Voxel-wise exact T1 Estimation for Accurate Quantitation of Perfusion Indices using Fast 3D-SPGR in Intracranial Mass Lesion

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Introduction: The conversion of signal (S) to absolute Gadolinium-DTPA concentration [Gd] for quantitative perfusion studies continues to be problematic. The conversion of the signal from a spoiled gradient echo sequence to concentration requires pre contrast T1 for which multipoint inversion recovery has been one of the most precise mean of measuring T1 in tissues; determination of T1 using this, however, requires a long scan time. Here we propose and demonstrate a very promising new method requiring less scan time for voxel-wise exact T1 estimation followed by a quantitative analysis of dynamic concentration curve for the measurement of various perfusion indices.

Materials and Methods: Dynamic contrast-enhanced imaging was performed using a three-dimensional spoiled gradient-echo (3D SPGR) sequence (TR/TE-6.6/2, flip angle-15º, The field of view (FOV)- 360 x 270mm, slice thickness- 6mm, matrix size- 256 x 192.). At the tenth 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 7.75 s for each time point. T1, T2 and PD weighted imaging before injection of contrast and T1 weighted imaging after 32 time points were performed for the same slice locations chosen for the 3D SPGR. In the current method the three pre-contrast images (T1, T2, PD) with different TR, TE was used for exact T1 estimation. Pre-contrast T1 is then used for the absolute computation of concentration curve from signal intensity curve. Absolute measurements of **CBV, CBF** were made using standard algorithms and an automated method for obtaining the arterial input function. These measurements are based on the assumption that during the first pass the contrast remains intravascular. Compartmental modeling [1] of tracer kinetics is used to model the behavior of contrast through different tissues. Fitting of the tri-exponential model to the given concentration curve lead to the quantification of parameters $\mathbf{k^{trans}}$ and $\mathbf{v_e}$

Theory: 1. Concentration curve: The signal from a SPGR is [5]: $S_t = G(PD)\exp(-TE(1/T_{20}^*+R_2C_t))\sin(\theta)((1-\exp(-TR(1/T_{10}+R_1C_t)))/(1-\exp(-TR(1/T_{10}+R_1C_t))))$, 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. 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 $R_1 = 4.5\ s^{-1}mmol^{-1}$,$R_2 = 5.5\ s^{-1}mmol^{-1}$ at 0.5 T [8]. The above equation is used to convert signal intensity curves into concentration curves.

2. First Pass Analysis: In first pass analysis we considered concentration curve before recirculation of contrast. Arterial Input Function (**AIF**) is obtained using Rijpkema's process [3]. Cerebral blood volume (**CBV**) is the volume of blood vessels within a volume of brain tissue. It is calculated by finding the area under the measured concentration curve $C_t(t)$ and normalizing it to the integrated $C_a(t)$ and density of the brain tissue (ρ =1.04 ml/g) [2, 4]. Cerebral blood flow (**CBF**) is the amount of arterial blood delivered to brain-tissue per-unit time. Tissue concentration $C_t(t)$ is represented in term of the convolution of $C_a(t)$ and R(t) using the equation: $C_t(t) = \rho((1-H_{cap})/(1-H_{art}))CBF.(C_a(t)*R(t))$ [2], $*$representing the convolution operation, R(t) is the residue function, CBF is the cerebral blood flow, $((1-H_{cap})/(1-H_{art}))$ accounts for the difference between hematocrit (H) between capillaries and large vessels. De-convolution of $C_t(t)$ with $C_a(t)$ results in CBF (R(0)=1).

3. Compartmental model: According to the model of Tofts and Kermode [1], after injection of bolus dose D mmole/kg body weight, given at time t=0, the plasma concentration decays bi-exponentially: $C_a(t) = a_1\exp(-m_1t)+a_2\exp(-m_2t)$. The amplitudes are a_1 = 3.99 kg/liter, a_2 = 4.78 kg/liter and rate constants m_1 = 0.144 min^{-1}, m_2 = 0.0111 min^{-1} [1,6].The resulting tissue concentration is, $C_t(t) = D\{b_1\exp(-m_1t)+ \{b_2\exp(-m_2t)+ \{b_3\exp(-m_3t)\}$, where $m_3 = K^{trans}/v_e$, $b_1 = K^{trans}a_1/(m_3-m_1)$, $b_2 = K^{trans}a_2/(m_3-m_2)$, $b_3 = -(b_1+b_2)$, K^{trans} (permeability surface area product/unit volume of the tissue or rate constant) and v_e is the leakage space, i.e., the proportion of the leaky tissue into which Gd -DTPA can leak ($0< v_e <1$)).

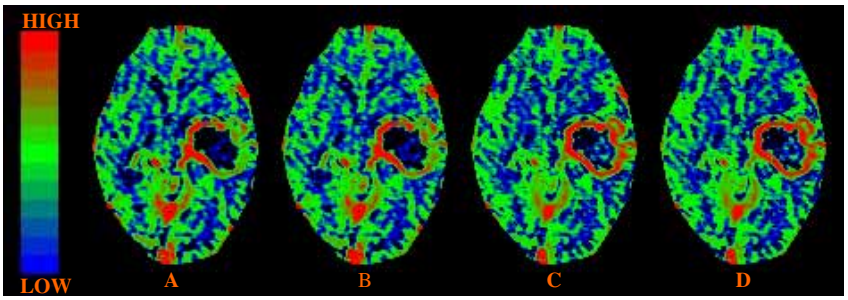

Figure 1

Results and Discussion: In **Figure 1**, A: CBV, and B: CBF are generated from first pass analysis of dynamic contrast curve, and C: K^{trans}, D: v_e by the compartmental model. All the four maps are showing a very high value at the boundary of the lesion and low value within the boundary of lesion. The absolute values of CBF and CBV in the normal gray and white matter are consistent with literature.

In **Figure 2**, the 1st image represents T1-weighted pre contrast, the 2nd calculated tissue T1 map, and the 3rd T1-weighted post contrast image after 32 time points (one time-point 7.75s). The 4th image is a reconstructed T1-weighted image generated for the same time point at which T1-weighted post contrast image was taken, by using calculated parameters from the three compartmental model.

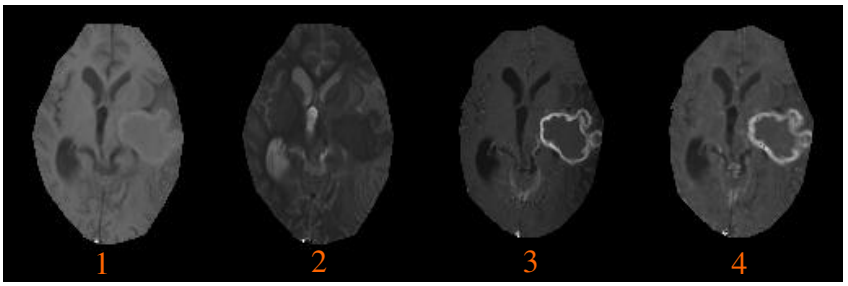

Figure 2

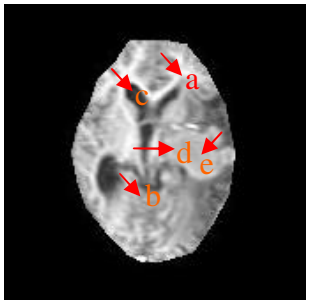

Figure 3

In **Table 1,** values of different calculated perfusion parameters in different tissues, labeled in **Figure 3** are listed. Values parameter $\mathbf{v_e}$ represents of the percentage of the total volume of a tissue occupied by leakage space. High values at the boundary of the lesion indicate high BBB break down. The table shows low values inside the boundary of the lesion.

Tissue type	*T1(ms)*	*CBF(mL/100g/min)*	*CBV(mL/100g)*	$K^{trans}(min^{-1})$	*v%*
a: White Matter	591.42	36.02	5.18	0.90	4
b: Gray Matter	701.04	72.97	10.41	2.23	12
c: CSF	1313.30	0.0	0.0	0.13	0.1
d: Lesion wall	758.32	312.07	40.56	13.08	71
e: Lesion interior	649.89	8.75	0.89	0.07	1.9

Table 1: T1, CBF, CBV, K^{trans} and v_e for different tissue types

Conclusion: The Exact voxel-wise T1 values made it possible to covert the dynamic signal time curve to dynamic concentration time curve more accurately. Analysis of dynamic curves resulted in an accurate estimation of perfusion indices. Concentration curve resulting from the compartmental model after substitution of $\mathbf{K^{tran}}$ and $\mathbf{v_e}$ enables a prediction of the behavior of contrast at future time, subject to the applicability of the compartmental model in the ROI.

References: [1] Tofts P. S. et al., MRM.17,357, 367(1991). [2] Ostergaard L et al., Part I: Mathematical approach and statistical analysis. MRM.1996; 36:715-725. [3] Rijpkema M. et al., J. Magn Reson Imaging., 2001; 14: 457-463. [4] Axel L. et al., Radiology1980; 137:679-686. [5] Wehrli F.W., Fast-Scan Magnetic Resonance, 1st ed., p.12, Raven Press, New York, 1991. [6]. Weinmann H.J. et al., NMR 16,167-172(1984).