# COMPARISON OF THE KINETIC PARAMETERS ESTIMATED WITH DIFFERENT NUMERICAL METHODS IN DCE-MRI

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**Introduction:** Dynamic contrast enhanced MRI (DCE-MRI) has been shown its ability to noninvasively assess characterization of tumor by the kinetic parameters, such as volume transfer constant ($K^{trans}$) and rate constant ($k_{ep}$). The Tofts and Kermode (TK) model [1] and modification of Tofts and Kermode (mTK) model [2] are both popular pharmacokinetic models. Nonlinear least-squares (NLSQ) method is often used to calculate kinetic parameters in TK and mTK models. However, a disadvantage of NLSQ method is the long calculation time. To overcome this disadvantage, an alternative method, linear least-squares method, have been developed in previous study [3]. The study had demonstrated that the LLSQ method not only can reduce calculation time but also can increase accuracy of estimation of kinetic parameter in lower SNR. However, the previous study only demonstrated that LLSQ is better method than NLSQ in solving mTK model equation. In this study, we further propose to apply the LLSQ method to solve TK model and use computer simulations to compare the accuracy of the kinetic parameters.

**Methods and materials:** Computer simulations includes the following steps: 1) The plasma concentration time curve $C_P(t)$ was simulated using a standard vascular input function (VIF), which was fitted to a bi-exponential decay [1]; 2) The tissue concentration time curves $C_t(t)$ were simulated by TK model [2]. The simulations were performed for a range of $K^{trans}$ = 0.004 ~ 0.016 $min^{-1}$, $k_{ep}$ = 0.04 ~ 0.16 $min^{-1}$ according to previous reports [4]. The Gaussian noise with different standard deviations were added to generate data sets with a range of SNR=10 ~ 80. 3) The kinetic parameters were calculated using the Matlab function lsqcurvefit to calculate a NLSQ solution to following equation:

$$C_t(t) = K^{trans} D \sum_{i=1}^{2} \frac{a_i}{m_i - k_{ep}} (e^{-k_{ep}t} - e^{-m_i t})$$

where $D$, $a_i$ *and* $m_i$ are the dose of contrast agent, amplitudes and decay rates, respectively.

4) The kinetic parameters were calculated using the Matlab function lsqnonneg to calculate a LLSQ solution to following equation:

$$\begin{bmatrix} C_{t1} \\ C_{t2} \\ C_{t_n} \end{bmatrix} = \begin{bmatrix} \int_0^{t_1} C_p(u)du & -\int_0^{t_1} C_t(u)du \\ \int_0^{t_2} C_p(u)du & -\int_0^{t_2} C_t(u)du \\ \int_0^{t_n} C_p(u)du & -\int_0^{t_n} C_t(u)du \end{bmatrix} \cdot \begin{bmatrix} K^{trans} \\ k_{ep} \end{bmatrix}$$

5) The simulations were performed with a range of SNR values and kinetic parameters. For each condition, 1000 simulations were run to calculate the percent mean errors (ME) percent standard deviations (SD) of $K^{trans}$ and $k_{ep}$ values estimated by LLSQ and NLSQ methods. Furthermore, patient data were processed. Three patients with brain tumor were included in this study. DCE-MRI T1 weighted images were performed using a 3D gradient-echo sequence at 3 Tesla. Three precontrast-data sets were acquired with TR/TE/θ = 5.8 msec/2.2 msec/5°10°30° for calculating intrinsic longitudinal relaxation $R1_0$. The bolus injection of 0.1 mmol/kg Gd-DTPA was administered through the antecubital vein by the power injector. After injection of contrast agent, dynamic images were acquired with θ = 30°. The relaxation rate function $R_1(t)$ was calculated from pre- and post-contrast data [4]. The contrast concentration C(t) was calculated from MR data by using $C(t) = (R1(t)-R1_0)/r1$, where the relaxivity r1 is 4 $second^{-1}mM^{-1}$ at 3 Tesla. The VIF measured from the superior sagittal sinus was used to analyze DCE- MRI data [1]. The values of $K^{trans}$ and $k_{ep}$ were calculated using the LLSQ and NLSQ methods. Two regions of interest (ROIs) were drawn on image. First, tumor pixels were selected with $K^{trans}$ value below 0.02$min^{-1}$ by LLSQ method. Second, ROIs of normal tissues were also selected to compare the parametric values.

**Results:** Figure 1 (a)-(c) shows the effect of different SNR, $K^{trans}$ and $k_{ep}$ on the estimated values of $K^{trans}$. The MEs of the $K^{trans}$ values calculated by LLSQ (dotted line) and NLSQ (solid line). The error bars are SDs for 1000 simulations. Fig 1a shows that the accuracy (ME) and precision (SD) of values of $K^{trans}$ calculated by LLSQ are better than NLSQ as SNR = 10. As SNR > 10, the MEs and SDs of estimated $K^{trans}$ values for LLSQ and NLSQ methods are similar. Fig 1b shows that the parameters obtained with NLSQ are significantly overestimated as $K^{trans}$ < 0.012, while the measured $K^{trans}$ was nearly unchanged with $K^{trans}$ with LLSQ method. Fig 1c shows that the accuracy (ME) and precision (SD) of estimated $K^{trans}$ are better than NLSQ at different $K_{ep}$ values. The calculation speed of LLSQ method was 17 times faster than NLSQ method when using MATLAB on a PC (0.33 s and 5.77 s for each 1000 simulations). Fig 2 shows the $K^{trans}$ maps obtained with LLSQ (a) and NLSQ (b) methods in a patient with glioblastoma multiforme. It can be seen that the $K^{trans}$ of LLSQ map shows better contrast between tumor and normal brain tissues than the $K^{trans}$ map by NLSQ. On the contrary, the $K^{trans}$ map of NLSQ presented overestimated $K^{trans}$ values in normal tissue. The mean $K^{trans}$ of selected low $K^{trans}$ tumor are 0.0133 ± 0.0053 by LLSQ and0.033 ± 0.109 by NLSQ. The mean $K^{trans}$ of normal tissue are 0.0095 ± 0.0103 for LLSQ and 0.0287 ± 0.0734 for NLSQ. The measure $K^{trans}$ values by NLSQ are much higher than LLSQ in these low $K^{trans}$ regions.

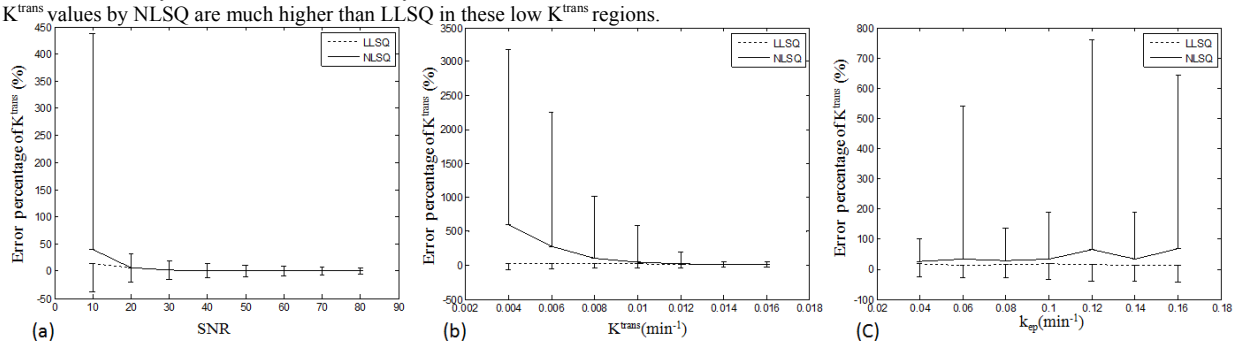


Figure 1 (a)-(c) shows that the effect of varying SNR, $K^{trans}$ and $k_{ep}$ on the estimated values of $K^{trans}$. The $K^{trans}$ values were calculated by LLSQ (dotted line) and NLSQ method (solid line). Note the high accuracy of LLSQ method.

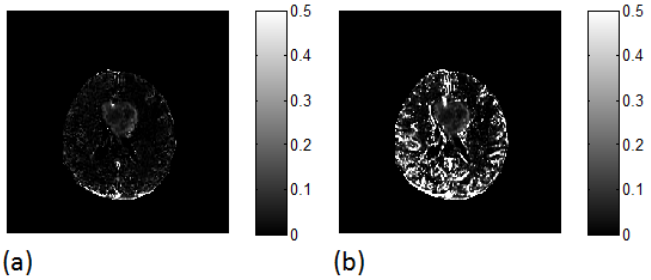


Figure 2 $K^{trans}$ maps derived with LLSQ (a) and NLSQ (b) method.

**Conclusion:** In this study, we demonstrated that LLSQ is an efficient method for solving TK model. The calculation speed of LLSQ method is much faster than NLSQ method. The MEs and SDs of the kinetic parameters are comparable for the LLSQ and NLSQ methods when SNR is high. However, at lower SNR, it is showed that LLSQ method can be immune from the influence of noise. It is also noted that LLSQ method are more accurate than NLSQ method when the $K^{trans}$ is low. In clinical application, $K^{trans}$ values should be quite low in normal tissue and some tumor regions such as necrosis. Our results showed the potential of overestimation for NLSQ method in patient data. Therefore, LLSQ method could be more preferable for assessing the kinetic parameters in these regions.

**References:**

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