Reliable estimation of capillary transit time distributions at voxel-level using DSC-MRI

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Introduction

DSC-MRI has proven very useful for characterizing tissue perfusion indices such as CBF, CBV and MTT. However, since CBF and MTT only represent average capillary flow and transit time, a more exhaustive characterization of local capillary flow patterns could be achieved by estimating the entire underlying transit time distribution. Flow heterogeneity in particular, or analogously transit time heterogeneity (TTH), has been suggested as an important physiological parameter correlating with outcome in acute ischemic stroke [1], and tissue oxygen extraction capacity (OEC) has been suggested to depend on both heterogeneity and MTT [2]. Estimation of these physiological parameters is contingent on accurate identification of the shape of the residue function. In this study we adopt a parametric, Bayesian model for the residue function and explore the feasibility of simultaneously estimating mean transit time and the shape related quantities OEC and TTH.

Materials and methods *Simulation.* We first generate concentration curves using the standard tracer kinetic principle relating tracer concentration to convolution between the arterial input function (AIF) and residue function. We use a gamma density function to characterize the distribution of trans-capillary transit times, which has previously been used to represent a range of microvascular flow patterns [3]:

$$C(t) = \mathrm{CBF}\int_0^t C_A(t-\tau)R(t|\alpha,\beta)d\tau, \qquad -\frac{dR}{dt} = \frac{1}{\beta^\alpha\Gamma\alpha}t^{\alpha-1}e^{-\beta t}$$

With this model, MTT and TTH correspond to the mean and variance in the gamma distribution, $\mathrm{MTT} = \alpha\beta$, $\mathrm{TTH} = \beta\sqrt{\alpha}$, and OEC is calculated as in [2], and these relations were used to generate concentration curves for given values of MTT and TTH. Concentration curves were generated with parameters corresponding to a digital phantom image consisting of 7 by 7 fields representing 49 unique combinations of TTH and MTT, with both parameters taking values from 2s to 20s with 3s increments, see left column in Figure 1. Each field consisted of 14 by 14 voxels, and a signal curve $S(t) \propto \exp\left[-T_E R_2\left(C(t)\right)\right]$ was generated for each of these with noise added to give an SNR of 100. We assume a linear relation between concentration and transverse relaxation rate. CBV was fixed at 4% and sampling rate was TR=1.5s, with 100 points simulated in total. The AIF was modeled using a gamma-variate function with parameters as in [4]. *Estimation.* The signal curves with added noise were converted to concentration, and to mimic standard analysis of DSC-MRI data, each frame in the time series was spatially smoothed with a 3x3 uniform filter. We then applied the Bayesian model estimation approach in [3] to estimate the parameters $(\mathrm{CBF},\alpha,\beta)$. In contrast to [3], we allow α and β to vary independently

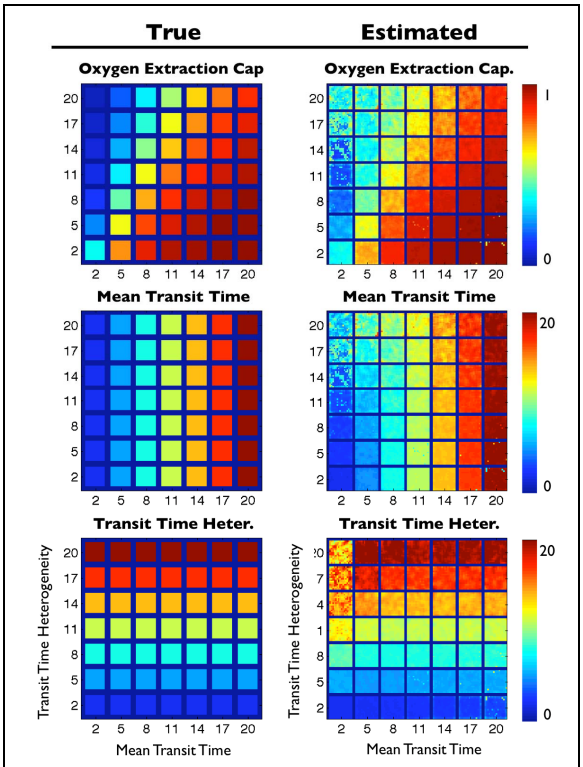

Figure 1

Results The right column in Figure 1 displays the simulation results. OEC values are well reproduced for most combinations of MTT and TTH. However some bias is observed when MTT is very short and TTH very high (top left corner of the grid). Moreover, both MTT and TTH estimates exhibit excellent overall agreement with ground-truth values, again with the possible exception of the low MTT, high TTH combination. We also observe low variation in estimated values within each field, suggesting adequate regularization was obtained using the Bayesian estimation approach.

Conclusion We have demonstrated that using a Bayesian estimation approach with a parameterized residue function, shape characteristics of the residue function can be reliably estimated, which in turn was shown to produce estimates of OEC in close agreement with simulated values. We also attempted to estimate TTH and OEC using SVD [4], but were unable to obtain similar agreement with simulated values (results not shown), suggesting that estimation of microvascular flow patterns requires dedicated modeling of the residue function. **References** [1] Østergaard, JCBFM 1999. [2] Jespersen, ISMRM 2008. [3] Mouridsen, Neuroimage 2006. [4] Østergaard, MRM 1996.