Correction of Partial volume Effects in Plasma Time Curve for Tracer Kinetic Analysis in DCE-MRI

R. Rathore[1], A. Singh[1], R. Gupta[2], M. Haris[2], S. Verma[1], A. Purwar[1], G. Bayu[1], M. Sarma[1], J. Singh[1], S. Agarwal[1], and D. Rathore[1]

[1]Mathematics & Statistics, Indian Institute of Technoloky, Kanpur, Kanpur, U.P., India, [2]Radiodiagonasis, SGPGIMS, Lucknow, U.P., India

INTRODUCTION: Tracer kinetic analysis of DCE-MRI data requires concentration of contrast agent (intravenously injected) in the plasma (as an input function). Both standard (8) and individually measured plasma concentration curves are being used. The use of individually measured plasma curve (if accurately measured) has advantages over standard plasma curve as it improves accuracy of measurements (4). Given a suitable image acquisition protocol (**3, 5**) the measurements of plasma curve is feasible, and was shown to be reproducible by Parker et al. 2003. Rijpkema et al., 2001 and Parker GJM, et al., 2003, 2006 used a semi-automatic selection criterion to find all 'arterial' voxels in brain images. In a brain DCE-MRI data the partial volume effect (PVE) is the main problem in the measurement of accurate plasma curve. Plasma curve measurements using the procedures described by Rijpkema et al., 2001 and Parker GJM, et al., 2003, 2006 suffers from PVE. This is mainly because of low spatial resolution of DCE-MRI data, due to which even a manual measurement suffers from PVE. In particular, PVE results in an underestimation of the amplitude of the plasma curve, due to which the tracer kinetic analysis (with and without intravascular term) in the high contrast enhancing regions can not be done accurately. The automated AIF extraction method proposed here is similar to that described by Rijpkema et al., 2001 and Parker et al., 2006, but it additionally corrects for the partial volume effect, and also does an automatic estimation of bolus arrival time (BAT) using PL model (2). Our procedure is fully automatic and does not require any operator interaction. We also compare the tracer kinetic analysis results from the present procedure with those obtained without the correction of PVE, and those from the standard plasma curve (8).

MATERIALS AND METHODS:

Patient and data acquisition: - Fifteen patients with high grade gliomas were studied using a 1.5T GE scanner. DCE-MRI was performed using a 3D-SPGR sequence (TR/TE-5/1.4, flip angle-15º, The field of view (FOV) - 360 x 270mm, slice thickness- 6mm, matrix size- 256 x 192.). At the 4th acquisition, Gd-DTPA at a dose of 0.2 mmol/kg of body weight was administered. A series of 384 images at 32 time points for 12 slices were acquired (≅ 5.25 s temporal resolution). As per our protocol (1) T1, T2, PD weighted FSE stacks (and an additional post contrast T1 weighted FSE stack for control purposes) for the same slice locations as chosen for the 3D SPGR were acquired.

Method for automatic plasma curve measurement: - Find BAT (using PL model fitting to C(t) (2)), peak value and time to peak (TTP) of each voxel's C(t) of a given data set. After this, threshold out all pixels with time difference [TTP-BAT] >10 s, find the 95th percentile of peak values of the remaining voxels, followed by exclusion of all pixels with peak value below 95-th percentile. Find minimum of BAT's (minBat) of the remaining voxels (arteries and veins). Finally all the voxels with BAT= minBat are the candidates for a choice of the plasma curves. Take average of all final candidate voxels to get an average plasma curve (take delay effects into account using BAT). Hematockrit label (0.4) was taken into account for obtaining the true plasma curve. The proposed new procedure to correct for PVE consists of using the relation: ***Corrected*** $C_p(t) = (C_p(t)/max)*MAX$, where max is the peak value of measured $C_p(t)$ curve and MAX is the global peak value during the first pass over the entire data set (or the concentration at a pure plasma voxel). For the case reported below MAX equalled 6 mmol/L. This choice of MAX value was the computed maximum value observed during first pass over the entire data sets.

Data processing: - The data was processed using in-house developed perfusion software (based on JAVA programming language) (1). Images were registered using in-house developed registration software for voxel wise analysis. Firstly voxel-wise tissue T_{10} was computed followed by conversion of S(t) into concentration time curve (C(t)) (1). BAT was estimated for each voxel using PL model (1) fitted to C(t) curve. Plasma curve was estimated for each patient using above described procedure and corrected for PVE. Generalized tracer kinetic model (GTKM) (inclusion of intravascular term to tracer kinetic model) (1, 4) was fitted to C(t). Fitting of GTKM to C(t) was carried out using least square minimization using Levenberg-Marquardt Method (Press et al 1997). Before fitting GTKM to C(t), hemotokrit level 0.4 was taken into account in plasma curve (Cp(t)). GTKM fitting was carried out using the earlier mentioned three different plasma curves.

RESULTS: - Figure 1(a) shows the graphs of automatically measured plasma curves using current procedure (*without correcting PVE*) in different slices of a given data set. Figures 1b and 1c show the graphs of automatically measured plasma curves using current procedure (*with PVE correction*) in different slices of a given data set without and with matching for peak position (TTP). **Figure 2** shows the results of GTKM fit parameters ($k_{ep}(min^{-1})$, $k^{trans}(min^{-1})$, v_e and v_p, respectively) obtained using different plasma curves. We used automatically measured plasma curve (without PVE correction) for the first row maps, automatically measured plasma curve (corrected for PVE) for the 2nd row maps and the standard plasma curve for the 3rd row parameter maps. These maps show that the tracer kinetic analysis without PVE correction results in over estimation of the parameters (sometimes even exceeding the physiologically acceptable range). The color scales in figure 2 represent absolute values. Results of all parameters using standard plasma curve were different (higher) from the maps obtained using individually measured plasma curve (as they are computed after well mixing requiring at least two circulations).

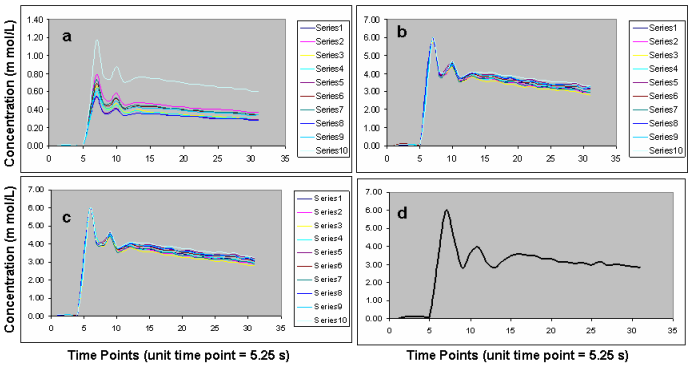

Figure 1

DISCUSSIONS: The determination of the plasma curve is quite sensitive because of its dependence on a number of factors like choice of the voxel, partial volume effect, heart beat and kidney action, time of flight effect, and field inhomogeneity. In brain studies, because of TOF effect, the measurements in major arterial voxels (bottom slices) are not possible. Measurement of plasma curve manually, or using any automatic procedure suffers from PVE. Automatically measured plasma curve with PVE (low amplitude) results in poor results of tracer kinetic analysis in high contrast enhanced voxels. However, after correcting for partial volume effect, tracer kinetic analysis was successfully carried out and provided good results in all the contrast enhanced tissues. Validation of the procedure of correcting PVE is based upon the assumption of well mixing of the contrast in plasma volume (based upon this assumption concentration of contrast at any location inside pure plasma has to be the same). Most of the automatic procedures for plasma curve result in an averaged plasma curve which can provide better reproducibility as compared to individually measured (manual) plasma curve. Plasma curve measurements with TTP match showed less variability of the curve over different slices as compared with those without TTP match. In conclusion, the proposed procedure for automatic plasma curve estimation and PVE correction results in more accurate and stable measurement of plasma curve which leads to improved accuracy in physiological parameter estimation (tracer kinetic analysis).

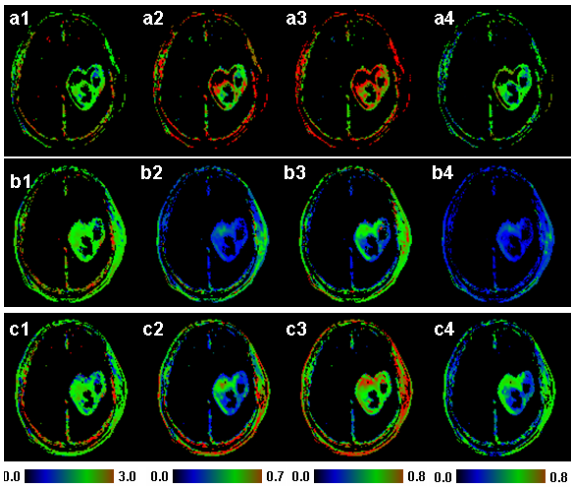

Figure 2

REFERENCES: [1] Anup et. al., JMRI (2007). [2] Anup et. al., ISMRM (2007). [3] Fritz-Hansen et al. (1998). [4] GJM Parker & DL Buckley. Springer-Verlag, 2004, pp. 81-92. ISBN 3-540-42322-2. [5] Li et al. (2000) [6] Parker GJM, et al., (2003), (2006) [7] Rijpkema et al., (2001). [8] Tofts et .al., (1991), (1999).