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 ≤ b ≤ 50 s/mm² for perfusion and 50 ≤ b ≤ 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, 1468 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 planar 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:

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

(1)

Parameter maps were calculated with a home-written MATLAB (The MathWorks, USA) routine. For ROI-based analyses, ROIs were placed in anatomic T₂-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 (T) 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 T₂ 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 ≤ b ≤ 200 s/mm²). Both, M. tibialis (T) and M. gastrocnemius medialis (Gm), demonstrated increased perfusion fractions f (T: 2.0/5.6 %; Gm: 2.4/4.2 %) and increased pseudo diffusion coefficients PD (T: 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 (T and Gm: 1.8 ± 0.1 × 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.

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.