Measurement of Blood Volume and Permeability Surface Product in Skeletal Muscle using Gadomer-17

A. Z. Faranesh[1,2], D. Lancaster[2], G. Orcino[2], J. Taylor[2], J. Bacher[3], D. L. Kraitchman[4], E. R. McVeigh[2]

[1]Department of Biomedical Engineering, The Johns Hopkins University, Baltimore, Maryland, United States, [2]Laboratory of Cardiac Energetics, NHLBI, NIH, DHHS, Bethesda, Maryland, United States, [3]Veterinary Resources Program, NCRR, NIH, DHHS, Bethesda, Maryland, United States, [4]Department of Radiology, The Johns Hopkins University, Baltimore, Maryland, United States

Introduction: The ability to characterize tissue microvasculature is useful in applications such as diagnosing tissue injury (1), tumor classification (2), and evaluation of angiogenic therapies (3). Blood volume (BV) and permeability surface product (PS) are useful physiologic parameters which relate directly to the status of the microcirculation. In this work a method for fast multislice T_1 mapping (TAPIR: T_1-mApping-with-Partial-Inversion-Recovery) (4) was used in conjunction with the administration of a macromolecular contrast agent (Gadomer-17, Schering, Berlin, Germany) to quantify BV and PS in rabbit hindlimb skeletal muscle. Values for normal fast-twitch and slow-twitch muscles were obtained, and the approach was also used to investigate regional variations under ischemic conditions.

Methods: Imaging studies were performed on New Zealand White rabbits (n=7) prior to and two weeks post induction of hindlimb ischemia by femoral artery excision. All imaging was performed on a 1.5 T GE clinical scanner using 3-inch surface coils placed on the lateral side of each hindlimb. The multiecho TAPIR method was used to acquire T_1 maps for 16 slices. A four echo readout was used with TR/TE = 11.5ms/2.6ms, which allowed the measurement of 16 points along the T_1 recovery curve for 16 slices with an in-plane resolution of 1.25 mm x 1.25 mm in approximately two minutes. Gadomer-17 was administered i.v. at a dose of 0.05 mmol/kg, and T_1 maps were acquired every ten minutes for 60 minutes. The effective longitudinal relaxation time, T_1^*, was calculated by fitting the data to a monoexponential recovery curve on a pixel by pixel basis, and ΔR_1 maps were made by taking the difference between post and pre contrast relaxation rates. The data was analyzed using a two compartment kinetic model described in ref. (5). Values for BV and PS were compared for the tibialis anterior and soleus muscles of animals prior to surgery using an unpaired two-tailed t test. The method was also used to compute BV and PS maps for animals post surgery to examine changes induced by ischemia.

Results: The average BV and PS values for normal muscle are shown in Table 1. The BV for the soleus muscle was significantly higher than that of the tibialis anterior ($p \leq 0.001$). The PS values for the two muscles were not significantly different. A sample image from an ischemic animal is shown in Figure 1, which displays a spin echo image, BV map and PS map for a mid-calf slice of an animal two weeks post surgery. Note the increases in both BV and PS in the region of the soleus muscle compared with the normal contralateral limb.

Conclusions: By combining a fast multislice T_1 mapping method with the use of an intravascular agent, high spatial resolution maps of BV and PS were obtained in skeletal muscle. This method does not rely on quantifying first-pass kinetics, allowing for the acquisition of multiple slices for greater coverage. Significant differences in BV were found between the soleus and tibialis anterior muscles, reflecting the higher degree of vascularity of the slow-twitch soleus muscle compared with the fast-twitch tibialis anterior muscle. Large regional variations in both parameters were observed in ischemic tissue, possibly indicating hypoxia induced angiogenesis and inflammation related permeability changes. The technique presented here may be useful in identifying pathologies in the microvasculature as well as changes in capillary density and integrity that may be associated with angiogenesis.

Muscle	BV (μl/g)	PS (μl/g/hr)
TA	59.5±14.8	54.7±16.2
SO	84.5±20.8	63.8±19.9

Table 1: Blood volume (BV) and permeability surface product (PS) for tibialis anterior (TA) and soleus (SO) muscles. Values are shown as mean ± standard deviation. BV for two muscles are significantly different ($p \leq 0.001$).

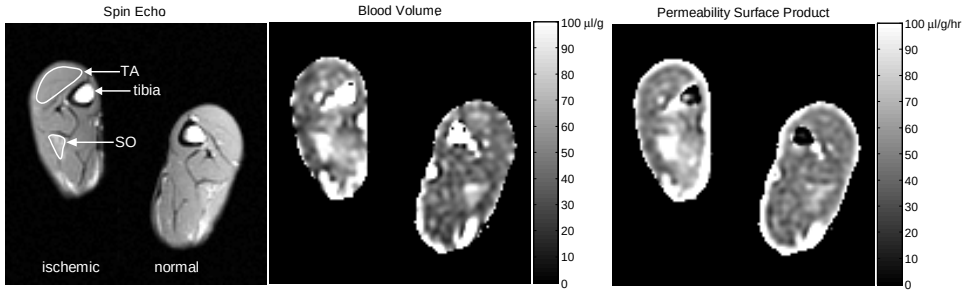

Figure 1: (Left) Axial spin-echo image of rabbit hindlimbs two weeks post surgery, with tibialis anterior (TA) and soleus (SO) muscles labeled on ischemic leg. (Middle) Blood volume map and (Right) permeability surface product map, showing increased values for both parameters in soleus muscle of ischemic leg.

References

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