Quantifying the mitochondrial content with diffusion MRI

Nicolas Moutal, Denis S Grebenkov, Sylvie Clerjon, Guilhem Pagès, J.-M. Bonny

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N. Moutal[1], *D. S. Grebenkov*[1], *S. Clerjon*[2], *G. Pages*[2], *and J.-M. Bonny*[2]
[1] PMC, Ecole Polytechnique, CNRS, IP Paris, F-91128 Palaiseau France
[2] AgroResonance - UR370 QuaPA, F-63122 Saint Genès Champanelle, France

Introduction: In this work, we show how diffusion MRI protocols with high b-values may be applied to a non-invasive quantification of mitochondria and other microscopic organelles. While mitochondria play a major biochemical role and are related to several diseases, their current studies require invasive microscopy techniques such as TEM. Therefore, solving this challenging problem with diffusion MRI would be of great clinical interest.

Methods: The experiments were conducted *ex vivo* on pork muscle at a temperature of 16°C. We applied a PGSE sequence with δ=3.2ms, Δ=10ms, and b-values up to 10000s/mm^2, for 6 non-collinear gradient directions and 32x32 (0.3mm)^3 voxels. Additionnally, a fat suppression scheme [1] was employed to reduce the contribution from lipids. Two different muscle samples were analyzed: Masseter (M1), an oxidative muscle with high mitochondrial content, and Longissimus Dorsi (LD2), a glycolytic muscle with low mitochondrial content.

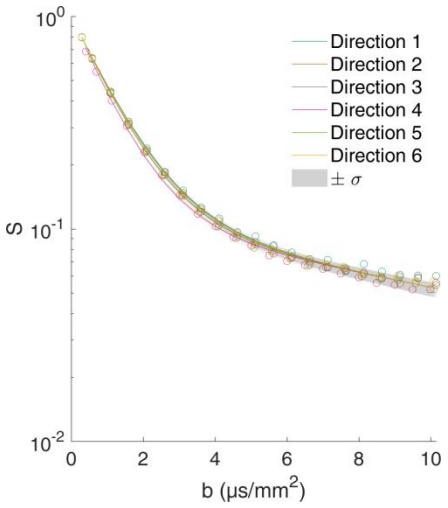

Fig.1 Signal from one voxel of sample M1 and different gradient directions (circles) and fit by Eq. 1 (lines). At high b-values, one observes a slow-decaying residual signal. The noise level is around 0.003.

Results and discussion: For both samples, the signal shows a fast decay at low b-values and a slow decay at high b-values (see Fig.1). The slow-decaying signal is attributed to water trapped inside mitochondria, a bi-exponential fit is applied:

$$S = S_0\left[(1-\rho)\exp\left(-b\sum_{i,j} e_i\, D^f_{i,j}\, e_j\right) + \rho\exp(-bD^s)\right] \quad \text{(Eq.1)}$$

where S_0 is the reference signal (at b=0), ρ is the mitochondrial water fraction, D^f is the apparent diffusion tensor of "fast" water inside muscle cells and D^s is the apparent diffusion coefficient of "slow" water inside mitochondria.

As mitochondria are filled with around 64% of water [2], one can infer the mitochondrial volume fraction (MVF) from ρ as $MVF \approx 1.5\rho$. Figure 2 shows the map of MVF for both samples. Sample M1 displays two regions with respectively high (~15%) and low (~5%) MVF whereas sample LD2 has a uniform low (~3%) MVF. These results are in qualitative agreement with the muscle type as discussed above, and the values are consistent with the literature (see [3] for a comparison with mouse and dolphin). Histological slices are planned in order to confirm and explain the existence of two different regions in sample M1.

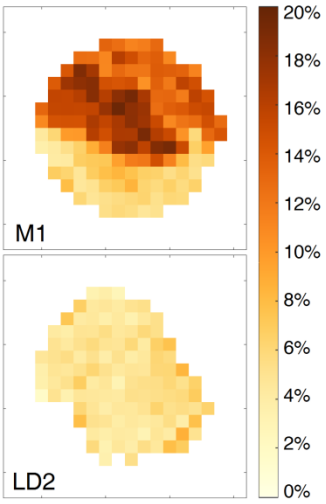

Fig.2 Estimated mitochondria volume fraction (MVF) for both samples.

Conclusion: The residual signal at high b-values in muscles is naturally explained by mitochondria. This work is a proof of concept and a prerequisite for developing *in vivo* methods to quantify the content of various organelles in muscle, e.g. for studying mitochondrial dysfunction in aging.

References: [1] J. M. Gomori et al., Radiology 168, 493-495 (1988).
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[3] B. Pathi et al., J. Exp. Biol. 215 (11), 1871-1883 (2012).