Quantifying in-vivo changes in myofiber diameter due to muscular atrophy with time-dependent diffusion MRI

Gregory Lemberskiy[1,2], Els Fieremans[1], Thorsten Feiweier[3], Leon Axel[1], and Dmitry S Novikov[1]

[1]*New York University School of Medicine, Bernard and Irene Schwartz Center for Biomedical Imaging, Department of Radiology, New York, NY, United States,* [2]*Sackler Institute of Graduate Biomedical Sciences, New York University School of Medicine, New York, NY, United States,* [3]*Siemens AG, Healthcare Sector, Erlangen, Germany*

Introduction: The analysis of tissue microstructure via MRI is possible by measuring the diffusion coefficient as a function of diffusion time. In particular, the random permeable membrane model[1] (RPBM) was developed to utilize time-dependent diffusion to quantify cell size and membrane permeability. This model assumes a system of randomly oriented barriers, Fig. (e). Here we apply RPBM to quantify myofibers within human calf muscle, where the walls act as the predominant restriction to water diffusion.[2,3] RPBM allows for estimation of the free diffusion coefficient D_0, cell membrane permeability κ, and mean fiber diameter a. **Purpose**: Validate the RPBM by comparing fiber sizes in the calf muscle in the immobilized leg and the calf muscle on the contralateral control leg. **Target Audience**: MR physicists and clinicians interested in quantifying cell size and permeability.

Methods: 2 male and 1 female volunteers aged 30-35 each had one leg placed in a non-weight bearing cast for injuries of the Achilles tendon or posterior tibial tendon. During the 6-week period, the calf muscle of the immobilized leg atrophied due to inactivity. For each volunteer, both calf muscles were scanned one week after transferring into a walking boot.

Scans were performed using a MAGNETOM Trio 3T Tim system (Siemens AG, Erlangen, Germany) with a Tx/Rx CP extremity coil. DWI images were acquired for $b = 0$, and along 20 gradient directions for $b = 500$ s/mm^2 using STEAM EPI preparations for 9 different diffusion times t from 38.8ms to 1500ms. Other imaging parameters include: 1 average, TR>7.4 s, TE = 72ms for 38.8ms and TE = 42ms for all other points, matrix = 64x64, 10 slices, voxel size = 3x3x5 mm^3, FOV = 190x190 mm^2. Scan time was 45 minutes per leg.

DTI parametric maps of diffusion eigenvalues $(\lambda_1, \lambda_2, \lambda_3)$ were calculated for all diffusion times using in-house software developed in MATLAB. The corrected b-matrix, as provided by the prototype sequence, was used to include the contributions of both applied diffusion gradients and imaging gradients. The accuracy of the acquisition was verified by testing the protocol in a 20% albumin phantom in which the diffusion coefficient was shown to be independent and isotropic over the range of employed diffusion times. Systematic signal attenuation due to local tissue vibration was observed in 10% of acquired DWI images and filtered via artifact correction based on diffusion coefficient.[4] These values were filtered out along each gradient direction and recombined into the DTI parametric maps. Regions of interest (ROIs) were manually outlined on T_2-weighted anatomical images, Fig. 1(a, b), to study the time-dependent diffusion in the Anterior Tibialis (AT), Extensor Digitorum Longus (EDL), Gastrocnemius Medialis (GM), Gastrocnemius Lateralis (GL), Peroneous Longus (PL), Posterior Tibialis (PT) and Soleus (SOL). For each ROI, the average value of the transverse diffusivity as a function of the diffusion time t, $D_\perp(t) = (\lambda_2 + \lambda_3)/2$, was used to fit to the RPBM to extract fiber diameter a, and membrane permeability κ (Fig (f)). Since fitted D_0 values agree well with the longitudinal eigenvalue λ_1, for fit robustness we fixed $D_0 = \langle\lambda_1\rangle$, the average over all time points.

Results: Muscle fiber sizes across all muscle ROIs for all volunteers were larger in the control leg, Fig. (g). There was no reported difference in membrane permeability between legs, Fig. (h). The sizes and permeabilities are consistent with values reported from histology.[5]

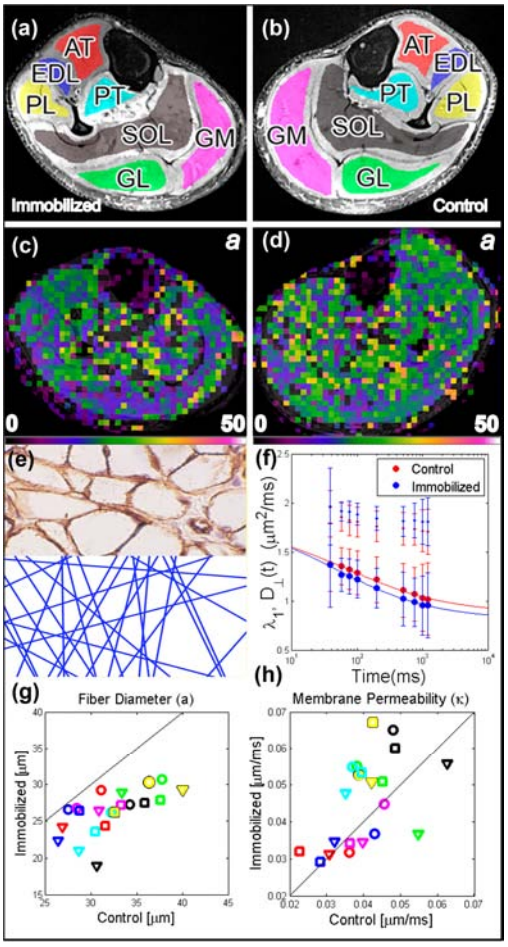

Figure: **(a)** Anatomical T_{2w} image showing muscle ROIs in immobilized leg and **(b)** control leg. Parametric map of fiber diameter a [μm] in immobilized **(c)** and control **(d)** legs. **(e)** Histological slice of skeletal muscle compared with RPBM. **(f)** Example of time-dependence of parallel and transverse diffusivity along GM. Comparison of fiber diameters **(g)** and membrane permeability **(h)** of muscle ROIs in control and immobilized leg.

Discussion: The RPBM has been shown to assess myofiber diameter and permeability.[2,3] Here we demonstrate that the RPBM robustly determines the myofiber diameter decrease as a result of atrophy. Myofibers of the immobilized leg were consistently smaller than in the control. Volunteers experienced the least amount of atrophy in AT and EDL since the casts offered room for slight dorsiflexion.

Conclusion: The time-dependent diffusion modeled with RPBM is shown to be a sensitive biomarker of the change in cell size due to atrophy. This method can be used as a diagnostic tool for physical therapists to assess microstructural muscle damage. Follow up scans during the volunteer's recovery could be used to identify optimal treatments for a given injury.

References: [1] Novikov et al. Nat Phys **7**:508,2011; [2] Fieremans et al, ISMRM 2011 1153; [3] Fieremans et al, ISMRM 2013 0489; [4] Lemberskiy et al. Submitted ISMRM 2014; [5] Polgar et al. J Neurol Sc **19**:307; **Acknowledgements:** Kecheng Lui (Siemens Medical Solutions, USA), Laith Jazrawi (NYU Langone Medical Center)