A modified Generalized Tracer Kinetic model for Perfusion Parameters in DCE- MRI for High Grade Intracranial mass Lesions

R. K. Rathore[1], P. sahoo[2], R. awashti[3], R. K. gupta[4], S. verma[5], and D. Rathore[5]
[1]Mathematics and Statistics, IIT Kanpur, KANPUR, U.P., India, [2]Mathematics and Statistics, IIT Kanpur, KANPUR, India, [3]SGPGI, [4]SGPGI, LUCKNOW, [5]IIT Kanpur

Introduction: Dynamic contrast enhanced (DCE) MRI is getting widely used for detecting, staging, and monitoring tumor pathologies. Perfusion measurements based on DCE imaging can simultaneously calculate cerebral blood flow (CBF), cerebral blood volume (CBV) and a number of blood brain barrier leakage parameters. In the case of blood brain barrier disruption contrast agent is assumed to permeate into the extra cellular extra vascular space (EES).according to the GTK model solution $C(t) = v_p C_p + v_e C_e = v_p C_p + k^{tr} \int_0^t C_p(u) \exp(-k_{ep}(t-u)) du$ in which v_p , v_e are, respectively, the volume fractions occupied by blood plasma and the permeability associated EES. The second term is due to a moderate BBB disruption permeability model. In this presentation we update the model by considering an additional BBB disruption as an accumulated flow into a leakage space. Note if the λ_{trans} compartment is absent in a voxel the fit would assign an insignificant value to the parameter.

Theory: The addition leads to a modified GTK model $C(t) = v_p C_p + k^{tr} \int_0^t C_p(u) \exp(-k_{ep}(t-u)) du + \lambda_{trans} \int_0^t C_p(u) du$ in which $0 \le \lambda_{trans} \le 1$ is the average fractional plasma volume flow per unit time (i.e., minute^{-1}). Without taking the λ_{trans} term into account the intra vascular the CBV calculations would be erroneous. *Cerebral blood volume CBV (mL/100g) is the volume in blood vessels within a volume of brain tissue as compared with that in the larger feeding vasculature (arterial input voxel) in the units of mL per 100g of tissue in a voxel*. It therefore is to be calculated by normalizing the area under the calculated $v_pC_p(t)$ by that of the $C_a(t)$ (AIF) (Østergaard et al., 1996a): $CBV = (H/\rho) \int v_p C_p(t) dt / \int C_a(t) dt$ where ρ (1.04 g/mL) (Axel, 1980) is the density of brain tissue (needed to provide the correct volume units, and presently assumed constant throughout), $H = (1-H_{lv})/(1-H_{cap})$ accounts for the difference between hematocrit of capillaries (H_{cap} = 25%) and that of large vessels (H_{lv} = 45%) (Gaehtgens, 1992), since only the plasma volume is accessible to the tracer. Because of the normalization by the AIF, CBV estimation remains independent of the amount of contrast injected. *The cerebral blood flow CBF (mL/100g/min) is the amount of arterial blood delivered to brain-tissue per-unit time*. Assuming a linear time invariant response, tissue concentration C(t) can be represented as a convolution of $C_p(t)$ and R(t): Since $C_p(t)$ is the concentration delivered at time t, $C(t) = (\rho/H) \cdot CBF \cdot (C_p(t) \otimes R(t))$ for the tissue as whole. The impulse response function R(t) is the corresponding tissue residue function. It ought to decrease monotonically from 1 to 0 and represents the residual fraction of unit concentration at t = 0 (due to a unit impulse input) remaining in the tissue at time t, so that the CBF is the maximum of the curve obtained when the deconvolution of the tissue C(t) with the corresponding $C_a(t)$ is performed (Ostergaard et al., 1996; Rempp et al., 1994): $CBF \cdot R(t) \cong (H/\rho) F^{-1}\{F\{C(t)\}/F\{C_p(t)\}\}$, where F and F^{-1}, respectively, are the discrete FT, and the inverse discrete FT operations.

Data processing: The data was processed using in house developed perfusion software (based on JAVA programming language). Voxel wise precontrast tissue parameter T_{10} was computed and used in the conversion of signal intensity time curve $S(t)$ into concentration time curve $C(t)$. An automated arterial input function (AIF) was measured by the method described in [3].The above model was fitted to $C(t)$ for measuring the constants $(k_{trans}, k_{ep}, v_p, \lambda_{trans})$. Fitting of the model to $C(t)$ was carried out using least square minimization using Levenberg-Marquardt Method (Press et al 1997) using initial approximation provided by the earlier GTK model procedures [3-4]. Before fitting, hemotokrit level 0.4 was taken into account in plasma curve $C_p(t)$. Bolus arrival time and delay effect are also taken care of as in [4].

Cerebral blood flow (CBF) and CBV was calculated by above described method.

Patient and data acquisition: - Ten patients with high grade gliomas, ten patients with low 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 0.2mmol/kg of body weight was administered. A series of 384 images at 32 time points for 12 slices were acquired (≅ 5.25 s temporal resolutions). 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.

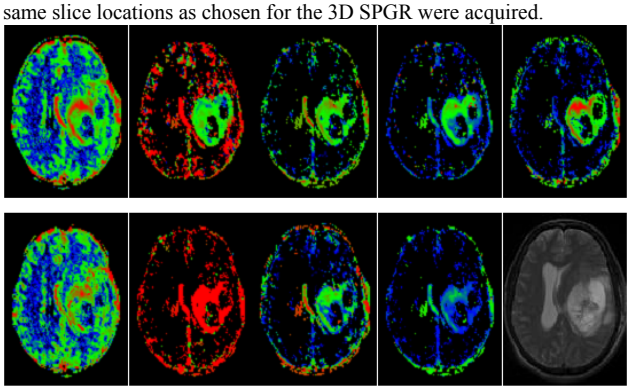

Figure-1

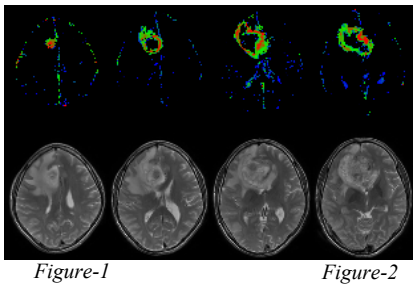

Figure-2

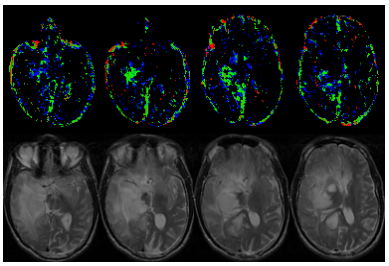

Figure-3

Results: Figure -1 Top L-R: (1) CBF, (2)Kep, (3) K^{tr}, (4) v_e, (5) λ_{trans}, Bottom L-R: (1) CBV, (2) K_{ep}, (3) Ktr, (4)Ve, (5) T2. Figure – 2 High Grade Glioma: Top L-R (1-4) λ_{trans}, Bottom L-R (1-4) T_2 , Figure – 3 Low Grade Glioma: Top L-R (1-4) λ_{trans}, Bottom L-R (1-4) T_2 . Absolute color scheme was used for coloring. All maps show high values at the boundary of the lesion. The absolute values of CBF and CBV in the normal grey and white matter are consistent with literature. In the Table mean values of different perfusion parameters at the lesion wall are listed. ROIs are placed where λ shows high value in the volume of lesion. The mean and standard deviation have been calculated over 10 patients in each of the categories.

n=10	High grade	Low grade
λ	.047±.021	.0009±001
c b f	6.67±1.51	1.86±.15
c b v	3.99±.64	1.93±.47
k t r	.113±.08	.032±.044
v e	.21±.11	.008±.010
k e p	3.8±.89	2.09±.83

Conclusion: In the proposed method the leakage correction in CBV automatically takes place (cf. [4]). Moreover we note that the model as such does not suffer from the problem of finding a neighboring feeding artery. The parameters λ_{trans}, CBF, as well as CBV shows significant differences in high and low grade glaiomas. The leakage parameter λ_{trans} shows much more significant differences compared to K_{trans} and v_e in these two cases and would be helpful in grading the tumors. The high values of indeed justify the modified GTK model.

References: [1] Tofts P. S. et al., MRM. 17,375,367(1991).[2] Ostergaard L et al., MRM.1996;36:751-725. [3] Singh A. et al. JMRI 2009 Jan;29(1):166-76. [4] Singh A, et al., 2007, J Magn Reson Imaging 2007;26:871-880.