An Analytical Approach for Quantification and Comparison between Signal Intensity and Longitudinal Relaxation Rate Change (ΔR_1) in MR DCE-T1 Studies

Hassan Bagher-Ebadian[1,2], Siamak P Nejad-Davarani[1,3], Rajan Jain[4], Douglas Noll[3], Quan Jiang[1,2], Ali Syed Arbab[4], Tom Mikkelsen[5], and James R Ewing[1,2]

[1]Neurology, Henry Ford Hospital, Detroit, Michigan, United States, [2]Physics, Oakland University, Rochester, Michigan, United States, [3]Biomedical Engineering, University of Michigan, Ann Arbor, Michigan, United States, [4]Radiology, Henry Ford Hospital, Detroit, Michigan, United States, [5]Neurosurgery, Henry Ford Hospital, Detroit, Michigan, United States

Introduction: In Dynamic Contrast Enhanced (DCE- MRI) studies, pharmacokinetic models rely on converting the time course of the signal intensity, S_t, to changes in the longitudinal relaxation rate, $\Delta R_1(t)$. This change is then assumed to be proportional to the tissue indicator concentration time profile [1,2,3]. However, many researchers employ the normalized Signal Intensity, SI(t) for quantitative and semi-quantitative DCE analyses instead of $\Delta R_1(t)$. To the best of our knowledge, there has been no quantitative comparison between the two techniques, and the equality of the profiles generated by these techniques is still in question [2,3,4]. We have recently presented an analytical approach [5, 6] for calculating $\Delta R_1(t)$ from dynamic 3D-T1-Weighted-Spolied Gradient Echo (SPGRE). This analysis requires the pre-contrast tissue T_1 and does not require knowledge of the tissue relaxivity or proton density, M_0, and thus avoids systematic errors associated with the assumption that the relaxivity of the Contrast Agent (CA) in a particular tissue is a known constant [5,6]. In this study, one-dimensional error propagation is applied to the previously described analytical approach in order to investigate the difference between $\Delta R_1(t)$ and SI(t) profiles. A full analytical methodology is presented for comparing the level of agreement in the profiles in both techniques (SI(t) and $\Delta R_1(t)$) for different contrast enhancement ratios. The technique was applied to an SPGRE dataset acquired in the brain of a patient with Glioblastoma to compare the difference between SI(t) and $\Delta R_1(t)$ time courses in different anatomical areas of the brain.

Theory: Equations 1 and 2 describe an analytical expression for calculating the ΔR_1 profile from the raw signal intensity (S_t) using the value of resting T_1, estimated from a Variable Flip Angle (VFA) technique, acquired prior to the dynamic study. The subscripts m and n denote the starting and ending time points for calculation of the average signal intensity (S_0) prior to the CA administration, and θ and TR refer to the flip angle and repetition time of the dynamic experiment. Equation 3 represents the relationship between signal intensity change, $d[S_t]$, and change in $\Delta R_1(t)$ or $d[\Delta R_1(t)]$. In equation 3, *x(t)* represents the time-dependent contrast enhancement ratio of the signal, assumed to be always less than or equal to 1. The normalized signal intensity, SI(t), is defined as the ratio of $(S_t - S_0)/S_0$ [3,4,7]. Equation 4 describes the partial derivative of ΔR_1 versus raw signal intensity (S_t), as a function of the dynamic flip angle (θ), resting longitudinal relaxation time, T_1, and the contrast enhancement ratio, *x(t)*. Combining equations 4, 5 and 6, and employing the partial derivative chain rule, yields equation 7 describing the relationship between the change in $\Delta R_1(t)$ and changes in normalized Signal Intensity, SI(t) at any time point. Ω (t) is defined as the ratio of $d[\Delta R_1(t)]$ to $d[SI(t)]$ normalized to its initial value(prior to CA administration). This parameter is considered to be the key equation for quantification and investigation of the behavior of the two temporal profiles in different anatomical areas (different values of resting T_1).

$$E^{pre} = e^{\frac{-TR}{T1(pre)}},\quad B = \frac{1-\cos\theta E^{pre}}{1-E^{pre}},\quad S_0 = \frac{1}{(n-m+1)}\sum_{t=m}^{n} S_t,\quad S_t = \begin{cases} S_0 & t < n \\ S_t & t \geq n \end{cases} \qquad (1)$$

$$\Delta R_1(t) = -\frac{1}{TR} Ln\left\{\frac{(n-m+1)(1-E^{pre})S_t - (1-\cos\theta E^{pre})\sum_{t=m}^{n} S_t}{(n-m+1)(1-E^{pre})\cos\theta E^{pre} S_t - (1-\cos\theta E^{pre})E^{pre}\sum_{t=m}^{n} S_t}\right\} \qquad (2)$$

$$d[\Delta R_1(t)] = \left(\frac{\partial[\Delta R_1(t)]}{\partial S_t}\right) d[S_t],\quad S_t = \begin{cases} S_0 & t < n \\ S_t & t \geq n \end{cases},\quad x(t) = \frac{S_0}{S_t} \leq 1 \qquad (3)$$

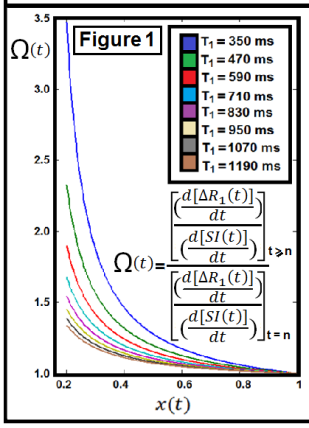
$$\frac{\partial[\Delta R_1(t)]}{\partial S_t} = \frac{B(1-\cos\theta)}{TRS_0}\left\{\frac{x(t)^2}{x(t)^2 B^2 - x(t)B(1+\cos\theta)+\cos\theta}\right\},\ \text{if}\quad SI(t) = \frac{S_t - S_0}{S_0} \qquad (4)$$

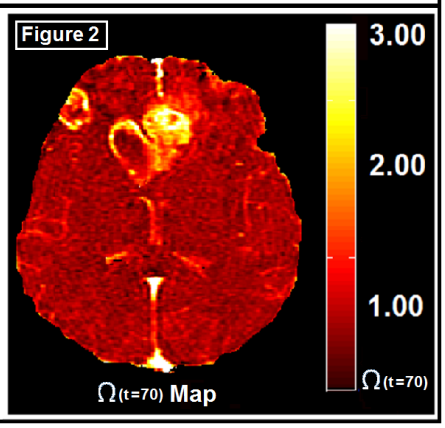
$$\left(\frac{\partial S_t}{\partial SI(t)}\right) = S_0 \Rightarrow \left(\frac{\partial[\Delta R_1(t)]}{\partial SI(t)}\right) = \left(\frac{\partial[\Delta R_1(t)]}{\partial S_t}\right)\left(\frac{\partial S_t}{\partial SI(t)}\right) = \left(\frac{\partial[\Delta R_1(t)]}{\partial S_t}\right)(S_0) \qquad (5)$$

$$\frac{\partial[\Delta R_1(t)]}{\partial SI} = \frac{1}{TR}\left\{\frac{B(1-\cos\theta)x(t)^2}{B^2 x(t)^2 - B(1+\cos\theta)x(t)+\cos\theta}\right\},\ d[\Delta R_1(t)] = \left(\frac{\partial[\Delta R_1(t)]}{\partial SI(t)}\right) d[SI(t)] \qquad (6)$$

$$\left(\frac{d[\Delta R_1(t)]}{dt}\right) = \frac{1}{TR}\left\{\frac{B(1-\cos\theta)x(t)^2}{[B^2 x(t)^2 - B(1+\cos\theta)x(t)+\cos\theta]}\right\}\left(\frac{d[SI(t)]}{dt}\right) \qquad (7)$$

Results: Figure 1 illustrates Ω(t) for different resting T_1 values at different contrast enhancement ratios, x(t). This figure shows that the conversion factor between the two profiles (Ω (t)) drastically diverges from 1 for short T_1s as the contrast enhancement ratio decreases. On the other hand, Ω(t) converges at higher values of x(t), almost regardless of T_1 values. Figure 2 plots a map of Ω(t) for a human brain study at the final time point (time-point=70~ 6.0 min after CA injection) of a dynamic series acquired at 3T. This map has been generated from 3D-SPGRE data (θ =20, 70 time points, interval of 5.7 s, total time: ~6.5 min, 256X256, TR=5.8 ms, TE~1.2 ms and VFA: 2, 4, 8, 10, 15 and 20 degrees) using equation 7. This map clearly shows that in the region of most clinical interest, the lesion area (where the x(t) gets smaller) there is a large difference between SI(t) and $\Delta R_1(t)$ (~140% to 210%). According to this map, the difference between the two profiles increases (e.g. ~230% to 300% at 6.0 min) as x(t) decreases (the areas with high resting T_1 value and high enhancement/high CA leakage) and it decreases as the resting T_1 increases(the areas with high plasma volume and less CA leakage).





Conclusion: This pilot study confirms that using the SI profile instead of ΔR_1 in analysis of DCE-MR data can result in significant biasing in estimation of permeability parameters for the areas with high leakage and low water content (low resting T_1). This study also suggests that semi-quantitative analyses that use SI instead of ΔR_1 need to be corrected with an Ω(t) factor to minimize the biasing effect due to the disagreement between SI and ΔR_1 profiles.

References:

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