Quantification of Reactive Hyperemia in the Femoral Artery and Vein by MRI-based Blood Oximetry

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Introduction

Several non-invasive modalities exist to quantify reactive hyperemia of peripheral circulation in response to a physiologic challenge such as cuff-induced ischemia. At rest peripheral vascular health often cannot be assessed because normal nutritive requirements are met even in the presence of multiple levels of occlusion [1] with the reduction of the vascular resistance below the normal level via establishment of collateral circulation. However, greater flow rates cannot be accommodated due to high vascular resistance of the collateral bed, which is the main cause of the pressure or energy loss. Depending on the imaging modality, the hyperemic response can be quantified with a time-course measurement of relative flow, flow-mediated dilatation (FMD) or the concentration of HbO_2 and Hb during hyperemia. The purpose of the time-course measurement is to extract parameters that may provide useful clinical information of endothelial function, which controls vascular tone and vascular fluidity [2], during hyperemia. The parameters of reactive hyperemia are often related to the maximal change, required time for the maximal change and recovery time to the baseline value of a given quantity, such as the relative blood flow. We demonstrate MR susceptometry-based oximetric quantification of reactive hyperemia in response to cuff-induced ischemia for the duration of 3 and 5 mins by making direct time-course measurement of oxygen saturation level in the femoral/popliteal artery and vein of both normal subjects and patients with peripheral arterial disease (PAD).

Methods

In MR susceptometry-based oximetry [3, 4] blood vessel is modeled as a long paramagnetic cylinder at some angle θ relative to the applied field B_o. The incremental field, ΔB, inside, is given as $\Delta B = ½\, \Delta\chi B_o(cos^2\theta - 1/3)$, where $\Delta\chi = \Delta\chi_{do} Hct\cdot(1 - HbO_2)$ is the susceptibility difference (in SI units) between the intravascular blood and that of its surrounding muscle tissue, $\Delta\chi_{do} = 4\pi\cdot(0.27$ ppm) [5] is the susceptibility difference in SI units between fully deoxygenated and fully oxygenated erythrocytes, HbO_2 represents the fraction of the oxygenated hemoglobin (*Hb*) and hematocrit (*Hct*) is the volume fraction of the packed erythrocytes in the whole blood. The incremental field is measured with a phase difference image, $\Delta\phi_{map} = \gamma\Delta B\cdot\Delta TE$, where ΔTE is the time duration between two successive equal-polarity gradient echoes. Phase difference images between two echoes were constructed as [6] $\Delta\phi = \arg(Z_2 Z_1^*)$, where Z_1 and Z_3 represent complex values of a particular pixel in the images of two echoes, respectively, the asterisk denotes complex conjugate. The phase difference computation performed in this manner maximizes SNR and a short interecho time avoids phase wraps. Images were acquired with a multi-echo RF-spoiled GRE sequence programmed with SequenceTree Version 3.1 [7]. The pulse sequence includes fat suppression and first-moment nulling along the slice (i.e. blood flow) direction. The key parameters were: voxel size = 1 x 1 x 5 mm^3, FOV = 128x128 mm^2, resolution = 1 x 1 x 5 mm^3, BW = 488 Hz/pixel, TE = 4 ms, echo spacing = 2.5 ms, TR = 39 ms, flip angle = 13°, total scan time/image = 5 s. An eight-channel knee array coil (InVivo Inc., Pewaukee, WI) was used to acquire axial images containing the femoral/popliteal vessels (**see Figure 1**) at 3T. To date 14 subjects, divided into three groups, have been scanned: PAD patients (n = 7, ABI < 0.8, ages = 52 – 80 yrs), age-matched control subjects (n = 2, ABI > 1.0, ages = 66 and 68 yrs) and healthy young (n = 5, ABI > 1.0, age = 23 – 40 yrs). The cuff paradigm consisted of three parts: 2 minutes baseline, 3 minutes cuff occlusion, and 6 minutes recovery, which was repeated with 5 min cuff occlusion. Written informed consent was obtained prior to all human studies following an institutional review board-approved protocol.

Results and Discussion

Sample images and oxygenation time-course are shown in **Figures 1** and **2**. The washout time and the upslope (**Figure 3**) were significantly longer and less, respectively, for PAD patients compared to normal. The washout time refers to the time required to observe oxygen depleted venous blood that is washed out of the capillary bed during the reactive hyperemia and the upslope correspond to the reoxygenation rate in the vein after the washout. Arterial saturation remained constant (within uncertainty) as expected since oxygen extraction only takes place in the capillary bed. Longer duration of ischemia should induce greater blood flow but it was not observed in the healthy subjects. We conjecture that 5 s temporal resolution may not be adequate for healthy subjects, whose blood flow can increase by as much as 6 times at the initial phase of hyperemia. On the other hand, greater upslope after the 5 min occlusion was observed (0.24 ± 0.07 vs 0.50 ± 0.10 $\%HbO_2$/sec; p = 0.0004) for the PAD patients. Lastly, average venous and arterial saturation at rest did not differ significantly in either healthy and PAD subjects: 65 (± 8) vs. 68 (± 8) and 95 (± 3) vs. 94 (± 4), respectively.

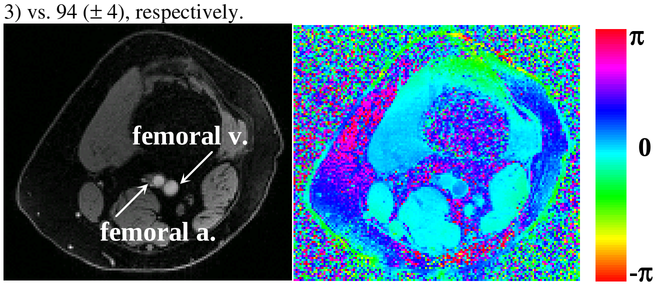

Figure 1 Sample axial magnitude and phase difference image of femoral vessels of a healthy 68 yr-old female.

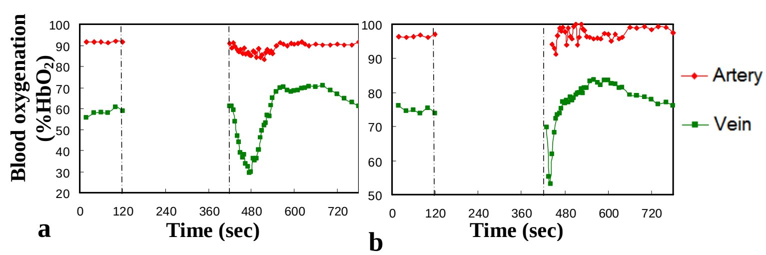

Figure 2 Blood oxygenation time-course of a PAD patient (**a**) and a control subject (**b**). Dashed lines indicate the beginning and end of the cuff occlusion.

Conclusions

MR susceptometry-based oximetry can distinguish PAD patients from healthy subjects by quantifying reactive hyperemia in response to cuff-induced ischemia. Washout and upslope of the venous saturation most clearly distinguish PAD patients from the normal subjects.

References:

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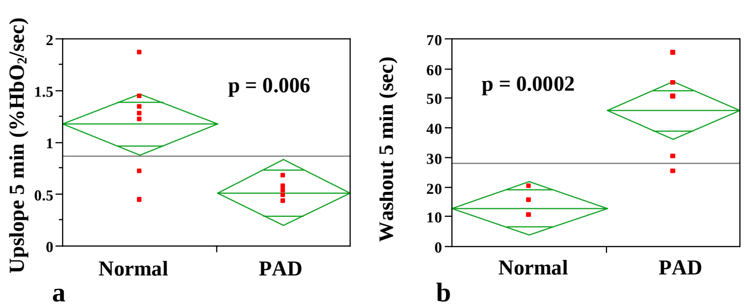

Figure 3 Scatter plots comparing (**a**) upslope and (**b**) washout time of healthy subjects and PAD patients after a 5 mins of occlusion. Reduced number of data points in (**b**) reflects degeneracy in the washout times among the normal subjects and patients.