Functional Muscle MRI in Human Calf Muscle using IVIM

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Introduction Diffusion Weighted Imaging (*DWI*) is increasingly gaining importance for a variety of clinical applications, and derived apparent diffusion coefficients (*ADC*) based on *DWI* data have been reported in a multitude of studies [1]. In biologic tissues, *ADC* is determined by the microscopic motion of water, including not only translational and rotational molecular diffusion but also microcirculation of blood in the capillary network, as described by the intravoxel incoherent motion (*IVIM*) model [2]. The *IVIM* theory, which predicts an additional component in the signal equation due to perfusion effects and bridges the gap between diffusion and perfusion, has recently been applied to MR studies of several abdominal organs [3,4] and skeletal muscles [5,6]. Previous *DWI* studies in human skeletal muscles have been analysed by calculating separately linear signal decays within predefined different intervals of *b*-values, e.g., $0 \le b \le 50$ s/mm² for perfusion and $50 \le b \le 750$ s/mm² for diffusion quantification. This approach is limited, however, due to the missing estimation of the perfusion fraction within the signal decay. Consequently, in this work we present an approach to determine diffusion and perfusion changes in exercised human calf muscles by employing bi-exponential fitting. Moreover, the feasibility of calculating parameter maps was investigated.

Materials and Methods Diffusion Weighted (*DW*) images of lower leg muscles were acquired from one healthy volunteer using a modified single-shot echo planar imaging (*EPI*) sequence at 3.0 T (clinical whole-body MR scanner, TIM Trio, Siemens Healthcare, Germany) and a 2-channel matrix coil. Transverse *DW* images were acquired with 110 × 110 pixel matrix and a FoV of 220 × 220 mm² (TE/TR = 69/2000 ms, 1466 Hz/px, GRAPPA factor = 2). Three 4-mm-thick slices were obtained with in-plane resolution of 2.0 × 2.0 mm². The total measurement time was 4:24 min for a series of trace weighted *DW* images (*DW* in three orthogonal directions), 15 different *b*-values (b = 0, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 150, 200, 400, 600 s/mm²) and 3 averages. *DW* images were obtained before and after exercise performed inside the *MR* scanner with a modified *MR*-compatible pedal ergometer [7]. The exercise required active plantar flexion (against weight) and ankle dorsiflexion (against frictional resistance of a tackle rope) and was performed until total exhaustion of the subject. The following parameters were extracted from the *DW* images: *ADC* by mono-exponential fitting, and *IVIM* parameters *D* (diffusion coefficient), *PD* (pseudo diffusion coefficient) and *f* (perfusion fraction) by bi-exponential fitting according to:

$$S_i/S_0 = (1-f)\cdot e^{-bD} + f\cdot e^{-b(D+PD)}. \quad (1)$$

Parameter maps were calculated with a home-written MATLAB (The MathWorks, USA) routine. For ROI-based analyses ROIs were placed in anatomic T_2-weighted *TSE* images (TE/TR = 8.3/2000 ms, 1.0 × 1.0 × 3.0 mm³) of the low leg muscles (see Fig. 1), including the *M. tibialis* (*Ti*) and *M. gastrocnemius medialis* (*Gm*) and were transferred to the *DW* images.

Results Figure 2 shows *DW* images for three different *b*-values (*b* = 0, 200, 600 s/mm²), revealing the well-known signal increase due to prolonged T_2 relaxation time in *DWI* of exercised muscles compared to skeletal muscles in rest. ROI-based analyses demonstrated bi-exponential signal decays in two different exercised human calf muscles which were fitted by the bi-exponential function in Eq. 1 (illustrated in Fig. 3 for *b*-values between $0 \le b \le 200$ s/mm²). Both, *M. tibialis* (*Ti*) and *M. gastrocnemius medialis* (*Gm*), demonstrated increased perfusion fractions *f* (*Ti*: 2.0/5.6 %; *Gm*: 2.4/4.2 %) and increased pseudo diffusion coefficients PD (*Ti*: 55.3/402.3 × 10^{-3} mm²/s; *Gm*: 55.9/196.4 × 10^{-3} mm²/s) after exercise. The diffusion coefficient D increased only slightly from 1.5 × 10^{-3} mm²/s to 1.6 × 10^{-3} mm²/s in both muscles. Conventional mono-exponential fitting detected no changes in ADC value before and after exercise (*Ti* and *Gm*: 1.8 × 10^{-3} mm²/s). Inspecting the parameter maps in Figure 4 revealed no significant differences between ADC or D maps, which were acquired in rest and post exercise. However, frequent non-convergence of the pixel-based bi-exponential fitting caused high standard deviations in the *f* and *PD* maps.

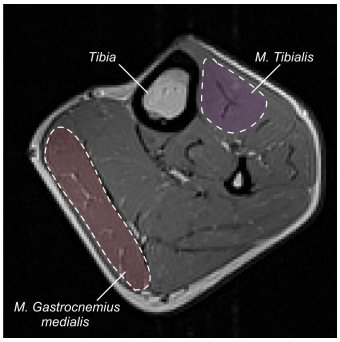

Fig. 1 T_2-weighted TSE image of a right lower leg with schematically overlaid ROIs.

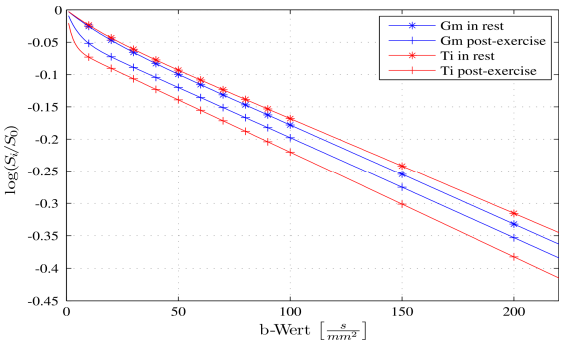

Fig. 3 Signal curves demonstrate bi-exponential signal decays as described by IVIM theory in two exercised muscles with increased perfusion.

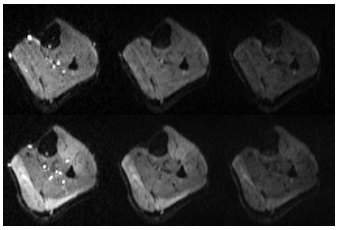

Fig. 2 DW images of right lower leg muscles before (top row) and after (bottom row) exercise (b = 0, 200, 600 s/mm²)

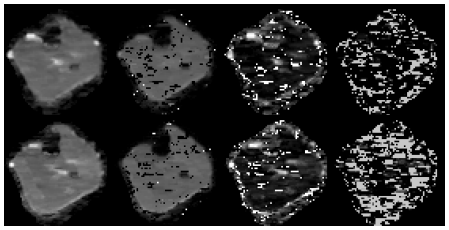

Fig. 4 Calculated parameter maps for ADC, D, f and PD values (from left to right) before (top row) and after exercise (bottom row). In ADC and D maps no changes in activated muscles could be observed. Maps of f and PD show high standard deviations.

Discussion In this study we demonstrated the feasibility of bi-exponential fitting based on *IVIM* theory in muscle functional *MRI* studies. Our results demonstrate the insensitivity of mono-exponential fitting, which, by disregarding perfusion effects, leads to overestimated *ADC* values. However, no changes before and after the exercise were detected in mono-exponential fits. Bi-exponential fitting based on ROI-analyses resulted in increased perfusion fraction *f* and increased pseudo diffusion coefficient *PD* after exercise, whereas the diffusion coefficient *D* remained nearly constant. The small increase of *D* may be explained by warming effects in exercised skeletal muscle [6]. Based on these first promising results, we feel encouraged to further investigate *IVIM* parameter changes during functional muscle *MRI*.

References

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