Statistical Comparison of Tofts-model Parameters with Descriptive and Approximated Descriptive Parameters

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Introduction: Dedicated tracer kinetics model for dynamic contrast-enhanced (DCE)-MRI data are gaining importance since they allow extracting vascular tissue properties. A number of different models have been proposed [1,2,3]. Most of these require extensive time for calculating parameter maps, especially with the increase of spatial and temporal resolution available today. These processing times are generally too long for the clinical routine, in particular for diagnosis directly performed after the examination. Descriptive parameters are faster and less vulnerable to optimization errors. Their drawback is the lack of linkage to physiological parameters and the higher sensitivity to noise. In this work, we correlated a number of simple descriptive parameters to the parameters of the Tofts-model [1] to identify candidates to bypass time consuming calculations. Since the use of pharmacokinetic models generally results in a smoothing effect on the concentration time curve, this was simulated using descriptive parameters derived from gamma variate and bi-exponential functions approximated to the enhancement curves (see Figure 1).

Methods and Materials: Imaging was performed using a Fast Low Angle Shot (FLASH) sequence at field strength of 1.5 T with Gd-DTPA administration. Volume datasets over a period of 4.5 minutes for prostates were acquired. The GD-DTPA is injected continuously over a period of 30 s with a temporal resolution of 11.25 s. 18 prostate data-sets were examined in which the prostate was selected as investigation area by manual delineation (see Figure 1). A fixed arterial input bi-exponential function with the parameters by [1] was assumed. The comparison was performed for the Tofts permeability k^{trans}, the interstitial volume fraction v_1 and exchange rate $k_{ep} = k^{trans}/v_1$ with a selection of descriptive parameters: peak enhancement (pE), Wash-In, Wash-Out, area-under-the-curve (AUC), time-to-peak (TTP) and maximum-intensity-to-time-ratio (MITR). Wash-in and Wash-out are defined as the difference quotient for the time points T_1 and T_2 and for the time points T_3 and T_4, respectively (see Figure 2). Here, the fixed time points T_1= 1.08 min, T_2= T_3 = 2.16 min, T_4= 3.32 min were chosen manually. The integration for AUC was performed from T_1 to T_4. Wash-In and Wash-Out are the parameters used in the three-time-point method [3]. The remaining parameters are usually used in the analysis of DSC-MRI [4] or cardiac MR [5] and were included in this comparison since they give a general description of the curve. The correlations between all these parameters have been determined for each dataset and the results were compiled with a mean statistic.

Results: Table 1 shows the results for this comparison. The conventional descriptive parameters show a high correlation for MITR and k^{trans} and for pE and v_1. Moderate correlations with k^{trans} can be found for AUC and MTT. The parameter v_1 shows moderate correlations with AUC and Wash-In. The correlations of k^{trans} with the smoothed parameters are largest for MITR where only the bi-exponentially approximated MITR is increased compared to the conventional MITR. The v_1 is highly correlated with pE and moderately with AUC and Wash-In. Both approximation methods increased the correlations. There was a slightly better performance for the bi-exponential method than for the gamma variate based one although this was not significant. The k_{ep} shows only moderate correlations with TTP, MTT and Wash-Out for the approximated parameters. The conventional descriptive parameters only achieve this for MTT.

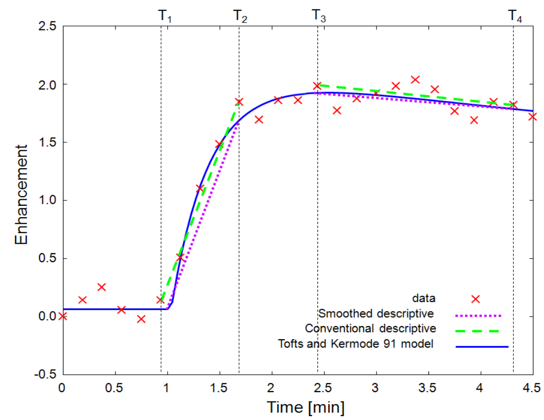

Figure 1: Sketch of descriptive parameters, Tofts-model and smoothed descriptive parameters. Red crosses: original enhancement. Blue line: Tofts-model fit. Green dashed lines: conventional Wash-In and Wash-Out. Purple dotted lines: smoothed Wash-In and Wash-Out. Note that the Tofts-model was replaced by gamma variate and biexponential functions to obtain the smoothed parameters.

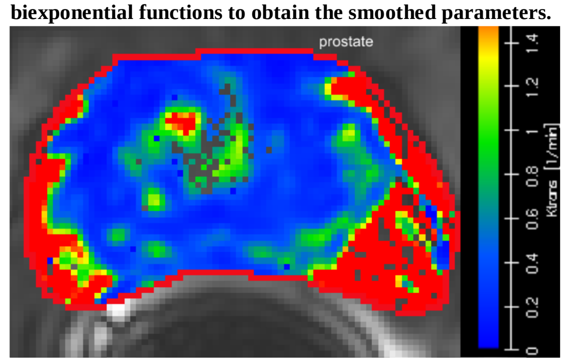

Figure 2: Example for the selected investigation area (red bordering voxel). Shown is the parameter map for the Tofts permeability k^{trans} as colour overlay over the original data.

Discussion: The high correlations found for k^{trans} with MITR and v_1 with pE, AUC and Wash-In indicates that these parameters are closely linked to the model derived parameters and are clear signs of increases k^{trans} or v_1, respectively. The approximation with gamma variate or bi-exponential function can increase the correlation for these parameters, especially for the parameters related to v_1. The approximation of data can benefit thus for both comparisons but it is to be discussed, if the computational requirements for the optimization is worth this effort. Surprisingly, the parameters proposed by the 3TP method did not show high correlations. This probably results from the non-linearity of the dependency. Future work on this topic will have to investigate this influence. Moreover, it will be worthy to carry out a comparison only for malignant tissue since the exchange rates are higher and probably influenced stronger by the nonlinearity of the relations. Another important topic is the stability of approximation lower temporal resolved data (e.g., DCE-MRI data used for breast MRI) with only a limited number of time-points.

Table 1: Correlations calculated for the comparison of descriptive and Tofts model parameter. High correlations (r>0.8) have been marked in green and moderate (r>0.7) correlations are emphasized with yellow.

	Average and standard deviation of correlation coefficient								
	k^{trans}			v_1			$k_{ep}= k_{trans}/v_1$		
Approx.	none	Gamma	Biexp	none	Gamma	Biexp	none	Gamma	Biexp
pE	0.65 ± 0.11	0.58 ± 0.09	0.61 ± 0.09	0.81 ± 0.10	0.92 ± 0.03	0.93 ± 0.03	0.34 ± 0.18	0.21 ± 0.14	0.21 ± 0.14
AUC	0.75 ± 0.11	0.66 ± 0.08	0.65 ± 0.09	0.73 ± 0.13	0.87 ± 0.05	0.90 ± 0.04	0.47 ± 0.20	0.31 ± 0.16	0.27 ± 0.16
Wash-In	0.66 ± 0.22	0.69 ± 0.22	0.66 ± 0.24	0.71 ± 0.12	0.80 ± 0.07	0.85 ± 0.05	0.40 ± 0.26	0.39 ± 0.26	0.32 ± 0.26
Wash-Out	-0.56 ± 0.15	-0.68 ± 0.15	-0.65 ± 0.19	0.09 ± 0.19	0.17 ± 0.19	0.09 ± 0.19	-0.62 ± 0.15	-0.76 ± 0.14	-0.76 ± 0.15
TTP	-0.62 ± 0.11	-0.71 ± 0.08	-0.68 ± 0.07	0.00 ± 0.13	-0.06 ± 0.15	-0.07 ± 0.13	-0.67 ± 0.10	-0.77 ± 0.10	-0.76 ± 0.09
MTT	-0.71 ± 0.10	-0.58 ± 0.16	-0.66 ± 0.08	-0.05 ± 0.16	-0.02 ± 0.14	-0.10 ± 0.17	-0.75 ± 0.11	-0.64 ± 0.18	-0.73 ± 0.09
MITR	0.85 ± 0.06	0.82 ± 0.05	0.86 ± 0.04	0.63 ± 0.12	0.77 ± 0.07	0.73 ± 0.09	0.61 ± 0.15	0.52 ± 0.15	0.58 ± 0.16

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