Quantification of blood oxygenation and flow in response to apneic challenge

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Introduction: The apneic response is central to many disease states, including sleep apnea, chronic obstructive pulmonary disease (COPD), and asthma. Normal physiologic changes during breath-hold induced apnea include reduced cardiac output, peripheral vasoconstriction, decreased arterial and tissue oxygen saturation, and decreased peripheral blood flow [1-3]. Previous studies of the apneic response have focused on healthy subjects, using Doppler ultrasound to measure peripheral blood flow and optical techniques (near-infrared spectroscopy and pulse oximetry) to monitor tissue and arterial saturation [4, 5]. Although portable, NIRS does not allow for quantification of intravascular hemoglobin saturation (%HbO_2), and there are concerns about the accuracy of pulse oximetry during peripheral vasoconstriction [6]. Modification of a multi-echo GRE pulse sequence allows simultaneous measurement of blood oxygen saturation and blood flow at high temporal resolution [7, 8], making it an ideal technique for studying physiologic and pathologic responses to apneic challenge. Because certain disorders, such as sleep apnea and COPD, involve chronic changes in ventilatory patterns and the body's sensitivity to hypercarbia and hypoxia, we conjecture that features of the HbO_2 and blood flow velocity curves during apnea may be altered in these diseases. MR-based characterization of the apneic response could potentially provide a new, non-invasive tool for evaluating these diseases, for example, as an adjunct to overnight EEG monitoring in the diagnosis of sleep apnea.

Methods: In order to simultaneously monitor blood oxygenation and flow velocity in femoral vessels and the superior sagittal sinus (SSS) as a result of apneic challenge, a modified multi-echo GRE pulse sequence (**Fig 1a**) [8] was used to collect velocity-encoded projections (phase encoding gradients inserted after TE1) in addition to full-image echoes (TE2 and TE4) for field mapping. The field map is used to quantify the difference in the induced magnetic field between the intravascular blood and surrounding muscle tissue [4, 9] for blood oxygenation quantification. Blood flow velocity is estimated from the phase difference between the velocity-encoded projections after removing signal contributions from the background static tissue using a reference image [7], which is collected at TE1 (**Fig 1b**, note that phase encoding gradients occur before TE1) prior to launching the pulse sequence of Fig 1a for the duration of the apnea paradigm. HbO_2 and velocity was quantified in the femoral artery and vein and SSS in 2 healthy subjects (ages 25 and 38 yrs) during baseline (1 min), apnea (45-75s breath hold beginning at end exhalation), and 3 mins of recovery. All experiments were performed on a 3T Siemens Trio and axial images of the femoral vessels and SSS were acquired with an extremity and head coil, respectively. The following imaging parameters were used: FOV=128 x 128 mm^2, voxel size = 1 x 1 x 5 mm^3, TE/TR = 5/39.1 ms, BW = 521 Hz/pix, Flip angle = 15º, VENC = 60 cm/s.

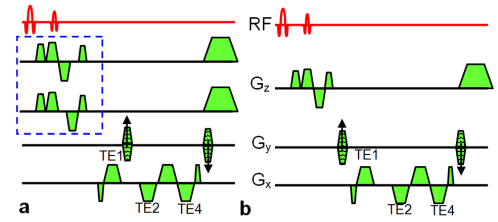

Figure 1: a) RF-spoiled multi-echo GRE pulse sequence with fat suppression and flow compensation. In **b**) the two-step velocity-encoding is toggled between TR (dashed box).

Results and Discussion: A representative plot of HbO_2 in the femoral artery and vein during apneic periods of 45 and 60 seconds is shown in **Fig 2**. The nadir of the arterial saturation was delayed by about 20 seconds from end apnea due to re-circulation time and decreases with prolonged apneic period. Venous saturation in both the femoral vein and SSS (**Fig 3, different subject**) was found to increase approximately 5 %HbO_2 during apnea, which together with the decreased arterial saturation represents a decreased arteriovenous (AVO_2) difference both centrally and peripherally. However, while velocity measurements in the femoral vessels (not shown) decreased during apnea, SSS velocity increased approximately 70% after 45 seconds apnea (**Fig 3a**) and 100% after 75 seconds apnea **(Fig 3b)**, thus maintaining oxygen delivery to the brain despite the reduced AVO_2 difference. These observations suggest that cerebral metabolic rate of oxygen ($CMRO_2$) was roughly preserved during apnea, while oxygen utilization decreased in the periphery. Such flow-mediated preservation of $CMRO_2$ has been observed in response to hypercapnia [10, 11], which occurs during apnea. It is notable that HbO_2 in the femoral vein (**Fig 2**) continued to decrease well after end apnea, perhaps representing peripheral regeneration of O_2 stores after reduced O_2 utilization during apnea.

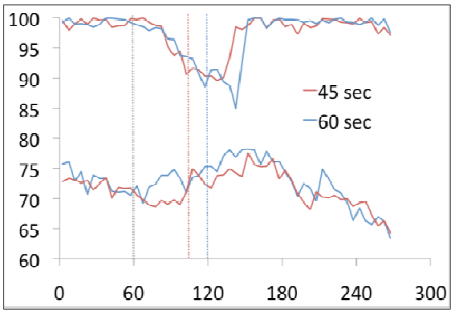

Figure 2: Time course of HbO_2 saturation in the femoral artery (top) and vein (bottom). Vertical lines correspond to apnea initiation and colored lines to apnea cessation after 45 & 60 sec.

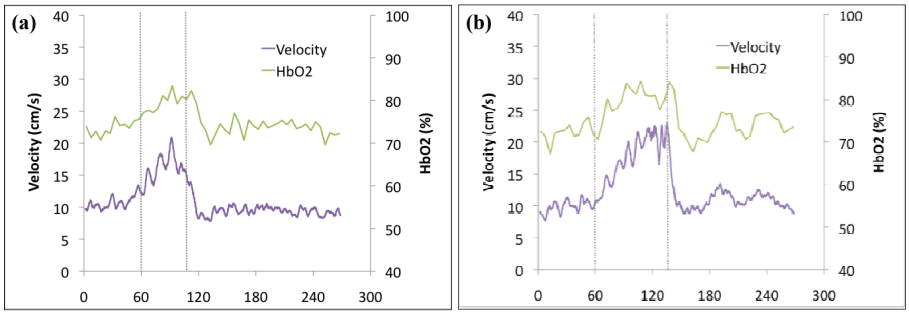

Figure 3: 5-sec sliding average of velocity measurements and discrete HbO_2 measurements versus time in the SSS after **(a)** 45 seconds and **(b)** 75 seconds apnea. Grey lines represent apnea initiation and cessation.

Conclusion: This study indicates the feasibility of a multi-GRE-based method for characterization of the apneic response. Future studies will focus on improving sensitivity and reproducibility of HbO_2 and velocity measurements, increasing the sample size of healthy controls, determining inter-observer and population variability in the apneic response, and investigating the apneic response in relevant disease states.

References: [1] Foster et al., Scand J Med Sci Sports (2005); [2] Andersson et al., Undersea Hyperb Med (1998); [3] Marabotti et al., J Appl Physiol (2009); [4] Fernandez-Seara et al., MRM (2006); [5] Andersson et al., J Appl Physiol (2002); [6] Lindholm et al., Aviat Space Environ Med (2007); [7] Langham et al., MRM (2010); [8] Langham et al., ISMRM (2010); [9] Haacke et al., Hum Brain Map (1997); [10] Kety and Schmidt, JCI (1948).

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