Accuracy of T1-Fitting for Pharmacokinetic Analysis of Dynamic Contrast-Enhanced MRI

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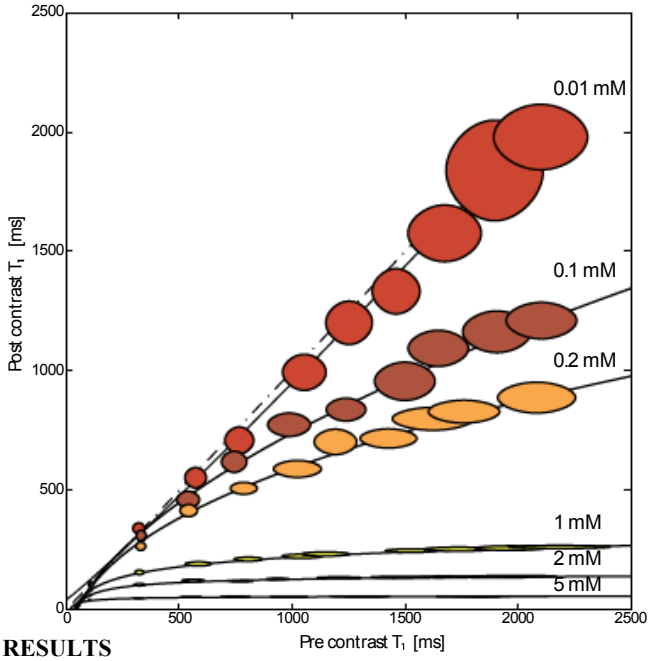
INTRODUCTION

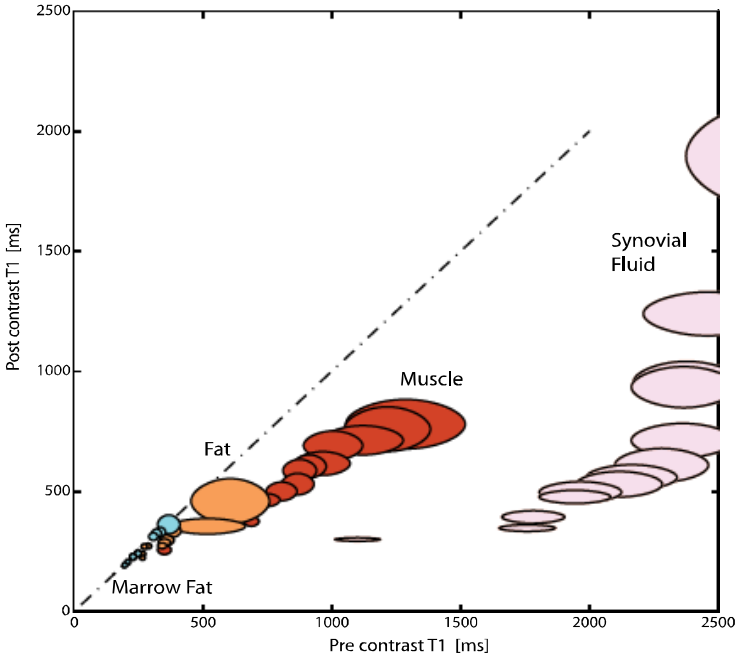
Pharmacokinetic Analysis (PKA) using Dynamic Contrast-Enhanced MRI (DCE-MRI) requires good estimates of the Arterial Input Function (AIF). In DCE-MRI a Gd-based contrast agent (CA) is injected and the bolus passage is monitored over time. Concentration curves are calculated based on measured signal enhancement, the relaxivity r_1 of the CA, and pre-contrast T_1-maps; concentration is usually approximated by $S(t)/S(0)-1 \approx T_{1pre}r_1[CA]$. The varying flip angle method (VFA) calculates a T_1-map using a series of spoiled gradient echo (SGE) scans with a range of flip angles. T_1-maps are generated by solving the SGE signal equations for T_1 and M_0 (Deoni, MRM(49), 515–526, 2003). After CA injection, the T_1 shortens in proportion to concentration, which results in two effects: signal increases, and the peak signal shifts to larger flip angles. Both effects are potentially beneficial for the accuracy of the T_1-fitting procedure, and thus more accurate concentration curves. This work examines the possibility of using post-contrast T_1-maps for concentration curve calculation, and effectively use $S(t)/S(e)-1 \approx T_{1post}r_1[CA]$ (where the *e* indicates end of dynamic scan). Goal is to show that in DCE-MRI studies the accuracy of T_1-mapping increases when the VFA method is acquired after CA administration.

METHODS & MATERIALS

Using the SGE signal equation ($S = M0*(1-\exp(-TR/T_1))*\sin(a)/(1-\cos(a)*\exp(-TR/T_1))$) curves are simulated for T_{1pre} values in the range 100-2000 ms, and for corresponding T_{1post} values in the presence of a range of contrast agent concentrations (0.01, 0.1, 1, 2, and 5 mmol L^{-1}). Normally distributed noise is added to both sets of curves with a standard deviation equal to 10% of the maximum signal of the T_{1pre} value (M_0=1 for both). T_1 and M_0 values are numerically fitted. For each set of T_{1pre}/T_{1post} this procedure is repeated 25 times.

In an ongoing study, three knee osteoarthritis patients are included. MR scanning is performed on a 3T system (Philips Achieva, Philips Health Care, Best, The Netherlands) using a 8-channel knee coil. T_1-mapping is performed using the VFA method (SGE sequence, TR/TE=8/4 ms, flip angles 2, 5, 7, 10, 15, 20, 25, 30, 40, and 60 degrees, 108x108 matrix size, 0.78x0.78 mm pixel size, 2.5 mm thickness, acquisition time 20s per angle). CA is administered intravenously (Dotarem, Guerbet, The Netherlands, 0.5 mmol ml^{-1}, r_1 = 3.4 L $mmol^{-1}$ s^{-1}), followed by a saline flush (MedRad power injector). T_1-scans are acquired before CA administration and after dynamic scan completion. Pre- and post-contrast T_1-maps are calculated and ROIs are drawn in homogeneous regions of 4 tissues (marrow fat, fat, muscle, and synovial fluid). For each ROI the mean and standard deviation of pre- and post-contrast T_1 are calculated. The signal-to-noise ratio (SNR) is calculated by dividing the mean by the standard deviation.





RESULTS

The left figure shows the results of the simulation experiment. For 0.01, 0.1, 0.2, 1, 2, and 5 mM concentrations of CA the mean and standard deviation of fitted T_1-values are shown. The axes of each ellipse are set to the standard deviation of the corresponding measurement. Circles indicate equal standard deviation in pre- and post-contrast estimates, "horizontal" ellipses indicate larger standard deviations for the T_{1pre}-measurement compared to T_{1post}. Clearly, for higher concentrations of CA the standard deviation of the T_{1post}-fit is smaller than for T_{1pre}. The right figure shows the standard deviation of the fitted T_1-values in the patient data. Fitted T_{1pre} and T_{1post} values in the same ROIs show a decrease in standard deviation which is, depending on the enhancement, varying from no change in bone marrow to a reduction to 30% in muscle and synovial fluid. Again, for higher concentrations of CA the standard deviation of the T_{1post}-fit is smaller than the T_{1pre}-fit. The SNR over all ROIs (n=46) is 12% higher for the T_{1post}-fit. Calculated for only the muscle and synovial fluid ROIs (n=25) the SNR is 20% higher for the T_{1post}-fit.

DISCUSSION

The use of CA increases the signal in T_1-weighted images and shifts the signal peak to larger flip angles. Both effects are beneficial for calculation of T_1-maps afer administration of CA. A more accurate estimate of T1 translates linearly to a more accurate estimate of the concentration curve, which is of importance for PKA. The results show that the standard deviation decreases and SNR increases using the post contrast T_1-fit. The post-contrast T_1-map yield estimates that are, in the worst case equal, and in all other cases better than the pre-contrast T_1-map for use in DCE-MRI and PKA.