The measurement and interpretation of intravoxel incoherent motion (IVIM) of skeletal muscle in vivo: preliminary results

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Introduction

The utility of skeletal muscle MRI has been largely limited in the clinical setting. However, recent research has focused on the assessment of the microscopic anatomy of skeletal muscle using MRI. For example, skeletal muscle cells and surrounding stroma were recently assessed at the micrometer level using water diffusion "direction" data acquired by diffusion tensor imaging (DTI) (1). However, diffusion "speed" in skeletal muscle has not been previously considered. We hypothesized that if skeletal muscle has a unique water diffusion speed, synergistic biological information might be obtained by considering the water diffusion "speed" in addition to "direction" when assessing microanatomy. The purpose of this study is to examine whether fast and slow diffusion components are present in skeletal muscle using the principle of IVIM, and to consider its significance in vivo (2, 3).

Materials & 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, and the flexor digitorum profundus muscle (FDP) was scanned by Flex-M 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:

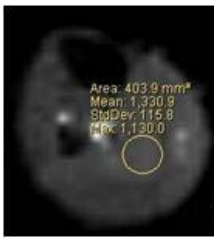

Figure 1
Measurement of the signal intensity and its SD at the SOL in a 26-year-old volunteer on DWI with of b-value = 0.

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 in the SOL and FDP.

A reproducibility study was also performed in two additional volunteers (A and B). SOL measurements were acquired six times in each volunteer using the same parameters and ROI settings described above. Average and standard deviations (SD) of the fast and slow diffusion fractions and the ADCfast and ADCslow were calculated for each volunteer.Fig. 2 shows semi-log plots of improved fits over monoexponential functions as assessed by F tests in all cases for the SOL and FDP ($P < 0.05$). Table 1 summarizes the intersubject means ± SD of the biexponential parameters and ADC of the biexponential fits for two muscles.

Results & Discussion

No statistically significant differences were observed for either the fast or slow diffusion fractions between the two muscles. Although ADCfast was also not significantly different between the SOL and FDP, ADCslow was significantly lower for FDP compared to SOL ($P < 0.01$; paired t-test). In the reproducibility study, all coefficients of variation (CV) were less than 10%.

The fast versus slow diffusion fractions were slightly greater than 9.0 versus less than 1.0, respectively, in both the calf and forearm. 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 for SOL, 0.02 for FDP); in addition, slow diffusion fraction values were also very small (3-8%).

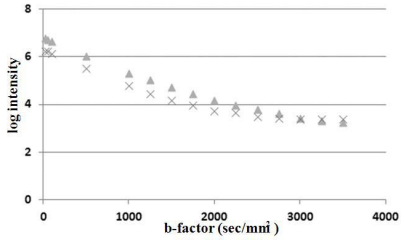

Figure 2
This semi-log plot shows typical signal decay vs. b-factor for the SOL and FDP ROIs of this volunteer.

The assessment of microscopic anatomy using DTI has primarily been performed using b-values of 400-700 mm/sec2 (i.e., medium b-values) (1). 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 (4). 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 (5). 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 suggest that fast diffusion of skeletal muscle is mainly observed in the intracellular space due to its massive size.

	Fast ADC (×10-3mm2/s)	Slow ADC (×10-3mm2/s)	Fast component fraction of (%)	Slow component fraction (%)
SOL	1.68 ± 0.14	0.26 ± 0.17	92 ± 5	8 ± 5
FDP	1.75 ± 0.22	0.02 ± 0.01	95 ± 1	5 ± 1

Table 1
Interindividual means ± SD of biexponential parameters ADCfast and ADCslow and the fast and slow diffusion component fractions at the SOL and FDP.

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.

References 1) J Magn Reson Imaging 2008;27:932-937 . 2) Invest Radiol. 2009;44:769-775 3) Radiology. 2008 ;249:891-899. 4) Magn Reson Med 1999;42:150-157 5) Am J Physiol 1982;243:271-280