An Efficient Method for Pharmacokinetics Parameter Calculation in Permeability Study Using Dynamic Contrast-Enhanced Magnetic Resonance Imaging

Chunhao Wang[1,2], Fang-Fang Yin[1,2], and Zheng Chang[1,2]

[1]*Radiation Oncology, Duke University Medical Center, Durham, North Carolina, United States,* [2]*Medical Physics Graduate Program, Duke University, Durham, North Carolina, United States*

Target audience: clinicians, physicists and other clinical professionals

Purpose

In dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI), high temporal resolution (Δt) is always desired for accurate quantitative pharmacokinetics (PK) analysis [(1)]. However, the current calculation methods for PK parameter estimation are computational intensive and may require long processing time, especially when the temporal resolution is high. This study developed an efficient calculation method for quantitative permeability PK parameters.

Methods

The two-compartment extended Tofts model was commonly selected to describe contrast agent (CA) concentration dynamics in the tissue-of-interest $C_t(t)$ and in blood plasma $C_p(t)$ [(2)]. In this proposed calculation method, the model equation was expressed in a derivative format with zero initial conditions. To minimize the potential noise effect in time domain on derivative calculation of $C_t(t)$ and $C_p(t)$ in the model, a low-pass filtering process using Kolmogorov-Zurbenko (KZ) kernel was adopted in considerations of its good high frequency resolution and efficient computation [(3)]. Three parameters were then solved analytically as a linear least-squares problem: rate constant K^{trans} and k_{ep}, and volume fraction of blood plasma in tissue v_p. The proposed method was tested using two simulation studies: single voxel simulation and 2D simulation based on a clinical brain study. The proposed method was also compared against the other two currently used methods: nonlinear least-squares based Levenberg-Marquerdt (LM) method, and a linear least-squares method using integrative model equation (ILLSQ) [(4)]. In the single voxel simulation, a group of intracranial PK parameters was selected to evaluate the performance of this proposed method at different temporal resolutions and noise levels. The $C_p(t)$ in the simulation was modeled as a population-averaged measurement results [(5)], and $C_t(t)$ was generated using the chosen PK parameters. Both $C_p(t)$ and $C_t(t)$ were then added with Gaussian random noise to obtain a certain level of CNR (ratio of the peak CA enhancement to the standard deviation of noise intensity). Two substudies were performed: 1) $\Delta\mathbf{t}$ = 1s with CNRs ranging from 5 to 100; and 2) a clinically realistic level of CNR = 10 with $\Delta\mathbf{t}$ ranges from 0.1s to 20s. At each condition, the simulation was performed with 5000 runs, and the calculated average value and the standard deviation of each parameter was recorded. The accuracy was evaluated by its difference to the true value for $C_t(t)$ generation. The efficiency was evaluated by the calculation time used in 5000 runs. The results of the proposed method were compared to LM and ILLSQ methods. The K^{trans} calculation of the proposed method was then furtherly evaluated against the two current methods in a 2D simulation using voxels with different K^{trans} intensities. Each voxel was simulated in the same fashion as the single voxel simulation at 1000 runs, and the accuracy was evaluated by difference map and the quantitative total relative error (TRE) [(6)].

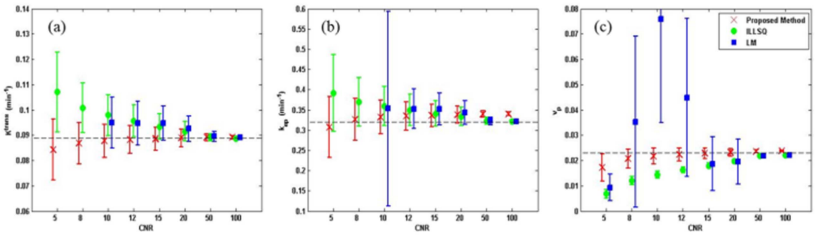

Fig 1. PK parameter calculation results with varying CNR

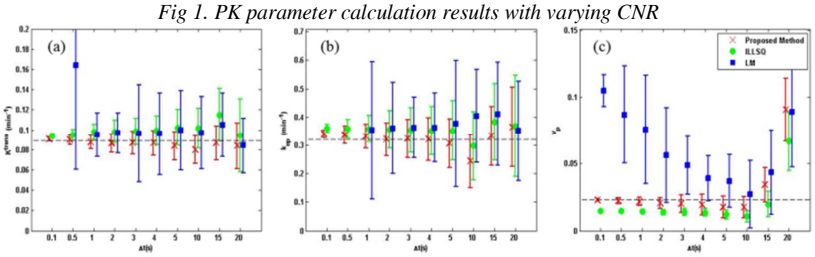

Fig 2. PK parameter calculation results with varying Δt

Results

When the noise level was high (CNR≤15) and Δt = 1s, the proposed method was able to calculate all parameters with improved or comparable accuracy (Fig 1). When the temporal resolution was high (Δt≤5s), the accuracies of the proposed method in all parameters' estimation were improved in comparison with the current methods. When Δt = 1s, the efficiency of the proposed method was improved by a factor of 7.3 compared with ILLSQ, and a factor over 300 compared with LM. Fig.3 demonstrates that the proposed method was able to estimate a group of K^{trans} values at varying intensities with improved or comparable accuracy. The TRE value was 0.002 for the proposed method, 0.007 for the ILLSQ, and 0.091 for the LM, respectively.

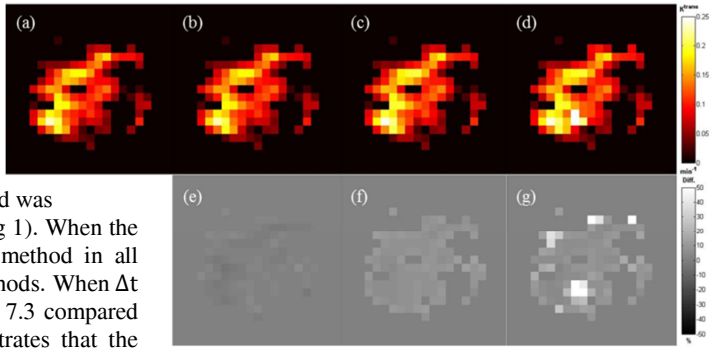

Fig 3. Distribution of true K^{trans} values in 2D simulation (a), K^{trans} calculation results of the proposed method (b), ILLSQ method (c) and LM method (d). (e)-(g) demonstrate the corresponding difference maps in percentage

Conclusion

A new efficient method was developed and demonstrated to accurately and efficiently calculate permeability parameters for quantitative permeability DCE-MRI study with high temporal resolution.

References: **1**. Henderson E, Rutt BK, et al. Magn Reson Img 1998;16(9):1057-1073; **2**. Sourbron SP, Buckley DL. Magn Reson Med 2011;66(3):735-745; **3**.Yang W, Zurbenko I. Wiley Interdisciplinary Reviews: Comp Stat 2010;2(3):340-351; **4**. Murase K. Magnet Reson Med 2004;51(4):858-862; **5**.Parker GJ, Roberts C, et al. Magn Reson Med 2006;56(5):993-1000; **6**. Chang Z, Xiang QS. Med Phys 2006;33(10):3758-3766