Measurement of the Oxygen Extraction Fraction in Patients with Steno-occlusive Cerebrovascular Diseases using Quantitative Susceptibility Mapping at 7T

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TARGET AUDIENCE: Researchers who are interested in QSM, noninvasive measurement of OEF, and cerebrovascular diseases

PURPOSE: Severe hemodynamic ischemia, i.e., misery perfusion, can be identified by an increased oxygen extraction fraction (OEF) and is one of the risk factors for future stroke events and embolic complications during surgery[1]. Currently, OEF can be directly measured only by positron emission tomography (PET); however, PET includes several issues such as radiation exposure and invasiveness, long examination time, limited number of clinically available scanners, and lower spatial and temporal resolutions. Although several studies[2-6] attempted to measure OEF using MRI techniques, the accuracy of these results remained suboptimal when compared with those of PET. Therefore, in this study, we attempted to investigate whether OEF maps generated using our newly developed quantitative susceptibility mapping (QSM) technique at 7T can readily demonstrate OEF changes in patients with major cerebrovascular steno-occlusive disease compared with OEF maps generated using PET.

METHODS: Twenty-seven patients (18 men and 9 women; age range, 32–82 years, median, 66 years) with chronic stenosis/occlusion of the unilateral internal carotid artery (ICA, n = 16) or middle cerebral artery (MCA, n = 9/2 MCA stenosis/occlusion) were examined using a 7T MRI scanner (Discovery MR950, GE Healthcare) and quadrature transmit and 32-channel receive head coils. Source images of QSM were obtained using a three-dimensional spoiled gradient recalled acquisition technique with the following scanning parameters: flip angle, 20°; echo time, 15 ms; repetition time, 30 ms; field of view, 256 mm; slice thickness, 0.5 mm; and matrix size, 512 × 256. OEF measurements were obtained using a PET scanner (SET-3000GCT/M, Shimadzu), with a 5-min scan during continuous inhalation of $^{15}O_2$. QSM images were generated from the source images using an in-house program with the modified method of multiple dipole-inversion combination with k-space segmentation (MUDICK)[7]. In this method, three sub-domains in the k-space were defined in Ref7 and susceptibility maps calculated by the least-squares method with different iteration numbers were applied to each domain. OEF maps were then generated from QSM images as follows. Venous structures were segmented using a threshold of more than +2SD for susceptibility values in a volume-of-interest (VOI) of 25 × 25 × 25 mm. Differences in susceptibility values between venous structures and surrounding brain tissues in each VOI, denoted by $\Delta\chi$, were obtained. Then, OEF values of each VOI were calculated using the following equation: $\Delta\chi = \Delta\chi_{do} \times Hct \times OEF$, where $\Delta\chi_{do}$ is the difference in susceptibility per unit hematocrit (Hct) between fully deoxygenated and fully oxygenated blood (1.8×10^{-7} in CGS units). The Hct value we used was 0.45. After coregistration of QSM-OEF maps with PET-OEF maps using SPM8, 18 spherical regions-of-interest (ROIs) with a diameter of 25 mm were automatically placed along the entire brain surface on the sections at the level of the centrum semiovale. Mean OEF values were calculated for the unilateral cerebral hemispheres, and OEF ratios for the affected hemisphere against the contralateral one were then obtained. The correlation between QSM-OEF and PET-OEF values was examined using Pearson's correlation coefficient and linear regression analysis.

RESULTS: Four patients were excluded because of a past history of subcortical hemorrhage or strong susceptibility artifacts. The remaining 23 patients were eligible for further analyses. Findings on QSM-OEF maps of the patients appeared comparable with those on the corresponding PET-OEF maps (Fig. 1). The scatter plot of the OEF ratio between QSM-OEF and PET-OEF maps is shown in Figure 2. A good correlation was found between the OEF ratio on the QSM-OEF maps and that on the PET-OEF maps ($r = 0.89$, $p < 0.001$). The slope and intercept of the regression lines were 0.97 and 0.04, respectively, indicating an excellent agreement between relative QSM-OEF and PET-OEF values.

DISCUSSION: In this study, we revealed that QSM-OEF maps corresponded well with PET-OEF maps, with an excellent correlation and agreement in patients with unilateral major vessel stenosis/occlusion. This successful result can be attributed to high-resolution, high-contrast images at 7T and sophisticated QSM-OEF algorithms that facilitated the accurate estimation of quantitative susceptibility values for minute intracerebral venous structures. On the other hand, this technique includes several limitations. The accuracy of estimating local OEF values strongly depends on the precision of extraction of small intraparenchymal veins and restoration of susceptibility values; these can be easily affected by many imaging and postprocessing conditions, which should be optimized. In addition, deposition of physiological iron and pathological hemosiderin in brain tissue and large extracerebral venous structures such as dural sinuses and cortical veins can cause substantial errors during OEF estimation, which should be avoided by further improvement of postprocessing algorithms.

CONCLUSION: OEF ratios on QSM-OEF maps at 7T showed a strong correlation with those on PET-OEF maps in patients with unilateral ICA/MCA stenosis/occlusion, suggesting that noninvasive OEF measurement using QSM at 7T can be used as a substitute to $^{15}O_2$-PET to assess patients with steno-occlusive cerebrovascular diseases.

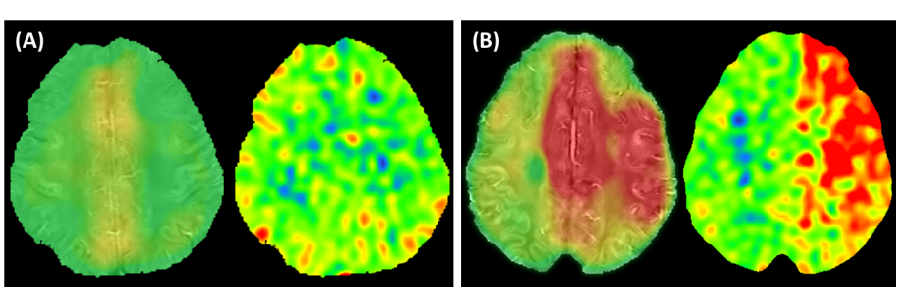

Fig. 1: QSM-OEF (left) and PET-OEF (right) in patients with right MCA stenosis (A) and left ICA occlusion (B). OEF ratios on QSM-OEF and PET-OEF were 0.97 and 1.02, respectively, in patient A and 1.37 and 1.41, respectively, in patient B.

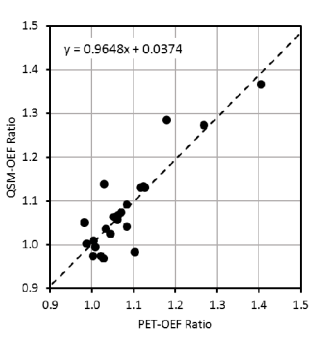

Fig. 2: Correlation of the OEF ratios between QSM-OEF and PET-OEF maps.

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