What is the Minimum Time Resolution Required for DCE-MRI Kinetic Analysis with Kety Model Using Single- and Dual-Temporal-Resolution Techniques?

K-L. Li[1], G. Thompson[1], X. Zhu[1], G. Buonaccorsi[2], and A. Jackson[1]
[1]Wolfson Molecular Imaging Centre, The University of Manchester, Manchester, Lancashire, United Kingdom, [2]ISBE, The University of Manchester

INTRODUCTION

Mapping kinetic parameters with high spatial resolution is necessary when lesions are small and the changes of tumor microvaculature are heterogeneous. However, accurate analysis of the fractional plasma volume, v_p, the transfer constant, K^{trans}, and the fractional volume of extravascular extracellular space, v_e, need high temporal resolution DCE-MRI when model-based analyses are used [1,2] . Conventional DCE-MRI uses a single temporal resolution (STR) DCE-MRI. The Arterial input function (AIF) and the tissue concentration-time ($C(t)$) curves are sampled at the same rate, typically with Δt = 1 – 3.5 sec per frame. The volume size of such high spatial and high temporal resolution DCE-MRI is currently limited by the MR hardware and providing coverage of the whole lesion and feeding vessels becomes challenging. A dual-temporal resolution (DTR) DCE-MRI technique has been proposed[3], where the AIF is sampled much more frequently than the tissue $C(t)$ curves. The purpose of the study was to assess the minimum sampling rate required for the estimation of accurate K^{trans}, v_e, and v_p, of tissues, using the DTR incorporating with the extended Kety model.

MATERIALS AND METHODS

Computer simulation to assess the effects of time steps on accuracy of Kety modeling

The modified Kety model [1] involves a convolution integration of the plasma input function with an impulse response function over a time space [0, t]:

$$C(t) = v_p C_p(t) + K^{trans} \int_0^t C_p(t') \exp\left(-\frac{K^{trans}}{v_e}(t-t')\right) dt' \qquad [1]$$

With a bolus injection, the very rapid concentration changes and high peak value in the first pass of the plasma input function make it not a typically smooth well-behaved integrand. Thus time steps (dt') should be chosen accordingly to ensure accurately modeling the 'true' tissue concentration-time curve, $C(t)$. Eestimating the error from the integration with various dt' isn't obvious. We therefore generated the $C(t)$ curves with various dt', and used their difference as an estimate of the error from the convolution integration.

The minimum C(t) time resolution needed under the conditions of zero noise and zero temporal jitter uncertainty

Computer simulations were performed to show the effects of the tissue $C(t)$ time resolution on accuracy of the parameter estimates using the STR and DTR method under the conditions of zero noise and zero temporal jitter uncertainty. For the DTR method, the $C(t)$ curves were simulated using a high temporal resolution (1 s) theoretical AIF, and then sampled with an array of Δt (5, 10, 20, 40, 60, 120, and 150 s). For the STR method, the tissue $C(t)$ curves were simulated using the theoretical AIF that has various temporal resolutions (5, 10, 20, 40, and 60 seconds). A range of v_p values (0.02, 0.05, 0.10, and 0.15), a K^{trans} of 0.2 min^{-1}, and a v_e of 0.35 were used in the simulations. Parameter estimates obtained from fitting Kety model (Eq. [1]) to the simulated concentration-time curves were compared with the parameters used for the simulations (the 'true' values). The accuracy of the 'measured' parameters (K^{trans}, v_e, and v_p) was expressed by percent deviations (PD) of the 'measured' values from the 'true' values: $PD(\%)$ = (measured – true)/true*100%.

Effects of Gaussian Noise at Various temporal resolutions and v_p Levels

The above simulated tissue concentration-time curves with various sample intervals (5, 10, 20, 40, and 60 s, respectively) were converted to signal intensity curves. Zero-mean Gaussian noises with four different noise levels (5%, 10%, 15%, and 20%) were added to the simulated SI-time curves to generate synthetic data sets, which were then converted to concentration-time curves [4] for kinetic analysis with the STR and DTR method. For each given condition (i.e., a set of K^{trans}, v_e, v_p, a given noise level, and temporal resolution), 1000 repetitions were performed. Accuracy and precision in each physiological parameter were assessed from the mean and standard deviation (SD) of the percent deviation calculated from the Monte Carlo repetitions.

RESULTS

Fig. 1 shows a simulated AIF [5] following a bolus injection of 0.1 mM/kg, and the theoretical $C(t)$ tissue curves generated using Eq. 1 with time steps of 0.5, 1.0, 2.0, 5.0, 10.0, 15.0, and 20.0 s, respectively. The $C(t)$ curves generated with the time steps less than 5 s did not show visible differences to each other, and can be referred as the 'true' $C(t)$ curve. When the time steps become greater than 10 s, the $C(t)$ curves negatively deviated from the 'true' one until t equal around 250 s. After ~250 s, all the $C(t)$ curves generated with different time steps overlap together. Fig. 1 tells that the time step of a half of the first pass duration is the critical value to ensure accurately modeling the 'true' $C(t)$ curve.

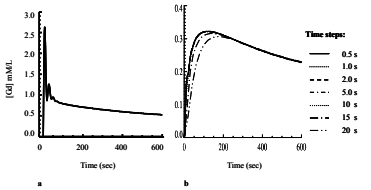

Fig. 1. simulated $C_p(t)$ curve (**a**), and tissue $C(t)$ curves (**b**) using various time steps. Kinetic parameters used in the simulation are K^{trans}, 0.4 min-1, v_e, 0.4, and v_p, 0.02.

Kinetic analysis of the simulated zero-noise $C(t)$ curves showed that, with the STR method, for a time resolution of 10 s, the errors were small for K^{trans} (PD = -0.4%) and v_e (PD = -1.1%) with no difference at various v_p levels; the errors in v_p estimates increased when the 'true' v_p decreased (PD=28%, 11%, 6%, and 4% for true v_p = 0.02, 0.05, 0.10, and 0.15 respectively). When the time resolution increased to 20 s, the errors jumped to PD of -14% for K^{trans}, -23% for v_e, 435% for v_p when the 'true' v_p is 0.02. With DTR analysis the errors in estimates of all the three hemodynamic parameters were either minimal (for K^{trans} and v_e) or small (8% for 'true' v_p =0.02) and no observable difference until the time resolution decreased to 150 s. The effects of Gaussian noise on the performance of the DTR method are demonstrated in Fig. 2. In contrast to the results from zero noise data, which showed consistently excellent accuracy over the whole temporal resolution range being studied, the accuracy and precision of the DTR method decreased as temporal resolution become lower. The precision (represented by SD of the PD values of the 1000 Monte Carlo repetitions for each given condition) of the DTR method was also dependent on the noise levels. The DTR method showed slightly better performance than the STR method at 10 s $C(t)$ time resolution, but greatly improved at 20 s $C(t)$ time resolution compared with the STR method

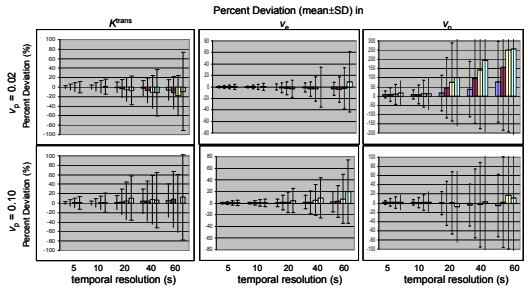

Fig. 2 Accuracy of K^{trans}, v_e, and v_p obtained by DTR method as a function of the temporal resolution of tissue $C(t)$ curve, and the noise levels. 'True' parameter values are: K^{trans} = 0.2 min^{-1}, v_e = 0.35, v_p = 0.02 and 0.10. noise levels are 0.05 (blue), 0.10 (rufous), 0.15 (yellow), and 0.20 (green).

DISCUSSION AND CONCLUSION

The DTR method showed potential to allow higher spatial resolution with larger imaging volume than the STR method. In this study, we have found that the critical time for the minimum time resolution is $\Delta t \approx 10$ s for STR and 20 s for DTR method. In-vivo study, using DTR of large volume and high spatial resolution series in its 2nd phase has been performed in our lab to validate the results from the Monte-Carlo simulation. The results have been presented elsewhere.

REFERENCES: 1. Tofts. J Magn Reson Imaging 1997;7(1):91-101. 2. Tofts et al. J Magn Reson Imaging 1999;10(3):223-232. 3. Henderson and Lee. Magn ResonImaging 1998;16(9):1057-1073. 4. Zhu et al. J Magn Reson Imaging 2000;11(6):575-585. 5. Horsfield et al. Phys Med Biol 2009;54(9):2933-2949.