Intra-observer and Scan-Rescan Reproducibility of Quantitative Oxygen Extraction Fraction from MRI Phase at 7 Tesla

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Target Audience. Radiologists interested in evaluation of oxygenation status for disease such as stroke, tumor, and multiple sclerosis.

Purpose. Oxygen metabolic disturbance forms a key pathological component of many neurological disorders such as multiple sclerosis (MS) [1]. Metabolic imaging can thus provide new diagnostic information about tissue health and function. Non-invasive MRI evaluation has adopted T_2^* magnitude as a surrogate for tissue oxygenation [2]. However, isolation of oxygenation-related T_2^* signal from changes due to cerebral blood volume and edema is challenging. Phase-based MRI methods, on the other hand, directly measure absolute oxygen extraction fraction (OEF) in single veins by applying MR susceptometry [3]. To extend phase-based OEF imaging toward clinical use, improved understanding of the variability in oxygenation values across scan sessions and readings is critical.

This work evaluates the reproducibility of quantitative OEF measurements from MRI phase in adult volunteers and in patients with MS. The study was performed at ultra-high field (7T) with high signal-to-noise ratio to achieve sub-millimeter phase resolution, allowing for OEF observations across multiple cortical regions.

Methods. *MRI Acquisition*. We recruited 10 healthy volunteers and 5 patients with MS to be scanned on a 7T Siemens MRI with an in-house 32 channel head coil. For OEF measurements, axial 3D flow-compensated FLASH images were acquired with magnitude and phase (TR=26ms; TE= 6-6.4, 10ms; resolution= $0.33 \times 0.33 \times 1.0 mm^3$; matrix=576x504x64; BW=130Hz). A subset of 5 controls was scanned twice in sessions a week apart, with repositioning based on localizers.

Vessel selection. Long cortical pial veins parallel to the main field (B_0) were manually identified on sagittal and coronal views. Vessels were selected only if the tilt angle was <20° relative to B_0 and the diameter was <2mm.

OEF quantification. Phase images were high-pass filtered (96x96 Hanning) to remove background magnetic fields. The field shift between the vessel and surrounding tissue, $\Delta B_{vein\text{-}tissue}$, was calculated using phase from both echoes. Applying MR susceptometry, local OEF was determined for each parallel vein as: $\Delta B_{vein\text{-}tissue} = 1/6 \cdot 4\pi\ \Delta\chi_{do} \cdot Hct \cdot \mathbf{OEF} \cdot (3\cos^2\theta - 1) \cdot B_0$. Here, vessel tilt was assumed $\theta=0$, $\Delta\chi_{do}=0.27$ppm, and hematocrit was measured or assumed $Hct=0.42$ [4,5].

Readings. In each subject, OEF was averaged from 8-10 veins across the cortex. One observer identified vessels and measured OEF in 5 patients and 5 controls, then repeated the analysis on the same dataset after one week. Separately, the same observer analyzed scan-rescan OEF in 5 distinct healthy volunteers; readings from the two sessions for each subject were also made a week apart.

Results. *Intra-observer*. 60.2% of vessels identified on the first reading were independently re-identified on the second reading. Mean cortical OEF was not different across readings for controls (p=0.71) and patients (p=0.95). The intra-observer reproducibility of OEF was excellent, with coefficient of variation (COV)= **2.1%**.The Bland-Altman plot for intra-observer OEF is shown (***Fig 1***) [6].

Scan-rescan. Consistent subject repositioning was achieved between scan sessions (***Fig 2***). 34.1% of vessels identified on the first week were the same as those independently identified on the second week. Mean cortical OEF across subjects was not different between the first session (mean ± SD = 29.3 ± 3.4%) and the second session (30.2±1.1%), p=0.50. The scan-rescan COV was **5.9%**, and a scatter plot of OEF is shown with confidence intervals based on the mean SD of the group (***Fig 3***).

Discussion. We observed high intra-observer agreement for OEF in healthy volunteers and in patients with MS. Scan-rescan reproducibility was also acceptable, with week-to-week COV = 5.9% compared to within-session COV = 2.3% in global phase OEF in the sagittal sinus reported by Jain et al [7].

Conclusion. This study supports use of quantitative phase-based OEF as a reliable MRI method to assess oxygenation in the brain.

References. [1] Sun, *Ann Nucl Med* 1998. [2] Christen, *Magn Reson Med* 2011. [3] Fan, *Magn Reson Med* 2012. [4] Haacke, *Human Brain Mapp* 1997. [5] Weisskoff, *Magn Reson Med* 1992. [6] Bland, *Lancet* 1986. [7] Jain, *J Cereb Blood Flow Metab* 2010. **We thank Drs. Lawrence Wald and Boris Keil,** NSF GRFP, R01-EB007942, NMSS 4281-RG-A1.

Intra-observer Cortical OEF % (mean ± SD)

	Reading #1	*Reading #2*	*p-value*
Controls (n=5)	32.8 ± 3.6	32.5 ± 2.7	0.71
Patients (n=5)	28.2 ± 1.7	28.8 ± 1.9	0.95

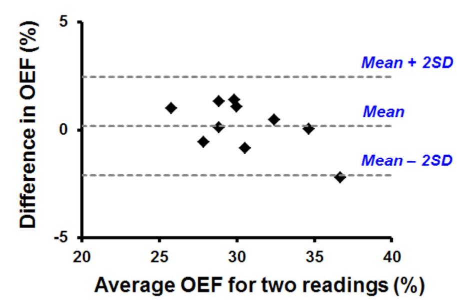

Fig 1. Bland-Altman plot illustrating excellent intra-observer reproducibility of OEF (COV = 2.09%).

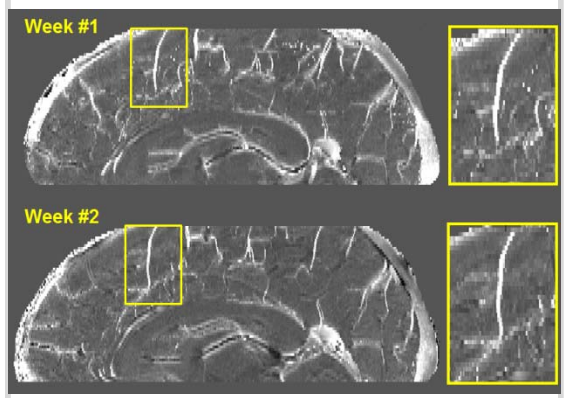

Fig 2. Phase images acquired one week apart in a healthy volunteer, with good repositioning. The same vein is highlighted from each scan.

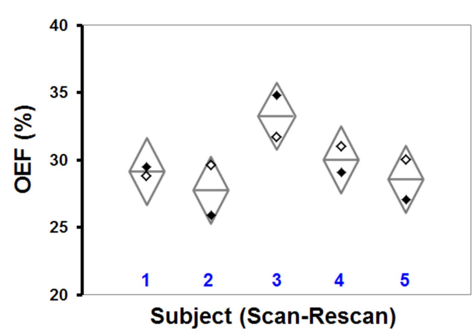

Fig 3. Scatter plot of cortical OEF over two sessions for each subject. The vertical span of each diamond represents the 95% confidence interval.