Dependence of Fractional Order Diffusion Model Parameters on Diffusion Time

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INTRODUCTION

At high b-values (e.g., ≥1,500 s/mm^2), it is well known that diffusion-induced MR signal loss in the brain tissue exhibits anomalous behavior that cannot be described by a mono-exponential function. This phenomenon has been attributed to tissue heterogeneity manifested by cellular structures, cell membranes, and/or intra- and extra-cellular spaces [1]. Over the past few years, a number of groups have proposed various models [2-7] to describe diffusion signals at high b-values with a common goal to establish the interrelation between diffusion measurements and tissue microstructures. Recently, a diffusion model employing fractional order calculus was reported [6, 7]. By generalizing the Bloch-Torrey equation using fractional order derivatives in space, this model describes anomalous diffusion by three parameters: diffusion coefficient (D), fractional order spatial derivative β ($0<\beta<1$), and a spatial variable μ (in units of μm). Although it has been suggested that β and μ can be correlated with the degree of tissue heterogeneity [6], the biophysical basis of this correlation is yet to be established. In this study, we have investigated the effects of diffusion times on the three parameters obtained from the fractional order diffusion model, and report experimental findings that will help establish the interrelation between the diffusion parameters and tissue microstructures.

METHODS

According to the fractional order diffusion model, the diffusion-induced signal loss S is given by [6, 7]

$$S = S_0 \exp[-D\mu^{2(\beta-1)}(\gamma G_d \delta)^{2\beta}(\Delta - \frac{2\beta-1}{2\beta+1}\delta)] \qquad (1)$$

where G_d, δ, and Δ are the gradient amplitude, pulse width, and pulse separation of a Stejskal-Tanner diffusion gradient pulse pair, respectively. To investigate the dependence of D, β and μ on diffusion times δ and Δ, two imaging experiments were carried out on healthy human brains at 3.0 T (GE HDx Signa scanner, GE Health Care, Waukesha, WI) using a customized single-shot EPI sequence with an 8-channel head coil. In the first experiment, three δ values were selected at 32.2, 35.2, and 38.2 ms. At each δ value, Δ was fixed at 55.68 ms while G_d was varied from 0 to 3.2 G/cm to produce 15 b-values from 0 to 4387 s/mm^2 with a constant TE of 108ms. In the second experiment, three Δ values were selected at 39.18, 47.43, and 55.68 ms. At each Δ value, δ and TE were fixed at 32.2 ms and 102 ms, respectively, and G_d varied accordingly to produce 15 b-values in the same range. In both experiments, the acquisition parameters were: TR = 3000 ms, slice thickness = 5 mm, slice gap = 1.5mm, FOV = (22 cm)^2, matrix size =256x256, and acceleration factor =2 for parallel imaging based on SENSE. For each diffusion data set, image intensities as a function of G_d were fitted to Eq. (1) using a Levenberg-Marquardt fitting algorithm to obtain parameters D, β and μ on a pixel-by-pixel basis.

RESULTS

Figure 1 displays a set of representative maps of D, β and μ with each column corresponding to each of the three Δ values. With increased diffusion time, the D and β maps (the first and the second row in Fig. 1, respectively) did not change substantially. However, the change in the μ map was striking for both gray and white matter. The dependence of μ on Δ is further illustrated in Fig. 2 for two regions of interest, a white matter region selected from the genu of the corpus callosum and a gray matter region from the putamen, where μ increased almost linearly with Δ. The dependence of D, β and μ on δ (data not shown) was similar to the results in Figs. 1 and 2, although the difference in μ maps was not as striking due to the relatively narrow range of δ values constrained by signal-to-noise considerations.

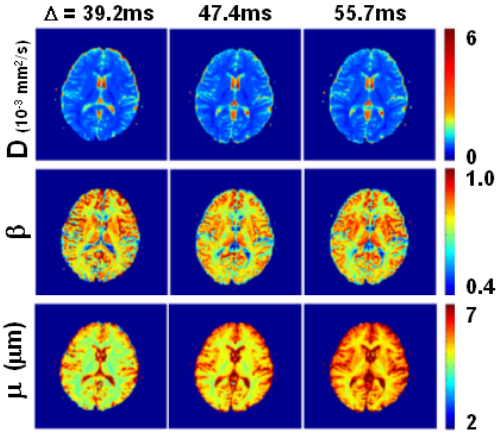

Fig. 1 Parametric diffusion maps obtained from the fractional order diffusion model at different Δ's.

DISCUSSION

Previous studies have reported that β decreases as the degrees of tissue heterogeneity or diffusion restriction increase [6,7]. The relationship between μ and tissue structural complexity has not been established. This is partly because of the relatively short δ and Δ values employed in the previous studies, and partly because μ becomes indeterminate when β approaches 1 (see Eq. (1)) as in the case of cerebrospinal fluid (CSF) where there are no barriers to diffusion for the given experimental conditions. At a relatively short diffusion time, the degree of diffusion restriction may not be fully experienced by water molecules, resulting in a low μ value and relatively low contrast between different tissue environments (Fig. 1). As the diffusion time becomes longer, the amount of diffusion restriction and tissue structural differences can be better explored by diffusing water molecules, revealing a larger μ value and increased tissue contrast (Figs. 1 and 2).

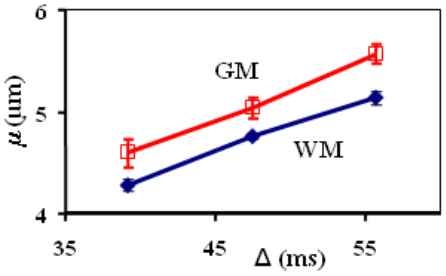

Fig. 2 μ as a function of Δ for a white matter (WM; blue) and a gray matter (GM; red) ROI.

CONCLUSIONS

We have observed a strong dependence of μ value in the fractional order diffusion model on diffusion time. This provides evidence suggesting that μ may reflect the degree of diffusion restriction and serve as a link to the mean diffusion free length on tissues or structured materials. The parameter μ, in conjunction with β, may provide a new way to probe tissue structures using high b-value diffusion imaging with a fractional order diffusion model. Future studies are planned to use this model in clinical studies of brain tumors.

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