The Effects of Locally Estimated Arterial Input Functions on Pharmacokinetic Parameters in DCE-MRI

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Introduction: Dynamic contrast-enhanced MRI (DCE-MRI) is physiological imaging tool used clinically to aid the diagnosis and treatment monitoring of a variety of diseases. Pharmacokinetic parameters can be estimated by fitting DCE-MRI data to one of many mathematical models. The two-compartment model used here describes the concentration of contrast agent (CA) in tissue with respect to three parameters as well as the CA concentration in the plasma through the relationship: $C_t(t) = K^{trans} C_p(t) \otimes e^{-k_{ep}t} + V_p C_p(t)$ where K^{trans} and k_{ep} are the transfer constant and rate constant respectively, $\otimes$ is the convolution operator, v_p is the blood plasma volume fraction, and $C_p(t)$ is the concentration of CA in the blood plasma (also known as the arterial input function or AIF) [1]. In many cases, direct measurement of the AIF from DCE-MRI data is difficult due to small arterial lumens, flow and signal saturation effects, and lack of a measurable artery within the field of view. Previous work by the authors has focused on developing an alternating minimization with model (AMM) method for jointly estimating AIF model parameters and tissue kinetic parameters directly from tissue concentration curves (TCs), also termed blind estimation. This method has been shown to provide good results for both simulated and clinically acquired data [2]. In some cases, the shape of the estimated AIF depended on the region from which the input TCs were selected. As the region of interest moved away from an artery towards a region of diseased tissue, the resulting AIF became increasingly dispersed in time [3]. This work first develops a method for calculating the expected confidence of a locally estimated AIF. AIFs are then estimated voxel-wise using a region-growing technique to ensure sufficient quality of data for each voxel as determined by the confidence measured. The changes in pharmacokinetic parameters when measured from a local input function are compared to measured and globally estimated input functions

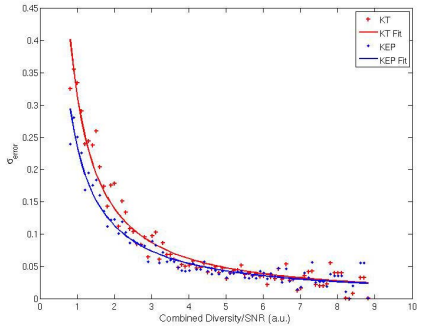

Figure 1 – The expected error in the estimated AIF as a function of SNR and diversity.

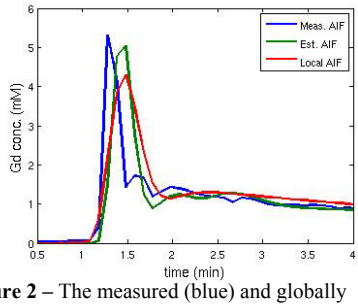

Figure 2 – The measured (blue) and globally estimated (green) AIFs plotted along side a single locally estimated AIF (red) for one sarcoma patient.

Methods: Empirical testing and observation of the AMM method's performance led to the hypothesis that the quality of AIF fit was mainly a function of the SNR and diversity of the input TCs. Temporal resolution also affected fit quality, especially with regard to v_p, but was approximately constant among typical clinical scans. Computer simulations with known truth were used to determine the response of the AMM method to various inputs. Each simulation involved the creation of eight TCs from a 'true' AIF. These curves were input to the AMM algorithm, which was initialized with a population-average initial estimate for the AIF. The error of the resulting AIF was assessed by calculating the percent error of kinetic parameter measures when the estimated AIF was used instead of the 'true' AIF. In each simulation, zero-mean Gaussian noise was added to the eight TCs and the range of kinetic parameters from which the TCs were created was altered to fully sample the entire expected SNR and diversity ranges seen in clinical data. The SNR and diversity measures for each simulation were combined into a single metric, and the expected error was plotted as a function of this measure (Fig. 1). Voxel-wise AIF estimates were obtained from clinical images by centering a region of interest on a particular voxel and growing a region with concentric shells around that voxel until the TCs in that region met a pre-determined SNR/diversity threshold. The curves from this region were clustered into 8 representative curves with an unsupervised k-means algorithm and these representative curves were then input to the AMM algorithm. The resulting estimated AIF was assigned to that voxel. This process was repeated for a particular area within the 4D image. Pharmacokinetic parameters were calculated for each voxel using the estimated AIF assigned to that voxel. In addition, a single AIF was estimated using the entire area as input. A measured AIF was also obtained from arterial voxels in the full dataset using an automatic thresholding routine. Pharmacokinetic parameters were calculated voxelwise for each of these global AIFs and the results were compared to that for the voxelwise AIFs.

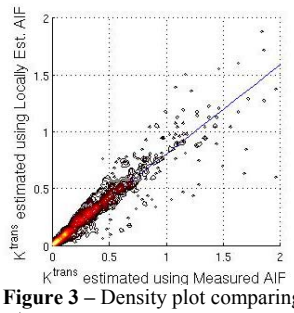

Figure 3 – Density plot comparing K^{trans} calculated with a measured AIF versus local AIFs for two patients.

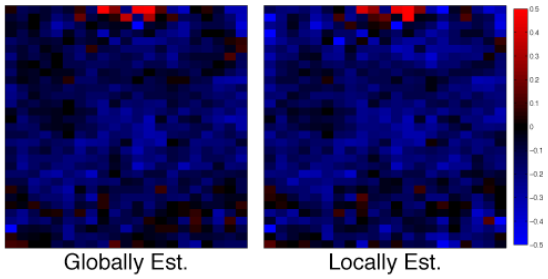

Figure 4 –Maps showing the percent difference in K^{trans} when a globally (left) or locally (right) AIF is used in place of a measured AIF in pharmacokinetic modeling.

Results/Discussion: The simulated results for the AMM method showed no bias in any of the parameters as a function of either SNR or diversity. The standard deviation of the error was used as a measure of error and the K^{trans} and k_{ep} errors are plotted as functions of the combined SNR/diversity metric in Fig. 1. Both error measurements follow a power law decay of the form $\sigma = Ax^b$ with K^{trans} parameters: A=0.32, b=-1. 2, and x refers to SNR/diversity. Fig. 2 displays the measured and globally estimated AIFs for a single patient, along with a representative locally estimated AIF selected from a voxel on the tumor rim. K^{trans} measurements obtained from the local AIFs are compared to those from measured AIFs from two patients and are shown in Fig. 3. K^{trans} tended to be larger using the measured AIF (y=.78x+.02 with R^2=.93) while k_{ep} measurements matched more closely (y=.98x-.04 R^2=.93). The median region size for the local AIF calculations in these two patients was 139 voxels (corresponding roughly to a 5X5X5 cube). Maps illustrating the percent differences in K^{trans} when estimated AIFs are used in place of the measured AIF are shown in Fig. 4. Parameters from local AIFs tend to match those from measured AIFs more closely than those from globally estimated AIFs. As seen in Figs 3 and 4, the parameters from both types of estimated AIFs tend to be lower than those from measured AIFs, likely due to dispersion in the AIF time course. This dispersion may be a function of slow CA uptake in regions of the tumor with tortuous vasculature. Although locally and globally estimated AIFs often give similar results as in Fig. 4, in some cases the locally estimated AIFs may provide additional insight on tumor vasculature and local blood supply, which may in turn aid treatment planning and monitoring.

Reference:

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2. Fluckiger JU, et al**.** Model-based Blind Estimation of Kinetic Parameters in DCE-MRI. Mag. Res. Med 2009 *Online view*
3. Fluckiger JU, et al. Local Arterial Input Functions in DCE-MRI. ISMRM 2008 Proceedings