Defining adequate complexity of compartment models in DCE-MRI

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INTRODUCTION

Pharmacokinetic models are typically used for the quantitative analysis of concentration time series obtained with Dynamic Contrast Enhanced Magnetic Resonance Imaging (DCE-MRI). Often, the concentration medium uptake is not adequately described by the simple one compartment model (1Comp) proposed by Tofts and Kermode [4]. Malignant tissue is heterogeneous [1], especially at tumor margins such that more complex models are needed. We propose a method to fit a two tissue compartment model (2Comp) to the concentration time series and a model selection criterion to decide whether additional complexity is needed.

METHODS

Pharmacokinetic parameters are obtained with a Bayesian non-linear regression approach [2]. Contrast agent concentration is modeled with the standard 1Comp model $C_T(t) = K^{trans}[C_p(t) * \exp(-k_{ep}t)] + \varepsilon_T$ [4] and with a two tissue compartment model as shown in Figure 1: $C_T(t) = C_p(t) * K^{trans1} \exp(-k_{ep1}t) + C_p(t) * K^{trans2} \exp(-k_{ep2}t) + \varepsilon_T$. Here, ε_T is assumed to be a Gaussian observation error.

To decide which model is appropriate per voxel, we propose a model selection technique based on the Deviance Information Criterion (DIC) that captures both the goodness of fit to the data and the suitability of model complexity [3]. The DIC is defined as sum of the median deviance – which measures the fit to the data – and the estimated number of effective parameters p_D. Obviously, data fit increases with the degrees of freedom in more complex models: The number of effective parameters p_D estimates the model complexity.

Thus, for a given voxel we select the 2Comp model if the DIC is smaller for 2Comp model than for the 1Comp model. In addition, we reject the the 2Comp model, if the p_D for the 2Comp model is less than the typical values of p_D for the 1Comp model (1.5). The quantities needed for model selection can easily be calculated, once the posterior distribution is obtained via Markov Chain Monte Carlo simulations [3].

Data consist of 12 DCE-MRI scans from a breast cancer study. The scans were acquired with a 1.5T Siemens MAGNETOM Symphony scanner, TR=11 ms and TE=4.7 ms. Each scan consists of three slices. Regions of interests cover the tumor and adjacent healthy tissue. A dose of D=0.1 mmol/kg Gd-DTPA was injected at the start of the fifth acquisition using a power injector.

RESULTS

We fit the standard 1Comp model and the proposed 2Comp to each voxel in each of the 12 DCE-MRI scans. For about 40% - 60% of the voxels the 2Comp model is selected. Within the tumor, the 2Comp model is rarely chosen as the p_D values of the 2Comp model is small. For voxels at tumor margins however, the 2Comp model typically outperforms the 1Comp model.

Figure 2 shows the difference in p_D between both models for the middle slice of one scan. At voxels for which the 2Comp model is more appropriate, the number of effective parameters in the 2Comp model is distinctly higher than in the 1Comp model. The improvement in fit when allowing for a second compartment can be seen in Figure 3, which shows the difference in the estimated variance σ^2 of the estimation error for both models. A typical concentration time curve (CTC) for a tumor edge voxel is shown in Figure 4. The fast uptake and slow washout is captured well by the 2Comp model, the 1Comp model, however, cannot adequately describe the observed uptake dynamics.

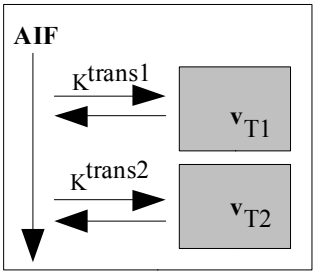

Figure 1: Schematic 2Comp model

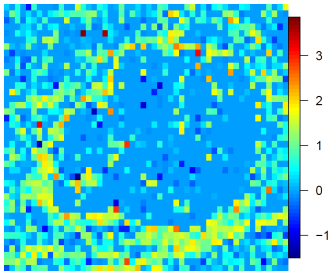

Figure 2: Parameter map p_D(2Comp) - p_D(1Comp)

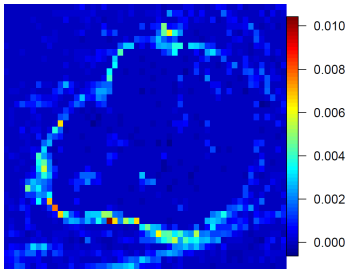

Figure 3: Parameter map σ^2(1Comp) - σ^2(2Comp)

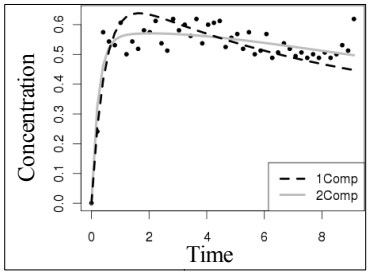

Figure 4: CTC in a tumor edge voxel and fit for 1Comp and 2Comp model

CONCLUSIONS

The Bayesian approach provides a model selection criterion that accounts for the adequacy of model fit as well as for the adequacy of model complexity. The proposed 2Comp allows for heterogeneity within voxels and outperforms the 1Comp model in describing the contrast medium uptake dynamics at tumor margins.

REFERENCES

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