Effect of b-Value and TE on the Estimation of Intramyocellular Diffusion Properties in the Presence of Edema

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Introduction

Muscle fiber damage can result from repeated, high intensity lengthening contractions in healthy muscle and by activities of daily living in diseases such as muscular dystrophy. This damage can include sarcomere disruption and a loss of membrane integrity and may provoke an inflammatory response. Because there are existing techniques for observing edema (*e.g.*, STIR and T_2-weighted imaging), it would be beneficial to have a tool that can examine muscle fiber damage distinctly from edema. Several recent studies have suggested that elements of the diffusion tensor (**D**), and in particular the third eigenvalue (λ_3) and fractional anisotropy (*FA*), may reflect muscle damage in a distinct manner from T_2 (1-4). However, the interpretation of these data may not be straightforward, as edema may introduce additional T_2 and diffusion components (4). The longer T_2 and larger magnitude, more isotropic diffusion tensor that is associated with edema ($T_{2,E}$ and $\mathbf{D}_E$, respectively) may introduce errors into the estimation of the intracellular diffusion tensor ($\mathbf{D}_I$) in echo time (*TE*), intracellular volume fraction (P_I), signal to noise ratio (*SNR*), and diffusion-weighting (*b*-) value dependent fashions. Therefore, the purpose of this study was to use Monte Carlo simulations in order to examine the dependence of $\mathbf{D}_I$ estimation on these variables, in regions of interest (ROI's) of varying size.

Table 1. Compartmental NMR and diffusion properties

Parameter	Intracellular	Extracellular
λ_1 (x10^{-5} cm^2/s)	2.1	2.1
λ_2 (x10^{-5} cm^2/s)	1.66	2.1
λ_3 (x10^{-5} cm^2/s)	1.32	2.1
T_1 (ms)	1200	1200
T_2 (ms)	35	125

Methods

Model Tissue Definition The simulations were performed in Matlab v 7.0.1 and were similar to those of Damon (5). A slowly exchanging, two-compartment model was assumed (Table 1).

Simulated Image Formation The signal S was calculated for simulated images according to:

$$S = P_I \cdot \left(1-\exp\left(-TR/T_{1,I}\right)\right)\cdot \exp\left(-TE/T_{2,I}\right)\cdot \exp\left(-b\cdot r\cdot \mathbf{D}_I \cdot r^T\right) + P_E \cdot \left(1-\exp\left(-TR/T_{1,E}\right)\right)\cdot \exp\left(-TE/T_{2,E}\right)\cdot \exp\left(-b\cdot r\cdot \mathbf{D}_E \cdot r^T\right)$$

where *r* indicates each row of a diffusion weighting matrix **R** formed with weighting along the *X, Y, Z, XY, XZ*, and *YZ* directions, the superscript *T* indicates the transpose, and P_E=(1-P_I). The *b*-values were 145, 290…1160 s/mm^2; *TR*/*TE*=5000/30, 40…90 ms; and P_I=0.6, 0.7, 0.8, and 0.9. Rician noise was added to form images with *SNR* values of 10, 15, 20, 30, 40, 60, 80, 100, 120, and 140. 1000 independent realizations of noise were performed for all combinations of *SNR, TE, b*, and P_I.

Data Analysis For each noise realization, the mean signal *S* was measured in a single-voxel and in 27- and 100- voxel ROI's. **D** was formed by weighted least squares regression of the natural log of *S* on *b* as previously described (5) and diagonalized using the *eigs* function. For each combination of *b, SNR, TE*, and P_I, the mean and standard deviation (SD) of the first-third eigenvalues (λ_1-λ_3), mean apparent diffusion coefficient (ADC), and *FA* were calculated; the angular uncertainty (*AU*) was calculated as the angular deviation of the estimated to known value for the first eigenvector (ε_1) and the distribution was characterized with its SD.

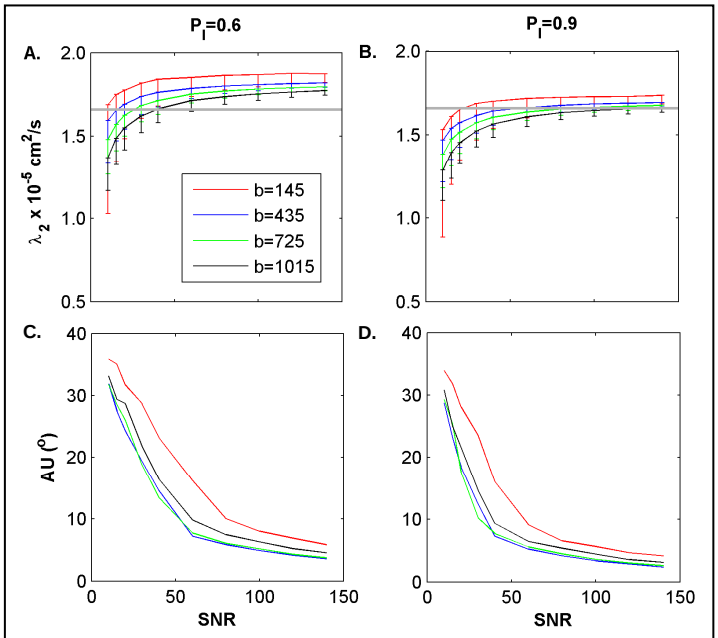

Figure 1. Effects of P_I, *SNR*, and *b*-value on selected elements of **D** for TE=30 ms in single voxels. **Panels A-B** show mean and SD of λ_2, increasing with decreasing P_I; increasing precisions with increased SNR; and lower λ_2 estimates with increasing *b*. **Panels C-D** show decreasing (ie, better) *AU* with increasing SNR and a minimum at *b*=435-725 s/mm^2; *AU* decreases with increasing P_I.

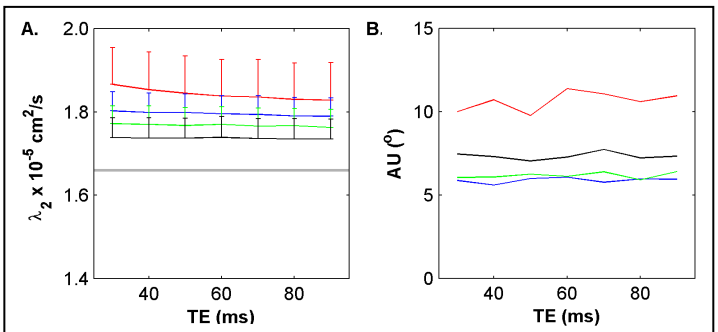

Figure 2. Effects of *TE* and *b*-value on λ_2 and *AU* at P_I=0.6 SNR=80 in single voxels. **Panel A** shows mean and SD of λ_2 with a relative absence of effect of TE for typical *b*-values (435-725 s/mm^2) . **Panel B** shows the lack of sensitivity of *AU* to *TE*. See legend to Figure 1.

Results and Discussion

Consistent with the assumptions, there was no effect of P_I on the estimate of λ_1 (not shown). The transverse diffusivity and ADC estimates increased with decreasing P_I , increasing *SNR*, and decreasing *b* (example single-voxel data are shown in Figure 1). *AU* also decreased (improved) with increasing *SNR*. Similar trends but with lower SD were observed for larger ROI sizes. For low values of *b*, there was a modest decrease in λ_2, λ_3, and ADC with increasing TE; but for typical values of *b* and higher, these parameters were essentially TE-insensitive. Also, *AU* was *TE*-insensitive.

These data indicate that for diffusion tensor imaging to be used for assessing muscle fiber damage *per se*, the degree of edema must be quantified through other means so that the transverse diffusivities can be appropriately interpreted. The estimates are insensitive to *TE*; however these simulations do not account for diffusion time variations that may occur as *TE* changes.

References

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