Conversion From Signal Intensity to Gd Concentration May Be Unnecessary for Perfusion Assessment of Tumors Using DCE-MRI

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Introduction: Dynamic contrast enhanced MRI (DCE-MRI) has demonstrated utility in both diagnosing and evaluating the progression and response to treatment of malignant tumors [1]. It is commonly assumed that precise tracking of changes in vascular parameters measurable using DCE-MRI requires conversion of the observed signal intensity changes seen in various tissues post-injection to Gd concentration values [2,3]. This conversion process relies on the accurate mapping of T1 relaxation times for the region of interest, and the subsequent registration of the T1 mapping data to the dynamic scans. Both these steps have the potential to introduce significant noise into the parameter estimation process. There are two primary reasons for making use of conversion to contrast agent concentration ([CA]): first, it is assumed that the relationship between signal change and [CA] is significantly non-linear over the range of [CA] present in tissues (including blood); second, it is assumed that the observed signal change will vary significantly depending on the initial T1 of the tissue in question [2]. The goal of this work was to evaluate whether use of the appropriate image acquisition and analysis techniques renders this process unnecessary, allowing a simplified and more robust parameter estimation process.

Methods: In order to test the relative accuracy and precision of K^{trans} measurements, with and without conversion of signal to [CA], we developed two phantoms, each containing 100 vials in a 10x10 grid. Each column in both phantoms was filled with a different concentration of a copper sulfate solution, yielding base T1 relaxation times ranging from 98ms to 1016ms at 1.5T field strength. Subsequently, different volumes of a gadolinium based contrast agent (Omniscan, GE) were added to each row of the second phantom, yielding [CA] ranging from 0 to 0.9 mM. T1 was measured with multiple inversion/recovery times (TI(s)/TR(s) of 1.65/1.88, 0.65/0.88, 0.35/0.58, 0.15/0.38, and 0.027/0.260). Both phantoms were scanned using a 3D SPGR sequence, with a flip angle of 30 degrees, TR/TE of 5.6/1.2, a 256x160 matrix, an 8 slice, 64mm slab, with 20 phases acquired in 3 min 38 sec. Eight ideal tissue time-concentration curves (shown in Fig. 1) were generated for K^{trans} ranging from 0.015 – 0.120 min^{-1} using the Kety-Tofts model [1] with a scaled model arterial input function [4]. Corresponding signal-time curves for each K^{trans} were generated using the signal from a single phase of the SPGR acquisition for four base T1 values (208 ms, 388 ms, 667 ms, and 1016 ms) by interpolating at each time point between the signals observed in the vials with known contrast concentrations above and below the ideal contrast concentration at the appropriate baseline T1 value. K^{trans} values were calculated in three ways: (1) using the known [CA] (considered ideal values); (2) using [CA] derived from baseline T1 and the signal changes in the dynamic data; and (3) using the absolute signal change, S(t)-S(0). Results for the derived [CA] and signal change based methods (2 and 3, respectively) were evaluated based on their correspondence to these ideal values (method 1).

Results: An indication of the quality of data likely to result from parameter estimation using absolute signal changes can be obtained by examining the relationship between signal changes and [CA] changes. Scatterplots of nominal [CA] vs. signal with baseline subtracted for initial T1 ranging from 208-1016 ms are presented in Figure 2. The coefficient of correlation between ideal and estimated K^{trans} using derived [CA] (method 2) was 0.88 (data not shown). Figure 3 shows the results for K^{trans} calculated using the absolute signal change (method 3). The coefficient of correlation between ideal and estimated K^{trans} values for this method was 0.91.

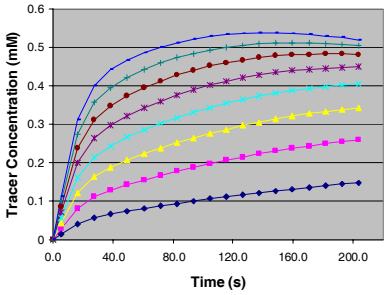

Figure 1. Ideal time-concentration curves for K^{trans} values ranging from 0.015 to 0.120 min^{-1}.

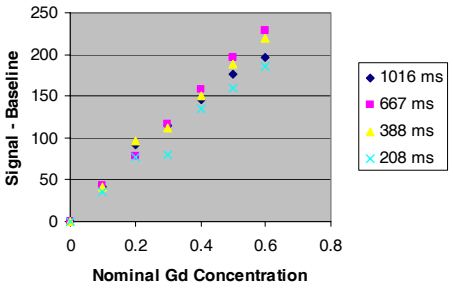

Figure 2. Scatter plot of S(t)-S(0) vs. nominal [CA] using four baseline T1 values. Note the linear relationship and minimal T1 dependence.

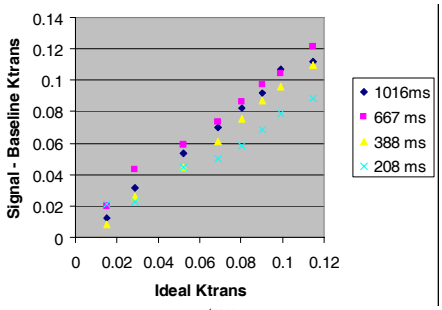

Figure 3: Scatterplot of K^{trans} calculated using signal difference for each curve in Fig. 2 and four baseline T1 values vs. Ideal K^{trans}.

Discussion: These results demonstrate that, for baseline T1 values and time-concentration curves typically seen in solid tumors, conversion from signal difference to apparent [CA] provides little or no perceptible benefit in terms of either accuracy or precision in the estimation of kinetic parameters such as K^{trans}. The failure of derived [CA] to provide a more reliable estimate of K^{trans} than signal differences may result from noise introduced by the conversion process and the lesser T1 dependence of absolute signal change than relative signal change. Noise is introduced into the derived [CA] through both errors in the T1 estimation and the registration processes needed to convert signal change to concentration. In clinical trials using human subjects, T1 maps are most frequently generated by scanning the subject using multiple flip angles, and then fitting the resulting signal intensity values at each pixel to a standard signal formation model [5,6]. Although the multiple inversion time method used in this study requires considerably more time than T1 measurement using multiple flip angles, it is generally considered to be both more accurate and more stable [7]. The probable greater T1 error in vivo and the impact of subject motion which complicates co-registration of T1 and dynamic data would likely result in greater noise added in clinical studies than that shown here. However, variation in the proton density and/or positioning relative to the coil could also introduce noise when absolute signal change is used. Hence, an evaluation of these two approaches with clinical test-retest data is needed to determine which approach should be used for clinical studies.

References: [1] Tofts P, Brix G, *et al*., JMRI, 10:223 – 232, 1999. [2] Evelhoch J, JMRI 10:254–259, 1999. [3] Leach M, Brindle K, *et al.*, Brit J Cancer 92:1599-1610, 2005. [4] Simpson N, He Z, Evelhoch J, Magn Reson Med, pp. 42 – 52, 1999. [5] Galbraith S, Lodge M, *et al.,* NMR Biomed, pp. 132 – 142, 2002. [6] Gupta R, J Magn Reson, 25:231, 1977. [7] Haacke M, Brown R, *et al.,* MRI: Physical Principles and Sequence Design, pp. 649 – 650, 1999.