Different kinetics of post-exercise perfusion fraction by diffusion-weighted imaging between athletes and non-athletes

Yoshikazu Okamoto[1], Graham J Kemp[2], and Tomonori Isobe[1]

[1]University of Tsukuba Hospital, Tsukuba, Ibaraki, Japan, [2]University of Liverpool, Liverpool, Liverpool, United Kingdom

Target audience This presentation will be beneficial for the musculoskeletal biologists, MRI researchers, cardiologists, and endocrinologists.

Purpose Diabetes mellitus, which is increasingly prevalent, has important effects on peripheral vascular function which are strongly related to prognosis and quality of life. Magnetic resonance imaging (MRI) has a number of diagnostic applications in conditions like diabetes mellitus. Here we explore the possibility that diffusion-weighted MRI (DWI) might be able to assess peripheral perfusion post-exercise in calf muscle. The concept of intravoxel incoherent motion (IVIM), initially described by Le Bihan et al (1) in brain imaging, can be used to quantify both true molecular diffusion and incoherent motion of water molecules in the capillary network, known as pseudodiffusion. Several investigators (2-4) have suggested that both pure molecular diffusion and capillary perfusion contribute to signal detected by DWI in the liver. The effect of pseudodiffusion on signal attenuation depends on the b-value (or b-factor), a term which gathers together several properties related to the gradient pulses (1): the pseudodiffusion contribution to IVIM occurs mainly at b-values < 200 s/mm2 (1, 5). We are interested in the potential pseudodiffusion might have for quantifying muscle perfusion. We therefore performed DWI at varying b-value in human skeletal muscle, and used the measured signal intensity of each image to calculate the 'perfusion fraction' (PF). It is difficult to validate this against gold-standard measures of tissue perfusion. However, a similar issue with the quantification of skeletal muscle microanatomy by diffusion tensor imaging (DTI), has been addressed indirectly by comparing results in subjects of different age, gender and training state and in response to different kinds of contraction, to make inferences about the microanatomical basis of the measurement (6-11). Here we take a similar indirect approach to DWI, comparing the kinetics of PF in both calves after unilateral calf muscle exercise between two very different groups, athletes and non-athletes.

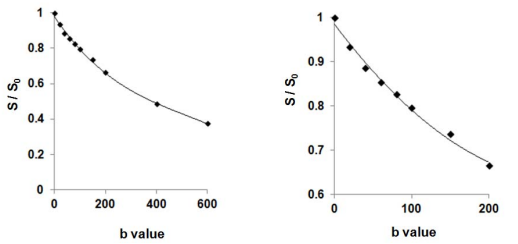

Figure 1 The left-hand panel shows the data and fitted curve for the ROI shown in Fig 1 using 10 b-values. Tne right-hand panel expands the b-value range 0-200s/mm2.

Methods

Materials. Twenty women volunteers aged 18-24 (mean 22) y were recruited. None had any history of cardiovascular and respiratory disease. Ten volunteers (Group A: mean age 21 y) were well-trained, high-achieving student athletes who had joined a University Department of Physical Education on sports scholarships. They were all tennis players. They had participated in sports since the age of 7–13 (average 10) y, and all had a record of advancing to the final 16 or better in national tournaments during high school. Their training schedule over the prior year (except during tournaments) averaged 6 days/week, 3 h/day. The other ten volunteers (Group B: mean age 22 y) had no habit of daily exercise. Written informed consent was obtained from all volunteers, and the study was approved by the institutional research ethics board. *MRI scanning.* MRI scans of both calves simultaneously were performed on a 3T MRI Achieva release 2.6 (Philips, Best, The Netherlands) using the 32 channel cardiac coil. The DWI scan was incremented every TR period to cover b-factors from 0 to 600 mm2/sec in 10 steps (0, 20, 40, 60, 80, 100, 150, 200, 400, 600). Other scan parameters were TR 3000 ms, TE 58 ms, FOV 320 mm, matrix size 64, voxel size 5 /5/10 mm, slice thickness 10 mm, gap 5 mm, number of slices 5, NSA 1. Total scan time was 2 minutes 30 seconds. *Experimental protocol.* After a resting scan (P0), each volunteer left the scanner and performed right calf exercise by standing (leaning on a wall for balance) and repeatedly raising and lowering herself using her right foot: raising and lowering were times to take 2 s each; one set of 10 raising and lowering cycles therefore took 40 s, and the volunteer performed 3 sets. Each volunteer then performed repeated right-leg hopping over a string 15 cm from the floor; this was performed in 3 sets, each of 10 steps. Within 5 min of cessation of exercise, perfusion scanning (parameters as in P0) was performed successively four times (P1-4). A sports trainer with 10 y experience supervised all exercise to standardize the procedure. *Data analysis.* Signal intensity of both SOL muscles was measured by a single experienced radiologist. The ROIs were chosen as 390-410 mm2 box-shaped, and the measurement was performed in ten DWI (from b=0 to 600 s/mm2) for each period (P0-4. Each measured signal intensity (S) were divided by that measured on b=0 s/mm2 image (S0). Data were fitted to biexponential kinetics by least-squares fit in Excel. Calculation of PF (i.e. 1 – the diffusion fraction) was performed using the equation below: $\mathbf{S=S0 \cdot PF \cdot exp(-bD^*) + S0 \cdot (1\text{-}PF) \cdot exp(-bD)}$ Here S is the signal intensity, b is the b-factor, D* is the pseudo-diffusion coefficient and D the diffusion coefficient. (The observed and fitted relationships between S/S0 and b-values is shown in Figure 1). We analyzed the time course of PF, comparing differences between A and B using two factor fractional ANOVA with repeated measures.

Results & Discussion

Figure 2 shows the kinetics of PF in right calf (i.e. the exercised calf) and left calf (the non-exercise calf) in group A (athletes) and B (non-athletes). In right (exercised) calf in Group A there is a slight increase in group A at P1, followed by a slight fall to a plateau. By contrast, group B shows rapid increase at P1, followed by a gradual decrease. There is a significant within-subject main effect in Phase ($P<0.01$), and an interaction effect between Phase and Group ($P<0.05$). Tests for between-subject effects shows no significance in Group ($P>0.05$). Exploring the interaction effects, there is a significant difference between groups A and B ($P<0.05$) at P1. PF shows statistically significant differences between P0 and P1, P2 and P3 ($P<0.05$) in Group A, and P0 and P1, P0 and P2 ($P<0.01$), and P1 and P4 ($P<0.05$) in Group B. In left (non-exercised) calf, in Group A there is little change in all phases, while in group B a slight increase at P1 is followed by gradual decrease. There is a significant within-subject main effect in Phase ($P<0.01$), and a between-subject main effect also in Group ($P<0.05$). There is no interaction effect in Phase and Group.

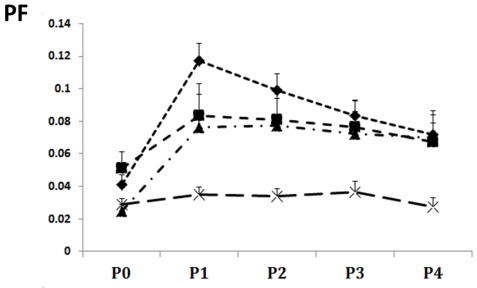

Figure 2 The figure shows the kinetics of perfusion fraction from Phases P0-P4 in right (exercised) calf and left calf (lower panels) in group A (athletes) and group B (non-athletes). See key for identification. ■Boxes express right, group A. ♦Diamonds express right, group B. ▲Triangles express left, group B, and ×Crosses express left, group A.

There have been reports (12-15) on PF in leg muscle by IVIM, but the possible clinical application has not been discussed. There is one report of an elevation of PF after exercise (13), but we report here the first attempt to compare the post-exercise kinetics of PF between athletes (Group A) and non-athletes (Group B). We did indeed find a significant difference between these groups in both the exercised (right) and non-exercised (left) calves. The ability of skeletal muscle capillaries to respond to changing demands plays an important role in fatigue and endurance. Capillary density responds to appropriate training e.g. (16), working through various angiogenic mechanisms (17, 18, 19). An increase in PF in response to exercise was expected in both groups. Subjects in our Group A were all well-trained players of tennis, a sport which requires repeated stopping and sprinting. That PF showed a smaller increase in these subjects than their untrained comparators might plausibly be explained in terms of a superior capacity of their muscle capillary system to respond to this demand. We had not expected any change in PF in the left calf, which was not exercise. This was so in the athletes of Group A, and the small but significant changes in Group B presumably reflect the local effects of systemic responses to exercise. This merits further investigation, particularly in relation to likely differences of capillary density between the two groups.

Conclusion We compared the post-exercise time-course of PF measured by DWI between athlete and non-athlete groups. The differences we identified may reflect aspects of muscle vascular physiology of potential sport-science and clinical use.

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