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Multi-site evaluations of a T₂-Relaxation-Under-Spin-Tagging (TRUST) MRI technique to measure brain oxygenation

Peiying Liu¹, Ivan Dimitrov^{1,2}, Trevor Andrews^{2,3}, David E. Crane⁴, Jacinda K. Dariotis⁵, John Desmond⁶, Julie Dumas⁷, Guillaume Gilbert^{2,8}, Anand Kumar⁹, Bradley J. MacIntosh⁴, Alan Tucholka⁸, Shaolin Yang^{9,10,11}, Guanghua Xiao¹, and Hanzhang Lu¹

¹Advanced Imaging Research Center, University of Texas Southwestern Medical Center, Dallas, Texas, USA

²MR clinical science, Philips Healthcare, Cleveland, OH, USA

³Department of Radiology, University of Vermont College of Medicine, Burlington, Vermont, USA

⁴Heart and Stroke Foundation Canadian Partnership for Stroke Recovery, Sunnybrook Research Institute, Toronto, Ontario, Canada

⁵Department of Population, Family and Reproductive Health, Center for Adolescent Health, The Johns Hopkins Bloomberg School of Public Health, Johns Hopkins University, Baltimore, Maryland, USA

⁶Department of Neurology, Johns Hopkins Medical Institutions, Baltimore, Maryland, USA

⁷Department of Psychiatry, University of Vermont College of Medicine, Burlington, Vermont, USA

⁸Department of Radiology, Notre-Dame Hospital (CHUM), University of Montreal, Montreal, QC, Canada

⁹Department of Psychiatry, University of Illinois at Chicago, Chicago, Illinois, USA

¹⁰Department of Radiology, University of Illinois at Chicago, Chicago, Illinois, USA

¹¹Department of Bioengineering, University of Illinois at Chicago, Chicago, Illinois, USA

Abstract

Purpose—Venous oxygenation (Y_v) is an important index of brain physiology and may be indicative of brain diseases. A T₂-relaxation-under-spin-tagging (TRUST) MRI technique was recently developed to measure Y_v . A multi-site evaluation of this technique would be an important step toward broader availability and potential clinical utilizations of Y_v measures.

Methods—TRUST MRI was performed on a total of 250 healthy subjects, with 125 from the developer's site and 25 each from five other sites. All sites were equipped with a 3T MRI of the same vendor. The estimated Y_v and the standard error of the estimation, ϵ_{Y_v} , were compared across sites.

Corresponding authors: Peiying Liu, Ph.D., Advanced Imaging Research Center, UT Southwestern Medical Center, 5323 Harry Hines Boulevard, Dallas, Texas 75390, Tel: 214-645-2806, Fax: 214-645-2885, peiyingliu.peiyingliu@gmail.com or Hanzhang Lu, Ph.D., Advanced Imaging Research Center, UT Southwestern Medical Center, 5323 Harry Hines Boulevard, Dallas, Texas 75390, Tel: 214-645-2761, Fax: 214-645-2885, hanzhang.lu@gmail.com.

Results—The averaged Y_v and ε_{Y_v} across six sites were $61.1 \pm 1.4\%$ and $1.3 \pm 0.2\%$, respectively. Multivariate regression analysis showed that the estimated Y_v was dependent on age ($p=0.009$), but not on performance site. In contrast, the standard error of Y_v estimation was site-dependent ($p=0.024$), but was all less than 1.5%. Further analysis revealed that ε_{Y_v} was positively associated with the amount of subject motion ($p<0.001$) but negatively associated with blood signal intensity ($p<0.001$).

Conclusion—This work suggests that TRUST MRI can yield equivalent results of Y_v estimation across different sites.

Keywords

blood oxygenation; TRUST; brain; venous oxygenation

INTRODUCTION

Venous oxygenation (Y_v) is the fraction of oxygenated hemoglobin in the venous blood. Quantification of Y_v in the brain can be used to assess the brain's oxygen homeostasis. When combined with other physiologic measures, such as arterial oxygenation and cerebral blood flow, one can estimate important physiological parameters like oxygen extraction fraction (OEF) and cerebral metabolic rate of oxygen (CMRO₂) (1–3), which are key markers for tissue viability and brain function. Altered Y_v , OEF and CMRO₂ have been found in studies on normal aging (4,5), early brain development (6), and a number of diseases, such as multiple sclerosis (7), carotid artery disease (8), congenital heart disease (9,10) and drug addiction (11). Quantification of Y_v is also important for understanding the mechanism of blood-oxygenation-level-dependent (BOLD) functional magnetic resonance imaging (fMRI), as it is well-known that the BOLD fMRI signal is a complex function of blood oxygenation, blood flow, and oxygen consumption in the brain (12,13). Previous studies showed that Y_v can be used to normalize BOLD fMRI signal and thereby improve the characterization of neural activity (14,15).

Quantification of Y_v is, however, not yet a standard procedure. Up until recently, it was considered a “niche market” of positron emission tomography (PET), which requires an onsite cyclotron, the use of ¹⁵O-labeled radiotracers, and an arterial line for dynamic blood sampling (16,17). Therefore, there is a growing interest to quantify Y_v using non-invasive methods. A few techniques have been reported to measure Y_v based on the susceptibility effects of deoxyhemoglobin on extravascular tissue (18,19) or intravascular blood (3,20). Previously, we have reported a T₂-Relaxation-Under-Spin-Tagging (TRUST) MRI technique to obtain quantitative value of Y_v in the superior sagittal sinus by measuring the T₂ of venous blood (21). An advantage of TRUST MRI in comparison with previous T₂-based techniques (22–24) is that, TRUST utilizes the spin-tagging principle on the venous side to automatically isolate pure venous blood signal and minimize partial voluming effects from surrounding tissue, rather than relying on the post-processing operator to manually select a region of pure blood. It has been validated in humans by comparing TRUST-derived arterial Y values with those measured with the gold-standard Pulse Oximeter (25), and has also been shown to be sensitive in detecting oxygenation changes due to hypercapnia (26), hyperoxia (27), hypoxia (27), glucose (28) and caffeine (29) challenges. The current TRUST

protocol has several attractive features including the absence of any exogenous agent, short scan duration of 1.2 min, and feasibility on a standard 3T scanner. Moreover, it has been shown that the single site TRUST test-retest variations was <2% (30,31), which is reliable enough potentially for use as a functional biomarker for brain diseases (4–7,11).

There is a growing interest in using TRUST to measure Y_v under various physiological and pathophysiological conditions. As an initial effort, the TRUST sequence has been disseminated to a number of sites over the world. However, the performance and reliability of TRUST MRI across different sites have not been assessed. Given that TRUST MRI requires special pulse sequence design and slice positioning, it is unclear whether differences in system configuration and operator experience would result in a significant variability in Y_v measurement across sites.

In the present work, we evaluated the TRUST MRI technique in a multi-site setting. The aims of this study are twofold: 1) to show that TRUST can be performed at different sites without the need for special hardware or on-site training of the operators; 2) to show that TRUST measurements are comparable across sites. Altogether, six imaging centers located in North America participated in the study, with a total of 250 healthy volunteers. The measured Y_v values (i.e. accuracy) as well as the standard error of Y_v estimation (i.e. precision) were compared across the six sites.

METHODS

TRUST MRI technique

TRUST MRI (21) is based on the principle that T_2 relaxation time of the blood has a well-established relationship with Y_v (32), thus one can measure pure blood T_2 and convert T_2 to Y_v through calibration. The technique uses an RF pulse to magnetically label the incoming venous blood, and acquires images with and without the labeling to obtain control and labeled images (Fig. 1a). The subtraction of the control and labeled images yields an image from pure venous blood signal (Fig. 1b). The labeled and control scans are repeated flow-insensitive T_2 -preparation pulses so as to modulate the signal with T_2 weighting (Fig. 1b). The blood signal (S) and the T_2 -preparation duration (termed effective echo time [eTE]) have the following relationship:

$$\Delta S(eTE) = S_0 \cdot e^{eTE \cdot (1/T_{1b} - 1/T_{2b})}, \quad \text{Eq. [1]}$$

where S_0 is the pure venous blood signal with no T_2 weighting, T_{1b} is the blood T_1 (assumed to be 1624ms (33)), and T_{2b} is blood T_2 . Therefore, the monoexponential fitting of S and eTEs gives the T_2 value of the venous blood (Fig. 1c). Using a calibration plot specifying the relationship between T_2 , Y and Hematocrit level (25), the blood T_2 can then be converted to Y_v . Due to relatively large flow velocities and therefore pronounced inflow of the labeled spins, TRUST measurement in large venous vessels, e.g. superior sagittal sinus, was found to be particularly robust (2,31) and is the focus of this study, which provides an estimation of the global venous oxygenation in the brain.

Sites and participants

Of the six participating sites, four were located in the United States and two in Canada. The sites were all equipped with 3T Achieva whole body MRI systems (Philips Healthcare, Best, The Netherlands). The developer's site, which is the site of the lead authors, scanned 125 healthy volunteers and these data served as the benchmarks. Each of the five remote sites recruited and scanned 25 healthy volunteers. As such, a total of 250 subjects were studied: 130 males and 120 females with an age range of 18 to 93 years. Table 1 lists demographic information of the participants in all sites. The ethnic composition was distributed such that there were 187 Caucasians, 46 African Americans, 15 Asians and 2 others. The Health Insurance Portability and Accountability Act (HIPAA) compliant protocol was approved by the ethics committee of each site, specifically the UT Southwestern Medical Center institutional review board (IRB), the Johns Hopkins Medicine IRB, the Sunnybrook Research Institute Research Ethics Board, the University of Illinois at Chicago IRB, the Research Ethics Board of Medical Center of the University of Montreal, and the University of Vermont IRB. Informed written consent was obtained from each participant. The TRUST data from each remote site were acquired by adding the sequence to an existing research study, thus the age ranges were not matched across the sites.

Data acquisition

The executable files of the customized TRUST pulse sequence were transferred electronically to all sites. Each remote site scanned 25 healthy volunteers and transferred the datasets to the developer's site for centralized analysis. Before data transferring, any personal information from subjects was removed in accordance with the patient protection regulations. The developer's site collected a relatively large sample size and age range so that the data would serve as a reference for comparison with the other sites.

Identical imaging parameters were used in all sites and the protocol was based on that optimized in a previous study (30). The imaging parameters were: voxel size $3.44 \times 3.44 \times 5 \text{ mm}^3$, TR=3000ms, TI=1022ms, four eTEs: 1, 40, 80 and 160ms, labeling thickness 100mm, gap 22.5mm, scan duration 1.2min.

To ensure consistent slice positioning across sites, an instruction document that included several examples (see Supporting Fig. S1) was sent to each site. Operators were instructed to position the TRUST imaging slice to be parallel to anterior-commissure posterior-commissure line with a distance of 20mm above the sinus confluence. This positioning scheme has been shown to provide sufficient labeling of venous blood in the superior sagittal sinus (SSS) in virtually all adult brains (5,31).

Data analysis

The TRUST MRI data were processed using in-house MATLAB (Mathworks, Natick, MA) scripts. The processing method followed that described previously (2,21,31). Briefly, after motion correction, pairwise subtraction between control and tag images was performed, the difference of which yields pure venous blood signal. A preliminary region of interest (ROI) was manually drawn on the difference image to include the superior sagittal sinus. Then four voxels with the highest signals in the difference images in the ROI were chosen as the final

mask for spatial averaging. The model described by Eq. [1] was then fitted to the averaged venous blood signals to obtain a T_2 estimate, which was in turn converted to Y_v via a calibration plot obtained by in vitro blood experiments under controlled oxygenation, temperature, and hematocrit conditions (25). In the T_2 - Y_v conversion, the hematocrit was assumed to be 0.40 for female and 0.42 for male (5). The precision of the Y_v measurement, reflecting the uncertainty of the estimation, was quantified by the standard error of the estimated Y_v (ε_{Y_v}). Specifically, the goodness-of-fit from the T_2 fitting gives a 95% confidence interval (CI) of the estimated T_2 , which was further converted to the confidence interval of the estimated Y_v via the calibration plot. Then ε_{Y_v} was calculated by $\varepsilon_{Y_v} = (\text{upper CI of } Y_v - \text{lower CI of } Y_v) / (2 * 1.96)$.

In addition to Y_v , two other parameters were also extracted from the TRUST data, the amount of subject head motion during the TRUST scan and the blood signal intensity, since we conceived that both of these variables could affect Y_v and ε_{Y_v} . The head motion amount was approximated by the standard deviation of the motion vector (in units of mm) obtained from the image realignment algorithm in the software Statistical Parametric Mapping (SPM) (University College London, UK). It is a measure of the subject cooperation in the scan. The blood signal intensity was calculated as the ratio between the difference (i.e. control minus labeled) signal and the control signal (which contains both blood and tissue signals) within the final mask of SSS at the first eTE. This parameter is indicative of the size of the SSS.

Statistical analysis

One-way Analysis of Variance (ANOVA) test was used to evaluate if there is a site difference in age, gender, motion, and the blood signal intensity. The statistical significance of these effects was assessed with a Bonferroni-corrected p value of 0.05. Next, to evaluate the site-effect on Y_v and ε_{Y_v} , a multivariate regression analysis was conducted with age, gender, motion and blood signal intensity as continuous variables and site as a categorical variable. This analysis was conducted separately for Y_v and ε_{Y_v} . If a significant site-effect was detected, each site was compared to the reference site (denoted as Site “a”) to identify which site(s) is different and whether the TRUST performance at that site is better or worse than the Site “a”. An examination of the site-effect was also performed using one-way ANOVA on the “residual” Y_v and ε_{Y_v} (denoted by $\overline{Y_v}$ and $\overline{\varepsilon_{Y_v}}$, respectively), in which the effects of age, gender, motion and blood signal intensity were regressed out. In all analyses, a Bonferroni-corrected p value of 0.05 or less was considered statistically significant.

RESULTS

General results

The transfer of the TRUST sequence and slice positioning procedures to the participating sites went smoothly. The investigators and MR technologists of each site were able to install the sequence and properly position the slice by simply following the written instructions. There was no instance of a need for onsite training.

The age and gender information from each site are shown in Table 1. The ANOVA test showed that there was a significant difference in age and gender across the six sites

($p < 0.001$ and $p = 0.031$, respectively), which was due to the differences in their respective parent studies. The amount of head motion and blood signal intensities are shown for each site in Fig. 2a and b, respectively. No site difference was found in these two parameters ($p = 0.80$ and $p = 0.95$ for head motion and blood signal intensity, respectively), indicating that subject cooperation and mean SSS size are comparable across the sites.

Evaluation of venous oxygenation (Y_v) across sites

The mean Y_v of all 250 subjects was $61.0 \pm 5.8\%$, ranging from 42.1% to 76.6%. This range of Y_v in healthy subjects is consistent with previous reports (5,34). The inter-subject standard deviation, 5.8%, is also similar to earlier studies and is thought to be primarily attributed to normal variations in venous oxygenation (5,31,34). Fig. 2c shows the measured Y_v categorized by sites. The inter-site standard deviation was 1.4%. Multivariate regression analysis of Y_v as a function of age, gender, motion, blood signal intensity and site revealed that, the performance site has no significant effect on the measured Y_v ($p = 0.85$), indicating that there was no site dependence in Y_v estimation using TRUST. As shown in Fig. 3a, there was a significant effect of age ($p = 0.009$ from multivariate regression analysis). No significant effects of gender ($p = 0.99$), motion ($p = 0.15$, Fig. 3b) and blood signal fraction ($p = 0.25$, Fig. 3c) in Y_v were found. When the effects of age, gender, motion, and blood signal fraction were regressed out, ANOVA test on $\overline{Y_v}$ still showed no significant effect of performance site ($p = 0.75$).

Evaluation of the standard error of Y_v (ϵ_{Y_v}) across sites

The mean ϵ_{Y_v} of all the 250 TRUST- Y_v measurements was found to be $1.4 \pm 0.6\%$, ranging from 0.4% to 3.9%. Fig. 2d shows the ϵ_{Y_v} categorized by sites, with an inter-site standard deviation of 0.2%. For all sites, the mean ϵ_{Y_v} were lower than 1.5%, suggesting a generally good measurement precision using TRUST. Multivariate regression analysis of ϵ_{Y_v} revealed that ϵ_{Y_v} is not dependent on age ($p = 0.26$, Fig. 3d) or gender ($p = 0.29$). However, significant effects of head motion ($p < 0.001$, Fig. 3e) and blood signal intensity ($p < 0.001$, Fig. 3f) were found. Subjects with greater head motion or lower blood signal intensity tended to have a larger ϵ_{Y_v} . The multivariate regression analysis also revealed that there was significant site-effect in ϵ_{Y_v} ($p = 0.024$). To confirm the presence of the site-effect, one-way ANOVA test was performed on $\overline{\epsilon_{Y_v}}$ after regressing out the effects of age, gender, motion and blood signal intensity, and a significant site-effect remained ($p = 0.015$). Post-hoc comparison of the ϵ_{Y_v} between the reference site and each of the participating site suggested that the site-difference was attributed to a significantly lower (i.e. better performance) ϵ_{Y_v} in Site “e” ($p = 0.024$) and a trend of lower ϵ_{Y_v} in Site “c” ($p = 0.081$), as the other sites showed no differences from the reference site ($p > 0.38$).

We further conducted exploratory analysis to examine the reason underlying the site-difference in ϵ_{Y_v} . We hypothesized that the degree to which the refocusing pulse is accurate could influence ϵ_{Y_v} , since deviation in the flip angle away from the ideal 180° will result in the signal decay that does not follow a monoexponential curve. Therefore, we quantified an additional parameter, the discrepancy between the measured blood signals and the monoexponential fitting curve, by calculating the difference between the mean experimental data and the fitted values, i.e.,

$\Delta_{m-f} = 1/4 \cdot \sum_{eTE} \left| \text{mean}(\Delta S(eTE)) - S_0 \cdot e^{eTE \cdot (1/T_{1b} - 1/T_{2b})} \right| / S_0$, where $eTE=1, 40, 80$, and 160ms . It was found that, after regressing out Δ_{m-f} (in addition to age, gender, motion, and blood signal intensity), ε_{Y_v} was no longer significantly dependent on site ($p=0.41$), suggesting that RF pulse flip angle accuracy may be one of the main reasons for the slight differences in ε_{Y_v} across sites.

DISCUSSION

The present study evaluated the TRUST technique for Y_v measurement in a multi-site setting. It is shown that the TRUST sequence can be implemented and performed on a standard 3T scanner at different sites. The TRUST results from the six imaging centers revealed that there was not a site difference on the estimated Y_v values. The precision of the Y_v estimation, measured by the standard error of Y_v , are in general good at all sites ($<1.5\%$), but showed some variability in some participating sites. To our knowledge, this work represents the first effort to conduct a multi-site evaluation of an MR-based oxygenation technique, which is a critical step toward broader availability and potential clinical utilizations of cerebral oxygenation and oxygen consumption measures.

Cerebral venous oxygenation is an important physiological parameter of the brain. Given that the arterial blood is typically fully oxygenated, the knowledge about venous oxygenation can inform how much oxygen has been extracted by the brain for its energy consumption. Indeed, when combined with blood flow measurement, venous oxygenation can be used to calculate the brain's metabolic rate based on Fick's principle (1). The brain's metabolic rate is closely related to neural activity and brain health, and its abnormality has been implicated in several neurodegenerative and metabolic diseases (7–11,35). Therefore, a clinically practical approach to determine cerebral venous oxygenation may provide a valuable tool for diagnosis and treatment monitoring in many brain disorders. Unfortunately, up until recently, PET based measurement using ^{15}O -labeled tracer was the only available approach for use in humans. While the PET method provides a quantitative, spatially resolved map of OEF and CMRO_2 , its technical complexity has limited its utility in routine clinical practice. For MR based methods, although BOLD fMRI has been used in brain mapping for more than two decades, it remains a qualitative method and its signal has no direct indication of the actual blood oxygenation in the brain. Over the past few years, several quantitative oximetry methods (3,20,21,24,36–39) have been proposed, of which the T_2 -based approach is one method. It remains to be seen which of these methods will make it to the clinical arena, and it is possible that it will depend on the particular disease type. The present work represents an initial effort to lay preliminary foundation for a broader availability of the global oxygenation method using T_2 -based approach.

In this multisite setting, the transferring of the TRUST sequence was smooth. Since the imaging protocol has been streamlined, no change or modification was needed at any of the individual sites. No datasets had to be excluded due to improper positioning, suggesting that the written instruction of positioning, together with example figures of the positioning (as shown in Supporting Fig. S1), were sufficient for investigators and MR technologists to plan the TRUST scan without previous experience with this sequence. The relatively short

duration (1.2 min) of the TRUST scan also allowed it be added to existing protocols without adding much burden to the participants. These features may enhance the potential of the TRUST technique to be disseminated to researchers and clinicians who are interested in non-invasive measurement of venous oxygenation in the brain.

The key advantage of TRUST is that the partial voluming effect is minimized. Specifically, partial voluming due to static tissue can be automatically removed by the control/label subtraction in data processing. Therefore, the TRUST results was shown to be independent of imaging resolution (21), and not relying on processing operator to manually select a ROI of pure blood.

The Y_v values measured by TRUST are in good agreement with those measured by other techniques that have been reported in literature (3,17,24,34,37,38,40). For example, Coles et al reported an averaged Y_v of $58 \pm 4\%$ in 10 healthy subjects between 18–60 years old using the gold-standard ^{15}O -PET (17). Recent studies using other MRI techniques reported an averaged Y_v between 59.6% and 67.2% in young healthy volunteers (3,24,37,38,40).

We found that there is no site-dependence in the TRUST-measured Y_v , suggesting that venous oxygenation can be measured reliably across scanners at different sites. The observation of an absence of effects of head motion and blood signal intensity on Y_v indicates that the TRUST- Y_v measurement requires no additional subject cooperation, compared to other physiological MR sequences, nor was the size of SSS an issue. Our multisite data showed that the measured Y_v significantly decreased with age ($p=0.009$, Fig. 3a). This observation is consistent with previous single-site studies of normal aging (4,5). The decrease of Y_v indicates that a greater fraction of the incoming oxygen is extracted in older individuals. Our previous studies have suggested that this may be due to a combination of two reasons (4,5). One is that CBF decreases with age, thus the brain has to increase the OEF to match the demand. The other reason is that the brain's metabolic demand, i.e. CMRO_2 , is actually greater in older individuals, which is postulated to be compensatory and due to a lower processing efficiency in the aging brain (4,5).

Gender did not have a significant effect on Y_v , when using the assumed hematocrit values of 0.40 and 0.42 in female and male, respectively. This may be expected as the optimal oxygen tension of the female and male brain is likely similar. We also tested to use other hematocrit assumptions and found that, when the assumed hematocrit difference is greater than 0.06 (i.e. 0.40 and 0.46 for female and male, respectively), a significant Y_v difference would be identified. However, this assumption of large difference is not compatible with the existing literature on hematocrit in female and male individuals.

The standard error of the Y_v measurement using the TRUST technique, ε_{Y_v} , was found to be less than 1.5% in all six sites. This amount of uncertainty is considerably less than the inter-subject normal variation of approximately 6% as well as disease-related change of 5.7% in Multiple Sclerosis (7), 45% in Stroke (41), 6.3% in Alzheimer's disease (42). Thus, this level of precision is considered good in general. Statistical analysis showed that the ε_{Y_v} depends on performing site ($p=0.024$). Comparing the five remote sites to the developer's site, one site showed significantly smaller ε_{Y_v} ($p=0.024$) and another site showed a trend of

smaller ε_{Y_v} ($p=0.081$). No site was found to have a larger ε_{Y_v} than the reference site. We also examined the potential correlation between ε_{Y_v} and Y_v , with the notion that a noisy dataset may result in a systematic bias (higher or lower Y_v values). We did not observe a significant correlation ($p=0.23$, $N=250$), indicating that noise affects the precision but not the accuracy of the Y_v estimation by the TRUST technique.

Regression analysis revealed that the site-difference in ε_{Y_v} could be explained by the difference in the measurement-fitting discrepancy (ε_{m-f}) across sites. When the ε_{m-f} effect was regressed out, ε_{Y_v} was no longer dependent on the performance site. ε_{m-f} is expected to be mainly due to the imperfection in the 180° refocusing pulses, i.e. B_1 inhomogeneity. Slight imperfection in the refocusing pulses could cause the measured blood signals to deviate from the ideal monoexponential decay curve, thereby resulting in a large ε_{m-f} . Therefore, we speculate that the site-difference in ε_{Y_v} may be due to the performance of the B_1 preparation on an individual scanner. However, we emphasize again that the value of ε_{Y_v} was in general low and the range of ε_{Y_v} across sites was relatively narrow (0.95%–1.48%, Fig. 2d).

The multivariate regression analysis also revealed that there are no age and gender effects on ε_{Y_v} . This finding suggested that the measurement precision of TRUST is comparable between young and older subjects and between females and males.

The blood signal intensity is the difference signal normalized to the control signal, and a measure of the intrinsic SNR of the TRUST data. In our data, the blood signal intensity is around 50% for all sites (Fig. 2b). As a reference, the difference signal in ASL is typically only 0.5–2% of the control signal (43–45). Thus, SNR of TRUST MRI is considerably higher than that of ASL, which allows a reliable T_2 fitting and measurement of Y_v . The main reason that the blood signal intensity does not approach 100% is that there exists partial voluming between tissue and blood in the voxels, thus blood may not occupy the entire voxel. In this regard, the blood signal intensity provides an indirect indication of the size of the SSS. The blood signal intensity in principle is also affected by the labeling efficiency of the labeling RF pulses. In a pulsed labeling scheme, however, the efficiency is usually close to 100% (46), thus this is not expected to be a major factor in determining the blood signal intensity.

There are a few limitations in this multi-site study. One limitation is that the age and gender distributions were not exactly matched across sites, due to the study design that the TRUST sequence was added to an existing study at the remote site and the studies at the remote sites had different subject demographics. A true multi-site trial in which subjects of each site are recruited solely for the purpose of the trial would involve a substantially greater budgetary requirement and should ideally include multiple MRI vendors, which will be the goal of our future studies. To alleviate this limitation, we included the participant's age and gender as covariates in the analysis and their effects were regressed out when evaluating the site-effect on the TRUST measurements. We also included a large sample over the adult lifespan at the reference site, to facilitate age and gender matched comparison. Another limitation is that this study has only included sites from a single MRI vendor, because of the convenience in implementing an identical pulse sequence (e.g. matching all gradient waveforms and RF

pulse shapes). Therefore, it is unclear if there would be a vendor-difference in the TRUST- Y_v measurements. Thus, a multi-vendor study should be performed in future. Furthermore, no participants were scanned at different sites in this study. To better assess the site-effect, future studies should consider scan the same participants at multiple locations.

CONCLUSION

In the present work, we evaluated the measurement of venous oxygenation using TRUST MRI across 6 imaging centers. The accuracy as well as the precision of the TRUST- Y_v measurement was assessed. The TRUST sequence can be implemented and performed on a standard 3T scanner at remote sites with high success rate. The results revealed that the estimated Y_v values are compatible across sites after age-related Y_v difference is accounted for. All six sites showed good precision of the TRUST measurements, with one remote site superior to the reference site. The precision of the Y_v measure was found to be affected by subject head motion and size of the blood vessel. This work suggests that TRUST MRI, as a promising MR technique to measure brain oxygenation, has the potential to be used effectively at a broad range of MRI facilities.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Fig. 1.

Illustration of the positioning of TRUST MRI and representative results. (a) Imaging slice (red) and labeling slab (blue) of the TRUST MRI scan. The imaging slice was positioned to be parallel to AC-PC line and 20mm above the sinus confluence. (b) Typical data of TRUST MRI. The subtraction of the control and labeled images yields pure venous blood signal, which is subject to increasing T_2 weightings. (c) Monoexponential fitting of the blood signal in superior sagittal sinus as a function of eTE results in T_2 estimation. The T_2 value can then be converted to venous oxygenation via a calibration plot (25).

Fig. 2.

Site-comparison of the TRUST measurements. (a) Averaged amount of motion in the scans at the six sites. (b) Averaged blood signal intensity at the six sites. (c) Averaged Y_v at the six sites. (d) Averaged ϵ_{Y_v} at the six sites. Significant site-difference was found in ϵ_{Y_v} .

Fig. 3.

Scatter plots between the TRUST results and factors including subject age, motion and blood signal intensity. (a–c) Scatter plots between Y_v and age, motion and blood signal intensity, respectively. (d–f) Scatter plots between ϵ_{Y_v} and age, motion and blood signal intensity, respectively.

Table 1

Demographic information of the subjects from all sites.

Site	a	b	c	d	e	f
Subject number	125	25	25	25	25	25
Age range (years)	18–93	21–70	31–82	22–44	18–24	20–40
Gender (M/F)	65/60	8/17	12/13	21/4	13/12	11/14