A Novel Vascular Transfer Function for Modeling the Local Arterial Input Function for More Accurate Estimation of Vascular Permeability Parameters in DCE-MRI Studies

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Target Audience: Neurologists, neuro-radiologists, physicists and scientists working in the field of Dynamic Contrast Enhanced imaging, and vascular permeability

Purpose: One of the key elements in Dynamic Contrast Enhanced (DCE) Image Analysis is the Arterial Input Function (AIF). The AIF is used for estimating permeability parameters such vascular forward transfer rate constant (k^{trans}), reverse transfer rate constant (k_b), plasma volume fraction (v_p), and extracellular-extravascular space fraction (v_e)[1]. Traditionally, in these studies a global AIF sampled from a major artery or vein is used for estimating these parameters; however, not addressing dispersion and delay of the AIF at the tissue level can lead to biased estimates of these parameters. We previously introduced a parametric basic transfer function (BTF) describing changes of the AIF profile at different levels of the human brain vascular structure[2], based on laws of fluid dynamics, Murray's vascular branching law and vascular morphology. Here, we introduce an extended version of this transfer function which in addition to dispersion and delay of the AIF, takes into account extravasation of the Contrast Agent (CA) into the Extravascular-Extracellular space (EES). This extended transfer function (ETF) can decompose the tissue response signal (TRS) sampled from DCE image regions with leaky vessels, to its intra-vascular and extra-vascular components. This can be used for more accurate estimation of permeability parameters of vessels.

Methods: The transfer function of a single vessel with laminar flow has been calculated as[2,3] $h(t) = \frac{t_0}{t^2}$ for $t \geq t_0$ where $t_0 = \frac{D_0}{v_0}$ (the ratio of the length of the vessel to the maximum blood velocity in that vessel) is a characteristic of every branch, assuming that blood flow is constant. The parametric equation of the transfer function of the vascular structure from the opening of a main branch to the end of one of the sub-branches at the n^{th} level of branching can be expressed as: $h(t)_{1\,to\,n} = g \times (h(t)_1 * h(t)_2 * \ldots * h(t)_n)$ where $h(t)_n = \frac{t_{0n}}{t^2}$ for $t \geq t_{0n}$ and $n = 1\ to\ 6$. Here g is a gain factor. By sampling the CA concentration ($C_t(t)$) from a voxel in the DCE-MR image series, and also sampling the AIF from the circle of Willis, we can write the following equation: $C_t(t) = h(t)_{1\,to\,n} * AIF(t)$. The problem is to find the transfer function that can best describe the relation between the AIF and $C_t(t)$ at each voxel in the image. Using the simplex algorithm as a non-linear fitting method and the sum of squared errors as the cost function, for every configuration of the transfer function (based on the number of branching layers (n)), the best function that can transform the AIF to the $C_t(t)$ is estimated. The fitting procedure is done for six configurations of one to six layers of branching, to find the following set of parameters for each of the configurations: $[g, t_{01}, t_{02}, \ldots t_{0n}]$. Next, model selection is carried out using the Akaike Information Criterion (AIC)[4] to find the best transfer function that can transfer the AIF to the sampled $C_t(t)$. This transfer function can describe delay and dispersion of the AIF after passing through the vascular structure down to the capillary bed; however, it models only intact vessels with no leakage. To address the effects of extravasation, we have extended this transfer function by combining it with the Extended Tofts Pharmacokinetic Model[5] to get the following equation: $C_t(t) = \frac{Ktrans}{v_p} e^{-k_b t} * AIF(t) * h(t)_{1\,to\,n} + AIF(t) * h(t)_{1\,to\,n}$. Here $C_t(t)$ is the superposition of the intravascular and extravascular components of the signal which are the two main components of this equation. By replacing $C_t(t)$ with $(1 - Hct)\Delta R_{1t}(t)$ and $AIF(t)$ with $\Delta R_{1a}(t)$, the observation equation for DCE-MR applications can be written which we have used in this study. Here $\Delta R_1(t)$ is the relaxation change.

DCE-T1 series of a patient with a Glioblastoma Multiforme Tumor was acquired (3D SPGRE DCE-T1, 70 image volumes with 20° flip angle and 5.31s time resolution, Magnevist (Bayer Healthcare Pharmaceuticals, Wayne, NJ) with a dose of 0.1 mmol/ kg injected at a rate of 4 mL/s). Figure 1-a shows a section of this image. The CA concentration profile was sampled from three locations as seen in Figures 1-b (The AIF from the circle of Willis), 1-c (an ROI in the tumor) and 1-d (an ROI in the normal tissue).

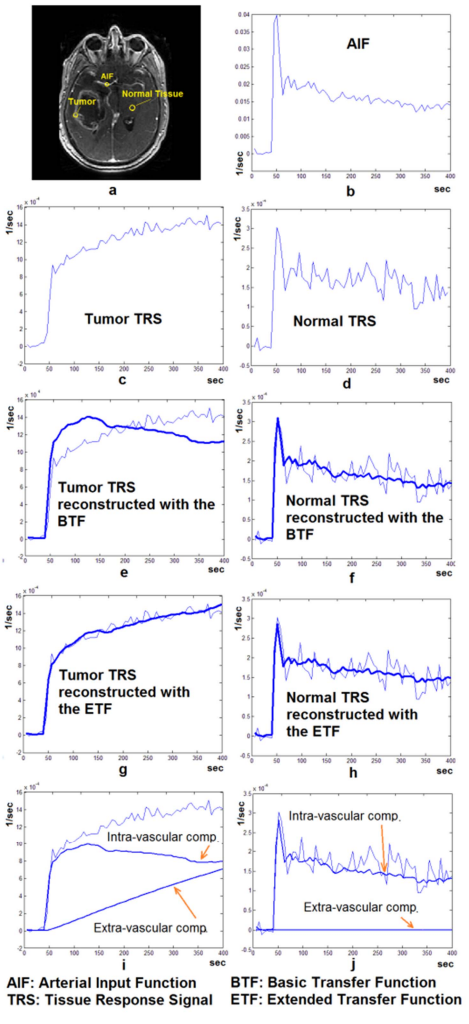

Figure 1

Results: The results of finding the best transfer function using the basic transfer function can be seen In Figures 1-e and 1-f. The bold curve shows the result of convolving the AIF with the optimal transfer function which is found after fitting the best model selected by the AIC. As seen in Figure 1-f, in the normal tissue, the reconstructed tissue response signal matches the original signal very well; however, since this basic transfer function does not explain extravasation, in the case of the signal being sampled from the tumor area, the reconstructed signal is far from the original sampled signal, even for the best fit transfer function (Figure1-e). In the next step, we repeated the same procedure stated above, but with using the extended transfer function. Figures 1-g and 1-h show the reconstructed signals in both cases. In the case where there is no leakage, even when the extended transfer function is used, the reconstructed signal is almost identical to that estimated with the basic transfer function (Figure 1-h). But when the extended transfer function is used for explaining the signal sampled from the tumor, the reconstructed signal matches the original signal very well. In Figures 1-i and 1-j, the intravascular and extravascular components of the reconstructed signals are plotted as separate curves. The intra-vascular component represents the local AIF and the extra-vascular component the leakage to the EES. In Figure 1-j, the extra-vascular component is zero which means there is no leakage to the EES.

Discussion and Conclusions: The results show that the extended vascular transfer function is able to explain the effects of dispersion and delay of the AIF, as well as the extravasation of the CA to the EES. By using this transfer function, the tissue response signal can be decomposed into its intra and extra-vascular components which are basically the intravascular and leakage components of the signal. The advantage of using this transfer function for solving the pharmacokinetic model is that it can estimate the local AIF found in each voxel and it employs this AIF (instead of the global AIF) in the calculations which can lead to more accurate estimation of the permeability parameters, especially in areas with leaky vessels. Also, extracting the extra-vascular component of the signal can lead to estimation of the permeability parameters using shorter scan times. Overall, this transfer function has the potential to address many open problems in DCE-MRI and DCE-CT applications where it can be used for simultaneous measurement of permeability and perfusion parameters.

References

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