ROI2)	0.37	0.96	0.43	0.36	0.155	0.081