Multiparameter functional MRI assessment of vascular reactivity

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Introduction: Endothelial dysfunction is believed to be one of the earliest manifestations of atherogenesis. Even though there is no noninvasive technique for its direct assessment, several approaches can yield indirect information on vascular health. Among these are brachial artery reactivity via flow-mediated dilation, aortic pulse-wave velocity (PWV), carotid intima-media thickness and coronary artery calcium score. Each of these techniques has limitations and, more importantly, each provides a single parameter only for evaluating systemic atherosclerosis. Here, we present an integrated MRI protocol that provides a spectrum of functional parameters as surrogates of endothelial dysfunction. The approach is being evaluated in patients with various severity of peripheral arterial disease (PAD -- ankle-brachial index [ABI] <0.9) as well as healthy subjects.

Methods: The pilot study in progress has a target enrollment of 100 subjects that will consist of 40 patients with PAD, 40 age-matched controls and 20 young healthy subjects. The enrolled subjects underwent an integrated MRI protocol that includes simultaneous time-resolved velocity and blood oxygenation [%HbO2] mapping in the femoral artery and vein, both at rest and during reactive hyperemia. The technique consists of interleaving MR susceptibility-based oximetry [1,2] and projection-based velocity quantification [3] in a single interleaved pulse sequence [4]. In addition, pulse-wave velocity (PWV) along the aortic arch was quantified via a non-triggered projection method [5]. Reactive hyperemia was induced with a cuff paradigm consisting of 2 mins of baseline, 5 mins of occlusion and 6 mins of recovery. During baseline, the velocity waveform and venous oxygen saturation (SvO2) were quantified. The interleaved pulse sequence was launched 10s prior to cuff release to quantify blood oxygenation and velocity with temporal resolution of 5s and 80 ms, respectively, during hyperemia. Following the procedure, which lasts about 25 mins total, aortic PWV was quantified. All studies were performed at 3T (Siemens Tim Trio) with an extremity and body matrix coil. Peripheral vascular reactivity was assessed in terms of washout time, upslope and overshoot (OS), which are derived from the time-course of femoral vein oxygen saturation (SvO2), and from the simultaneously acquired time-resolved arterial blood flow velocity, arterial pulsatility (AP), changes in shear rate (ΔSR) and duration of forward flow (TFF) during hyperemia are quantified. Lastly, the vascular reactivity of the central artery is assessed with PWV.

Results: Figure 1 shows representative time-courses of SvO2, blood flow velocity and rate in the femoral artery and vein, and a sample complex difference (CD) intensity time-curve for one cardiac cycle in the ascending (Aa) and descending (Da) aorta for PWV estimation in a healthy 26 yr-old subject. Upon cuff deflation (t=0, Fig 1a) the oxygen-depleted capillary blood drains resulting in a “dip” in SvO2 at the imaged slice and the elapsed time to observe the dip is defined as the washout time. The dip is followed by an increase (upslope) and above-baseline saturation (overshoot) as a result of hyperemia. The time-resolved blood flow velocity (Fig 1b) during hyperemia shows a transient increase in shear rate leading to a period of time (TFF) where forward flow is maintained, i.e. significant increase in the flow rate compared to baseline flow (Fig 1c). Lastly, Fig 1d is a sample time-resolved [CD] curve used to estimate PWV. The vascular reactivity data of select subjects are shown in Table 1. The peripheral vascular reactivity of patients with advanced PAD (rows in gray) is characterized by longer washout time, reduced upslope, loss of arterial pulsatility (PI), lower shear rate during hyperemia and significantly prolonged TFF (arterial flow quantification during hyperemia was not possible on the patient with severe PAD (ABI=0.38)). The absence of retrograde flow (Fig 1b), i.e. “monophasic” flow waveform, during early phase of hyperemia is likely the result of the reduction in vascular resistance. Thus, TFF may reflect the period of hyperemia during which the release rate of NO is most pronounced as a result of significant increase in shear rate. In general, we observe a linear relationship between aortic PWV and age consistent with previous findings [5], but significant difference was not found between healthy subjects and patients with PAD. Although anecdotal, the MRI metrics of the 58 year-old smoker without symptomatic CVD (pink) are in stark contrast to the other two healthy subjects (equal FRS, rows in blue). We attribute the disparities between our measures and FRS to the latter measure’s ignoring some effects pertaining to life style.

Conclusions: Functional changes that reflect impaired vascular reactivity associated with PAD, advancing age and detrimental lifestyle (e.g. smoking) include longer washout time, reduced upslope, OS, arterial pulsatility and shear rate. The modulated reactivity appears to be compensated with an increase in the duration of forward flow TFF.


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Table 1 Sample vascular reactivity data.

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<th>Age</th>
<th>Sex</th>
<th>ABI</th>
<th>FRS (%)</th>
<th>Washout (sec)</th>
<th>Upslope (%HbO2/sec)</th>
<th>OS (%HbO2)</th>
<th>AP (sec)</th>
<th>ΔSR</th>
<th>TFF (sec)</th>
<th>PWV (m/s)</th>
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Figure 1 Quantitative assessment of vascular reactivity in a healthy 26 yr-old: Time-course of femoral vein SvO2 (a); temporally-resolved blood flow velocity (averaged across the lumen) during hyperemia (b); flow rate (averaged over several cardiac cycles) (c); sample [CD] curve acquired without gating at 10 ms temporal resolution (d).