Correcting for bolus delay and dispersion in the AIF using a constrained local AIF (LAIF) model

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Target audience: Clinicians and imaging scientists interested in DCE-MRI and tracer kinetics.

Purpose: Dynamic contrast enhanced (DCE) MRI is widely employed in the detection and characterization of cancer. Many DCE MRI data models employ a directly determined upstream arterial input function (AIF). Determining an AIF is technically challenging, due to partial volume and flow artifacts. Further, the actual AIF at the capillary inlet of any given region of interest is both delayed and dispersed compared with the AIF measured in a major feeding vessel. In the case of tumor tissue, where the vasculature is expected to be highly heterogeneous, a single global AIF is likely a poor approximation to the desired voxel-specific local AIFs (LAIFs). The goal of this project is to better model DCE-MRI data, accounting for both delay and dispersion with a constrained LAIF model.

Methods: *Data:* Clinical cervical cancer DCE-MRI data were acquired prospectively as part of EMBRACE, an international study on MRI-guided brachytherapy in locally advanced cervical cancer. Each DCE-MRI dataset consisted of two dynamic (time-resolved) MRI sub-datasets: (i) the remote AIF dataset obtained from monitoring of the external iliac artery and (ii) the tissue response dataset obtained from monitoring of the cervix. *Model:* The use of a locally modelled AIF has been previously investigated in dynamic susceptibility enhanced (DSC) MRI experiments (1). We have extended this strategy to DCE-MRI data analysis. Each voxel-specific LAIF model includes two gamma distributions, mimicking the contrast agent's initial and recirculation boluses, a steady-state contrast agent circulation phase term, and an exponential decay term, accounting for contrast agent washout. The LAIF model was constrained by fixing the values of several model parameters extracted from the measured AIF. Two model parameters, the initial bolus arrival time, and the relative bolus size, accounting for delay and dispersion, respectively, were not constrained. The tissue response function was characterized by the three-parameter (F_p, v_p and PS) Compartmental Tissue Uptake (C-TU) model (2), which was shown previously to be the preferred model for these same cervical cancer DCE data (3). Here, F_p is the plasma flow, v_p is the fractional plasma volume, and PS is the permeability-surface area product. The unconstrained (modeled) LAIF parameters and the tissue response function parameters were estimated using Bayesian probability theory methods (4), with Markov-chain Monte Carlo simulations.

Results and Discussions: **Figures 1A and 1B** compare measured AIF (mAIF) *vs.* constrained LAIF (cLAIF) modeling results averaged over the whole tumor. Systematic deviations in the residual for the Compartmental Tissue Uptake (C-TU) model are substantially reduced with use of the cLAIF approach. Fits obtained with the mAIF and cLAIF provided very similar estimates for v_p and PS. However, compared to the cLAIF approach, the mAIF tends to underestimate F_p. Voxel-wise model selection analyses (**Figures 1C & 1D**) show the cLAIF approach is highly preferred (more probable). Simulation studies (data not shown) confirm Bayesian parameter estimation employing cLAIF correctly extracts tissue response function parameters under noise conditions typical of clinical DCE-MRI data (baseline noise SD 0.01~0.02 mM).

Conclusions: Cervical Cancer DCE MRI data were better modelled using the constrained LAIF than using a single remotely measured AIF. Application across the entire EMBRACE patient population will be the subject of future efforts.

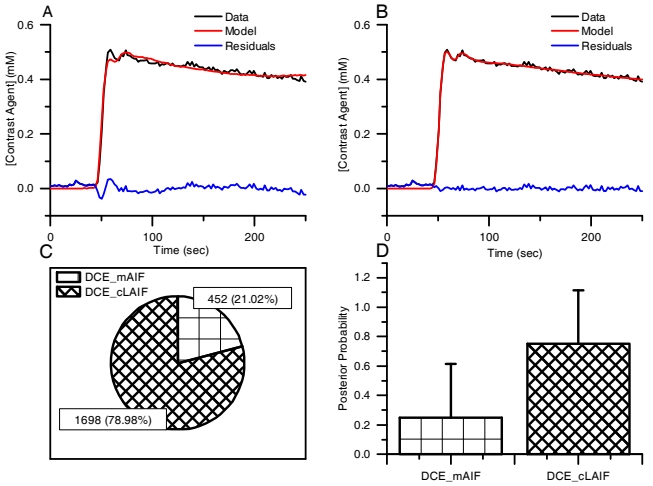

Figure 1. Panel A & B: Bayesian modeling of a DCE MRI contrast agent concentration-time curve for a cervical tumor (full tumor average), employing either a remotely measured AIF (**Panel A**) or a constrained LAIF (**Panel B**). Parameters obtained with the mAIF approach: F_p = 0.49 min^{-1}, v_p = 0.22 and PS = 0.042 min^{-1}. Parameters obtained with the cLAIF approach: F_p = 1.2 min^{-1}, v_p = 0.23 and PS = 0.042 min^{-1}. **Panels C & D**: Voxel-by-voxel model selection between approaches employing either mAIF or cLAIF on the same cervical tumor (2150 total tumor voxels). **Panel C**: 79% (1,698) of the tumor voxels favor use of the cLAIF; 21% (452) of the tumor voxels favor use of the mAIF. **Panel D**: The posterior probability across the whole tumor obtained using the mAIF is 0.25 ± 0.36, while the posterior probability obtained using the

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