Vessel-specific quantification of blood oxygenation with T2-Relaxation-Under-Phase-Contrast (TRU-PC) MRI

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Introduction Measurement of human brain metabolism is of great importance in brain disorders and functional brain imaging, but for decades it has been a niche market of Positron Emission Tomography (PET) [1]. This is largely attributed to a lack of MRI methods to quantitatively measure regional venous oxygenation (Y_v). The present study aims to fill this gap by developing a non-invasive, rapid, and reproducible method to measure Y_v in a vessel-specific manner in the brain. Feasibility of this technique, T2-Relaxation-Under-Phase-Contrast (TRU-PC) is demonstrated. Furthermore, several technical aspects were examined, including validation with an established global Y_v technique, test-retest reproducibility, sensitivity to detect oxygenation changes due to hypoxia and caffeine challenges, applicability of EPI acquisition to shorten scan duration, and the ability to study veins with a caliber of 1-2 mm.

Theory The TRU-PC pulse sequence (Fig. 1) is featured by a combination of a T_2-preparation (red box) with phase-contrast MRI (green box). The phase-contrast module serves to isolate pure venous blood signal, and the T_2-preparation modulates T_2-weighting of the signal. A post-saturation pulse is applied following the signal acquisition to remove spin history (blue box), so that the magnetization can be accurately modeled regardless of the previous RF pulses experienced [4]. The MR signal of the TRU-PC sequence follows a mono-exponential decay as a function of effective TE (eTE). One can therefore acquire the signals at a range of eTE values to obtain a fitting for $T_{2,blood}$. $T_{2,blood}$ can in turn be converted to Y_v using a calibration plot [8].

Methods Experiments were performed on 28 healthy subjects (age 31 ± 10 years, 14 Male) using a 3T MRI scanner (Philips). A series of 5 studies were conducted. *Feasibility:* The feasibility study (N=8) was conducted to optimize the sequence parameters, which yielded the following working protocol: single slice, FOV=200x200mm^2, matrix=276x83, slice thickness=5mm, V_{enc}=15cm/s in AP, RT=668ms, TE=4.9ms, T2-preparation using τ_{CPMG}=10ms, three effective TEs (eTE=40ms, 80ms, 120ms), scan duration=7min 13sec. *Validation:* In N=7 subjects, Y_v measured with TRU-PC was compared to a validated global Y_v technique, TRUST MRI [2]. *Vascular reactivity:* In N=3 subjects TRU-PC MRI was performed before and during the breathing of 13% O_2 [6], and subsequently compared. N=3 subjects also performed a caffeine challenge. The subjects were scanned before, and 1 hour after the ingestion of a 200 mg caffeine tablet. *Reproducibility and EPI-acquisition study:* In N=5 subjects, the reproducibility of TRU-PC was investigated with three types of acquisition strategies: the standard TRU-PC (7.2 min), a segmented-EPI acquisition with EPI-factor of 3 (2.4 min), and EPI-factor of 5 (1.5 min). This set of scans was repeated four times in an interleaved fashion. Reproducibility of each acquisition strategy was evaluated by the intra-session coefficient of variation (CoV), defined as the standard deviation across repetitions divided by the mean [7]. The Y_v values across different acquisition strategies were also compared. *Small Vessel:* In N=2 subjects, the feasibility of measuring Y_v in pial veins and deep veins on the order of 1-2 mm in diameter was examined.

Results and Discussion *Feasibility:* Figure 2a shows maps of pure blood signals as a function of eTE. Figure 2b shows the corresponding Y_v map. It is apparent that the T_2 fitting is stable across the entire path of the venous structure. Interestingly, the mid-sagittal slice also includes a feeding artery, i.e. basilar artery, and Y_v in the artery was found to be close to 100%, as expected. ROI analyses were carried out in 8 regions as illustrated in Figure 2c. Figure 2d shows Y_v values for each ROI. Significant differences were observed in three neighboring ROI pairs (P<0.05). *Validation:* The average TRU-PC Y_v value of 61.3 ± 6.7% (mean ± SD) showed no difference (P=0.90) from the TRUST average Y_v of 61.4 ± 8.3%. Figure 2e shows the scatter plot between the TRU-PC and TRUST measured Y_v values. A linear relationship close to the unit line was observed between them (N=7, P=0.001). *Vascular Reactivity:* For the hypoxia maneuver, Y_v during hypoxia was lower than that during normoxia in all ROIs, consistent with the expected effects of this type of challenge. The average decrease in Y_v was 6.9±3.4%. For the caffeine challenge a decrease in Y_v was observed in all ROIs with an average reduction of 10.1±2.5%. *Reproducibility and EPI-acquisition:* The coefficient of variation (CoV) averaged over all ROIs was 3.5±1.0% for the non-EPI TRU-PC protocol, showing an excellent test-retest reliability. The use of EPI was able to shorten the scan duration with a minimal impact on the quality of the data: the CoV for EPI-factor 3 and EPI-factor 5 scans were 3.8±1.6% and 3.9±1.1%, respectively. *Small Vessel:* We measured Y_v in smaller veins (1-2 mm in diameter as determined from SWI images) in two subjects. In one subject, we applied a sagittal planning to measure pial veins that drain cortical gray matter. Figure 3a shows blood signal map as a function of eTE. Y_v values of representative veins are also displayed (note: these veins do not have designated names). In a different subject, we applied an axial planning to measure Y_v of deep veins that drain deep gray matter (e.g. basal ganglia, thalamus). The resulting TRU-PC images and the corresponding oxygen saturation are shown in Figure 3b.

In summary, we presented a novel technique, TRU-PC MRI, to non-invasively quantify cerebral oxygenation in regional draining veins with a diameter of 1 mm or greater. Methodological evaluations revealed that this technique is accurate when compared to established approaches, is reproducible, and has sufficient sensitivity in detecting oxygenation changes due to typical physiologic challenges. Thus, this simple technique may provide a critical step toward region-specific measurement of oxygenation and metabolism in the brain.

References [1] Mintun, et al. J Nucl Med 25:118 (1984) [2] Lu & Ge. MRM 60:357 (2008) [3] Xu, el al. MRM 62:141 (2009) [4] Xu, et al. MRM 68:198 (2011) [5] Bernstein & Ikezaki. JMRI 1:725 (1991) [6] Xu, et al. JCBFM (in press) [7] Liu P, et al. MRM (in press) [8] Lu, et al. MRM 67:42 (2012).

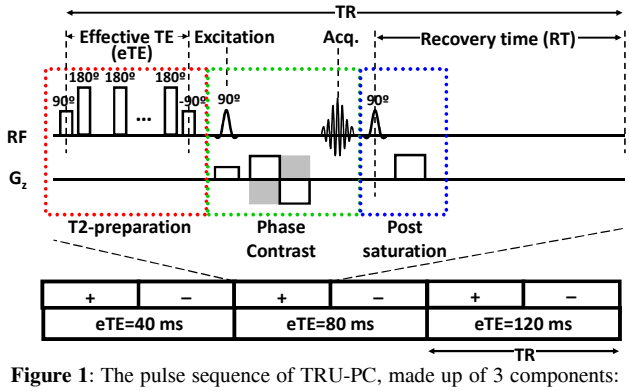

Figure 1: The pulse sequence of TRU-PC, made up of 3 components: a T2-preperation module (red box), a Phase-Contrast module (green box), and a Post-saturation module (blue box). The phase-contrast module allows for the separation of blood and tissue via the bipolar gradient applied in '+' or '−' orders. Three different T2-prep schemes (40, 80, and 120 ms) are played out. The post-saturation pulse resets the magnetization.

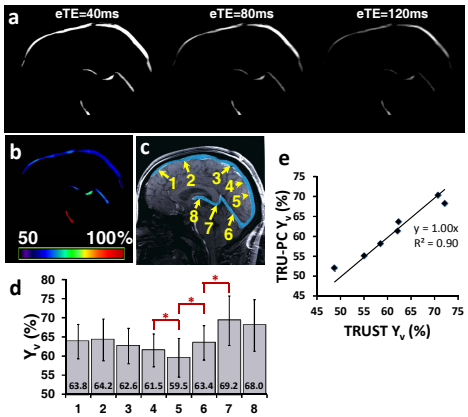

Figure 2: Representative results of TRU-PC MRI. (a) TRU-PC images acquired with eTE=40, 80, and 120 ms. (b) The corresponding oxygen saturation map. (c) Illustration of eight ROIs on a mid-sagittal anatomic image. (d) Average Y_v in ROI 1-8 (N=18). (e) Scatter plot between TRUST and TRU-PC Y_v.

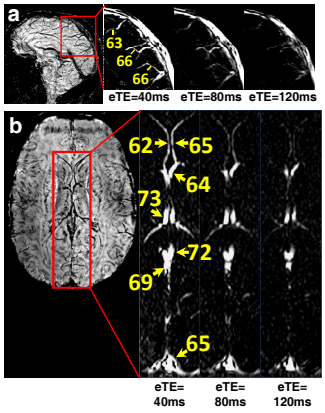

Figure 3: TRU-PC applied to (a) pial veins and (b) deep veins. Estimated Y_v of discernable pial veins are listed in the image. The anatomic image is a SWI image.