Analyzing Error Propagation in Semi-quantitative DCE MRI Parameters in Brain Tumors: a Comparison Study to Monte Carlo Simulation Predictions

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INTRODUCTION

Calculation of semi-quantitative DCE MRI parameters in tumor studies is simple and has found widespread clinical application. Semi-quantitative parameters are calculated by performing mathematical operations on measured signal intensities; consequently error can propagate into parameters due to MRI noise. We have performed parametric uncertainty analysis for the error propagation in commonly used semi-quantitative DCE-MRI parameters using Monte Carlo methods. The aim of this study is to test the predictions of these Monte-Carlo simulations with *in vivo* data acquired in patients with brain tumors.

MATERIALS AND METHODS

The key point for in vivo error analysis is definition of 'true' values. We proposed use of theoretical signal enhancement curves, SI(*t*), fitted to a 2 compartment kinetic model to generate 'true' values. However, fitting errors depend on both random noise and modeling error. We have therefore used the autocorrelation function to distinguish the contributions of these two error sources [1].

Five patients with type 2 neurofibromatosis (NF2) were examined on 3 occasions: baseline, 2 days, and 3 months post treatment with bevacizumab. The study was approved by local research ethics committee. High temporal resolution (Δt = 1s) and high spatial resolution (1 x 1 x 2 mm) DCE-MRI data series were collected sequentially using a dual injection technique. For each subject the three data sets (baseline, 2 days, and 3 months post treatment) were spatially aligned to enable direct longitudinal voxel-by-voxel comparison of derived maps (Fig. 1). Seven vestibular schwannoma and five meningiomas were automatically segmented for each visit using high-spatial resolution 3D Bayesian probability maps.

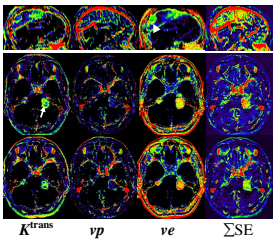

Fig. 1 Typical high spatial resolution 3D maps in a patient with VS(arrow) and meningiomas (arrow head) before and 3 month after bevacizumab treatment

3D high-spatial resolution parametric maps of the transfer constant (K^{trans}), the fractional plasma volume (v_p), and the fractional volume of the extravascular extracellular space (v_e) were calculated using a modified Tofts model. SI(*t*) curves representing each voxel with $0.03 < K^{trans} < 0.09$ min^{-1}, $0.55 < v_e < 0.90$, $0.001 < v_p < 0.07$, resembling the simulated persistent enhancement type curve from the previous Monte Carlo simulation (K^{trans} = 0.08 min^{-1}, v_e =0.6, v_p = 0.05), and voxel curves with $0.3 < K^{trans} < 1.0$ min^{-1}, $0.20 < v_e < 0.45$, $v_p < 0.15$, resembling the simulated washout type curve (K^{trans} = 0.62 min^{-1}, v_e =0.27, v_p = 0.02), were selected. Voxels with considerable modeling errors were excluded. Five semi-quantitative parameters were calculated from the theoretical and experimental SI(t) curves to produce the 'true' and the 'measured' values for calculation of percent deviation (PD) distribution. The five parameters are: SE_{1min} (= $S_{1min,post}$ − SI_{pre}), $SE_{rel,1min}$ (= SE_{1min}/ SI_{pre}), $\sum SE$, $\sum SE_{rel}$ and $R_{se1/se2}$ (=SE_{1min}/ SE_{5min}).

In Monte Carlo simulation, 1,000,000 iterations were used to calculate the PD distribution. However, the number of in vivo samples was only 10000 for persistent type curves, and 500 for washout type curves. We therefore divided the 1000000 Monte Carlo simulated persistent type curves into 100 groups (each has 10000 samples), and the 1000000 simulated washout type curves into 2000 groups (each has 500 samples). PD distributions were calculated for each of the subgroups. A range of values for each of the descriptive statistics of the PD distribution were produced and used for comparison with the in vivo data.

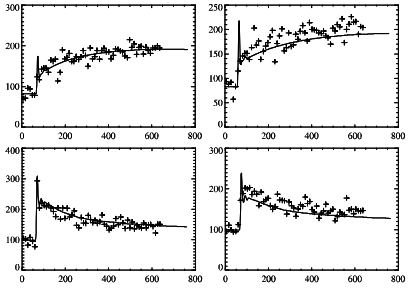

Fig. 2 Left column: curves with 'good fitting'; Right column: curves with considerable modeling error.

RESULTS

Fig.2 shows example curves to be used in the PD distribution analysis (left column); and those to be excluded from the analysis (right column), based on temporal autocorrelation analysis.

Fig. 3 compares PD distribution obtained from Monte Carlo simulation (1000000 iterations) and in vivo data. Both simulation and in vivo data showed that: (1) The sum of SE (or SE_{rel}) can have greater precision than non-summed metrics for persistent type curves, but not for washout curves; (2) The "normalized" parameters show poorer precision than the non-normalized metrics depending on the noise level of the pre-contrast baseline; (3) $R_{se1/se2}$ is much more accurate and robust for the persistent type than for the washout type of SI-time curves; (4) $R_{se1/se2}$, showed very wide spread of the extreme values of its PD distribution, which means that outliers must be treated for pixel-by-pixel mapping of this parameter.

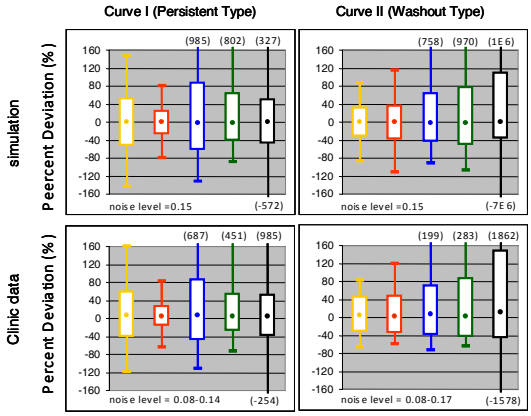

Fig. 3 The Box-and-whisker plots showing the locations of the median, the majority (5% - 95%), and the spread (extreme values) of the PD distributions for SE_{1min} (yellow), ∑SE (red), $SE_{rel,1min}$(blue), $\sum SE_{rel}$ (green) and $R_{se1/se2}$ (black).

Table1: the descriptive statistics of PD distribution in semi-quantitative parameters

PD distribution		min	5%per	median	95%per	max	skew	kurto
SE	Simu	-87, -42	-39, -25	-4, 3	25, 37	39, 88	0, 0	-1, 1
	In vivo	-67	-32	5	46	82	0	0
∑SE	Simu	-113, -51	-47, -30	-5, 4	29, 45	46, 115	0, 0	-1, 1
	In vivo	-59	-35	2	47	118	0	1
SE_{rel}	Simu	-92, -53	-50, -35	-7, 4	49, 86	90, 758	0, 8	0, 118
	In vivo	-72	-38	7	71	199	1	2
$\sum SE_{rel}$	Simu	-108, -64	-60, -42	-9, 5	59, 102	111, 970	0, 9	0, 144
	In vivo	-65	-43	3	86	283	1	4
$R_{se1/se2}$	Simu	-7E6, -44	-42, -31	-6, 5	70, 186	210, 1E6	-22, 22	5, 493
	in vivo	-1577	-45	11	148	1862	1	70

Table 1 lists the values of the descriptive statistics of PD distribution from Monte Carlo simulations and the in vivo data, for washout type curves. It can be seen that the in vivo values generally lie within the range (minimum and maximum) given by the 2000 Monte Carlo simulated PD distribution. Similarly, for persistent type SI curves, the in vivo statistics values were seen to lie within the range (minimum and maximum) given by the 100 Monte Carlo simulated PD distribution.

DISCUSSION Monte Carlo simulation methods have been used to improve understanding of the expected accuracy and precision of semi-quantitative parameters derived from DCE-MRI under different pharmacokinetic and signal-to-noise condition. However, simulation data shows the effect of noise on identical data sets, whilst patient data shows spatial heterogeneity of data in addition to noise effects. In this study, we selected a huge number of SI(t) curves (N = 12,000) with homogeneous kinetic properties from high spatial resolution DCE-MRI with 12 tumors x 3 visits in 5 patients. Autocorrelation of the residues in the process of fitting the in-vivo data to the chosen model was examined to further exclude those voxel whereas extra correlation was found, indicating systematic errors. The direct comparison of in-vivo analysis with Monte Carlo simulation supports the findings of previous Monte Carlo studies on synthetic data. **Reference:** Balvay et al, MRM 2005;54:868-877.