Non-invasive quantification of venous oxygenation and cerebral metabolic rate of oxygen in humans

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INTRODUCTION: Cerebral venous oxygenation (Y_v) is an important physiologic parameter reflecting the balance between oxygen consumption and supply, and is also relevant for quantitative interpretation of BOLD fMRI signal. Recently, we have proposed a T2-Relaxation-Under-Spin-Tagging (TRUST) MRI technique to quantify Y_v non-invasively in humans (1). The previous work has primarily focused on venous oxygenation in sagittal sinus (SS) (1). Here we aim to extend the measurement to the internal jugular veins (IJV). The challenge for imaging the neck region is that there are multiple blood vessels and many tissue types, and magnetic field inhomogeneity is large. On the other hand, the significance of Y_v measurement in IJV is that IJV drains virtually all blood in the brain and, therefore, is a more accurate indicator of whole-brain venous oxygenation. Furthermore, combined with a phase-contrast (PC) scan (2) measuring the flux of blood at the same location, one can quantify the whole-brain cerebral metabolic rate of oxygen (CMRO2) completely non-invasively. The establishment of such a method may be useful for studying CMRO2 characteristics during aging, sleep, and physiologic challenges.

METHODS: Experiments (12 healthy controls, 4 M, 8 F) were performed on a 3T Philips System. The TRUST sequence was described previously (1). Briefly, TRUST uses the spin labeling principle to separate out the pure (venous) blood signal and then uses T2-preparation pulses to modulate the signal with different T2-weightings (sequence diagram illustrated in Fig. 1). The measured venous blood T2 can be converted to Y_v with a well-known relationship between Y_v and blood T2 (3). TRUST applied on SS used: axial plane, voxel size 3.44x3.44x5mm^3, TR=8000ms, TI(inversion recovery time)=1200ms, labeling thickness 80mm, gap 20mm, single-shot EPI, T2 decay modulated by four TE times: 0ms, 40ms, 80ms and 160ms, each TE performs 8 dynamic scans(four label and four control interleaved); TRUST in IJV used the following parameters: voxel size 2x2mm^2, FOV 160x160mm^2, TI=1000ms, labeling thickness 170mm, gap 5mm, two-shot EPI, T2 decay modulated by three TE times: 0ms, 40ms and 80ms. Segmented EPI instead of single-shot EPI was used for IJV to reduce image distortion. Scan planning for SS TRUST was based on middle sagittal survey image (Fig. 2a). IJV TRUST scan planning was based on survey (Fig. 2b) as well as a time-of-flight venograph (Fig. 2c). The slice location is about 2-4mm below the jugular bulb. Phase contrast scan (0.45x0.45 mm^2 in-plane resolution) had identical slice location as IJV TRUST. Whole brain oxygen consumption was calculated as $CMRO_2 = Flux \cdot (1 - Y_v) \cdot C_a$, where C_a is the amount of oxygen molecules that a unit volume of blood (with a typical Hct of 0.44) can carry, assumed to be 833.7 μmol O2/100ml blood based on hematology and pulmonary physiology literature (4). In addition, T1W MPRAGE (1x1x1mm^3) was acquired for brain volume determination and was used to normalize whole brain CMRO2 to unit volume CMRO2 (in μmol/g/min).

RESULTS and DISCUSSION: TRUST images are shown in Fig. 3 for SS (upper row) and IJV (bottom row). The label (left column, Fig. 3) and control (middle column) images are almost identical except for the venous vessel regions (arrows). SS and IJV are evident in the difference images (right column, Fig. 3). The blood T2 values in the left and right IJVs were 63.6±17.5ms (mean±STD, n=12) and 59.0±11.8ms, respectively and the values for the combined ROI including both left and right IJVs were 62.8±10.6ms. The corresponding Y_v were 65.1±8.5%, 63.2±6.3% and 64.3±7.2%, respectively. There was a significant correlation between Y_v in the left and right IJVs across subjects (Fig. 4a), as expected since the blood originates from the same (venous) sinuses. The T2 of SS blood was 57.9±9.12ms and Y_v was 62.2±6.1%. There was no difference between left/right IJV Y_v (p=0.28), nor was there a difference between IJV and SS (p=0.13). The estimation errors in SS (2.42±0.62ms) were smaller than those in IJV (3.30±1.86ms) (paired t test, p=0.02), suggesting that TRUST MRI in SS is more robust. This is possibly because flow in IJV is more pulsatile compared to SS.

Fig. 2d shows the magnitude image of the phase-contrast scan which clearly shows the internal jugular vein and internal carotid arteries. In the corresponding phase image (Fig. 2f), the arteries are white because of upwards flow direction whereas the veins (circles) are black due to downwards flow direction. Flux in IJV was 619.45±127.33ml/min (combining both sides) obtained by integrating the negative-velocity voxel values within IJV regions (Fig. 2f circles). The flux normalized by the brain volume (computed based on MPRAGE image, with skull stripping using the software FSL, Oxford University, United Kingdom) was 52.7±11.1ml/100g brain/min, consistent with typical CBF values reported in literature using PET or ASL MRI. Y_v and flux shows a positive correlation across subjects (Fig. 4b), suggesting that individuals that have higher blood flow tend to have higher oxygenation in veins. This finding is consistent with our previous data comparing SS Y_v and ASL CBF (5). Whole-brain CMRO2 was found to be 1714.9±240.8 μmol/min. After accounting for brain volume, the unit volume CMRO2 was 1.46±0.20 μmol/g/min, in excellent agreement with PET result of 1.50±0.07μmol/g/min (6). In summary, we present the first results of quantitative CMRO2 measurements in humans with completely non-invasive procedures.

REFERENCES: 1) Lu ISMRM Abstract, 256 (2007); 2) de Boorder, M.J. et al. Stroke 35: 1350 (2004); 3) Silvennoinen et al. MRM 49: 47 (2003); 4) Chanarin et al. Blood and its Disease (1984) 5) Lu et al. ISMRM 613, (2007); 6) Fox et al. Science 241: 462 (1988);

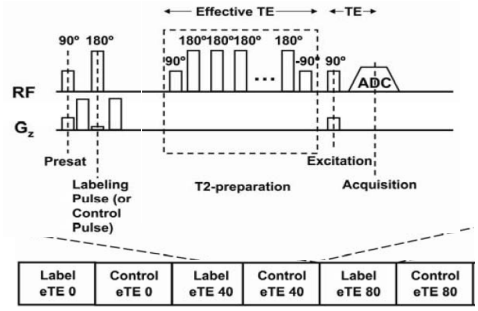


Fig. 1 TRUST sequence diagram. The sequence consists of interleaved label and control scans with different T2-weighting. For each scan, the sequence is similar to an ASL, except that the labeling slab is above the imaging slice and a T2-prep block is added.

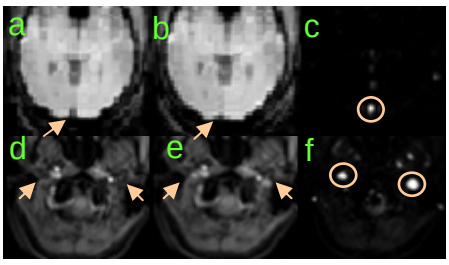


Fig. 3 TRUST images, (a) SS label, (b) SS control, (c) SS difference image; d) IJV label, (e) IJV control, (f) IJV difference image.

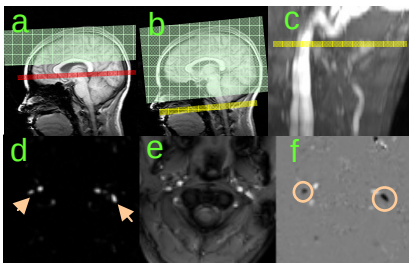
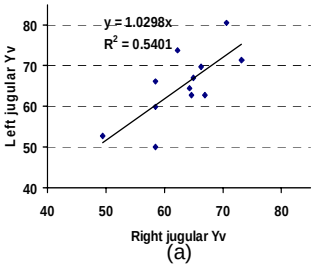
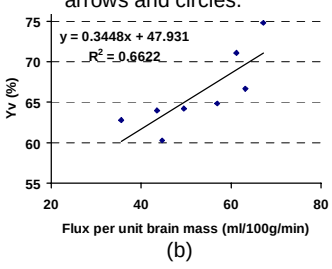


Fig. 2 Position of labeling slab (green) and imaging slice (red and yellow) for (a) SS and (b) IJV TRUST MRI. (c) illustrates the IJV slice location in a venograph (sagittal view). (d-f) Phase contrast magnitude image, anatomical image, and phase image (velocity map), respectively. IJV are shown in arrows and circles.



(a)



(b)

Fig. 4 (a) scatter plot between left IJV Yv and right IJV Y_v across 12 healthy subjects. (b) scatter plot between IJV flux and Y_v across 8 subjects.