Segmentation of Gd-DTPA Enhancing Lesion of Brain using Time to Peak of Concentration Time Curve and its Pharmacokinetic Analysis in Dynamic Contrast Enhanced (DCE) MRI

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INTRODUCTION: Perfusion MRI is widely used for the 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). In case of BBB breakdown contrast leaks into EES which results in enhancement of contrast in corresponding tissues/lesions. Lesion segmentation from MR images may help in assessing the therapeutic response by tracking the progress of its growth and/or shrinkage. Lesion volume is a significant prognostic factor as is a measure of therapeutic response. The task of manually segmenting brain lesions from magnetic resonance imaging is generally time-consuming and difficult. Semi-automatic and automatic segmentation of lesions is an active area of research [1, 2]. Here, we propose a new simple method for automatic segmentation of enhancing regions (lesions) of various brain pathologies using the parameter time to peak (TTP) derived from CTC and also carried out the voxel-wise pharmacokinetic analysis of the CTC using Toft's compartmental model.

METHODS: With informed consent the study was carried on 15 patients with different pathologies (brain tumor (5), brain tuberculomas (5) and brain abscess (5)). The final diagnosis of these pathologies was based on histopathology and culture of aspirated pus. DCE-MRI was performed using a three-dimensional spoiled gradient-echo (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.

***CTC*:** The signal from a SPGR is [3]: $S_t = G(PD)\exp(-TE(1/T_{20}^*+R_2C_t))\sin(\theta)((1-\exp(-TR(1/T_{10}+R_1C_t)))/(1-\cos(\theta)\exp(-TR(1/T_{10}+R_1C_t))))$, where G is the gain, PD is the proton density, and T_{20}^*, T_{10} are the values of T_2^*, T_1 before injection of Gd-DTPA. Voxelwise pre-contrast T_{10} was computed as in [4] using pre-contrast T1, T2 and PD weighted images. The increase in relaxation rates are linearly related to Gd concentration in the tissue: $1/T_1 = 1/T_{10} + R_1 C_t$; $1/T_2^* = 1/T_{20}^* + R_2 C_t$; where $R_1 = 4.5\ s^{-1}mmol^{-1}$, $R_2 = 5.5\ s^{-1}mmol^{-1}$. The above equation is used to convert S_t into C_t. Graphs of C_t were generated for all voxels (i.e., normal tissues and lesions) for simultaneous TTP analysis.

***Automatic segmentation procedure*:** The parameter TTP, which represents the point (time) where CTC attains its peak (maximum) value i.e. $C_{TTP} = \text{Max}(C_t)$, (t=1, 2,…, N). TTP is computed for individual voxel. Now different tissues have different TTP values depending on the vasculature. It has been observed that TTP of all normal tissues falls in first pass time interval while for all enhancing tissues (lesions) it occurs after first pass time interval [Figure 1.]. This knowledge of TTP behavior is the base of current method for automatic segmentation of lesion. We label with non zero value all the regions whose TTP occurs after first pass time interval and with zero value for the regions whose TTP falls during first pass interval. The labeled regions represent the enhancing lesions. Segmented regions were compared with post contrast T1 images. Segmented lesion was also used for the computation of total volume of the lesion. The "ground truth" (GT) lesion volume (enhancing), against which measurement results from current automated methods could be compared, was determined by an experienced radiologist, who traced the tumor outline manually. The area inside the outline was automatically labeled, calculated and multiplied by the MR slice thickness plus the inter-slice gap to calculate a per-slice tumor volume. The total tumor volume was obtained by summing the volume calculations for all slices. The volume validation of automatic segmented lesion was carried out by summation of the areas of contiguous slices. The areas were calculated by pixel counting using automatic segmentation.

***Pharmacokinetic analysis*:** Pharmacokinetic analysis of CTC was performed using Tofts compartmental model [5] for the quantitation of physiological parameters (permeability (k^{trans}) and fraction of leakage space volume (v_e)) on segmented enhancing lesion.

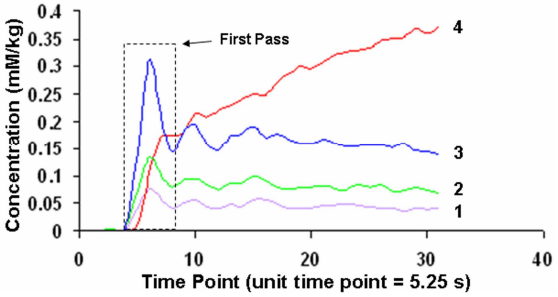

Figure 1. Concentration time curves after bolus injection of Gd-DTPA contrast agent into a tumor patient. Curves 1, 2, 3 and 4 represent the concentration time curves in normal white matter, normal gray matter, artery and lesion.

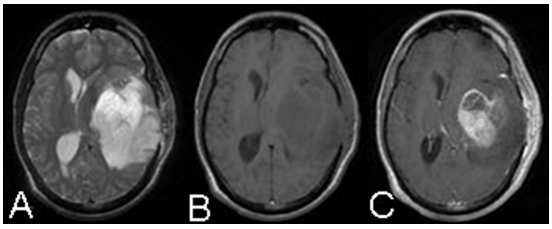

Figure 2. T2 (A), T1 (B) and post contrast T1 (C) weighted FSE images of patient with high grade tumor.

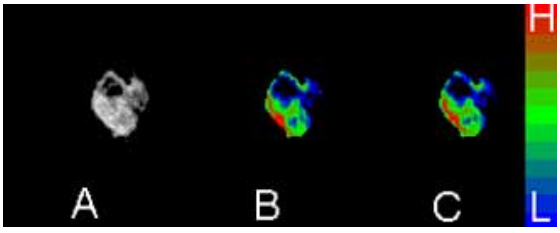

Figure 3. Gray map of TTP (A) and color maps of k^{trans} (B) and v_e (C) of segmented lesion.

RESULTS AND DISCUSSION: Figure 1 shows CTC of normal regions attaining its peak value during the first pass while CTC of lesion attains its peak after the first pass. There is clear distinction between the TTP values of normal regions and lesions. There is enhancement of contrast in regions of BBB breakdown (lesion) and due to this TTP occurs after a long time of first pass. Figure 2 shows the maps of T1, T2 weighted pre-contrast FSE images and T1 weighted post contrast image. Figure 3 shows the maps of TTP (gray label is directly related to TTP value) and physiological parameters of automatic segmented lesion. Over lesion (high grade tumor) k^{trans} ranges from 0.1037 to 1.993 min^{-1} while v_e ranges from 7% to 69%. Automatically segmented tumor volume and GT tumor volume were found to be comparable. Segmented lesion not only results in total volume estimates of lesion but also useful in reducing the time for performing pharmacokinetic analysis. Instead of carrying the pharmacokinetic analysis for whole brain one can restrict to only segmented lesion. Before application of this method the data should be preprocessed (desculped). Because there is also enhancement of contrast in some other tissues outside the brain like durra matter and can be segmented out by a desculping.

CONCLUSION: Proposed method makes it possible to automatically segment the enhancing lesions (for all the pathological cases in current study) using simple procedure which is better in terms of both time and computation. Automatically segmented lesion volume and GT lesion volume were found to be comparable which validates the volume estimation. Current method also tells us whether enhancement of contrast is there or not. Exact knowledge of the lesions enables a better analysis of lesion. Segmentation enables one to find complete range of k^{trans} and v_e values over the lesion.

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