Impact of the Model Impulse Residue Function on Quantitative Separation of Perfusion and Permeability

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Introduction:

There is a considerable interest in the quantitative determination of tissue parameters in dynamic contrast enhanced MR imaging (DCE-MRI). Tracer kinetic modeling is used to derive physiological parameters, such as plasma perfusion F_p, permeability-surface area product PS, plasma volume v_p and the interstitial volume v_e, from the measured tissue contrast agent washout curve. The adiabatic approximated solution of the Johnson and Wilson (aaJW) model, introduced by Lawrence and Lee [1], is commonly used to separate perfusion and the permeability-surface area product. In general, the different models are characterized by their impulse residue function ($R(t)$). The aaJW model uses a box shape in $R(t)$ to model the vascular influence on the concentration-time curve of the tissue. A more realistic and physiological description of the residue function was developed by Griebel [2]. This tracer kinetic model is an approach based on the indicator dilution theory [3]. It was originally designed for the application on intravascular tracers but it can easily be generalized for the application on permeable, extra cellular tracers. In current work, we have compared the physiological parameters provided by these different models using in vivo MR data and numerical simulations.

Methods:

For analyzing the concentration-time data the following convolution (⊗) equation was used:

$$c_t(t) = F_p\, c_a(t) \otimes R(t) \qquad (1)$$

where $c_t(t)$ represents the concentration-time curve in the tumor tissue and $c_a(t)$ the arterial input function (AIF). F_p denotes the tissue perfusion and $R(t)$ the residue function. The impulse residue function $R(t)$ of the aaJW model and the model described by Griebel are given by expression (2) and (3).

$$R(t) = \begin{cases} 1 & 0 \le t \le T_c \\ Ee^{-F_p / v_e (t - T_c)} & t \ge T_c \end{cases} \qquad (2)$$

$$R(t) = e^{-k_{iv}t} - \frac{\left(e^{-k_{iv}t} - e^{-k_{in}t}\right) k_{iv} E}{k_{iv} - k_{in}} \quad \text{where } k_{iv} = \frac{1}{T_c} \text{ and } k_{in} = \frac{F_p E}{v_e} \qquad (3)$$

where T_c denotes the capillary mean transit time ($=v_p/F_p$). The extraction ratio E can be calculated by E=1-exp(-PS/F_p). For simulations, measured and subsequently fitted DCE-MRI data were used for AIF modeling (figure 1) and a set of representative physiological parameters for the tissue residue function. Reference parameters were chosen from a breast tumor and were defined as 0.57 ml/g/min, 0.33 ml/g/min, 0.06 ml/g and 0.45 ml/g for F_p, PS, v_p and v_e, respectively [4]. These parameters, except v_e, were then varied to calculate different concentration-time curves in the tissue. For both models the concentration-time responses of the tissue were calculated using equation (1). The relative error provided by the different methods was calculated for various parameters. In addition dynamic MR data were analyzed with both models to separate F_p and PS.

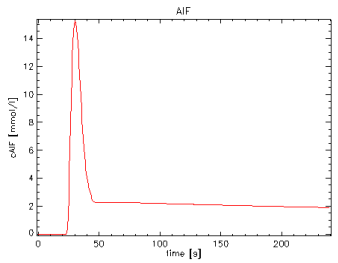

Fig. 1: Fitted AIF used for simulation from a double dose bolus with an injection rate of 5 ml/s and a 20 ml NaCl flash.

Results:

Figure 1 shows the used AIF for the simulations. In figure 2 the differences between the two models are shown. The most significant difference between the models was evident during the phase of contrast agent uptake of the tissue. Depending on the specific tissue parameters, simulations showed a relative error of up to 30%. Additionally, an essential impact on the slope and the early curvature of the curves for different tissue parameters was observed. A significant difference between the two compared models was also found for physiological parameter estimation from measured dynamic MR data (figure 3). The relative difference for estimates of F_p and PS were up to 44% (mean 18%) and 23% (mean 7%), respectively.

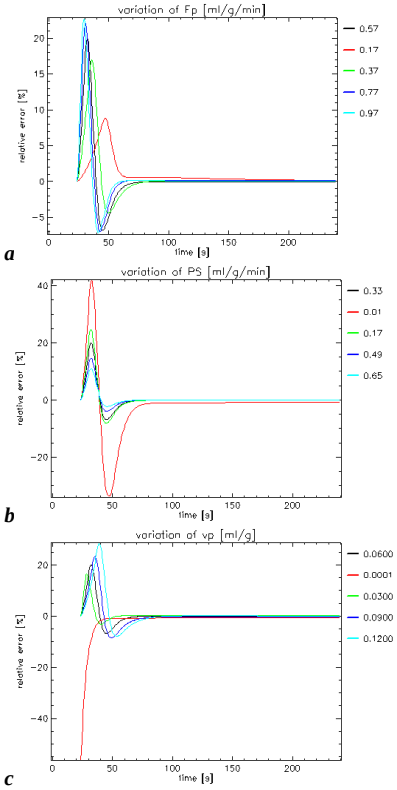

*Fig. 2: Influence of physiological parameters on concentration-time curves by using different tracer kinetic models. The black curve represents the baseline error of the compared models (values see text). The additional influence of parameter changes in **(a)** plasma perfusion, **(b)** permeability-surface area product, and **(c)** plasma volume are shown in the relative deviation.*

Discussion:

For quantitative analyses of DCE-MRI data it is necessary to use a realistic physiological model. Our simulations showed a significant difference in the concentration-time curves between the generally used aaJW model and the model developed by Zierler and extended by Griebel. There is a considerable overlap of the single physiological parameters in the concentration-time curves which complicates parameter estimation. Consequently, an immediate influence on quantitative separation of perfusion and therefore permeability-surface area product is given. Theoretical considerations that the aaJW model underestimates perfusion (and therefore a overestimation of PS) compared to the model introduced by Griebel could be confirmed with parameter estimations on DCE-MRI data. It should be considered, that fitting of small concentration changes in noisy DCE-MRI data causes a bias in parameter estimation. Furthermore the choice of the aaJW model for data analyses requires a sampling interval less than the capillary mean transit time of the tracer.

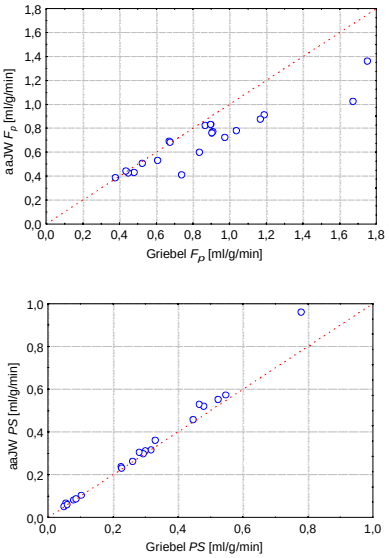

Fig. 3: Comparison of estimated parameter. The red line indicates equal parameter value.

References:

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Acknowledgments:

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