Does skeletal muscle contain fast and slow diffusion components in high b-value diffusion weighted imaging (DWI)?

Yoshikazu Okamoto[1], Tomonori Isobe[1], and Yuji Hirano[1]

[1]*University of Tsukuba Hospital, Tsukuba, Ibaraki, Japan*

Target audience This presentation will be beneficial for the musculoskeletal biologists and MRI researchers

Purpose

The extent of water diffusion is defined by the b-value in diffusion-weighted imaging (DWI) acquired using MRI. The relative contribution to the diffusion-weighted MRI signal becomes significant only at very low b values, allowing diffusion and perfusion effects to be separated. Moreover, previous studies have found that the brain and prostate have two different diffusion rates, namely, fast and slow diffusion components [1-5].

The assessment of microscopic anatomy of the skeletal muscle using DTI has mostly been performed using b-values of 400-700 mm/sec^2 (i.e., medium b-values) [6-9] because skeletal muscle has low T2 values. Such studies have concluded that water diffusion measurement primarily reflects intracellular water diffusion, and that muscle cell membranes can account for most of the water diffusion restriction [6-9]. Hatakenaka et al. reported that λ_1 and λ_3 varied in response to the diameter of the long and short axes due to passive muscle contraction and elongation, which suggests that the eigenvalues reflected intracellular water diffusion [6]. Galbán et al. observed changes in diffusion properties due to aging using DTI, and they reported that λ_1, λ_2, and λ_3 values decreased with age, which they attributed to changes in muscle fiber size. They argued that atrophy of the skeletal muscle fiber itself caused the decreased eigenvalues, which represented intracellular water diffusion [7]. Both studies were performed using medium b-value for DTI.

However, these conclusions may not fully explain the findings from these studies if skeletal muscle had both fast and slow diffusion components as observed in brain and prostate. Slow diffusion generally reflects intracellular water diffusion and fast diffusion generally reflects extracellular water diffusion according to the past literature [10-13]. In this situation, if the signal from the skeletal muscle truly represented intracellular water diffusion in the medium b-values on DTI as Hatakenaka and Galbán et al. concluded, the slow diffusion had to be a main signal in the medium b-values on DTI, and the effect of fast diffusion to the main signal had to be disappeared until at most 400 mm/sec^2 of b-value. I supposed it was unrealistic.

To investigate this possibility, we tried to elucidate whether fast and slow diffusion components exist in the skeletal muscle. The purpose of this study is to examine whether fast and slow diffusion components are also present in skeletal muscle using DWIs with multiple b-values, and to consider its relevance to the microanatomy.

Methods

Eleven healthy male volunteers in their 20s were recruited (mean age, 27.2 years). 3T MRI (Achieva release 2.6, Philips, Best, the Netherlands) was used in this study. The soleus muscle (SOL) was scanned by 32-channel cardiac coil. The following scan parameters were used: TR, 3,000 msec; TE, 58 msec; FOV, 320 mm; Matrix, 64; voxel size, 5/5/10 mm; slice thickness, 10 mm; gap, 5 mm; number of slices, 5; NSA, 1; the total scan time was 9 minutes 12 seconds. Scans were exponentially incremented every TR period to cover b-factors from 0 to 3,500 s/mm2 in 16 steps. The acquired datasets were transferred to a personal computer, and data analysis was performed with in-house software.

Regions of interest (ROIs) were chosen as 390-410 mm2 circular shapes by an experienced radiologist based on exact measurements of the coordinate point on T2-weighted images (Fig. 1). Fitting was performed using both monoexponential functions and biexponential decay functions of the following equation:

S = Afastexp(-ADCfastb)+Aslowexp(-ADCslowb) (1)

Here, S is the signal intensity; b is the b-factor; Afast and Aslow are the apparent amplitudes of the fast and slow components, respectively; and ADCfast and ADCslow are the apparent diffusion coefficients (ADCs) of the fast and slow components, respectively. The first b-factor (b = 0) was excluded from the analyses to decrease contamination from any perfusion component. A statistical comparison between monoexponential (i.e., Aslow = 0 in Eq. (1)) and biexponential fits was performed in each individual case by F tests using $\chi 2$ values for each type of fit. A statistically improved fit was considered for $P < 0.05$ in the F test.

Results & Discussion

Detailed diffusion datasets using multiple b-factors up to 3500 s/mm2 were successfully acquired from all subjects. Fig. 1 shows semi-log plots of improved fits over monoexponential functions as assessed by F tests in all cases. Decay curves are characterized with biexponential functions for all SOL ($P < 0.05$). Table 1 summarizes the intersubject means ± SD of the biexponential parameters, ADC of the biexponential fits, and ADC of the monoexponential fits.

	Fast ADC (×10-3mm2/s)	Slow ADC (×10-3mm2/s)	Fast component fraction of (%)	Slow component fraction (%)	Monoexponential ADC (×10-3mm2/s)
SOL	1.68 ± 0.14	0.26 ± 0.17	92 ± 5	8 ± 5	1.43 ± 0.05

Table 1
Interindividual means ± SD of biexponential parameters ADC_{fast} and ADC_{slow} and the fast and slow diffusion component fractions at the SOL

The fast versus slow diffusion fractions were slightly greater than 9.0 versus less than 1.0. Therefore, water diffusion in skeletal muscle appears to consist primarily of mono-exponential fast diffusion, with a very small amount of slow diffusion. These biexponential components differ from those of other organs, such as the brain, prostate, and liver, in which fast diffusion primarily occurs in the extracellular space, while slow diffusion occurs in the intracellular space; thus, the cell membrane functions as a restrictive factor. Slow diffusion in skeletal muscle might be restricted by water or another substance, because ADCslow values were very small (0.26); in addition, slow diffusion fraction values were also very small (8%).

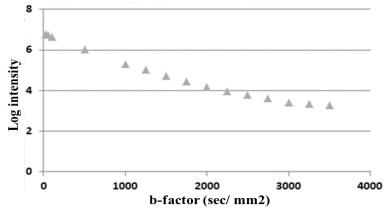

Figure 1
This semi-log plot shows typical signal decay vs. b-factor for the SOL.

The assessment of microscopic anatomy of the skeletal muscle using DTI has primarily been performed using b-values of 400-700 mm/sec2 (i.e., medium b-values) [6] as we described above. Such studies have concluded that water diffusion measurement primarily reflects intracellular water diffusion. However, this is not possible in other organs, because fast diffusion, which generally reflects extracellular water diffusion, must appear and disappear until 400 mm/sec2 is reached. Several studies have reported that the intracellular space in skeletal muscle is much larger and wider compared to that of other organs. Saab et al. studied the ratio of intra- and extracellular space fractions using a custom-made MRI. These investigators reported an extracellular to intracellular space ratio of 88:11 [14]. Additionally, studies published in the 1980s that calculated the extracellular to intracellular space ratio of skeletal muscle by frequent needle biopsy and blood testing after exercise also reported it to be approximately 9:1 [15]. Moreover, the size and shape of skeletal muscle cells is unique: while the diameter of the short axis is micrometer level, that of the long axis occasionally approaches the millimeter or centimeter scale. Therefore, skeletal muscle cells have an extremely long long axis, resulting in a massive intracellular space. We hypothesized that fast diffusion of skeletal muscle is mainly observed in the intracellular space due to its massive size.

Conclusion The results of this study indicate that skeletal muscle has both fast and slow diffusion components. However, we suggest that the water diffusion of skeletal muscle should be considered to be primarily monoexponential, with a very small slow diffusion component. The fast diffusion of skeletal muscle might be mainly observed in the intracellular space due to its massive size.

References 1) NMR Biomed 1999; 12: 51-62.2) Magn Reson Med 1996; 36: 847-857.3) Magn Reson Med 2004; 51:278-285.4) Magn Reson Imaging 2009; 27:355-359.5) Magn Reson Imaging 2006; 24:563-568.6) J Magn Reson Imaging 2008; 27:932-937.7) J Gerontol A Biol Sci Med Sci 2007; 62:453-458.8) Eur Radiol; 2008:18:2303-2310.9) NMR Biomed 2009; 22:1047-1053.10) Magn Reson Med 1997; 37:825-832.11) NMR Biomed 1998; 11:11–18.12) Neuroscience 1999; 93:487–490.13) Magn Reson Med 1999; 41:137–142..14) Magn Reson Med 1999;42:150-15715) Am J Physiol 1982;243:271-280