Comparison of MRI and US assessment of vascular reactivity in relation to CVD risk factors in old and young healthy subjects

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Introduction: Endothelial dysfunction and increased inflammation lead to atherosclerosis[1] and it is accelerated by aging. As endothelial dysfunction is an early marker of cardiovascular disease (CVD) and can be assessed indirectly with a physiological challenge such as cuff-induced ischemia. In this study, we evaluate an integrated MRI protocol that consists of three quantitative techniques against established ultrasound (US) measures: flow-mediated dilation (FMD) of brachial artery[2] and intima-media thickness (IMT) of carotid arteries. The MRI techniques include simultaneous measurement of blood flow velocity and the time-course of oxygen saturation during hyperemia in the femoral artery and vein, respectively, as well as regional quantification of pulse-wave velocity in the aortic arch, thoracoabdominal aorta and iliofemoral arteries.

Methods: Young healthy (YH; N = 21; age = 29.4±4.4) and old healthy (OH, N = 12; age = 57.4±4.4) subjects without a history of CVD, participated in this study. The quantitative MRI protocol to evaluate central and peripheral vascular reactivity comprised of two parts: 1) Dynamic oximetry and velocimetry of femoral artery and vein: Reactive hyperemia in the leg 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 in the femoral artery[3] and blood oxygen saturation[4,5] in the femoral vein were quantified. The interleaved pulse sequence[6] (MR susceptometry (**Fig 1** and **2**) and velocimetry) was launched 10s prior to cuff release to quantify SvO_2 and arterial velocity with temporal resolution of 1.25s and 120 ms, respectively, during hyperemia. 2) Regional quantification of PWV: Following the procedure, which lasts about 25 mins total, regional PWV along the aortic arch (**Fig 3a**), thoracoabdominal aorta, and iliofemoral (**Fig 3b**) arteries was quantified via a non-triggered projection method[7,8] that is immune to gating errors and can achieve "real-time" temporal resolution of 7.4 to 12 ms. To quantify PWV, velocity waveform has to be monitored simultaneously at two arterial segments in order to measure the transit time of pressure pulse. For the aortic arch single slice across the ascending and descending aorta is needed (Fig 3a). On the other hand, to quantify PWV along two distal arterial sites (**Fig 3b**) velocity data are acquired at both locations after exciting them essentially simultaneously with two successive RF pulses of different frequencies. All MRI studies were performed at 3T (Siemens Tim Trio) with an extremity and body matrix coil. Peripheral vascular reactivity in response to cuff-induced ischemia was assessed in terms of washout time, upslope and overshoot[9], which are derived from the time-course of SvO_2, and from the simultaneously acquired time-resolved arterial blood flow velocity, arterial pulsatility index (PI), peak-to-baseline flow rate (rQ_{max}) and duration of forward flow (T_{FF}) during hyperemia were measured. US imaging was performed using standardized imaging protocols and procedures[2,10]. Carotid IMT: The common carotid artery proximal to the bifurcation, the carotid bifurcation and proximal internal carotid artery were imaged. Brachial Flow-mediated dilation (FMD): Vasodilation was induced in the brachial artery with 5 min of cuff occlusion and images were recorded at the R wave before inflation and every minute for 5 mins after the pressure deflation to quantify FMD.

Results:

Part 1: Dynamic oximetry and velocimetry

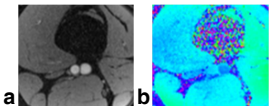

Fig 1 Sample **a**) magnitude and **b**) phase difference images at the level of femoral artery and vein (darker blue in **b** as a result of lower HbO_2.

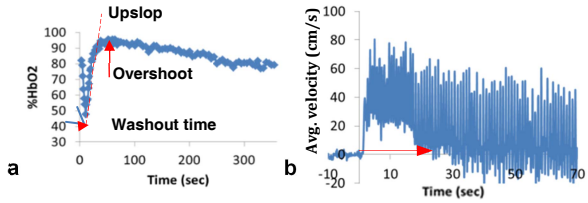

Fig 2 Time courses of **a**) venous HbO_2 and **b**) average blood flow velocity in femoral artery and vein, respectively. Each spike in **b**) represents a systolic peak. The red arrow denote the duration of forward flow (T_{FF}) during hyperemia. The washout correspond to the elapsed time to observe desaturated blood after the cuff release, upslope represent the resaturation rate and overshoot represent the temporary increase in HbO_2 due to transient increase in blood flow rate as indicated by the elevated peak systolic velocity in **b**).

Part 2: Regional PWV

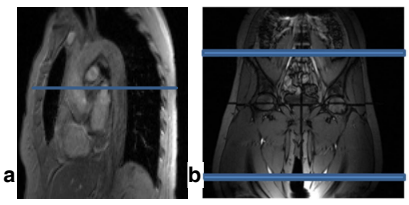

Fig 3 a) Representative oblique sagittal and **b**) coronal images showing prescribed slices (blue bars) for quantifying PWV along the aortic arch, and iliac and femoral arteries.

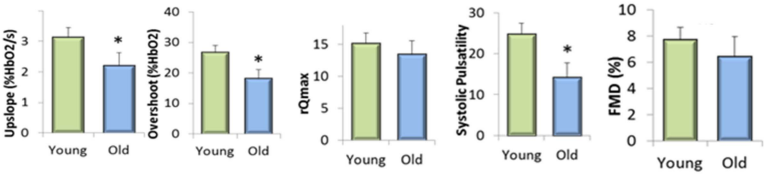

Fig 4 From the Part I of MRI protocol, decreased vascular reactivity in OH compared to the YH is characterized by lower upslope, overshoot and pulsatility index; * indicate $p < 0.05$. Significant difference in the peak-to-baseline flow rate (rQ_{max}) was not observed but the trend is consistent with previous studies. Similarly, FMD was reduced in OH as expected from vascular aging but was not statistically significant.

	Young	Old	p-value
aPWV	6.9	8.7	0.03
DaPWV	3.9	4.8	0.05
IMT	0.45	0.68	0.0004
CA diam.	7.2	6.3	0.008
CA area	9.7	16.8	0.0007

Table 1 Comparison between traditional CVD risk markers between YH and OH. Aortic (aPWV) and thoracoabdominal (DaPWV) pulse-wave velocities are quantified with the Part 2 of the MRI protocol (**Fig 3**). IMT and carotid artery (CA) diameter and area are derived from US images.

Discussion: Initial results indicate that oximetric parameters (upslope and overshoot), aPWV and DaPWV are indicators of vascular aging. Among US data, significant differences were observed in IMT, carotid artery diameter and lumen area between YH and OH (**Table 1**) but not in FMD.

References: [1] Libby, AJCN 2006 ; [2] Coretti et al, JACC 2002; [3] Langham et al, MRM 2010; [4] Haacke et al, Human Brain Mapping 1997; [5] Fernández-Seara et al, MRM 2006; [6] Langham and Wehrli, JCMR 2011; [7] Langham et al, MRM 2010; [8] Langham et al, JCMR 2011; [9] Langham et al, JACC 2010; [10] Roman et al, J Am Soc Echocardiogr 2006.**Acknowledgment**: NIH RO1 HL109545 and K25 HL111422.