Characterization of intra-axial neoplasms by histogram analysis of total tumor volume from MR-derived cerebral blood volume maps

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Purpose: To develop a histogram based analysis of MR cerebral blood volume maps with the aim of reducing user dependence in tumor grading.

Background: The value of normalized cerebral blood volume ratio (nCBV) analysis to differentiate malignant high grade tumors from low grade has been shown in multiple studies [1]. This method utilizes first-pass bolus tracking analysis to derive relative cerebral blood volume maps (rCBV) and viable malignant tumor tissue is identified as regions of elevated microvascular blood volume ('hot spots'). One limitation with this method is the user dependent selection of tumor 'hot-spots' which is critical for correct tumor grading. We propose an alternative method based on histogram analysis of the entire tumor volume, using the histogram shape and frequency distribution to differentiate high-grade from low-grade tumors in MR-derived blood volume maps.

Methods: Nine patients with known intra-axial tumor histology have so far been included. All imaging was performed at 1.5 T (Siemens Sonata) prior to surgery. rCBV maps were generated using established tracer kinetic models [2] applied to the first-pass data obtained by i.v. bolus injection of 0.1 mmol/kg of Gadovist (Schering AG). The time resolution of the first-pass gradient echo (GRE)-EPI sequence was 1.5 s and the voxel size was 1.8 x 1.8 x 6.5 mm^3. Histogram analysis was performed as followed: The location of the tumor was established from the rCBV maps, combined with post contrast T1-w SE images and T2-w FSE images. The rCBV maps were coregistered and overlaid on the morphological data to aid in accurate localization of tumor volume. Regions of interest (ROI's) were drawn as freehand regions individually in each slice, taking care to avoid large vessels. Histograms were generated by classifying the obtained rCBV in all the ROI's into 25 bins and normalizing the values to the rCBV value measured in an unaffected region. The area under the resulting histogram curves was then normalized to 1. All image analysis was performed using nICE™ (NordicIceMedical, Norway). The cut-off point for peak significant nCBV value for each histogram distribution was set using a nonparametric frequency distribution analysis of the resulting histograms with p=0.05.

Results: Of the nine tumors investigated, four were confirmed to be high-grade (three glioblastomas and one solitary metastasis). Four tumors were low grade and one tumor was an astrocytoma with mixed grading (I-III). The histogram analysis revealed a distinctive shape for all high-grade tumors, characterized by a wide distribution of nCBV values and a long tail into high nCBV values. The low-grade tumors exhibited a much narrower nCBV distribution with a frequency distribution similar to normal brain parenchyma. Figure 1 shows the obtained histogram curves in all nine patients. The distribution of normal white matter is also included as reference. Note the distinct shape difference between the high-grade and low-grade tumors. Only the high-grade tumors had significant number of pixel values above an nCBV value of 2.0 ($p<0.05$). Figure 2 shows sample rCBV maps obtained in a high-grade and low-grade tumor, respectively.

Discussion: We propose an alternative method to differentiate high-grade from low-grade brain tumors based on the nCBV histogram distribution of rCBV values measured in the entire tumor volume. It is hypothesized that this method provides a more objective and robust approach compared to the traditional approach whereby the tumor 'hot-spot' is subjectively identified by the operator. In the traditional definition of tumor hot-spot the grading is in effect made on the basis of a very few number of pixels compared to the total tumor volume whereas in the method proposed here the entire tumor pixel histogram is used to characterize the tumor. Although the current method so far is tested in a limited number of patients only, the initial results suggest that this may be an improved alternative to grading brain tumors from rCBV maps with less user bias.

Conclusion: A histogram based analysis of MR-based blood volume maps is introduced as a means of differentiating high-grade from low-grade brain tumors. In the current pilot study, the method proved to accurately differentiate high-grade from low grade tumors based on the histogram shape and distribution of nCBV values in the entire tumor volume.

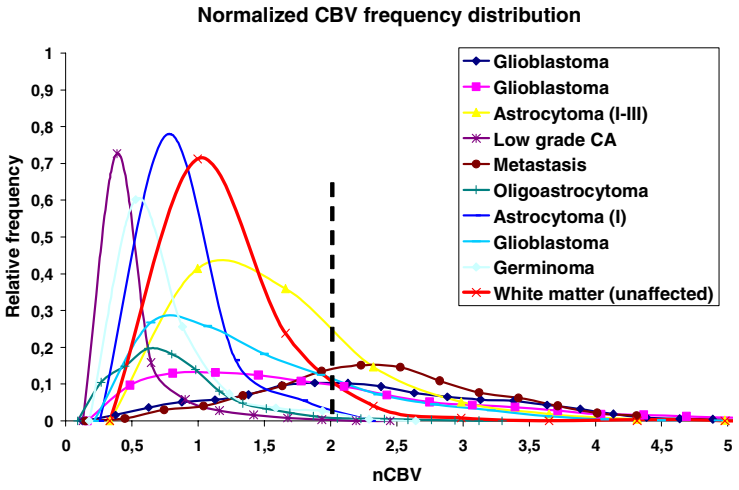

***Figure 1**. Histogram distribution of nCBV values in all tumors investigated. Note the distinct shape difference between the high-grade and low-grade tumors. A cut-off nCBV value of 2.0 ($p<0.05$) was found to differentiate high-grade tumors from low-grade.*

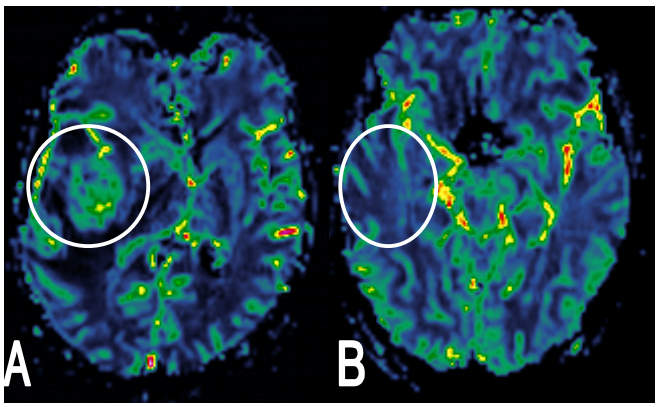

***Figure 2**. Sample rCBV maps in a patient with glioblastoma (A) and low grade oligoastrocytoma (B). The white circles indicate the tumor region in both cases. The higher heterogeneity and larger peak nCBV values are reflected in the corresponding histogram analysis (Fig 1).*

References:

[1] Covarrubias DJ et al, The Oncologist, 2004;9:528-537

[2] Ostergaard L et al, Magn Reson Med, 1996;36:715-725