Monte Carlo Simulation to Study the Robustness of Empirical DCE-MRI Kinetic Parameters to Gaussian Noise

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INTRODUCTION

T1-weighted DCE-MRI data can be assessed using two distinct approaches: 1) by quantifying contrast agent concentration changes using pharmacokinetic modeling techniques or 2) by the analysis of signal intensity (SI) changes using a number of empirical (semiquantitative) descriptors. The latter is simpler to perform and has proven popular, particularly in clinical applications. While investigators have extensively examined the reliability of pharmacokinetic parameters obtained from kinetic modeling and made considerable efforts to improve it, the effects of MRI noise on the reliability of empirical kinetic parameters have not been systematically investigated. In practice it is likely that significant errors may occur during the estimation of these semiquantitative parameters, particularly when they are estimated on a pixel-by-pixel basis to produce parametric distribution maps. The purpose of this study is to investigate the robustness of several empirical DCE-MRI kinetic parameters to Gaussian noise using Monte Carlo simulation.

MATERIALS AND METHODS

Simulation of Vascular Input Function and Tissue Uptake Curves

Vascular input function (VIF) was simulated using a function form described by Horsfield et al[1]. Theoretical tissue uptake curves ($C(t)$) were generated using the simulated vascular input function and the generalized kinetic model[2]. Three sets of parameters were used for the simulations: (i) $K^{trans} = 0.05$ min^{-1}, $v_e = 0.4$, $v_p = 0.018$, representing weak contrast enhancement; (ii) $K^{trans} = 0.2$ min^{-1}, $v_e = 0.6$, $v_p = 0.018$, representing persistent enhancement; (iii) $K^{trans} = 0.8$ min^{-1}, $v_e = 0.3$, $v_p = 0.018$, representing washout following initial enhancement; where K^{trans} is the transfer constant, v_e is the fractional volume of extravascular extracellular space, and v_p is the fractional plasma volume. The simulated concentration-time curves were then converted to signal intensity vs. time curves by assuming $SI_{pre} = 400$, $T_{10} = 1$ s, TR = 8 ms, and $\alpha = 30°$, where SI_{pre} and T_{10} are pre-contrast SI and native longitudinal relaxation time of tissue, respectively.

Choosing empirical kinetic parameters for error analysis

We divided the candidate empirical kinetic parameters into five categories based on the results of error propagation: (i) signal intensity subtraction, e.g., $SE_{1min} = SI_{1min,post} - SI_{pre}$; (ii) relative signal enhancement, e.g., $SE_{rel,\,1min} = (SI_{1min\,post} - SI_{pre})/\,SI_{pre}$; (iii) signal enhancement ratio, e.g., $R = (SI_{1min\,post} - SI_{pre})/\,(SI_{7min\,post} - SI_{pre})$; (iv) sum of SE over all the post-injection time points, $\Sigma(SE)$, which is similar to the area under the curve (AUC); (v) sum of SE_{rel} over all the post-injection time points, $\Sigma(SE_{rel})$, which is similar to AUC_{rel}[3]. The five empirical parameters, SE_{1min}, $SE_{rel,1min}$, R, $\Sigma(SE)$, and $\Sigma(SE_{rel})$ were calculated for each of the simulated SI vs. time curves without noise added (zero noise), to produce the 'true' values for each of the five parameters.

Monte Carlo simulation for error analysis

Zero-mean Gaussian noise with five different noise levels (5%, 10%, 15%, 17%, and 20%) were added to the simulations to generate synthetic data sets, with which the above five empirical parameters were calculated to produce the so-called 'measured' values. Any negative 'measured' values were set to zero. Percent deviations of the 'measured' values from the 'true' values were calculated by: deviation (%) = (measured – true)/true * 100. For each given condition (i.e., a set of K^{trans}, v_e, v_p, and a given noise level), 100000 trials were performed. Accuracy and precision were assessed from the mean and standard deviation (SD) of the percent deviation calculated from the Monte Carlo trials.

RESULTS

Fig. 1 shows the simulated AIF curve following a bolus injection of 0.1 mM/kg. Fig. 2 shows simulated SI-time curves without noise added. A 1-minute temporal resolution was used to extract data from the simulations. Fig. 3 shows accuracy and precision of the five empirical parameters under different noise and pharmacokinetic conditions. Among the five parameters, signal enhancement images (SE) from straightforward image subtractions and $\Sigma(SE)$ are of the best accuracy. $\Sigma(SE)$ shows also improved precision compared to SE images, whereas the accuracy and precision of $\Sigma(SE_{rel})$ may only slightly improved compared with SE_{rel}. Signal enhancement ratio (R) is mostly sensitive to noise and pharmacokinetic conditions. R is much more accurate and robust for the persistent type than for the washout type.

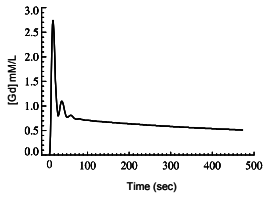
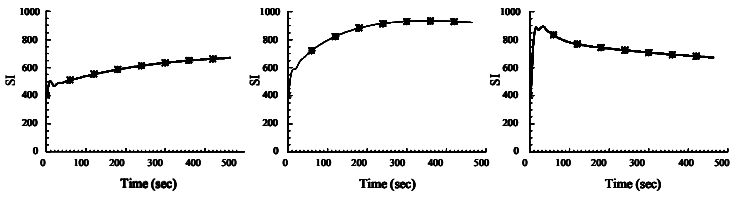


Figure 1. Simulated plasma concentration curve.



a. Weak Enhancement b. Persistent Enhancement c. Washout

Figure 2. Simulations of three types of kinetic enhancements.

DISCUSSION AND CONCLUSION

The findings from the Monte-Carlo simulation can be used to assist selection of appropriate parameters for a specific study. For example, the signal enhancement ratio (R) may not be a parameters appropriate for tumor hot-spot study supposing a noise level higher than 10%, but may be appropriate to study cancerous voxels infiltrating into breast parenchyma, which are generally of persistent type enhancement (low R values)[4]. $\Sigma(SE)$ have been shown as the most robust method for measuring images with low signal-to-noise ratio. In addition, the Monte Carlo simulation has entailed some implicit yet rarely emphasized issues, which are important for improving the robustness of the empirical kinetic parameters to noise, for example, the use of multi-baseline points to obtain a truthful mean value of SI_{pre}, wherever it is possible. In conclusion, the Monte Carlo simulation has improved our understanding of the effects of noise on the accuracy and precision of measured empirical kinetic parameters, leading to a better interpretation of these empirical parametric images.

REFERENCES: 1. Horsfield et al. Phys Med Biol 2009;54(9):2933-2949. 2. Tofts. JMRI 1997;7(1):91-101. 3. Evelhoch. JMRI 1999;10(3):254-259. 4. Li et al. Radiology 2008;248(1):79-87.

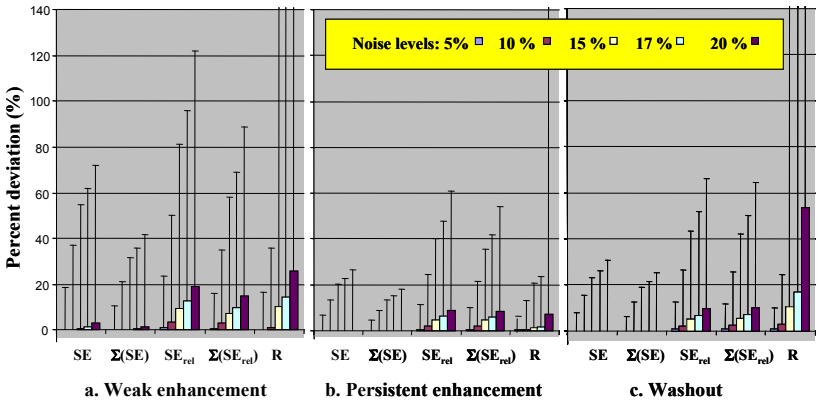


Figure 3. Percent deviations (mean±SD) calculated from 100000 Monte Carlo trials over a range of noise levels for five empirical parameters under tree different kinetic conditions.