Perfusion Tensor Imaging of Human Skeletal Muscle

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Introduction: The ability to non-invasively measure tissue perfusion is critical for assessing the physiological functions of human skeletal muscle in both healthy and disease states. The traditional techniques to measure tissue perfusion in human muscle are invasive and measure only bulk properties which do not render information on either spatial or temporal heterogeneity. Velocity selective arterial spin labeling (VSASL) MRI has been shown previously to be sensitive to muscle perfusion in humans [1], but does not allow a full exploration of important properties associated with the muscle perfusion, such as perfusion anisotropy and perfusion directions. Perfusion Tensor Imaging (PTI) was proposed in 2004 by Frank and Wong [2] in a study of perfusion anisotropy in the human brain, where VSASL was applied with a spherical velocity encoding scheme similar to that used in diffusion tensor imaging (DTI). The perfusion measurements can then be characterized by a perfusion tensor (*P*), analogous to the diffusion tensor in DTI, from which the estimates of the mean perfusion, fractional perfusion anisotropy and principle perfusion direction can be derived. This study demonstrates that PTI can also be used to measure perfusion properties of human skeletal muscle.

Methods: A healthy human subject with normal muscular functions was studied. All perfusion data were acquired on a General Electric (GE) Signa HDx 3.0 Tesla research scanner with a standard quadrature knee coil (GE, Milwaukee, Wisconsin). An in-house VSASL pulse sequence [3] with spiral readouts was used and is capable of encoding velocity in arbitrary directions. The subject was placed feet first in supine position such that the right lower leg was centrally located within the knee coil. Since the previous study [1] and our initial tests showed that the resting perfusion in human leg muscle is too low for a reliable detection by VSASL, we requested the subject to perform dorsal flexion of the right foot during the study in order to elevate the perfusion levels in the lower leg muscle. The exercise required significant use of the tibialis anterior, but was not considered strenuous by the subject. To maximally reduce the possible movements in the leg position associated with the exercise, the subject wore a customized rehabilitative boot on her right leg, and the boot was tightly strapped around the subject's leg and also fixed on the scanner table. Because the velocity encoding pulse is very sensitive to motion, the dorsal-flexion was performed only during the period between the end of the data acquisition of each TR and the beginning of the velocity encoding pulse in the next TR. The subject was also instructed to end the dorsal flexion well before the start of the next velocity encoding pulse so that the leg remains still in a consistent position during each image acquisition. This timing is also maximally sensitive to perfusion changes since peak arterial blood flow occurs between, rather than during muscle contractions. A total of 3 perfusion measurements were obtained and the subject was instructed to carefully maintain a constant level of effort in executing the exercise throughout the experiments. The cut off velocity (*Vcut*) for the VSASL was set to 5, 10 and 15 cm/sec for the three scans, respectively, and 6 non-coplanar encoding directions were used. Each scan lasted 8 minutes during which 96 interleaved VSASL images (16 images per direction) were acquired. Other imaging parameters were: FOV 24cm^2, slice thickness 8mm, gap between slices 4mm, matrix size 64x64, TR 5 sec, TE 9msec, TI 1.65sec. Eigenvalue decomposition of the perfusion tensor *P* was performed using AFNI command 3dDWItoDT [4]. Mean perfusion was then estimated from the trace of *P*, fractional anisotropy from the variance of the eigenvalues, and principle perfusion direction from the principle eigenvectors. The PTI analysis was confined only to the region where significant perfusion was detected.

Results: Figure 1 shows the mean perfusion, fractional perfusion anisotropy, and principle perfusion direction maps measured at three different *Vcut* values during exercise. Significant muscle perfusion is clearly seen in the tibialis anterior and is consistent with the dorsal flexion. There is no obvious perfusion measured in the gastrocnemius due to the low blood flow in the resting muscle and also the compression of gastrocnemius against the coil. The measured perfusion signal in the tibialis anterior decreases as *Vcut* increases. This is because larger vessels are encoded at higher *Vcut* values and a longer transit delay is required for the blood in these larger vessels to reach the targeted tissue. In the current study, the same delay time (1.65sec) was used for all three *Vcut* values. For the same reason, intravascular effect (bright spots in the mean perfusion maps that are localized to major arteries) is more prominent at higher *Vcut*. The fractional perfusion anisotropy increases with *Vcut*. This is consistent with the fact that blood supply from larger vessel groups is more directionally dependent than that from smaller vessel networks. Principle perfusion direction maps indicates a dominant longitudinal blood flow perpendicular to the imaging plane (as seen by the heavy presence of blue color in the maps), especially at higher *Vcut*. This agrees with the anatomical feature of the perfusion structure in the lower leg where most blood vessels travel longitudinally in the direction of the muscle fibers.

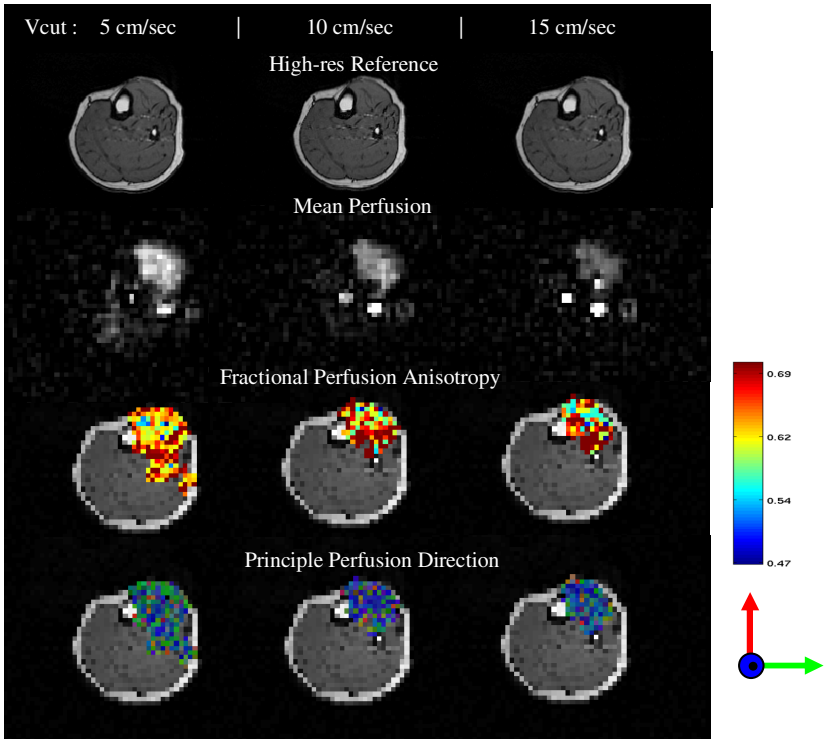

Figure 1: Mean perfusion, fractional perfusion anisotropy and principle perfusion directions measured at three different Vcut values. The high resolution structural images on the top row are provided for localization references. The color encoding for the principle direction maps are as follows: red -> up/down, green -> left/right, blue -> in/out.

Discussion: We have demonstrated the sensitivity of PTI in measuring the perfusion properties of human skeletal muscle in a healthy human subject. PTI can provide valuable information on the spatial flow heterogeneity as well as the direction of feeding vessels to each region, which is very important for studying muscle physiology. Future work includes optimization of the imaging parameters and quantification of the perfusion measurements, high angular resolution perfusion imaging for more complex muscle structures, and development of potential clinical applications for a range of medical conditions such as muscular dystrophy and compartment syndrome.

References: [1] Frank LR and Wong EC, ISMRM 2004, p2401. [2] Frank LR and Wong EC, ISMRM 2004,p1371. [3] Wong EC et al, ISMRM 2002, p621. [4] Cox RW and Hyde JS, NMR in Biomedicine,10:171-178,1997.