Multiband BOLD acquisition enhances the sensitivity of cerebrovascular reactivity (CVR) mapping

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Targeted Audience: Researchers interested in using BOLD MRI for CVR mapping.

PURPOSE: Cerebrovascular reactivity (CVR) reflects the ability of the brain vasculature to dilate in response to a vasoactive stimulus[1]. CVR can give a wealth of information beyond baseline cerebral blood flow (CBF) and cerebral blood volume (CBV) measures, and have demonstrated important utilities in brain vascular disorders[2]. CVR is usually measured with CO_2 inhalation while continuously acquiring BOLD MRI images. However, like other functional and physiological indices, the biggest drawback of CVR is its poor sensitivity and reliability. Multiband EPI is a fast-imaging technology that allows the excitation and acquisition of multiple 2D slices simultaneously[3]. In fMRI and DTI applications, it has been shown that multiband EPI provides an SNR advantage over single-band (conventional) EPI[3,4], owing to its higher temporal sampling rate. To our knowledge, the use of multiband acquisition for CVR mapping has not yet been investigated. In this work, we examined the SNR benefit of multiband acquisition in CVR mapping, by comparing the data collected using multiband 2 (MB2) and multiband 3 (MB3) with those using conventional EPI (MB1).

METHODS: Experiment: All experiments were conducted on a 3T (Philips) system. Five healthy volunteers (Age 30±4 years) were scanned. We used three different multiband factors (MB1, MB2, and MB3) and two different spatial resolutions (3.2x3.2x3.5 mm^3 and 2.5x2.5x3 mm^3), resulting in a total of six scans on each participant. The two spatial resolutions examined represents typical values used in the literature. The scan parameters are listed in Table 1. During each scan, the participant underwent a simultaneous hypercapnia and hyperoxia respiratory task lasting for 9.3 minutes, which can provide a concomitant estimation of CVR (to CO_2) and O_2-reactivity[5]. The paradigm of the task is shown in Figure 1. Briefly, the timing of the CO_2 and O_2 inhalation were carefully designed so that they are orthogonal to each other in the time domain and they have different frequencies in the frequency domain. BOLD signal change to CO_2 is used as CVR; BOLD signal change to O_2 (O_2-reactivity) reflects venous CBV (vCBV). During the 9.3min respiratory challenge, end-tidal CO_2 ($ETCO_2$) and O_2 (ETO_2) were recorded and BOLD images were continuously acquired. Data analysis: General linear regression was used between the BOLD time course, end-tidal CO_2 ($ETCO_2$) and O_2 (ETO_2), yielding CVR map in %/mmHg CO_2 and O_2 %/mmHg O_2 reactivity map (Fig. 1). Statistical analysis: We examined histogram of the T scores of the regression analysis, as this informs us the extent to which the estimated CVR is statistically meaningful. Additionally, we also conducted a paired T test on this T score on a voxel-by-voxel basis. Separate analyses were conducted for the CVR and O_2-reactivity maps.

RESULTS AND DISCUSSION: Visual inspection: Figure 2 shows high-resolution CVR and O_2-reactivity maps in a representative subject. It can be seen that the image contrasts are similar but the quality is improved in the multiband scans. The CVR values for "MB1", "MB2" and "MB3" protocols were 0.15±0.02, 0.19±0.02, and 0.21±0.02 %/mmHg, respectively. However, greater CVR values do not necessary indicate higher statistical significance. We therefore examined the T scores associated with these maps. Histogram comparison: Figure 3 shows a comparison of T score histograms for each of the map types, i.e. (A) high-resolution CVR map, (B) high-resolution O_2-reactivity map, (C) standard-resolution CVR map, and (D) standard-resolution O_2-reactivity map. In all comparisons, it is apparent that the multiband data has a distribution centered at higher T score values compared to conventional EPI data, suggesting that multiband acquisition yields statistically more significant data. When directly contrasting MB2 to MB1 data in a voxel-by-voxel comparison, it was found that 10% of the voxels in the brain showed a greater T score in the MB2 data. When comparing MB3 to MB1, this fraction was 9%. No apparent difference was observed between MB2 and MB3, suggesting that a greater MB factor does not increase the sensitivity further. Similar observations can be made for O_2-reactivity data and for standard-resolution data. Comparison between standard-resolution and high-resolution data: Figure 4 shows the comparisons of averaged T scores between the two resolutions for CVR and O_2-reactivity maps. In general, standard-resolution maps showed higher mean T score than high-resolution maps, indicating a better sensitivity for standard-resolution maps. The resolution difference is most pronounced in MB1 data (p=0.09 for CVR and 0.03 for O_2 reactivity), but reduced in MB2 and MB3 data. This observation suggests that high resolution scans might benefit more from the use of multiband acquisition in terms of sensitivity improvement. O_2-reactivity maps showed more significant resolution-difference than CVR maps, so we further compared the sensitivity between CVR and O_2-reactivity. Comparison between CVR and O_2-reactivity: It was found that the averaged T score of the O_2-reactivity map was significantly higher($p<0.004$) than that of the CVR map for all three multiband factors and for both high- and standard-resolutions, which indicates an over-all higher sensitivity of O_2-reactivity mapping than CVR mapping.

Recently, there has been a surging interest of applying CVR mapping in cerebrovascular diseases[6,7]. CVR mapping was also found to be useful in understanding the effects of pharmalogical agents on cerebrovasculature[8] and presurgical planning[9]. The quantitative mapping of vCBF (indicated by O_2-reactivity) could provide insight into pathopysiological mechanism and novel targets for therapy[10]. Therefore, the higher sensitivity achieved by multiband acquisition in CVR and O_2 reactivity mapping might benefit a large range of clinical applications and could also open doors for use CVR in unexplored research territories.

CONCLUSION: We have showed the successful use of multiband in CVR mapping. Furthermore, we showed that the sensitivity of MB scans was higher compared to conventional EPI scans owing to faster data acquisition rate. The availability of a sensitive technique would further encourage clinicians to adopt the use of CVR for future clinical applications.

3**REFERENCES:** 1) Yezhuvath et al. NMR in Biomed., 22:779 (2009); 2) Andrea et al. JMRI, 31:298 (2010); 3). Feinberg et al. PLos One 5:e15710 (2012); 4). Setsompop et al. MRM 67:1210(2012); 5) Liu et al. ISMRM proc. (2014); 6) Yezhuvath et al. HBM, 31:80 (2009); 7) Fierstra et al. Brain, 134:100(2011);) 8) Pattinson et al. JCBFM 27:414 (2002); 9) Zaca et al. WJCO, 2:289 (2011); 10) Johnston et. Al., BJA 90: 774 (2003).

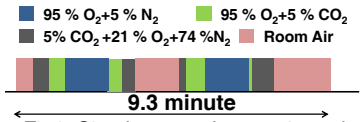

Fig1: Simultaneous hyperoxia and hypercapnia paradigm design.

Table1. Summary of scan parameters for multiband (MB) scans.

	MB1	MB2	MB3
standard	TR=1550 ms, TE=21ms, Dynamic=362	TR=900ms, TE=25ms, Dynamic=624	TR=650ms, TE=27ms, Dynamic=862
High	TR=1950 ms, TE=19 ms, Dynamic=288	TR=1100 ms, TE=24ms, Dynamic=510	TR=850 ms, TE=26ms, Dynamic=660

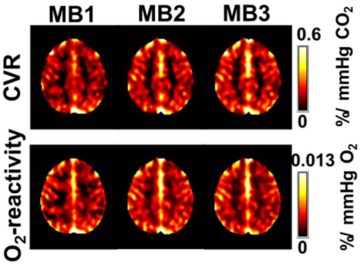

Fig 2. CVR and O_2 reactivity maps from a representative subject.

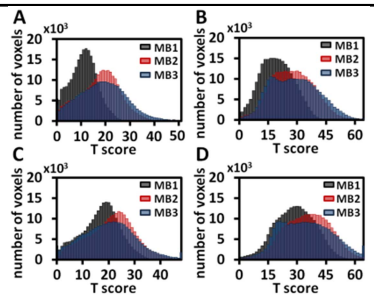

Fig 3: T score histograms. (A) High-resolution CVR map, (B) High-resolution O_2-reactivity map, (C) Standard-resolution CVR map, and (D) Standard-resolution O_2-reactivity map.

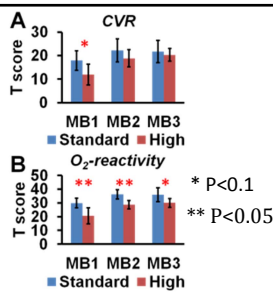

Fig 4: Comparisons of T scores between standard-resolution and high resolution. (A) CVR comparisons. (B) O_2-reactivity comparisons.