PET VALIDATION OF VASCULAR-SPACE-OCCUPANCY CBV MEASUREMENT

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INTRODUCTION: Cerebral blood volume (in unit of ml blood in 100 ml brain) is an important parameter for BOLD fMRI and a number of brain diseases (1,2). Conventionally, CBV is measured using PET with ^{15}O or ^{11}C-labelled carbon monoxide which labels the erythrocytes (3,4). While this approach is known to provide quantitative estimation of CBV, the use of radioactive isotopes limits its application due to invasiveness and high cost. Alternatively, CBV can be measured by DSC-MRI method. However, the DSC-MRI approach suffers from difficulties in estimating the arterial input function (AIF). Due to large spatial inhomogeneities in the brain tissue and partial volume effect of different tissue types, accurate estimation of AIF is not trivial and is still the topic of ongoing research (5,6). As a result, the quantification of absolute CBV (aCBV) is often difficult, and many studies use relative CBV. We have recently developed a vascular-space-occupancy (VASO) MRI technique (7,8) for quantitative assessment of aCBV. In this work, we report the validation of the aCBV measured by VASO MRI. We performed PET scans as well as VASO MRI scans on the same subject to directly compare the aCBV values measured by the two methods.

METHODS: Four healthy subjects (age 30±12, 3 males) were studied after informed consent was obtained. The MRI scans were conducted on a Siemens 3T TIM Trio MRI scanner. The imaging parameters of VASO MRI sequence were: TI/TR/TE=1088ms/6000ms/5.9ms, FOV=220x220mm^2, resolution=1.7x1.7mm^2, EPI factor=7, 11 slices with slice thickness=5mm, duration per scan=1min 42sec. A Gd-DTPA contrast agent (OMNISCAN^{TM}) was administered intravenously with a standard dosage (0.1 mmol/kg). Two pre-VASO images were acquired before the injection of contrast agent and averaged to give the pre-VASO image. Five post-VASO images were acquired starting 7min after the injection (to allow the contrast agent to be ready a steady state (8)) and the images were averaged to give the post-VASO image. The CBV map was calculated from the difference of pre- and post-VASO images, which were normalized against the CSF proton density to give absolute maps (7,8). To assess the intra-session reproducibility of VASO itself, we also calculated two independent VASO CBV maps –"VASO CBV 1", which was calculated from 1st pre-VASO and 1st post-VASO images, and "VASO CBV 2", which was calculated from 2nd pre-VASO and 2nd post-VASO images. For comparison, DSC MRI scan was also acquired before the post-VASO scans to yield a relative CBV map (9).

The PET CBV measurement was conducted on the same day as the MRI scan using a CTI Siemens HR+ scanner. ^{15}O-labeled carbon monoxide ($C^{15}O$) (half life 2 min) was used. The PET scan started at t=0 with a brief inhalation of $C^{15}O$ gas (40-56 mCi) and continued until t=10min. The PET data was reconstructed into three frames (t=0-2min, 2-5min, 5-10min). Only the third frame at the steady-state condition was used for the CBV calculation. The PET signal was calibrated by the radioactivity of pure blood obtained from venous blood samples to give absolute CBV values. The difference between microvessel and large-vessel hematocrit levels (0.85) was also corrected. The entire procedure for PET CBV measurement was conducted twice on each subject 1) for averaging and improving SNR; 2) to generate "PET CBV 1" and "PET CBV 2" for PET reproducibility assessment.

The CBV maps from VASO-MRI, PET and DSC-MRI were spatially registered to the MPRAGE image and smoothed (FWMH=12mm) using SPM. For correlation analysis, 32 circular ROIs of 15mm in diameter were drawn on the smoothed CBV maps in each subject.

RESULTS and DISCUSSION: Fig. 1 shows the result of the reproducibility test on VASO CBV, suggesting that the two independently measured VASO CBV maps are highly consistent. The VASO CBV and PET CBV maps of a subject are illustrated in Figs. 2a-2c. The MRI approach has a higher spatial resolution (Fig. 2a), but the smoothed version (Fig. 2b) is visually similar to the PET maps (Fig. 2c) which have lower intrinsic resolution. Correlation analysis between the VASO CBV and PET CBV results (Fig. 2d) showed that regional CBV values from VASO and PET are in excellent agreement. Furthermore, the slope of the regression curve was close to unity (1.05±0.13), suggesting that the absolute values of the VASO measurement were also in reasonable range. We noticed that the correlation coefficient between the VASO and PET results (r=0.72) is lower than that from the VASO reproducibility study (r=0.93, Fig. 1). To assess whether this is due to systematic difference between VASO and PET or due to SNR differences, we investigated the reproducibility of the two PET CBV maps. "PET CBV 1" and "PET CBV 2" indeed showed a significant correlation (Fig. 3) with a slope of close to 1, but the correlation coefficient (r=0.63) was even lower than that between VASO and PET. Therefore, it is likely that the discrepancy between VASO CBV and PET CBV is primarily due to the relatively low SNR in the PET CBV maps rather than any fundamental differences between the two measurements.

For completeness, we have also compared the VASO CBV maps to the relative CBV maps obtained from DSC MRI (Fig. 4). The results confirmed an earlier report that VASO and DSC CBV maps are spatially consistent (7). However, we would like to emphasize that VASO MRI provides CBV in absolute units (in ml blood in 100 ml brain) while DSC CBV is in relative units (a.u. of MRI intensities), which may present difficulties in comparison across subjects or when the whole brain CBV is changed.

To our knowledge, this is the first study to validate an MRI measurement of CBV using the gold standard PET method. The results showed that VASO-MRI provides quantitative and accurate estimations of CBV values in the human brain. Our data also demonstrated that VASO CBV has a higher SNR compared to the PET technique in addition to providing a higher spatial resolution.

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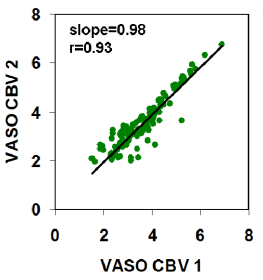

Fig. 1: Reproducibility test of VASO CBV. The CBV values of ROIs from all four subjects were superimposed.

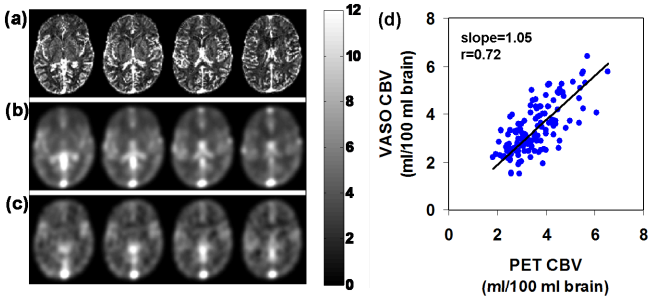

Fig. 2: Comparison between VASO CBV and PET CBV. (a) VASO CBV map (b) smoothed VASO CBV map (c) smoothed PET CBV map (d) correlation between VASO CBV and PET CBV.

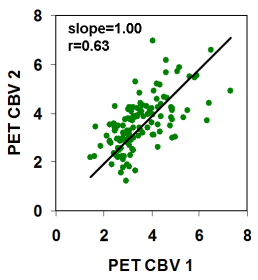

Fig. 3: Reproducibility test of PET CBV.

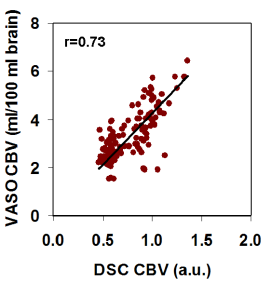

Fig. 4: Comparision between VASO CBV and DSC CBV.