# Vessel-specific mapping of cerebral venous oxygenation of small veins

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**Target Audience** MR Physicists and Clinicians interested in venous oxygenation quantification, especially effect of artifact on accuracy.

**Purpose** The ability to measure human brain metabolism on a routine basis will have a large impact on the diagnosis and treatment of brain disorders. A key component in quantifying oxygen metabolism is the measurement of venous blood oxygenation ($Y_v$)[1] . Several potential approaches have been proposed to quantify $Y_v$ using MRI, including intravascular $T_2$-based methods which rely on a simple and calibratable relationship between blood $T_2$ and oxygenation[2]. Recently we introduced such a $T_2$-based method to measure $Y_v$ along the major draining vessels of the brain called $T_2$-Relaxation-Under-Phase-Contrast (TRU-PC) MRI[3]. We showed that TRU-PC is a non-invasive, rapid, and reproducible method to measure vessel-specific $Y_v$, but fell short of mapping the $Y_v$ of small veins (caliber of 1-2 mm). The ability to generate such a "small-vessel map" of $Y_v$ may help in better characterizing variations in venous oxygenation across brain regions, identifying regions at risk of ischemia attack or stroke, and may find immediate applications in clinical conditions that affect specific brain regions. The present study aims to optimize TRU-PC to generate a complete $Y_v$ map of the vasculature in the mid-sagittal brain, including small veins. The optimization includes removing an eddy-current induced artifact to improve the $Y_v$ quantification, performing multiple scans to sensitize the maps to vessels with different flow velocity and orientation, and merging these scans into a single, comprehensive $Y_v$ map.

**Methods** *Removing eddy-current induced artifact*: The TRU-PC MRI technique applies the Phase Contrast (PC) principle[4] to separate pure blood signal from the surrounding static tissue. The $T_2$ value of pure blood is then determined using non-selective $T_2$-preparation pulses, which minimizes the effect of flow on $T_2$ estimation[2]. PC MRI applies two bipolar gradients in opposite directions in order to cancel out the tissue signal during complex subtraction of the images, resulting in a complex difference (CD) image. However, the application of flow-encoding bipolar gradients can generate eddy-currents that cannot be cancelled out by the application of an opposite bipolar gradient, resulting in an imperfect removal of tissue signal. This tissue signal will superimpose on the vessel signal, resulting in an inaccurate $T_2$-quantification. We propose to use a method developed to remove field-imperfections[5] to remove the arbitrary phase generated by eddy-currents. This correction will remove unwanted tissue signal and improve the $T_2$-quantification of blood. We assume that the measured phase difference ($\Delta\varphi$) is a linear combination of the true phase difference ($\Delta\theta$) and a phase caused by eddy-currents ($\Delta\varepsilon$): $\Delta\varphi=\Delta\theta+\Delta\varepsilon$. We reconstruct the $\Delta\varphi$ images from the complex data[4], and calculate a hyper-plane of field inhomogeneity ($\Delta\varepsilon$)[5] from the $\Delta\varphi$ images using all eTEs simultaneously for the fitting. By subtracting $\Delta\varepsilon$ from $\Delta\varphi$, the true phase difference, $\Delta\theta$, remains. By using the law of cosines[4], the CD images are reconstructed using the true phase difference, $\Delta\theta$. *Sensitizing the $Y_v$ maps to more vessels*: To acquire the complete vasculature in the mid-sagittal brain at 3T (Philips Achieva, 32 Ch. Receive headcoil), four separate TRU-PC scans were employed: one small-vessel scan with flow-encoding in Anterior-Posterior (AP) direction, one small-vessel scan with flow encoding in Foot-Head (FH) direction, and two large-vessel scans, also in AP and FH. The MR protocols for the large-vessel and small-vessel scans are similar, with the only difference being the flow-encoding cut-off velocity ($V_{enc}$) ($V_{large}$=15 cm/sec, $V_{small}$=3 cm/sec for Male, and 5 cm/sec for Female), and recovery time (RT) ($RT_{large}$=475 ms, $RT_{small}$=668 ms). The $T_2$-preparation incorporates hard composite pulses, MLEV-16 phase cycled, with $\tau_{CPMG}$=10 ms. This results in four sets of complex images with two effective TEs (eTE = 0 and 40 ms). Due to short blood $T_2$*, the TE was set to "shortest" with a conventional gradient echo (FOV = 200x200 $mm^2$, acq matrix = 276x83, reconstruction matrix=400x400, 1 slice, slice thickness = 5 mm). The total scan time is ~15 minutes. *Merging multiple scans*: After the session, the CD images for each eTE were reconstructed individually for each of the four scans as described above. Then the signal intensity from the four scans was thresholded at an SNR of 2.5, and the voxel-wise $T_2$ value was thresholded to be less than 140 ms based on venous blood $T_2$ at 3T[6]. Finally, the signal from all four scans was merged using sum-of-squares method, and the arteries were removed with a vein mask generated from Susceptibility Weighted Imaging (SWI)[7]. The $T_2$-map was generated on a voxel-by-voxel basis along the entire vascular path using a mono-exponential model, where the signal from non-zero voxels within a 35x35 voxel block were incorporated in the $T_2$-fitting to reduce error due to noise. The $T_2$ was then converted to $Y_v$ using a known calibration plot[6]. Five subjects (3 Female/2 Male, age 21-40) were scanned twice with the entire protocol. We compare the results with and without eddy-current correction.

**Results and Discussion** Figure 1 shows a representative $\Delta\varphi$ and CD image for one eTE before and after eddy-current correction for a single TRU-PC scan. Before correction, a non-zero $\Delta\varphi$ is present in some of the regions of static tissue that should ideally be zero (red arrow). This non-zero $\Delta\varphi$ translates to an aberrant tissue signal in the CD image (yellow arrow). After correction, the $\Delta\varphi$ image is closer to the true phase, $\Delta\theta$ (blue arrow), which translates to a better reconstructed CD image (green arrow). Since the small vessel map fuses four separate scans, there will be an accumulation of error during the merging of scans. By correcting for eddy-currents, there was a 30±17% reduction of accumulated error (i.e tissue signal) in the prefrontal region ($p$=0.001), 33±18% reduction of accumulated error in the parietal region ($p$=0.008), and 27±19% reduction of accumulated error in the occipital region ($p$=0.009). Figure 2 shows representative $T_2$ and $Y_v$ maps before and after correction. The average $T_2$ value before and after correction was 70.5±7.1 ms and 66.7±5.3 ms, respectively. The corrected $T_2$ is smaller than the uncorrected one for all five subjects (between -2.17 ms and -7.16 ms), which is expected since the tissue $T_2$ at 3T is higher (90-95 ms) than blood $T_2$ (55-85 ms). The amount of correction is dependent on the severity of the artifact being removed, and the voxel's tissue to blood content. The voxel-wise coefficient of variation (CoV) averaged over the entire vascular path of 2.5±1.5% before correction was not significantly different than the CoV of 2.9±1.8% after correction ($p$=0.23), showing that the excellent test-retest reliability was not perturbed by the correction. In Figure 3, a representative (corrected) $Y_v$ map is super-imposed on its anatomical SWI magnitude image. The named vessels in the image are marked with red letters. Many more un-named vessels (including pial vessels draining into the SSS) are also visible in the map. After correction, we still observe that the vessels draining the deep brain tend to have a higher $Y_v$ than the vessels draining the cortex, and that the anterior portion of the SSS has a slightly higher $Y_v$ than the posterior portion.

**Conclusion** In summary, we have optimized TRU-PC MRI to obtain a complete map of $Y_v$ from the brain's mid-sagittal draining veins (diameter of 1 mm or greater). This includes the removal of aberrant static tissue signal generated by eddy-currents, which improves the $T_2$-quantification of venous blood signal. We have also sensitized our acquisition to many more vessels, and we have shown that a single complete $Y_v$ map can be generated from these scans. This improved vessel-specific $Y_v$ map provides a better region-specific measurement of oxygenation and metabolism in the brain.

**References 1.** Xu et al. MRM 62:141 (2009). **2.** Lu & Ge. MRM 60:357 (2008). **3.** Krishnamurthy, et al. MRM, in press (2013). **4.** Bernstein, et al. MRM 32:330 (1994). **5.** Langham, et al. MRM 61:626 (2008). **6.** Lu, et al. MRM 67:42 (2012). **7.** Haacke, et al. MRM 52:612 (2004).

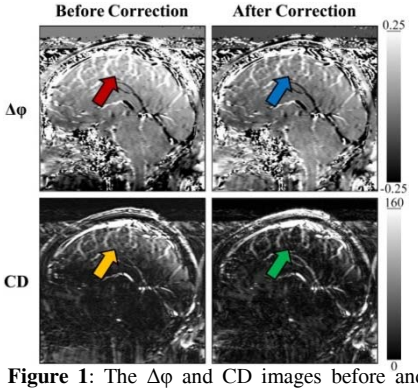


**Figure 1**: The $\Delta\varphi$ and CD images before and after eddy-current correction for one eTE from a representative scan. $\Delta\varphi$ has units of radians, the CD has units of arbitrary magnitude.

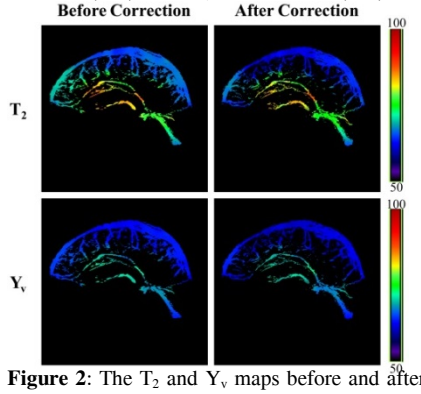


**Figure 2**: The $T_2$ and $Y_v$ maps before and after eddy-current correction from a representative scan. The $T_2$ map has units of ms, the $Y_v$ map has units of %.

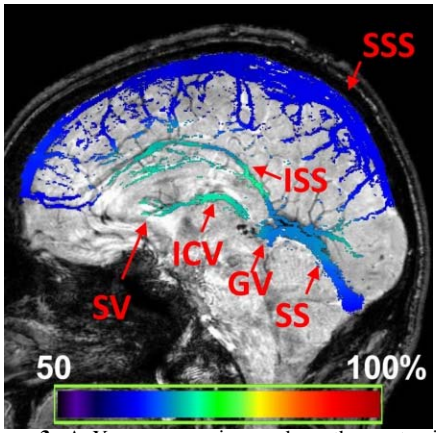


**Figure 3**: A $Y_v$ map superimposed on the anatomical SWI magnitude image. SV=septal vein, ICV = internal cerebral vein, GV=great vein, SS=straight sinus, ISS=inferior sagittal sinus, SSS=superior sagittal sinus.