Skeletal Muscle

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Target audience: This presentation is intended to inform those interested in the practical application of diffusion imaging methods to probe structure, function or pathology in skeletal muscle.

Objectives: To consider the properties of skeletal muscle pertinent to DWI and explain how and why optimal acquisition parameters may differ from those adopted in more familiar CNS applications.

Skeletal muscle makes up around 40% of adult human body mass and plays a vital role in health and function. Recently a number of potentially important diffusion imaging applications muscle have emerged for diagnosis and disease assessment, to provide biomarkers for trials of new therapies in neuromuscular diseases, and to study healthy muscle function and physiology [1].

The highly ordered structure of this tissue suggests the directional sensitivity of diffusion imaging may provide an almost perfect tool to probe myocellular organisation and function non-invasively, an observation recognised in early reports of MR diffusion imaging [2,3,4].

Diffusion imaging studies in humans have typically adapted the standard EPI sequences used for DTI of the brain, taking advantage of their temporal efficiency and robustness with respect to macroscopic tissue motion. However, the physical properties of skeletal muscle necessitate the adoption of acquisition parameters which may differ from those considered optimal in studies of the central nervous system:

Choice of Echo Time

Muscle water T_2s are quite low– around 35-40ms at 3T[5], implying low SNR[6] in DWI unless measures are taken to minimize TE while maintaining appropriate diffusion weighting. This has been achieved by careful choice of geometric parameters minimizing the EPI echo train-length and hence TE in spin-echo EPI acquisitions[7], or use of a stimulated echo diffusion preparation module[8,9].

Diffusion Weighting and Measurement Directions

The low T_2 of muscle is partially mitigated in SNR terms because healthy skeletal exhibits relatively high diffusivities, with tensor eigenvalues of the order of $\lambda_1 = 2.1\ 10^{-3}$ mm^2/s, $\lambda_2 = 1.6 \times 10^{-3}$ mm^2/s, and $\lambda_3 = 1.2 \times 10^{-3}$ mm^2/s [see table 41.2 in ref[1]], suggesting that optimal diffusion-weighting may be obtained with lower b-factors than commonly used for brain studies, and hence potentially shorter TEs. For accurate and precise tensor component estimation, optimal diffusion weightings must be derived taking into account practical SNR limitations, and being aware that in low signal regimes SNR changes caused e.g. by disease or other physiological processes may produce confounding bias in the tensor component estimation[6]. In practice values have been chosen in the range of b=400-700 s/mm^2(ref[10] and table 1).

While muscle tissue is highly structured and fibrous, the fibre geometry is less complex than in cerebral white matter reducing the need for high angular resolution diffusion-direction sampling. Studies of skeletal muscle in the limbs have typically used 6-15 directions (table 1).

Physiological and geometric dependence of diffusion metrics

In contrast to the brain, where changes in water diffusion are generally attributed to disease or the long term processes of maturation and aging, the diffusion properties of healthy muscle may change acutely as muscles contract due to loading or limb orientation[11,12], and after exercise[14]. While

opening up exciting avenues for muscle-function research, these observations may have implications for acquisition parameter optimisation, and suggest potential confounds which may require control in longitudinal studies of disease.

Fat infiltration

A common feature of neuromuscular diseases is the replacement or infiltration of muscle fibres with fat. The avoidance of chemical shift artefacts in EPI acquisitions, which may confound tractography studies or post-acquisition distortion correction procedures, requires effective fat-suppression[13]. On the other hand, there may also be intrinsic value in direct study of the diffusion properties of intra-or extra muscular fat by imaging[14] or spectroscopy[15], although the slow diffusivity of fat may require rather high b-values with risk of confounding macroscopic tissue motion artefacts.

Triggering

Cardiac triggering to reduce physiological motion artefacts has not been widely used in skeletal muscle DTI, although one study has suggested triggering may reduce measurement variance[9] and that the use of an outlier rejection procedure[16] during tensor reconstruction may further mitigate errors due to occasional macroscopic incoherent motion.

Discussion

Studies to date have demonstrated the rich possibilities of diffusion imaging in skeletal muscle using methods more or less directly translated from those routinely applied in CNS applications.
Future work will see improvements in spatial resolution and SNR with increasingly sophisticated acquisition strategies targeting the complementary measurement domains of muscle functional geometry and histopathologically relevant muscle microstructure.

Table 1 Selected acquisition parameters used for *in vivo* SE EPI-DTI studies of human skeletal muscle

Study	**Field Strength**	**Target**	**TE**	**averages**	**Sense factor**	**Spatial Resolution**	**Higher b-factor**	**diffusion directions**
Froelin 2012[7]	3T	Forearm	41ms	6	2	voxel size: 2 x 2 x 5 mm^3, matrix size 96 x 60	400 s/mm^2	15
Okamoto 2010[11]	1.5T	Lower limb	59ms	10	2	voxel size: 3.1 x 2.3 x 6 mm^3 matrix size 128 x 128	500 s/mm^2	6
Heemskerk 2009[17]	3T	Lower limb	48ms	n/a	1.2	voxel size: 6 x 1.5 x 1.5 mm; matrix size 96 x 64 slice	500 s/mm^2	10
Sinha 2011[18]	1.5T	Lower Limb	46ms	8	2	Voxel size 1.9x1.9x5 mm; voxel size 128x128	500 s/mm^2	6 and 13
Saupe 2009[10]	1.5T	Lower limb	44.3–67.4 ms	6	2	Voxel size 0.7x0.7x3mm matrix size, 256 × 256	125-1000 s/mm^2 (625 s/mm^2 with TE 60.6ms optimal)	15

Selected References

A number of groups have made important contributions to skeletal muscle diffusion imaging methods: the references cited are intended to be illustrative rather than comprehensive. The article by *Strijkers et al.*[1] provides an excellent overview.

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