5238

Direct Comparison of Dynamic Susceptibility Weighted MR Perfusion with CT Perfusion in Brain Tumors

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Introduction:

Contrast Agents (CAs) are widely used as indicators to study quantitative perfusion and Blood Brain Barrier (BBB) permeability in MRI, and are useful in characterizing pathology [1]. A common assumption is that the relationship between longitudinal relaxation rate change and Gd concentration is linear. In general, this assumption depends on the size of the molecules to which the Gd ion is attached and the MR pulse sequence parameters (TR, flip angle, etc) used to measure the relaxation rate. MR measurement of CA concentration plays a crucial role in quantification of kinetic model parameters (K^{trans}, PS product, cerebral blood volume – CBV - and cerebral blood flow - CBF). However, nonlinearities in the MR response (usually a measure of the change in R_1, where $R_1 = 1/T_1$) with CA concentration can substantially bias parametric estimates of cerebrovascular physiology. Look-Locker (LL) methods for estimating ΔR_1, show no evidence of bias in their estimates of tissue CA concentration [3, 4]. In other sequences, the T_2* contrast mechanism can bias the temporal estimate of T_1 [5], because only the image intensity of the n^{th} study after contrast administration is available to calculate T_1. A Dual-Echo Gradient Echo (2GE) sequence is a modified version of a sequence in common use for dynamic contrast enhanced (DCE) estimates of vascular physiology. This sequence will allow the separate assessment of T_1- and T_2* contrast mechanisms. We hypothesized that, given 2GE data as a basis set, nonlinearities due to water exchange and T_2* contrast in 2GE imaging could be addressed by training an ANN against an MRI measure that is known to be linear (LL) in concentration. In this study an adaptive neural network (ANN) was trained by LL sequences (known to be linear in CA concentration) to estimate CA concentration from 2GE pulse sequence (linearity unknown).

Material and Methods:

In this study it is hypothesized that, given a set of extracted features from 2GE sequences, an ANN can be trained to estimate temporal R_1 changes. To train and test the ANN, four Fisher rats (Female, 0.150 Kg) with 9L tumor were studied. Mean tumor age was 17.2 ± 0.8 days (range 16 to 18 days) for all animals. In MRI procedures, two initial LL image sets (24 small-tip-angle ~ 18º, TE 4 ms, at 50 ms intervals, TR=2.2 sec , 128X64, FOV=32 mm, three 2 mm slices) were followed by 2GE images (two gradient echoes at 3.4 and 6.8 ms, ~18° pulse, TR=60 ms, 3 slices of 2 mm thickness, FOV= 32 mm, 128x64, 4 seconds per image set) with the CA injection (140 μM Gd-BSA in 0.5 ml, slow IV push over ~ 1 min) at time point 14, and then two more LL data sets were collected (See Figure-1). As shown in Figure-1, using a physically meaningful and independent from system gain feature set (μ_1, μ_2, μ_3, and μ_4) extracted from 7T Dual Gradient Echo signals, an ANN was trained and tested with the ΔR_1 maps estimated by the LL technique. The feature set was constructed from the pure components (R_1, and R_2) of 2GE sequences before and after CA administration. The R_1 maps fitted from the pre and post injection Look-Locker sequence were used as the training set. Features extracted from the last part (last 8 sets of echoes in an approximate steady-state with CA constant in the tumor and vascular bed), and the 3rd through the 10th echoes (first part) before CA bolus injection were averaged and presented to the feature extractor system. The ANN was trained by at small value (~0) for the first part and the actual R_1 change estimated by the LL for the last part. The ANN was trained and validated using KFCV method, optimized by maximizing the Area Under Receiver Operator Characteristic (AUROCC) [6], and validated by 10500 samples with 60 folds and 175 samples in each randomly split fold.

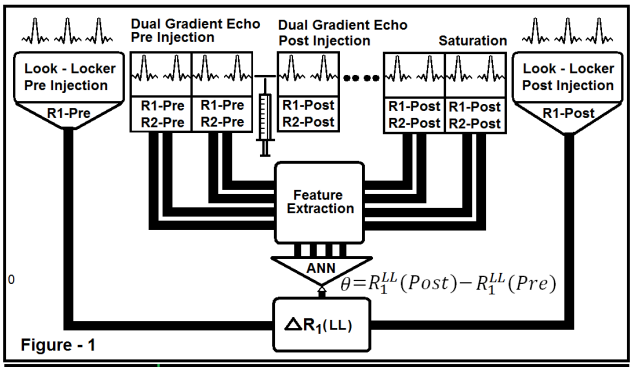

Figure - 1

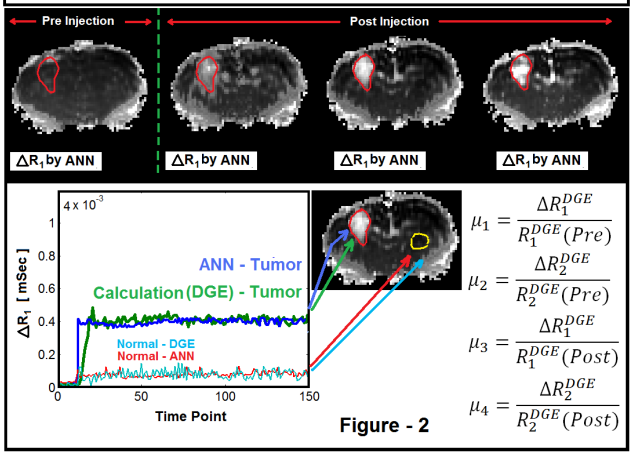

Figure - 2

Results and Discussions:

The ANN: 4:7:5:1 was optimal at AUROC=0.910. The trained ANN (4:7:5:1) was applied to the 2GE images of the four animals to generate a time course of R_1 maps, including the pre and post injection time points. Figure 2 shows a set of ΔR_1 maps in tumor and normal areas of one animal, generated by the trained ANN for all time points (150) before and after CA administration. The plots in figure-2 compare the trained ANN's estimate of the time course of ΔR_1 in the normal and tumor ROIs to the ΔR_1 calculated by the 2GE equation. As shown in this figure, the ΔR_1 estimated by the ANN for the tumor area is highly correlated (*r=0.89, p<0.0001*) with ΔR_1 generated by calculation. Note that in the tumor the raising time is quite different between the two estimates, but the general shape of the time behavior appears consistent. Of particular note is the agreement between the ANN estimate of ΔR_1 (averaged pixel-by-pixel) and the ROI estimate of ΔR_1 by calculation. Results imply that in the normal and leaky areas, the trained ANN with the slow pulse sequence (LL) produces the same levels of CA concentrations as the fast imaging technique (2GE) does. However, the ANN provides a fast rising time compare to the calculation. Because the ΔR_1 time course appears to generate linear Patlak plots (i.e., the systematic error introduced affects both input and response equally). The ANN, on the other hand, appears to be generating estimates of ΔR_1 that are close to known values of ΔR_1 in tumorous tissue at 7T. Thus, this example demonstrates the feasibility of applying an ANN to the problem of estimating ΔR_1 in fast imaging techniques (2GE) as function of time before and after injection of CA.

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