Evaluation of vessel size heterogeneity in brain tumors with dynamic contrast-enhanced dual echo perfusion weighted imaging.

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Introduction: Several studies have hypothesized the existence of vessel size heterogeneity in neoplasms. This hypothesis is difficult to evaluate in brain tumor patients, since biopsy is usually confined to one or two portions of a tumor. Relative cerebral blood volume (rCBV) information, acquired from dynamic susceptibility-contrast studies using either a gradient-echo (GE) or spin-echo (SE) method, constitutes a suggested non-invasive method to assess tumor vascularity. Given the fact that each method is theoretically sensitive to a different population of vessels, we used an interleaved GE / SE EPI sequence to assess tumor vascularity and vessel size heterogeneity in brain tumor patients that were scanned for clinical reasons. Moreover, by collecting both GE and SE information simultaneously, the ratio of GE and SE relaxation rate changes ($\Delta R2^*/\Delta R2$) could be calculated, which could serve as a marker of vessel diameter.

Methods: We retrospectively reviewed the MR examinations of patients scanned for a history of known or suspected cerebral neoplasm over a 6 month period. Criteria for inclusion of patients in this retrospective study were pathological or radiological confirmation of malignancy, diameter of the lesion at least 1cm, location of the lesion in the brain parenchyma, and scanning during the time that the GE/SE sequence was in routine use. Nine patients met criteria for inclusion in the study, 1 with the clinical diagnosis of anaplastic oligodendroglioma and 8 with diagnosis of an astrocytic tumor: 1 pilocytic astrocytoma, 1 low-grade astrocytoma, 3 anaplastic astrocytomas, 3 glioblastomas. All patients underwent clinical examination on a 1.5T Siemens Sonata scanner (Siemens Medical Solutions, Erlangen, Germany), which included dynamic contrast-enhanced dual echo perfusion weighted imaging (PWI). A multislice interleaved T2* / T2 weighted EPI-sequence was used for PWI, after intravenous bolus injection of 0.2mmol/Kg Gd-DTPA. The sequence parameters were: Repetition Time 1.4 sec, Echo Time 35 ms (GE), 90 ms (SE), Slice thickness 6mm, Interslice gap 1 mm, FOV 220*220, Matrix 128*128, Slices 10, Timepoints 72. Perfusion data sets were used to calculate T2* ($\Delta R2^*$) and T2 ($\Delta R2$) rate changes and relative cerebral blood volume (rCBV) maps were generated for both gradient and spin echo.[1,2] These maps were corrected for T1 leakage (agent extravasation) effects due to the disrupted blood brain barrier, that is often the case with brain tumors, and corrected rCBV maps were created.[3] We also created vessel size maps using the principles previously published in the literature, by determining the $\Delta R2^*/\Delta R2$ ratio for each voxel.[4]

Structural MR images (T2, FLAIR pre-contrast and T1 post-contrast) were used to define the lesion and its borders for each case. Our research approach included the visual inspection of the rCBV maps to detect noticeable differences between the GE and SE methods, as well as placement of regions of interest (ROIs) in various areas of the tumor to detect more subtle differences. The rCBV maps were reviewed and, in 6 of the 9 patients, we were able to determine areas of the tumor that had visibly higher intensity on the R2* maps than on the R2 maps. This difference between the two maps was only noticeable in part of the tumor and the rest of the lesion did not appear to be brighter on one map or the other. To quantify this observation, regions of interest (ROIs) of at least 14 pixels each were placed on the rCBV and vessel size maps within the tumor, in the region where there was visible difference between the GE and the SE rCBV maps and in another region of the tumor where no such difference was visible. Similar ROIs were also placed in regions of the tumor for the remaining 3 patients in order to pick differences that were not visible by simple observation. The mean value for each ROI was then calculated. Since the rCBV mapping method yields a relative rather than an absolute value of CBV, the comparison of the patients was facilitated by reference to an internal contralateral standard. The normal gray or white matter in the contralateral hemisphere was used as a reference and the ratios were computed. The tumor rCBV and vessel size map results are presented as normalized to contralateral brain.

Results: We compared the values of the GE (total) rCBV maps to those of the SE (microvascular) rCBV maps for every patient in the study. We found that in 6 of the 9 cases, R2* values were greater than R2 values by more than 50% in part of the tumor whereas the rest of the tumor showed similar R2* and R2 values. Similarly, the vessel size maps generated for these subjects demonstrated increased signal in the same tumor area that had different R2* and R2 values and significantly lower signal in other areas of the tumor. For the remaining 3 patients, the rCBV maps did not reveal R2*/R2 differences within the tumor.

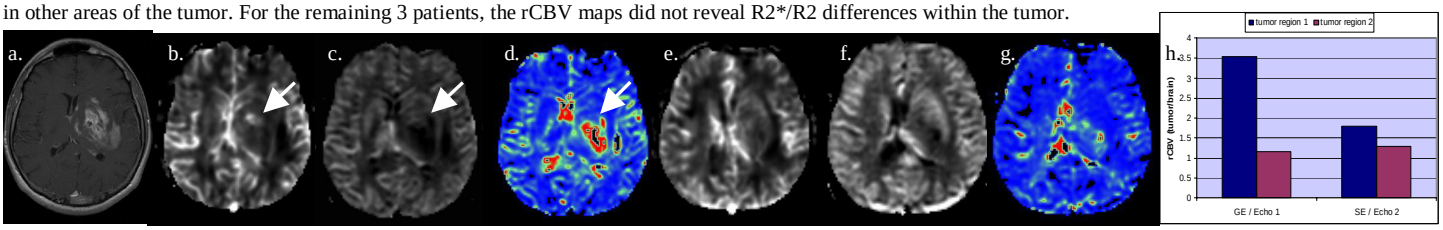

Figure 1. Patient with pilocytic astrocytoma. a. T1 post-gd structural image. b,c. GE and SE rCBV maps (slice one) show increased signal of the GE map in the area of the lesion compared to the SE map. d. Vessel size map shows increased signal in tumor area. e,f. GE and SE rCBV maps (next slice) show similar signal intensity for both GE and SE maps in other region of same tumor. g. Vessel size map shows signal intensity of tumor similar to normal brain. h. rCBV values of GE vs SE maps, showing a 97% greater R2* than R2 value in one area of the tumor, whereas the values are similar in another area.

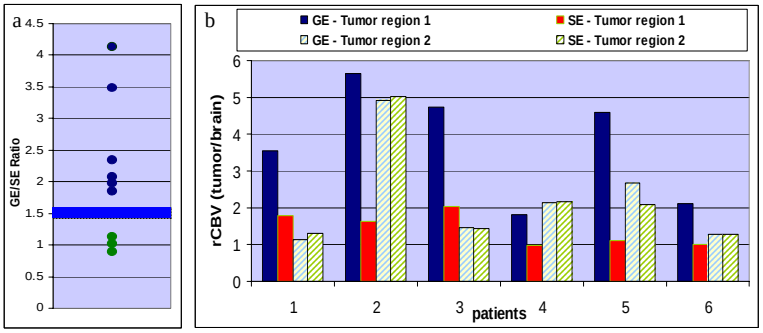

Figure 2: a. Graph showing the ratio of GE to SE rCBV values for all 9 patients. It is obvious that 3 of the 9 patients failed to show considerable difference between GE and SE maps in any area of the tumor. b. Comparison of GE and SE rCBV values (ratio of tumor to contralateral brain) for each of the patients that demonstrated significantly higher R2* than R2 values within an area of the tumor. For each patient, we show the rCBV values in two different areas of the tumor: Region 1 is the area that demonstrates the different GE / SE values and Region 2 is another area of the tumor in which this difference is not observable.

Discussion: In this preliminary study, 6 of 9 patients demonstrated areas of the tumor that showed significant rCBV differences between the GE and SE method, while other areas of the same tumor had essentially similar rCBV values in both GE and SE derived maps. This is preliminary evidence, but still highly suggestive of vessel size heterogeneity within the neoplasm. Although earlier reports have shown that rCBV differences between T2* and T2 methods exist in some brain tumor patients[5], we were able to show that differences between the two maps might become evident even within the same tumor. We can presume that the different areas observed within the tumor consist a meaningful finding, which might indicate that certain areas of the tumor have different aggressiveness than other areas adjacent to them. Our results need further investigation and warrant correlation with clinical progression and follow-up studies of these patients to determine the behavior of each region of the tumor.

References: 1. Sorensen AG, et al, Radiology. 1999 Feb;210(2):519-27. 2. Ostergaard L, et al, Magn Reson Med. 1996 Nov;36(5):726-36. 3. Weisskoff R, et al, Proceedings of the 2nd Annual Meeting of SMRM, San Francisco, 1994. p 279. 4. Dennie J, et al, Magn Reson Med. 1998 Dec;40(6):793-9. 5. Donahue KM, et al, Magn Reson Med. 2000 Jun;43(6):845-53.