Evaluation of a model-free approach to contrast-enhanced MRI in lung tumors

F. Risse[1], T. A. Kuder[2], C. Hintze[2], C. Fink[3], H-U. Kauczor[2], and W. Semmler[1]

[1]Medical Physics in Radiology, Deutsches Krebsforschungszentrum, Heidelberg, Germany, [2]Radiology, Deutsches Krebsforschungszentrum, Heidelberg, Germany, [3]Clinical Radiology, Medical Faculty Mannheim - University of Heidelberg, Mannheim, Germany

Introduction

The use of DCE-MRI has been proven to characterize the microvasculature of tumors[1]. The signal after administration of a low molecular weight contrast agent (CA) is either analyzed directly or quantitatively using pharmacokinetic (PK) models [1,2]. Differentiation of lung nodules obtained by MRI was reported recently [3,4]. The aim of this work is to present a simple approach to analyze contrast-enhanced MR perfusion images for a clinical setting that enables comparisons between follow-up examinations of patients without using a PK model.

Material and Methods

To evaluate the tumor kinetics in a bolus injection protocol in patients with lung tumors, the following kinetic parameters are calculated from the normalized tumor signal curves: the initial maximum $S_{max,tI}$, the maximum of the curve S_{max}, the bolus onset time T_0 with respect to the AIF onset time, the time to the initial maximum T_I, the initial slope $(dS_{tumor}(t)/dt)|_{max}$, and a time constant describing the behavior of the curve for $t > t_I$ τ (figure 1). T_0 is determined to obtain a parameter independent of the individual CA injection timing. Two major types of enhancement curves were found in lung tumors relevant for the analysis (figure2). To characterize both behaviors, the curves are subdivided into two phases: the first phase is the early enhancement due to the first pass of the contrast agent ($t \leq T_I$), the second the time $t > T_I$. To assess the perfusion of the tumor, $(dS_{tumor}(t)/dt)|_{max}$ of the initial signal increase is determined using linear regression [5]. Considering the tumor as one compartment during the first pass of a narrow CA bolus, and assuming no venous outflow, the perfusion of a voxel F may be calculated as [6]: $F=[(dS_{tumor}(t)/dt)|_{max}]/AIF(t_{max})$. The calculation of τ is used to characterize the shape of the curve's tail. The signal is fitted simply using an exponential model for $t > t_I$ to characterize the curve's tail. Curves with a distinct maximum and decreasing signal for $t > t_I$ are fitted by $y=\alpha[\exp(t/\tau)]+\beta$, otherwise by $y=\alpha[1-\exp(t/\tau)]+\beta$. The two curve types are easily identified by the algebraic sign of τ.

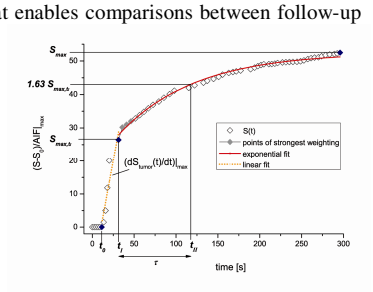

Figure 1. *Curve parameters.*

To evaluate the data analysis with known conditions, simulations using a PK model published by Brix et al.[7,8] were performed. The advantage of this model is the assessment of the hemodynamic parameters regional blood flow (RBF) and volume (RBV) as well as the capillary transfer coefficient K_{PS}. The two compartments are described by the following equations:

$$V_p \frac{dC_p(t)}{dt} = F(C_a - C_p) - K_{PS}(C_p - C_i) \qquad V_i \frac{dC_i(t)}{dt} = K_{PS}(C_p - C_i)$$

where V_p is the blood plasma volume, C_p the CA concentration within the plasma compartment, V_i the volume of the interstitial space, C_i the CA concentration in the interstitial space. F is the capillary plasma flow and C_a the arterial input. The exchange between the compartments is described by K_{PS}. The tissue concentration C(t) related to the MR signal is given by $C(t) = f_pC_p(t) + f_iC_i(t)$ with $f_p = V_p/V$ and $f_i = V_i/V$ [7,8]. The simulations were performed using nine real input functions from patients with lung tumors. Since the hemodynamic parameters and the permeability might vary widely in tumors two parameter sets derived from the article of Brix et al. [8] were used for the simulations. The tumor curves were modeled using the PK model with the input parameters F/V_p, K_{PS}/V_p, f_p and f_i. RBF and RBV are related to these parameters by $RBV = f_p/(1-h)\rho$ and $RBF = RBV \cdot F/V_p$, where the hematocrit of small vessels was set to h = 0.25 and the tissue density to $\rho = 1.04$ g/cm³ [7].

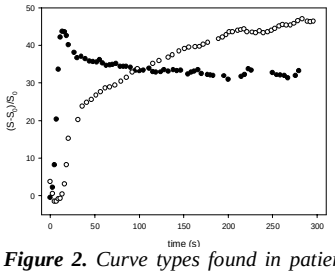

Figure 2. *Curve types found in patients with lung tumors. Type A with distinct maximum and following wash-out phase. Type B with continuous wash-in.*

Results

The simulation with the first parameter set revealed good linear correlation between the initial slope and RBF ($R^2 = 0.96$, $P < 0.0001$) (figure 3) and moderate correlation between S_{max} and RBV ($R^2 = 0.71$, $P < 0.0001$) but with a high standard deviation of S_{max}. In contrast, the other curve parameters showed only low or no correlation to the PK parameters. The second parameter set revealed a correlation of $R^2 = 0.98$ ($P < 0.0001$) between the initial slope and RBF (figure 4). Furthermore, good correlation was found between $S_{max,TI}$ and RBV ($R^2 = 0.99$, $P < 0.0001$) (figure 5), S_{max} and RBV ($R^2 = 0.95$, $P < 0.0001$). The latter curve parameters depended not only on RBF and RBV but also on tK_{PS}/V_p, f_p and f_i.

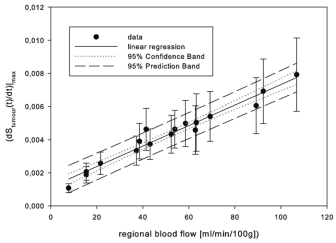

Figure 3. *Initial slope compared to simulated perfusion (RBF=8–107 ml/min/100g; RBV = 13–22 ml/100g).*

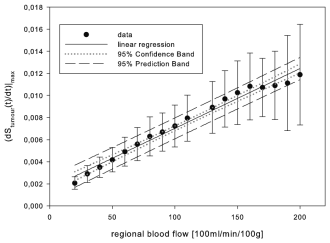

Figure 4. *Initial slope compared to simulated perfusion (RBF=20–200 ml/min/100g; RBV=10–32 ml/100g).*

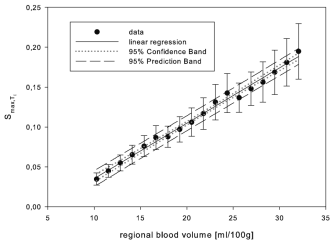

Figure 5. *Initial maximum calculated using model-free approach compared to RBV (parameter as in figure 4).*

Discussion

The initial slope had good linear correlation with RBF for most parameter combinations. The range of flow in the simulations covers the range of RBF in CT lung tumor measurements by Kiessling et al [9]. Furthermore, S_{max} and $S_{max,TI}$ showed good linear correlation with RBV. These parameters should thus be useful in the interpretation of hemodynamic changes since the initial slopes and the maxima are directly related to perfusion parameters. However, no time parameter (T_0, T_I, τ) revealed a linear correlation to parameters of the PK model. Non-linear relationships between two values do not seem to be very helpful when a simple investigation of the curve parameters is to be performed, particularly if parameter maps are used for the evaluation of tumors. A defined link between the model-free parameters of the presented approach, particularly τ, to the underlying patho-physiology of the late phase of the tumor contrast enhancement is missing.

In conclusion, the examination of the hemodynamic conditions and their heterogeneity within tumors is feasible with the model-free approach. The implementation is simple and the initial slope and the maxima are related to tumor flow and volume and thus easy to interpret. The normalization with an AIF should enable an intra-individual comparison of these parameters under therapy. However, the permeability cannot be determined directly with the model-free approach and PK models might still be necessary to obtain additional information about the permeability.

References

[1] Padhani AR. Br J Radiol 2003;76 Spec No 1:S60-80.
[2] Tofts PS et al. J Magn Reson Imaging 1999;10(3):223-232.
[3] Ohno Y et al. Radiology 2002;224(2):503-511.
[4] Schaefer JF et al. Radiology 2004;232(2):544-553.
[5] Miles KA. Br J Radiol 1991;64(761):409-412.
[6] Blomley M and Dawson P. In: Miles KA, Dawson P, Blomley M, editors. Functional computed tomography. Oxford: ISIS Medical Media; 1997. p 47-60.
[7] Brix G et al. Radiology 1999;210(1):269-276.
[8] Brix G et al. Magn Reson Med 2004;52(2):420-429.
[9] Kiessling F et al. Eur Radiol 2004;14(7):1226-1233.