IntraVoxel Partially Coherent Motion (IVPCM) Technique: Application on Skeletal Muscle Microvasculature

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Introduction:

Phase-sensitive methodologies have been developed for the characterization of tissue microcirculation since the late 1980's. Depending on the capillary geometry, IntraVoxel blood perfusion can be modeled as an Incoherent Motion (IVIM technique) or Coherent Motion (IVCM technique) [1]. The application of these methods has been complicated by their high SNR requirement and the ambiguity in the interpretation of their results [2]. On the other hand, an important advantage of those Diffusion-Weighted (DW) based techniques, which has not been sufficiently explored, is the directional sensitivity they afford when applied in tissues with anisotropic microcirculation like the myocardium [3] and the skeletal muscle [4]. The aim of the present study is the reformulation of IVIM to characterize IntraVoxel blood perfusion as Partially Coherent Motion (IVPCM) for a generic microvascular network with a preferential orientation and the implementation of the proposed methodology to probe in vivo discrete microcirculation territories in skeletal muscle.

Materials and Methods:

Theory: According to LeBihan's IVIM formulation [1], an analytical description of the diffusion echo attenuation signal can be derived by considering that the MR signal within each voxel during the diffusion time Δ is the sum of an intravascular component (transport due to flow and diffusion with D_{in}) and an extravascular component (diffusion with D_{ex}). If no interaction between the two compartments is assumed then the echo attenuation is given by a signal-weighted average of intra- and extravascular terms. Let f be the signal weighted fraction of the intravascular compartment. Callot et al [3] first addressed the issue of the anisotropy of the IVIM signal by assuming that microcirculation can be modeled as a pseudo-diffusion process with a pseudo-diffusion coefficient D^* and an apparent signal-weighted intravascular fraction f_{ap} with both parameters depending on the angle α between the average microvasculature orientation and the applied diffusion direction (Eq. (1)). Our proposed approach is based on the assumption that certain microcirculation territories are composed of a population of capillaries with an anisotropic distribution of orientations (Fig. 1). We chose the Fisher axial distribution [4] which relies on a single parameter, the concentration parameter K, to quantify the degree of microvascular anisotropy. For each capillary, the velocity profile follows the Poiseuille law and the direction of the flow is equally probable forward and backward (u_{av}=0) with a maximum velocity magnitude u_{max}. If the average capillary preferential orientation is known (directions $\parallel$ and $\perp$ are defined), estimates for u_{max} and K can be derived from DW measurements covering multiple b-values and judiciously chosen directions.

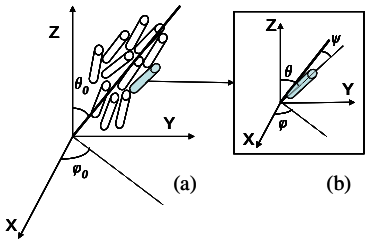

Figure 1 (a) Geometry of microvascular network and (b) an individual capillary. The angles θ_o and φ_o define the average orientation.

$$\frac{S(b,\alpha)}{S_0} = f_{ap}(\alpha)\exp\left[-b\left(D_{in}+D^*(\alpha)\right)\right]+\left[1-f_{ap}(\alpha)\right]\exp\left[-bD_{ex}(\alpha)\right] \quad (1)$$

$$\frac{S(q_{\parallel},q_{\perp})}{S_0} = fF(q_{\parallel},q_{\perp})\exp\left[-\sum_{i,j=1}^{3} b_{ij}(q_{\parallel},q_{\perp})D_{in}\delta_{ij}\right]+(1-f)\exp\left[-\sum_{i,j=1}^{3} b_{ij}(q_{\parallel},q_{\perp})D_{ex,ij}\right] \quad (2)$$

$$F(q_{\parallel},q_{\perp}) = \frac{\int_0^{2\pi}\int_0^{\pi/2}\exp\left[K\cos(2\psi)\right]\sin c(2\pi q_{\parallel}u_{max}\Delta\cos\theta)\sin\theta\, d\theta\, d\varphi}{\int_0^{2\pi}\int_0^{\pi/2}\exp\left[K\cos(2\psi)\right]\sin\theta\, d\theta\, d\varphi} \quad (3)$$

In vivo experiment: The skeletal muscle capillary network pattern is well-known to be anisotropic [5]. In the current study, the proposed framework was tested to characterize in vivo the microvascular anisotropy of the right calf muscle of one healthy volunteer. A 3-directions (aligned with the logical directions of the acquisition, X=L/R, Y=A/P and Z=S/I), 15-gradient amplitudes, diffusion-weighted stimulated-echo single-shot EPI sequence was implemented on a 3T GE scanner with the following parameters: FOV= 20 cm, axial slice with 9 mm thickness, 64×64 acquisition matrix, 5/8 partial phase encoding, N_{ex}=10, TR/TE=1500/52 ms, δ=15 ms, Δ=40 ms and g ≤3.0 G/cm. Fat suppression was performed using a spatial-spectral RF pulse.

Results and Discussion:

Simulations: The echo attenuation signal was simulated using Eq. (2) for typical parameters of the skeletal muscle microvascular network ($D^{\parallel}_{ex}/D^{\perp}_{ex}$=2.0/1.5 10^{-9} m^2/s, D_{in}=3.0 10^{-9} m^2/s, f=0.04, u_{max}=1 mm/s) for various diffusion directions and for various degrees of the microvasculature anisotropy K. The synthetically generated signal was then fitted to Eq. (1) for b>200 s/mm^2 to extract the direction-sensitive apparent vascular volume fraction f_{ap}. Fig. 2a shows the dependence of f_{ap}/f with the degree of microvasculature anisotropy and the orientation of the applied diffusion direction. For K=0, the capillary network is isotropic and therefore f_{ap} is independent of diffusion direction. As K increases however the capillaries tend to orient parallel to the preferential direction and f_{ap} becomes strongly diffusion direction dependent. The current analysis is consistent with the experimental f_{ap} results of Callot in the myocardium [2], and relies on the preferential orientation of capillaries in muscular tissue to explain the anisotropy of the measured apparent vascular volume fraction.

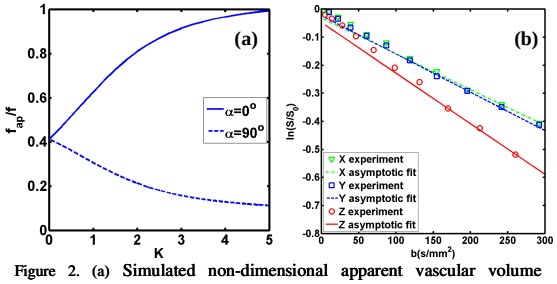

Figure 2. (a) Simulated non-dimensional apparent vascular volume fraction for two diffusion directions, (b) experimental data and asymptotic linear fit at high b-values for 3 diffusion directions of the normalized signal averaged within a 4x4 ROI in the medial gastrocnemius (MG) muscle.

	D (10^{-9} m^2/s)			f_{ap} (%)			f	$u_{max}/2$ (mm/s)	K
	X	Y	Z	X	Y	Z			
MG	1.28	1.37	1.81	3.11	2.28	4.65	4.54	0.63	1.8
LG	1.58	1.31	1.76	1.98	0.67	5.64	5.10	0.56	3.2

Table 1. IVIM and IVPCM fit results for ROIs in the medial gastrocnemius (MG) and the lateral gastrocnemius (LG) muscles.

In vivo results: The DW data from various muscle regions within the calf muscle cross-section were first fitted for b>200 s/mm^2 to Eq. (1) to extract the asymptotic fit limit, where the perfusion-related signal is almost completely attenuated (Fig. 2b), and then to the full model of Eq. (2). As Fig. 2b shows, the variation of the normalized signal as a function of b-value for 3 diffusion directions shown in Fig. 2b is consistent with the higher extravascular diffusion coefficient and higher apparent vascular volume fraction for the Z-direction (along average muscle fiber for small pennation angles) and agrees with the results of Morvan [6]. Table 1 summarizes the results of the full model for ROIs in two different muscle regions. The estimated values for the mean magnitude of the velocity ($u_{max}/2$) are within the range of reported values for blood flow in microvessels in skeletal muscle (< 1 mm/s). We have to point out that the low sensitivity of the method to the intravascular signal compartment contribution and the lack of temporal and spatial resolution prevents the extraction of accurate perfusion maps with the spatial and time resolution of the standard perfusion MRI techniques (DSC, ASL). Nevertheless, the directional sensitivity of IVPCM can provide non-invasively important insights into the territorial microvascular orientation, which cannot be studied with any alternate perfusion MRI technique.

Conclusion: A model-based analysis of diffusion-weighted MRI measurements extending the IVIM technique, labeled as IVPCM technique, is formulated and applied to the skeletal muscle. The reported results indicate that **IVPCM can characterize in vivo the anisotropy of discrete capillary network territories** in the case of tissues with preferential microvascular orientation.

References: [1] LeBihan D. *Diffusion and Perfusion Magnetic Resonance Imaging* (Raven Press, 1995), [2] Conturo T. E. *NMR Biomed.* 8: 307-332 (1995), [3] Callot V. et al. *Magn. Res. Med*., 50: 531-540 (2003), [3] Karampinos D. C. et al. *Proc. ISMRM* 2007, 1537, Berlin, [5] Weibel E. R. *Stereological Methods* (Academic Press, 1980), [5] Mathieu O. *J. Microscopy* 131: 131-146 (1983), [6] Morvan D. *Magn. Res. Imag.* 13: 193-199 (1995).