Accurate brain tumor blood volume estimation using DCE-MRI with Bookend T1 measurements and phase-derived AIFs

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Introduction: Quantitative dynamic contrast-enhanced (DCE) MRI of human brain tumors has demonstrated diagnostic potential. Currently, however, there is no single, widely implemented DCE data acquisition protocol. Instead, institutions often choose their own DCE pulse sequence and parameters, depending upon familiarity, scanner hardware and software. Protocols thus often vary widely from institution to institution, even changing over time at the same institution. This lack of standardization can make many comparisons, especially inter-institutional, difficult. We propose a strategy for standardizing the data acquired with any DCE pulse sequence by saving phase data during DCE (1) and by performing "Bookend" T_1 measurements before and after DCE (2,3). The phase and Bookend data enable reliable estimation of the arterial input function (AIF) and tissue response function (TRF), respectively, both in terms of absolute concentrations of contrast agent ([C]), thereby minimizing the dependence of the measurements on hardware or pulse sequence protocol. As a first step in testing this strategy, we performed DCE-MRI on a group of brain tumor patients and compared the results to a similar, separate CT perfusion study, the latter being considered as a reference standard.

Methods: Magnitude and phase data were saved from 13 DCE-MRI studies of grade IV astrocytomas, performed on a 1.5T Siemens Symphony using a phased array head coil. A 2D SPGR sequence was chosen for DCE, due to the high temporal resolution available, with parameters: TR=46 ms, double TE=2.06 & 5.48 ms, flip angle=90 deg, thickness=5.5 mm, gap=2.75 mm, 4 transverse slices through the tumor and superior sagittal sinus, Δt=2.2 s, total 3.6 min, Gd dose=0.1 mmol/kg. T_1 measurements were performed before & after DCE using the variable flip angle method (TR/TE=50/2.16, flip angles=10,20,40,70 deg) (4). The AIF was obtained from the superior sagittal sinus. Prior to tracer kinetic modeling, the DCE data were pre-processed with four different standardization methods, in order of increasing sophistication: "ΔS", magnitude signal minus baseline; "T_{1pre}", [C] calculated in the conventional way, using the pre-DCE T_1 measurement (2); "Bookend", with [C] calculated using the Bookend Method, which uses both pre- and post- T_1 measurements (2,3); "Bookend + phase", with [C] calculated with the Bookend Method, but with the AIF calculated using phase (1). For each of the four methods, tumor blood volume (TBV) was calculated with tracer kinetic modeling (5). It is important to note that these were not relative blood volume measurements, i.e. no reference tissue such as white matter was needed to calculate TBV in tumor. A separate group of 15 patients with grade IV astrocytomas was studied at our institution using CT perfusion (6), to establish reference TBV values for this tumor type. TBV values for the four DCE-MRI methods were analyzed using a repeated measures ANOVA with post-hoc Neuman-Keuls tests. Comparisons of mean TBV values with those found from CT perfusion were done using a two-tailed non-paired student's t-test.
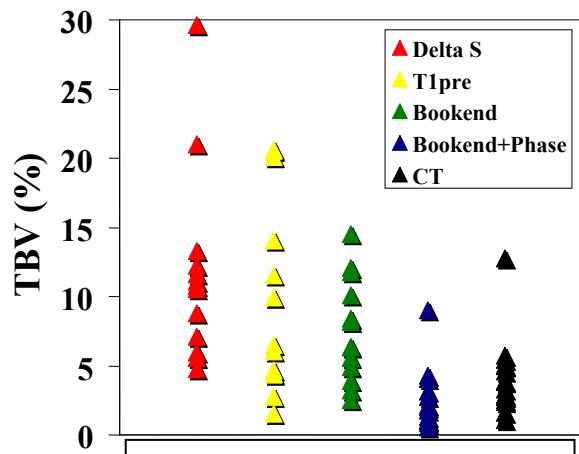

Fig 1: Distribution of TBV values for the 4 different MRI methods & CT.

Results: Repeated measures ANOVA showed a significant DCE-MRI technique effect (p<0.001). Post-hoc Neuman-Keuls testing revealed no significant differences among the mean TBVs determined by ΔS, T_{1pre}, and Bookend (p≥0.07 for each comparison), whereas the TBV determined by the Bookend + phase technique was significantly different from each of the other methods (p≤0.01). The mean CT-determined TBV was significantly different from each of the DCE-MRI methods (p≤0.01), except for the Bookend + phase approach (p>0.1).

Table 1: Mean ± standard deviation of TBV (%)

ΔS	T_{1pre}	Bookend	Booknd+Phas	CT perfusion
11.7 ± 6.8	9.8 ± 7.0	7.5 ± 3.7	2.6 ± 2.3	4.2 ± 2.7

Discussion: We observed increasing agreement between DCE-MRI and CT perfusion with increasing sophistication of DCE-MRI pre-processing. The most sophisticated DCE-MRI pre-processing (Bookend + phase) provided TBV values which were statistically similar to those found with CT perfusion (p>0.1).

Conclusion: We have proposed a strategy for standardizing DCE-MRI brain tumor data, using a combination of the Bookend Method (2,3) and phase-derived AIFs (1). This strategy can be implemented for any DCE pulse sequence, as long as the phase data are saved. Initial testing has shown that tumor blood volume values found from DCE-MRI are consistent with those of CT perfusion, thus supporting the validity of the strategy.

References: 1. Foottit et al. MRM 2010;63:772. 2. Cron et al. MRM 1999;42:746. 3. Cron et al. MRM 2004;51:1066. 4. Fram et al. MRI 1987;5:201. 5. Tofts et al. JMRI 1999;10:223. 6. Shankar et al. ASNR annual meeting 2009;May 16-21, Vancouver, poster 56.