Quantitative evaluation of cerebral venous oxygenation using T2-Relaxation-Under-Spin-Tagging (TRUST) MRI

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INTRODUCTION: The venous oxygen saturation fraction (Yv) in the brain has been the interests of many studies, because non-invasive and accurate measurement of Yv is not only important in terms of the fMRI signal, but also has directly clinical implications regarding the metabolic state of the brain. However, a robust method to measure this parameter has not been established. One of the main hurdles is that, in order to quantify the absolute value of blood oxygenation, one needs to isolate the blood signal (i.e. not having any partial volume from tissue or CSF) (1-3). To overcome this problem, we propose to apply spin labeling technique on the venous side (instead of on the arterial side as the conventional ASL does) and perform paired-subtractions just like the ASL data processing. Then the subtracted image only contains the venous blood signal. This signal by itself is not particularly interesting per se because it reflects the venous outflow but not perfusion. However, the T2 signal decay of this signal is interesting because the T2 relaxation time can be converted to Yv with a calibration plot. Various technical aspects of this method were investigated and measurements were also made under hypercapnia conditions to further test the technique. This technique is dubbed T2-Relaxation-Under-Spin-Tagging (TRUST) MRI.

METHODS: The TRUST sequence diagram and the geometric locations of the labeling slab and imaging slice are shown in Fig. 1. This pulse sequence is similar to the PICORE ASL sequence (4) except that the labeling slab is above the imaging slice and a series of non-slice-selective T2-preparation pulses are inserted in front of the excitation pulse to modulate the T2-weighting. T2-preparation rather than conventional T2-refocusing is used to minimize the blood outflow effect in T2 measurement. Two schemes (5) were applied to minimize the imperfection in the T2-prep pulses: 1) Composite pulses were used, i.e. $90_x180_y90_x$ for the 180 pulses and $270_x[-360_x]$ for the -90 pulse. 2) The signs of the 180 pulses were arranged in a MLEV pattern (e.g. 1 1 -1 -1 etc). MR experiments (3T Tim Trio, Siemens) were performed on a total of 24 healthy subjects with informed consent. Four effective TEs (TE_e) (the T2 weighting generated by the T2-prep pulses, not the TE used for the signal acquisition) are used: 0ms, 40ms, 80ms and 160ms, which correspond to 0, 4, 8 and 16 refocusing pulses in the T2-preparation (τ_{CPMG}=10ms). Other Imaging parameters: FOV=230mm, matrix=64x64, single-shot EPI, slice thickness=5mm, TR=8000ms, TE=19ms, TI=1200ms, repetition=4, scan duration 4'16". In two of the subjects, hypercapnia challenge (by breathing through a plastic tube with 600ml of volume, thereby increasing the dead-space) was applied and TRUST MRI was performed before, during and after the challenge. End-tidal CO2 was monitored throughout the experiment and was compared to MRI results. In 22 subjects, the labeling slab was also positioned on the arterial side and arterial TRUST was performed to determine $T_{2,blood,arterial}$ in vivo. TR/TI=3000/800ms.

RESULTS and DISCUSSION: Figs. 2a and b shows the control and label images, respectively, at different effective TEs. Fig. 2c shows the corresponding subtracted images. Note that only large venous vessels have discernable signal intensities due to relatively large flow velocities (arrow). An ROI was drawn in the sagittal sinus area (Fig. 2d) and the signals from 4 voxels with highest amplitudes were averaged. It is important to point out that the ROI selection did not significantly affect the fitted T2 values. Neither does the choice for number of voxels. Fig. 2e shows the experimental data and fitting results of the subtracted signal as a function of effective TE. Excellent fitting is achieved for all subjects. The resulting CPMG-T2 values are compared to a calibration curve (Fig. 2f) obtained from in vitro blood measurements at similar conditions (3T, τ_{CPMG}=10ms, Hct=0.44, courtesy of van Zijl and Clingman, personal communications) to estimate Yv in the human subjects. Over the entire subject group, the CPMG-T2 was found to be 62.4±12.0ms (mean±SD, n=24). The corresponding Yv was 64.8±6.3%. Comparing male and female groups, the male group (T2=58.0±11.5ms, n=16) has a significantly (p=0.008) shorter T2 than the female group (T2=71.1±7.7ms, n=8), which could be due to hematocrit differences. To test the robustness and reproducibility of the method, we performed 5 independent measures on each subject at 10 minutes of interval. Fig. 3 shows the time-courses and it can be see that, while the inter-subject variations are considerable, the temporal stability of the measurements is excellent (small error bars). We believe that the inter-subject variations are physiologic and reflect the normal variations among subjects (6). Fig. 4 plots the Yv values and end-tidal CO2 pressure before, during and after a hypercapnia challenge, showing a 9.8% increase due to the challenge. Arterial blood T2 was determined from branches of MCA using short TI (800ms) arterial TRUST. It was found to be 150.0±17.0ms (n=22), which is very consistent with the in vitro results (right end of the curve in Fig. 2f). In summary, TRUST MRI can be used to selectively measure blood T2 values, from which physiologic parameters such as Yv can be quantified.

REFERENCES: 1) Haacke et al. HBM 5:341-346 (1997); 2) Oja et al. JCBFM 19:1289-1295 (1999); 3) Golay et al. MRM 46: 282 (2001); 4) Wong et al. NMR in Biomed 10: 237 (1997); 5) Brittain et al. MRM 33: 689 (1995); 6) Nagdyman et al. Int. Care Med. 31: 846 (2005).

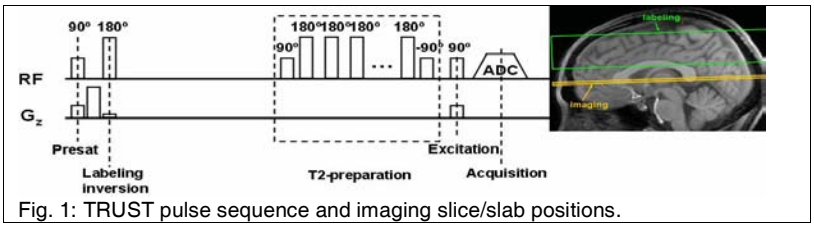

Fig. 1: TRUST pulse sequence and imaging slice/slab positions.

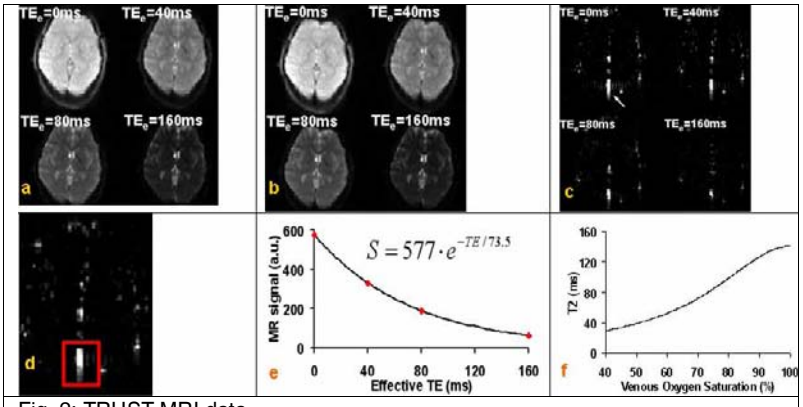

Fig. 2: TRUST MRI data.

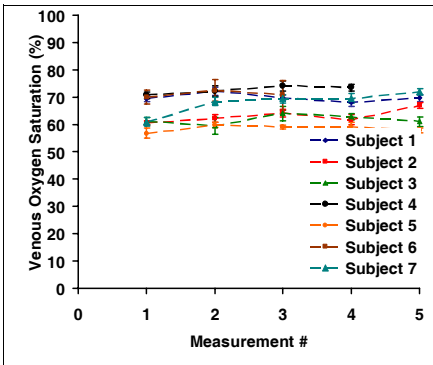

Fig. 3: Reproducibility of Yv measurements. Each subject was in the scanner for 45 minutes. Every 10 minutes, a TRUST MRI was performed. The TRUST MRI scan takes about four minutes.

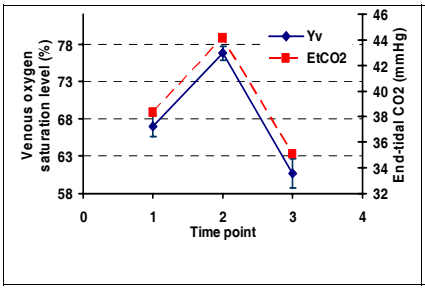

Fig. 4: Yv and end-tidal CO2 before (point 1), during (point 2) and after (point 3) hypercapnia challenge. The points are measured at about 10 minutes apart.