Dynamic changes in DTI eigenvalues and eigenvectors following ischemia-induced skeletal muscle damage

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Introduction:

Diffusion tensor imaging (DTI) is more and more used for tissue characterization in health and disease and for fiber tractography. The DTI indices derived from the diffusion tensor include the mean diffusion coefficient (ADC=Tr(D)/3)), calculated eigenvalues (λ_1, λ_2, λ_3) and eigenvectors (e1, e2, e3) and indices of diffusion anisotropy, e.g. fractional anisotropy (FA), which all provide information on the local tissue microstructure and geometry. Although the diffusion tensor measurement offers all the above indices, most studies limit the analysis to the ADC, FA and principal eigenvector.

In our studies on the utility of the DTI-based characterization of skeletal muscle injury, we also investigated the individual eigenvalues and eigenvectors. Our findings in a mouse model of femoral artery ligation stress the importance of using the complete diffusion tensor information.

Materials and Methods:

Animal model: Skeletal muscle damage was induced by unilateral ligation of the right femoral artery of 19 C57Bl6 mice. This results in severe muscle damage in the right lower hind limb. The damage is maximal 3 days after ligation, whereafter the tissue starts to recover.

MRI: MR was performed with a horizontal 9.5 cm bore, 6.3 Tesla MRI scanner. A diffusion-weighted spin echo sequence with fat suppression was used. The diffusion gradients were applied along 6 non-collinear directions and one reference image was recorded without diffusion weighting. Scan parameters were: FOV=20x20 mm^2, matrix size=128x64, slice thickness = 1.5 mm, TE=30 ms, NSA=2, TR=1.5 s, Δ=13 ms, δ=8 ms and b-value=0 or 572 s/mm^2.

Data analysis: From the DTI datasets the eigenvalues ($\lambda_1>\lambda_2>\lambda_3$), eigenvectors, and ADC were calculated.

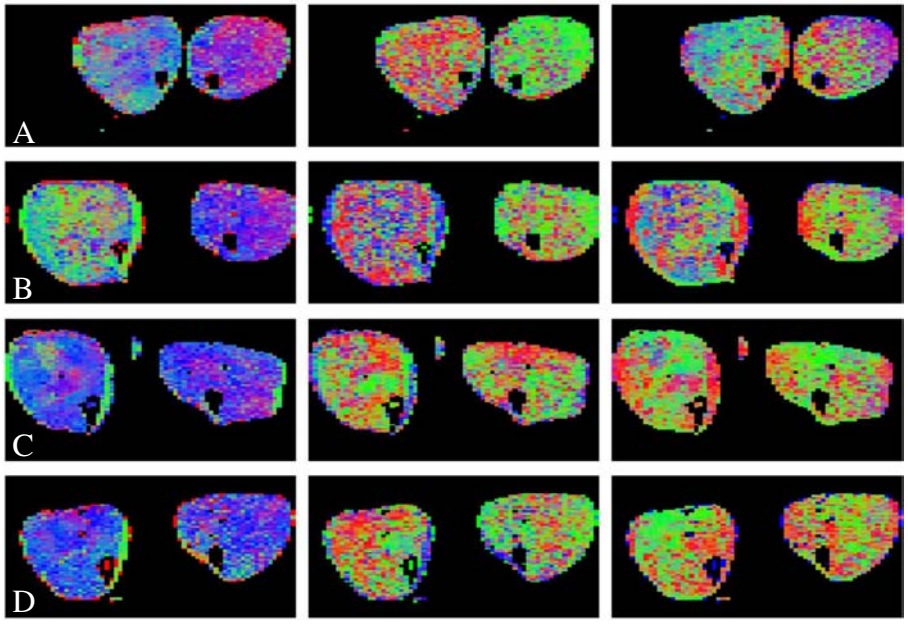

Figure 1) Color plot of the direction of the eigenvectors. Transverse slices were obtained from the same mouse that was followed over 21 days. A) directly after ligation, B) 3 days after ligation with severe tissue damage and increased eigenvalues, C) 10 days after ligation, D) 21 days after ligation. The ligated limb is situated on the left. Left images: e1; middle: e2; right: e3. Blue: out of plane; green: top to bottom; red: left to right.

Results and Discussion:

It has been shown that in intact skeletal muscle the direction of the principal eigenvector is along the direction of muscle fibers (1,2). However, in severely damaged muscle tissue this may no longer hold. The right limbs in Figure 1 visualize the direction of the eigenvectors for control muscle. As expected the vector pointing out of the transversal plane is associated with the principal eigenvalue in the normal situation except for the upper limb muscles. However, this was changed, for 6 out of 12 mice, 3 days after ligation (Fig 1b) where the diffusivities were elevated (Fig 2) and the fibers were swollen as evidenced by histology (data not shown). The direction out of plane is now associated with λ_2 and in some areas even with λ_3. This indicates that the diffusion perpendicular to the fiber direction is higher than diffusion parallel to the fibers. After 10 days a spot was still present with both altered direction (Fig 1c) and elevated diffusivities. After 21 days the principal eigenvector was along the fibers again for the entire limb (Fig 1d), in agreement with regeneration of the tissue, as evidenced by histology.

The three eigenvalues showed a different time course (Fig 2) following induction of tissue damage. Changes in λ_3 preceded and were larger than changes in λ_2.

In the calculation of the eigenvalues, $\lambda_1>\lambda_2>\lambda_3$ by definition, without taking the direction of the vector into account. As seen above the principal eigenvector can change its direction from parallel to perpendicular and thus the changes in diffusion parallel to the fiber direction were most likely overestimated. Therefore, in studies in which the eigenvalues are of interest it is important to verify the direction of the eigenvectors.

We also observed that λ_1 was hardly affected by damage, whereas both λ_2 and λ_3 were, with the largest increase for λ_3. Because λ_3 has by definition the smallest diffusion values the contribution to the ADC is relatively small. Therefore, changes in ADC might not be significant whereas changes in λ_3 can be.

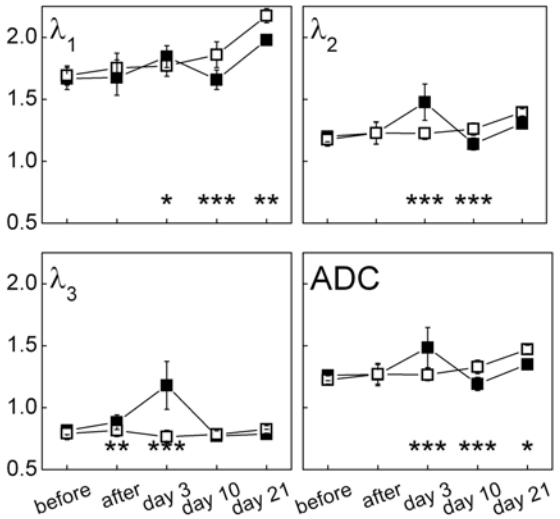

*Figure 2) Changes in MR indices as a result of femoral artery ligation. The values are the mean values of the modus of frequency distributions per limb per mouse. Black squares: ligated limb; and open squares: non-ligated limb. Error bars represent ± SDs. * p<0.05, ** p<0.01, *** p<0.005 of ligated versus non-ligated limb. ADC and λ's : x10^{-3} $mm^2 \cdot s^{-1}$.*

Conclusion:

We have shown that upon skeletal muscle damage the direction of the principal eigenvector can change.

References: 1) van Donkelaar et al. J. Anat 1999;194(Pt 1):79-88
2) van Doorn et al. Eur J Morph 1996;34:5-10