Sensitivity Analysis of Cross-relaxation Imaging

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Introduction: Cross-relaxation imaging is an efficient method of obtaining quantitative maps of the bound pool fraction (*f*) and the cross-relaxation rate (*k*) of brain tissue (1). The maps are calculated using a nonlinear fitting procedure that relies on the two-pool pulsed MT model (2) and depends on a priori assumptions of the parameters T_2^B and R_1^B ($1/T_1^B$) for the bound pool, as well as the product $T_2^F R_1^F$ for the free pool. We performed a sensitivity analysis of the fitting procedure to determine the a priori parameters that give the best fit to the two-pool model.

Procedure: Our measurement procedure replicates the method of Yarnykh and Yuan (1). Three volunteers are subjected to four variable flip-angle T1-weighted scans (TR = 20ms, α = 4°, 10°, 20°, 30°) followed by four variable offset frequency MT scans (TR = 32ms, α = 10°, Δ = 3, 6, 9, 12 kHz) on a 1.5-T GE scanner using a 8-channel head coil. The T1-weighted scans provide a R_1^F map (3), which is used to predict the measured signal of the MT scans. The prediction model makes a priori assumptions about all unknown parameters except for *k* and *f*. A non-linear least-squares algorithm is used to find the *k* and *f* values that minimize the prediction error. In order to determine the sensitivity of the *k* and *f*-maps to a priori parameters, we varied these parameters over the biologically plausible range (T_2^B = 1-3μs, R_1^B = 0-3ms, and $T_2^F R_1^F$ = .03-.07) (1, 4, 5). For each combination of parameters we obtained unique *k* and *f* maps, and then we calculated the mean RMS difference between the model fit and the data.

Results: The *k* and *f* maps in the top half of Figure 1 are reconstructed with the a priori parameters recommended by Yarnykh and Yuan, and our results match their findings. The bottom half of Figure 1 represents the proportion change in the *k* and *f* values as the a priori parameters are varied across their plausible range. The *f* values were nearly linearly proportional to the parameter changes, but the *k* map variations were less predictable. In order to determine how this variability reflects on the quality of the fits, we looked for the parameters that give the best quality of fit (smallest mean RMS difference). While the fit quality was not significantly affected by the variations in R_1^B and $T_2^F R_1^F$, it turned out that varying T_2^B from 9μs to 13μs resulted in changes in the quality of fit on the order of 30% for subject 2 and 50% for subjects 1 and 3 (see Figure 2). Additionally, we discovered that lower T_2^B values favor the fit quality, with all three subjects showing best fits when the T_2^B parameter was on the order of 8-9μs. We then did a gray/white matter brain segmentation and found that the white matter fits were better. The white matter also seemed to exhibit a shorter T_2^B value, although this was more noticeable in subject 1 than in the other two subjects.

Discussion: Cross-relaxation imaging is sensitive to the choice of a priori parameters used in the fitting procedure. While it is hard to determine the optimal parameters for accurate *k*-and *f*-map reconstruction, the quality of fit provides a robust and stable metric in deciding on them. The convex shape of the residual with respect to the T_2^B parameter strongly suggests that bound pool relaxation rates of 8-9μs are in best agreement with the proposed two-pool model.

References:

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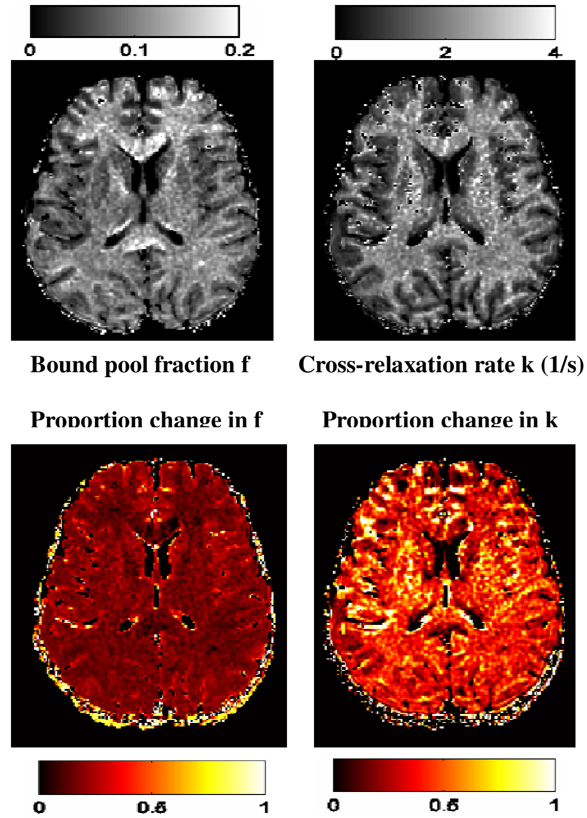

Figure 1: *Top*: *f*-map (left) and *k*-map (right) reconstructions for T_2^B= 11μs, $T_2^F R_1^F$ = .055, R_1^B= 1ms. *Bottom:* Plot of the proportion change of *f* (left) and *k* values (right) when the a priori parameters are varied from one extreme to the other. The colormap shows that the *k*-maps are more sensitive to the a priori parameters (hence the more intensive colors), and they also show more variability across tissues (hence the color non-uniformity)

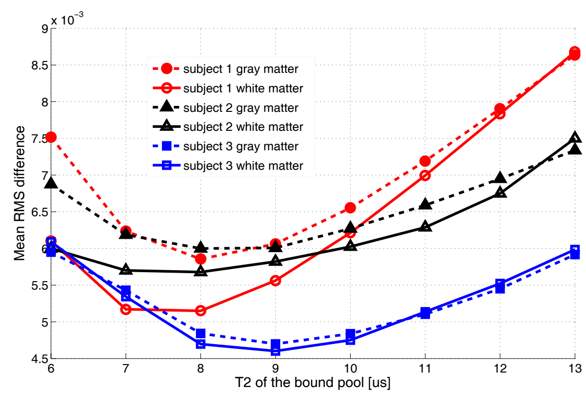

Figure 2: Quality of fit plotted as a function of T_2^B. All three subjects have a U-shaped quality of fit curve, with a minimum around 8-9μs. Also, white matter tends to be better fitted compared to gray matter and to have a slightly lower optimal T_2^B value.