Repeatability of cerebral perfusion measurements using susceptibility contrast MRI

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Purpose

Dynamic susceptibility contrast (DSC) magnetic resonance imaging (MRI) can measure cerebral perfusion and other related hemodynamic parameters [1]. In anti-angiogenic therapy of brain tumors, and gliomas in particular, cerebral blood volume (CBV) and cerebral blood flow (CBF) correlate with tumor grade, response to therapy, and survival. Although promising, the repeatability (test-retest reliability) of DSC in a clinical setting has received less attention. The range of normal variations in the estimated perfusion parameters, which depends on both the repeatability of the method and physiological variations in blood perfusion, may in part determine the measured response to cancer therapy. In our study, we have evaluated the repeatability of DSC based perfusion imaging using a double baseline MRI acquisition setup in adult patients with newly diagnosed glioblastoma (nGBM).

Methods

We included 31 patients (18 M, 13 F, age 23-72, mean 56) with nGBMs from a study of cediranib, a small molecule pan-VEGF tyrosine kinase inhibitor. All patients were on a stable or decreasing dose of steroids for 5 days prior to each MRI scan. Each subject was scanned at two baseline time points (hereafter referred to as baselines 1 and 2), typically 3-4 days apart using an identical imaging protocol on a 3.0 Tesla MRI system (TimTrio, Siemens Medical Solutions, Malvern, PA). DSC-MRI was acquired as follows; a 78 mm slab of tissue was imaged using a dual-echo, combined gradient-echo (GE) and spin-echo (SE) echo planar imaging sequence, with echo times (TE) of 31 ms and 94ms, respectively. Repetition time (TR) 1.48 s, flip angle 90º, 1.2 mm in-plane resolution (160×160 matrix), 6.5 mm through-plane resolution and 12 slices. A total of 100 volumes were acquired and 0.1 mmol/kg of Gd-DTPA was injected at 5cc/s after approximately 81s of imaging. The DSC acquisition was preceded by a dynamic contrast enhanced acquisition (0.1 mmol/kg of Gd-DTPA injected at 5cc/s) and this CA injection acted as a pre-dose to minimize errors in CBV estimates due to T1-shortening effects induced by CA extravasation in regions of blood–brain barrier breakdown or resection. In addition to DSC-MRI, post-contrast axial T1-weighted (T1W) images and axial fluid-attenuated inversion recovery (FLAIR) were acquired.

Prior to perfusion analysis, potential motion artifacts in the DSC data were detected and corrected using FSL (mcflirt). Perfusion analysis was performed in a modified version of nordicICE (NordicNeuroLab AS, Bergen, Norway). Contrast agent extravasation was corrected based on the correction technique proposed by Weisskoff et al [2] and later elaborated by Donahue et al [3] and Boxerman et al [4]. The arterial input functions (AIFs) were determined automatically in each patient by an established clustering method [5-6]. Reference tissue masks representing unaffected GM and WM were generated automatically from the DSC images as previously described [6-7] and then used to generate the reference tissue response curves for CA extravasation correction and also to normalize CBV and CBF maps.

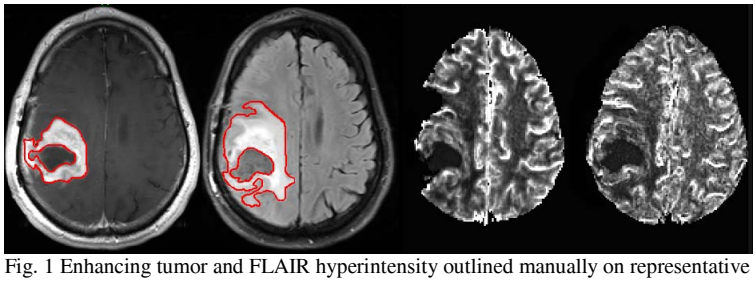

Fig. 1 Enhancing tumor and FLAIR hyperintensity outlined manually on representative images along with CBF maps from GE and SE MRI.

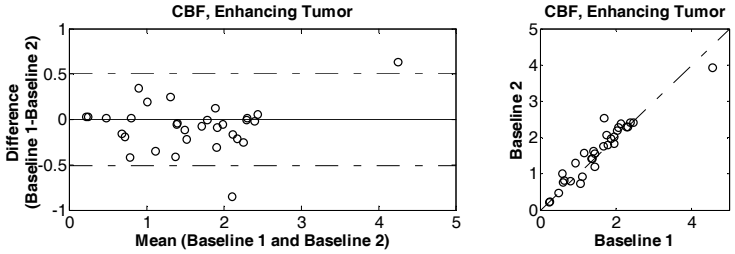

Fig. 2. Bland-Altman scatter plots of the GE parametric maps.

Table 1. The values of ICC for CBV and CBF maps.

	GE Signal		SE Signal	
Map	Enhancing Tumor	FLAIR Hyper-intensity	Enhancing Tumor	FLAIR Hyper-intensity
CBV	0.95	0.95	0.92	0.91
CBF	0.95	0.94	0.91	0.89

An experienced neuroradiologist outlined enhancing tumor on post-contrast T1W axial images and the total tumor region-of-interests (ROIs), including edema, on FLAIR images (Fig. 1). For each subject, the ROIs from baseline 1 were mapped to baseline 2 by rigid coregistration to ensure the same regions were evaluated in both baselines. Finally, all ROIs were mapped to the perfusion maps by rigid coregistration. The mean values of the generated perfusion maps were then calculated within each ROI. Repeatability was assessed using the intra-class correlation coefficient (ICC). Here, values close to 0 represent poor repeatability and values close to 1 represent good repeatability. The ICCs were calculated for CBV and CBF generated from both GE and SE MR images.

Results

Very high repeatability was obtained in tumor for GE CBV and GE CBF with ICCs > 0.94 and SE CBV and SE CBF with ICCs > 0.89 (Table 1). A scatter plot and a Bland-Altman plot comparing baseline 1 and baseline 2 are shown in Figure 2.

Discussion

Repeatability of perfusion parameters using DSC MRI has been previously reported for brain tumors [8] for a limited number of subjects and using a non-AIF-based technique (ICC=0.90 for rCBV of GE signal). Compared to [8] we obtained higher ICCs from a larger and more homogeneous population of subjects, as well as increased overall SNR with a 3T MRI with advanced multichannel receiver headcoil.

Conclusion

We have obtained high repeatability for perfusion maps derived from both GE and SE DSC using an optimized double baseline protocol aimed at high degree of standardization of all relevant parameters between scan sessions combined with automated image analysis methods. This study showed that DSC MRI has satisfactory repeatability for clinical use.

References

[1] Willats L and Calamante F, NMR Biomed, 2012.
[2] Weisskoff R et al, ISMRM, 1994; 279.
[3] Donahue KM, Magn Reson Med, 2000; 43(6): 845-53.
[4] Boxerman JL, AJNR Am J Neuroradiol, 2006; 27(4): 859-67.
[5] Mouridsen, K, Magn Reson Med, 2006; 55(3): 524-31.
[6] Bjornerud A et al, J Cereb Blood Flow Metab, 2010; 30(5): 1066-78.
[7] Emblem KE, et al, AJNR Am J Neuroradiol, 2009; 30(10): 1929-32.
[8] Jackson A, et al, J Magn Reson Imaging, 2001; 14(5): 510-6.