Fitting of the Piecewise Linear Function to Signal Intensity Time Curve and its Application in improving the Analysis of Concentration Time Curve of Dynamic Contrast Enhanced-MRI Data

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

[1]Mathematics, IIT Kanpur, Kanpur, Uttar Pradesh, India, [2]Radiodiagonasis, SGPGIMS, Lucknow, Uttar Pradesh, India

INTRODUCTION: Perfusion MRI can be used for studying the vasculature of different tissues/lesions of brain based on their response to the passage of intravenously injected contrast agent. Dynamic contrast enhanced (DCE) MRI data results in signal intensity time curve (S_t) at individual voxel which can be converted into concentration time curve (CTC or C_t). The shape of the curve is an important criterion for differentiation/characterization of different tissues. A variety of methods for analyzing the curves (S_t) both qualitatively as well as quantitatively has been reported in literature. Here a new method is presented for analyzing S_t. In this method a piecewise linear function is fitted to the curve. The parameters of the fit provide qualitative as well as quantitative information about tissue vasculature. Slop of 3rd line segment of fitting model was used for generating gradient color map which provides the vasculature information in terms of colors. Fit parameters were used in segmentation of contrast enhancing lesions. Bolus arrival time (BAT) is an important parameter in perfusion studies [1]; its accurate estimation improves the precision of various methods of analysis like pharmacokinetic analysis. The standard method for obtaining BAT is from estimation as a free parameter in the Gamma Variate fit. However, this method fails to give accurate estimation of BAT. Here BAT is one of the parameter of current fitting model.

METHODS: Ten 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 0.1 mmol/kg of body weight was administered. A series of 384 images in 32 time points for 12 slices were acquired with a temporal resolution approximately of 5.25 s. T1, T2, PD and post contrast T1 weighted imaging were also performed for the same slice locations chosen for the 3D SPGR. The data was processed using in-house developed JAVA based perfusion software [2]. Images were registered [3] for voxel wise analysis and de-scalped manually.

Theory: S_t can be viewed in two parts: base line (pre-contrast) part and post contrast part. In [4] three basic types of S_t were identified as shown in Figure 1. Type I curves are characterized by rapid early post-contrast rise followed by a continued straight line or curved rise (these are the regions where contrast leaks into lesion due to blood brain barrier breakdown), type II by a rapid initial rise followed by a plateau, and type III curves by a rapid initial rise followed by washout. Base line (pre contrast part) is common in all types of curves. In current study a piecewise linear function is fitted to the S_t. Given a random sample of i = 1 to n observations on S_t of a given pixel at a corresponding time ti, the model has the form:

$$f(i)=\begin{cases} c; & t_i < \alpha \\ c + m_1(t_i - \alpha); & \alpha \le t_i < \beta \\ c + m_1(\beta - \alpha) + m_2(t_i - \beta); & t_i \ge \beta \end{cases}$$

where the parameter α is BAT, β is the time for end of 2nd line segment, c is the constant (base intensity level), m_1 and m_2 are the slops of 2nd and 3rd line segment respectively of fitting model function. Here the model is fitted on enhancement curve S_t. Model can be fitted using Liebenberg-Marquardt. In current study the procedure adopted for fit is as follows: Based on the knowledge of time of contrast injection we assign a range of values to α and β (in neighborhood of first pass). Now for each of the combination of α and β we do the fitting of the function to the data and best fit (For which total fitting error is minimum) is used to decide the right set of parameters. The reason for the use of this procedure is simplification of computation and reduction of fitting error due to non linear fit. Graphs of S_t along with the fitting function were generated. Pre contrast tissue parameter T_{10} was computed and used for the conversion of S_t into C_t as in [2]. Slop m_2 was used for the segmentation of enhancing lesions (type-I). Tofts compartmental model [5] was used for the pharmacokinetics analysis of C_t over enhancing lesion for the estimates of physiological parameters permeability (k^{trans}) and fraction of leakage space volume (v_e). Voxelwise estimated BAT using current model was used for analysis. These parameters were also generated using fix BAT value for entire brain. Gradient (Slop) c*olor map* was generated using m_2 values. Red and green colors were weighted with positive and negative values of m_2 respectively.

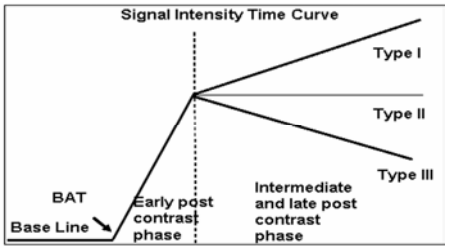

Figure1 Signal Intensity time curve characterization.

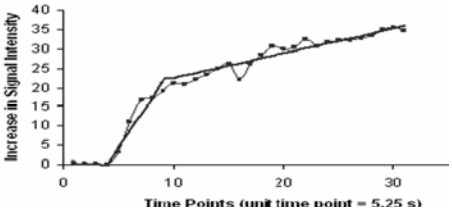

Figure 2: Example of piecewise Linear Fitting

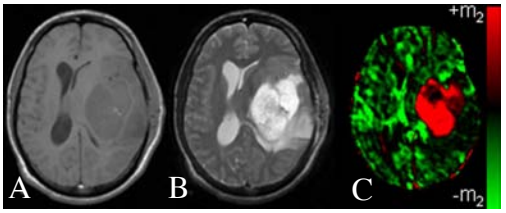

Figure 3: T1 (A), T2 (B) weighted FSE images and Gradient color map of patient with high grade tumor.

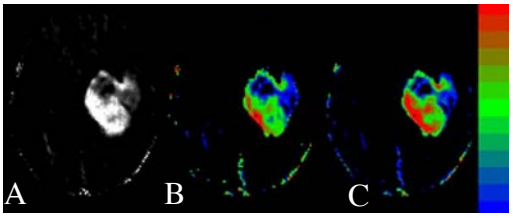

Figure 4: Gray map (A) of positive values of m_2 (slop) which represents type I curves (regions), k^{trans} (B) and v_e (C) map of patient with high grade tumor

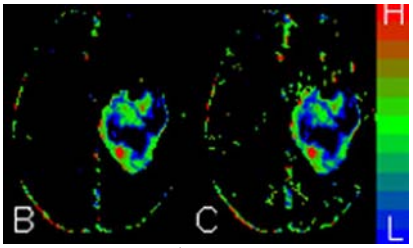

Figure 5: Maps of k^{trans} using voxelwise BAT (B) and fix BAT (C) of tumor patient

RESULTS AND DISCUSSION: Figure 1 represents the different types of S_t and Figure 2 represents the example of fitting current model on S_t (type I). Slope m_1 tell about the rate of initial rise of post contrast, m2 about the rate (rise, fall) of intermediate and late post contrast. In normal tissues m2 observed to be negative or zero but positive in enhancing regions (lesions). Current model provided simple and accurate estimation of BAT at each voxel and was used for further analysis. In Figure 3 high grade tumor is shown on T1, T2 and gradient color map. Color map provide clear distinction (visually) of type-I (enhancing lesion) from rest tissues and also tells about the rate of change at each voxel in terms of colors. Figure 4 shows the gray map of positive values of m_2 (representing segmented enhancing regions), color map of k^{trans} and v_e of segmented enhancing regions. Figure 5 represents maps of k^{trans} (B) computed using voxelwise BAT computed using current model and fix BAT value(C). Significant effect of BAT was observed on k^{trans}. One should estimate voxelwise BAT before further analysis for accurate parameter estimation. Total volume of enhancing lesion was estimated after removal of non brain enhancing voxels (at boundary, dura matter etc.). Fitting of pharmacokinetic model only on segmented enhancing region (lesion) significantly reduced time and complexity of computation (k^{trans} and v_e maps in Figure 4 (B and C)) (In Figure 4). Gradient color map is interpreted as; the pixel with color in red range belongs to enhancing lesions (type-I) and those with green color range belongs to normal or non enhancing tissues (type II and III). Brightness of color is related to high rate of change (high absolute value of slop). Here the fitting was restricted to integral points.

CONCLUSION: Piecewise linear fitting of signal intensity time curve results in a sequence of parameters which are important for medical diagnosis of various pathologies. Gradient color map provides vasculature information in term of colors and offer clear identification of enhancing lesions. Voxelwise BAT estimation using current fitting model before pharmacokinetic analysis improves the accuracy of estimation of physiological parameters. Parameters of current fitting model can be used for segmentation of enhancing lesion [Figure 4 (A)] and estimation of its volume. A complete range of physiological parameters (k^{trans} ranges from 0.1027 min^{-1} to 1.383 min^{-1} while v_e ranges from 10% to 58%) were obtained over segmented enhancing lesion.

REFERENCES: [1] Lucy EK et al, MRM 2005; 56: 986 – 992. [2] Rathore R, Singh A, Gupta R et.al. , Proc. Intl. Soc. Mag. Reson. Med. 14 (2006). [3] Woods RP et al, JCAT 1998; 22:139-152. [4] C. K. Kuhl et al, Radiology 1999; 211:101-110. [5] Tofts P. S. et al., MRM 1991;17:357-367.