Towards Robust and Automated Identification of Vascular Input Function in DCE-MRI

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Introduction Dynamic contrast enhanced MRI (DCE-MRI) holds potential for characterizing key physiological markers of tumor vascularity such as blood brain barrier permeability, which is believed to predict response to therapy and correlate with overall survival time [1]. Robust quantification of permeability is contingent on reliable characterization of contrast agent concentration in feeding vessels. However, three factors compromise estimation of the vascular input function (VIF). First, at high concentrations T2* effects attenuate the T1-weighted signal, entailing underestimation of concentration. Second, even with T2* correction, typical T1-weighted sequences can be insensitive to changes in vascular concentration during peak concentrations. Third, manual identification of VIFs can be difficult and compromises reproducibility. We propose utilizing dynamic estimates of T2* to device a completely automatic procedure for identifying the VIF using cluster analysis. We compare manual and automatic AIF selection and examine reproducibility of features of corrected and uncorrected signals as well as T2* based estimates of contrast concentration in two pre-therapy baseline scans of 10 patients with newly diagnosed glioblastoma.

Materials and methods

Patients (N=10) with confirmed glioblastoma multiforme were scanned on a 3T TimTrio, Siemens Medical Solutions. A dynamic T1-weighted series employing two echo times (TE=2.73ms, 3.89ms) was acquired at a 6s time frame resolution and 2.6 x 1.8 x 2.1 voxel resolution in 20 slices. A 0.1 mMol/kg dose of Gd-DTPA was injected at 5 cc/s within 2.5 minutes of the start of the acquisition. Patients were scanned at approximately day -5 and -1 (no intervening therapy) prior to treatment with a VEGF inhibitor. Two patients were excluded due to movement artifacts. Pointwise estimates of T2* were obtained using the ratio between the signals at the two echo times [2], and used to correct the original T1-weighted signal with the shortest TE. Exploiting the fact that the Gd-DTPA induced T2* shortening is most pronounced in the vasculature, a vessel mask was constructed based on maximum T2* change. K-means cluster analysis was used to automatically group the corresponding T1-weigted curves with similar temporal characteristics [3]. The group with maximum curvature during bolus passage was employed as VIF. An experienced neuro-oncologist performed manual identification of VIF based on T2* corrected T1-weighted signal curves. Vascular concentration of contrast agent was calculated using both the T2* signal component [4] and corrected T1-based relative signal.

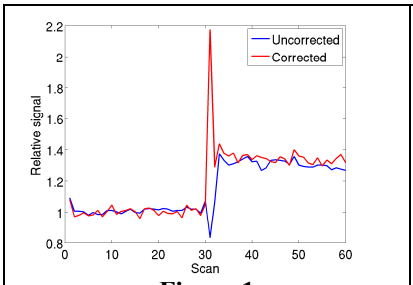

Figure 1

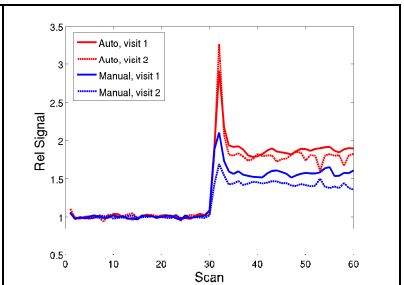

Figure 2

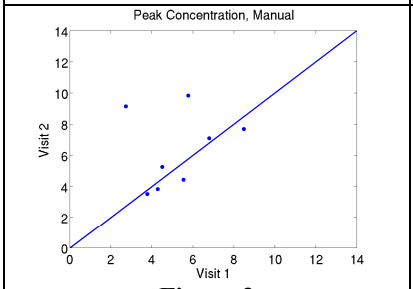

Figure 3

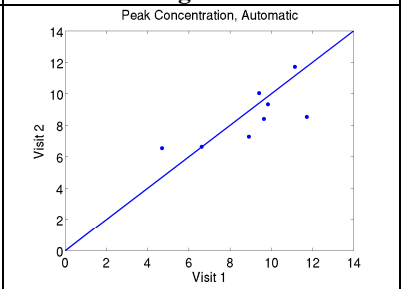

Figure 4

Results T2* correction increased peak relative signal in manually selected VIFs by a factor of 1.54 [1.36, 2.05] and in automatically identified VIFs by 2.91 [2.03, 3.33] (median, inter-quartile range) (Fig 1). However, maximum relative signal was significantly higher using the automated technique 3.73 [3.37, 3.98] compared to manual selection 1.81 [1.54, 1.89] (p=0.008, Wilcoxon). Absolute difference between peak signals at the two consecutive scans, relative to minimum peak, was lower for the automated approach 0.11 [0.04, 0.49] than manual 0.21 [0.13, 53], but not significant, indicating comparable reproducibility (see Fig 2 for an example). Peak concentration estimated using T2* was significantly higher using automated approach 9.31mM [7.36, 9.93] compared to manual 5.47mM [4.48, 7.37] (p=0.02, Wilcoxon). Additionally, a higher correlation between visits was observed for automatic (r=0.74) than for manual approach (r=0.23) (Figures 3,4). In contrast, peak concentration estimated using T1 based signal failed in several cases due to instability of the conversion from signal to concentration at high relative signals.

Conclusion Automated selection of VIF in combination with T2* based estimation of vascular concentration of contrast agent leads to peak-signal reproducibility comparable to manual selection, but higher peak concentrations. We speculate that automated VIF identification incorporating proper T2* correction will facilitate robust quantification of pharmacokinetic parameters in multicenter settings

References [1] Sorensen et al, Cancer Research 2009. [2] Kuperman et al, JMRI 1991. [3] Mouridsen et al, MRM 2006. [4] Bazelaire et al., Eur. Radiol 2006.