Minimizing Inaccuracy and Variability for Quantitative Estimates of CBF in Unilateral Carotid Artery Occlusion Patients: a PET and MR study

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Introduction

Recently, it has been shown that a quantitative estimate of CBF can be obtained with a singular value decomposition (SVD) deconvolution approach (1). Although some success has been reported in normal volunteers, relatively little attention has been given as to how this approach can be applied to the patient populations. In addition, the limited spatial resolution associated with the EPI sequences and inconsistent fractional cardiac output to the brain can potentially lead to inaccuracy and variability in the CBF measurements. In this study, a correction scheme is proposed to correct these errors. In addition, patients with unilateral carotid artery occlusion were studied with both MR and PET so that the accuracy of MR measured CBF under a pathophysiological condition can be assessed.

Methods

In total, 5 healthy volunteers and 5 patients with unilateral carotid artery occlusion were studied. For the patient group, both PET and MR images were acquired on the same day while only MR studies were performed for the volunteer group. Written inform consent was obtained from all subjects. All MR images were acquired on a Siemens 1.5 T VISION whole body clinical scanner. A 2D single-shot GE EPI sequence was utilized for acquiring images. This sequence was repeated 40 times prior to, during, and after the injection of contrast agent while the subjects were lying still inside the MR scanner. All images were transferred to a Sun Workstation for post-processing. Two pixels were separately placed within the middle cerebral artery and the superior sagittal sinus to obtain the arterial input function (AIF) and venous output function (VOF). An exponential fitting was employed to minimize the recirculation of the contrast agent. Subsequently, SVD was employed to deconvolve the tissue function (or curve) by the experimentally measured AIF and thus quantitative estimate of CBF was obtained. In addition, the area of VOF of each subject was also estimated by integrating the $\Delta R2^*$ curve obtained from the superior sagittal sinus. A VOFmean was defined as the mean VOF area obtained from all the volunteers. Finally, a correction factor (CF) was derived as the ratio of the area of the VOF of each patient and the VOFmean. The experimentally derived CF was then employed to globally scale the CBF values for each patient. Finally, AIR program (2) was applied to co-register the MR CBF maps with the PET CBF maps.

In order to compare the CBF estimates obtained from both the MR and PET studies, a total of 12 circular ROIs with 3 ROIs in each hemisphere across two adjacent slices were pre-defined. These ROIs were placed in both the PET and MR CBF maps and were used to obtain regional estimates of CBF in the patient group. In contrast, for the volunteer group, a total of 20 ROIs were defined across 5 slices with 10 ROIs placed in the gray matter and the remaining 10 ROIs located in the white matter, respectively. Mean and standard deviation from all ROIs were recorded for comparison.

Results

$\Delta R2^*$ time curves for the AIF and VOF of all volunteers are shown in Fig. 1a and Fig. 1b, respectively. The arrival times for both the AIF and VOF have been adjusted to be identical between subjects so that a comparison of the shape as well as the distributions of the two functions can be made. The experimentally measured AIFs exhibit a substantial variability from subject to subject while a more consistent pattern is observed for the VOF among subjects. Regional CBF of gray matter and white matter for all volunteers are in accordance with the reported values in the literature (1), a mean rCBF of 68.1 ± 9.5 ml/100gm/min was obtained for the gray matter while 26.7 ± 5.0 ml/100gm/min was obtained for the white matter.

Finally, MR estimated rCBF are correlated with those obtained from PET measurements and results are shown in Fig. 2. Note that no clear relationships between MR and PET estimates of CBF are obtained (Fig. 2a). In contrast, a substantial improvement (Y=1.02+20.3, r=0.8) is obtained in the relationship between PET and MR estimates of CBF after the application of the VOF correction scheme (Fig. 2b).

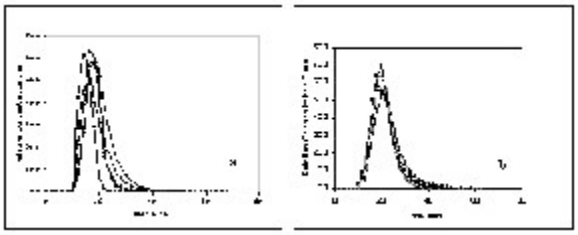

Fig. 1

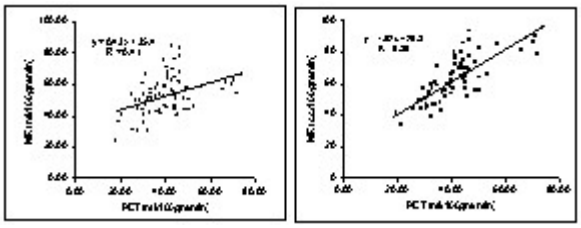

Fig. 2

Discussion

Despite the fact that results obtained from the volunteer studies are consistent with the reported values in the literature, no clear relationships are observed in the patient group when the MR measured CBF is correlated to that obtained via PET (Fig. 2a). Although several factors can potentially account for the observed variability in the patient studies, the two most plausible explanations are the partial volume effects of the AIF caused by the limited spatial resolution of the EPI sequence and the inconsistent fractional cardiac output to the brain, resulting in a substantial dispersion of the bolus of the contrast agent. As shown in Fig. 1, a substantial variability is observed for the AIF while a more consistent pattern is observed for the VOF. As a result, the areas of AIF may be underestimated in both the patient and the volunteer groups, leading to an overestimation as well as variability in the CBF estimates. In addition, one of the original assumptions made by Zierler (3) in deriving the tracer kinetics is that no tracers leave the ROI until all tracers have arrived. Because of the thin slice thickness of the MR images as well as the employment of an intravascular contrast agent, this assumption may no longer be valid for MR imaging approaches. In other words, the maximal height of the normalized residue function will not be equal one since some of the tracers may have left prior to the arrival of all tracers in the ROI. As a result, inaccuracy as well as variability in the measurements of CBF may occur. This is particularly true for the patient studies where a compromised fractional cardiac output to the brain may be present, leading to a substantial dispersion of the bolus of contrast agent. With the experimentally derived CF for each patient, a substantial improvement is observed not only in the linearity but also the slope of the linear regression line (nearly one for the slope), indicating that a more accurate estimate of CBF across a wide range of physiologically relevant CBF can be achieved with MR when the proposed correction algorithm is employed (Fig. 2b). However, the non-zero y-intercept still limits the accuracy of this technique, especially at lower CBF values. Further work will be necessary to improve the accuracy of the MR CBF measurements.

References

1. Ostergaard L, Sorensen AG, Kwong KK, et al. MRM 36:726-736, 1996.; 2. Woods RP, Cherry SR, Mazziotta JC. J Com Assist Tomogr 16:620-633, 1992.; 3. Zierler CL. Circ Res 16: 309-321, 1965.