INTRODUCTION: CMRO₂ (cerebral metabolic rate of oxygen consumption) is an important index of cerebral oxygen metabolism found to be altered in many neurological diseases [1,2]. Although recently developed MR-based methods achieve CMRO₂ quantification with 25 s temporal resolution [3,4], improving this temporal resolution further is needed to quantify CMRO₂ changes in response to short term physiologic stressors, such as breath hold apnea. While the normal physiologic response to apnea involves central vasodilation to maintain cerebral oxygen delivery [5], it is hypothesized that this response becomes blunted in patients with obstructive sleep apnea (OSA) [6,7], potentially contributing to the neurological complications associated with the disease. We present a CMRO₂ quantification method with 5-second temporal resolution and apply it to a breath hold paradigm, illustrating the potential of the method to investigate changes in cerebral metabolism and cerebrovascular reactivity during dynamic stressors.

METHODS: An interleaved, multi-slice GRE pulse sequence (Fig. 1) was developed to simultaneously measure total cerebral blood flow (tCBF) in the carotid and vertebral arteries of the neck and venous oxygen saturation (SO₂) in the superior sagittal sinus (SSS) of the head. The sequence alternates between two interleaves: 1) a neck-level non-phase encoded single-echo acquisition (TE1) with tagged first gradient moment to generate 1D projection velocity images to quantify total cerebral blood flow (tCBF) and the arterio-venous difference, normalized to body volume and hematocrit (Hct): CMRO₂ = tCBF x VO₂/100, and 2) an identical head-level single-echo acquisition (TE2) to quantify SSS blood flow (SSSBF) followed by a phase-encoded multi-echo acquisition (TE3&4) in the same TR to generate 2D phase difference maps to quantify SSS SO₂ [8]. Venous signal in the neck is suppressed by a saturation band inserted before each neck interleave. Prior to running the main sequence loop, a 2D flow-compensated reference image (Fig. 1a) is generated by inserting phase encoding lobes before TE1&2. The central k-space line of this reference image, with vessels masked prior to k-space transformation, is subtracted from the velocity-encoded projections to eliminate signal contribution from static tissue [8]. tCBF in the neck vessels is then determined by taking the phase difference between consecutive projections with alternating positive and negative first gradient moments. SO₂ is determined by measuring the phase accumulation in the SSS between TE3&4, as a result of the paramagnetic properties of deoxyhemoglobin [10-12]. During the main loop (Fig. 1b), the number of phase encodes is reduced by four fold to 52, and 2D phase maps are reconstructed using keyhole with outer k-space filled from the fully sampled reference image. CMRO₂ is quantified by Fick’s principle as the product of tCBF and the arterio-venous difference, normalized to brain volume and hematocrit (Hct): CMRO₂ = tCBF x (SO₂ - SSS SO₂). tCBF and SO₂ are determined from phase images, SO₂ measured with pulse oximetry, brain volume measured with a 3D MPRAGE image set [13], and hematocrit assumed as 0.4.

Two healthy subjects (24 y.o. F, 26 y.o. M) were scanned during a breath hold paradigm involving an initial 90 s baseline followed by two end-expiratory breath holds of 40 s and 30 s with 90 s recovery after each. Projection velocity data were time averaged to match the 5 s temporal resolution of the susceptometry acquisition. All experiments were performed on a 3T Siemens Trio scanner using a 12-channel head and 2-channel neck coil.

RESULTS AND DISCUSSION: S₀₂, tCBF, SSSBF, and CMRO₂ are plotted for a healthy 26 y.o. subject during a breath hold paradigm (Fig. 2a). Pulse oximetry derived S₀₂ did not change and therefore was assumed to remain constant at 98%, CMRO₂ averaged over the initial 90 s baseline was 118 ± 6 µmolO₂/100g/min, in agreement with literature [3]. Flow and S₀₂ are observed to increase during breath hold and drop during recovery, undershooting before returning to baseline, while CMRO₂ remains relatively constant during breath-hold, dropping during recovery before returning to baseline. The transient CMRO₂ drop post-apnea results from the ~5-10 s delay in S₀₂ recovery relative to tCBF recovery after cessation of breath hold. This delay may result from the time needed for blood measured in the neck slice to reach the head slice, but, surprisingly, it becomes more pronounced (~15 s) when considering flow in the SSS. Furthermore, SSSBF increases about twice as much relative to baseline than tCBF (105% vs. 48%). For this reason, calculating CMRO₂ with SSSBF substituted for tCBF (Fig. 2b) changes the observed CMRO₂ response significantly, causing a marked increase during breath-hold with return to baseline during recovery. The lack of drop in pulse oximetry derived S₀₂ values during breath hold is questionable given the demands of the paradigm. In the future, we will attempt to measure S₀₂ in addition to SSS SO₂ in cerebral arteries to eliminate the need for pulse oximetry.

CONCLUSIONS: This study indicates the feasibility of using keyhole susceptometry and projection velocimetry to increase the temporal resolution of CMRO₂ quantification to 5 s, thereby enabling observation of temporal dynamics of the cerebrovascular response to dynamic stressors. This technique will be applied to answer questions such as how CMRO₂ responds to apnea and whether this response is altered in diseases such as OSA.