Clinical Evaluation of Vessel Size Imaging in 31 Cases of Human Glial Brain Tumor

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Introduction Glial tumors of different grades have a very variable extent of microvascular density which is a prognostic factor for the survival of patients. The ability of tumors to form new vessels, or to engage native vessels, correlates with malignancy (1,2). As previously presented, a non-invasive method for evaluation of microvascular density is vessel size imaging (VSI) (3,4). VSI is closely related to the mean vessel caliber, and is able to visualize local differences in microvascularity. Therefore, in the present study VSI maps were calculated to evaluate their diagnostic use in correlation with biopsy proven diagnosis in human glial brain tumors.

Methods In 31 patients with glial brain tumors, the VSI was measured with a 3.0 Tesla scanner (Siemens TRIO) before neurosurgery. Four patients with astrocytoma°II (A°II), six with oligoastrocytoma°II (OA°II), two with oligodendroglioma°II (OA°II), two with oligodendroglioma°III (OA°III), one with oligoastrocytoma°III (OA°III), six with astrocytoma°III (A°III) and ten patients with glioblastoma multiforme°IV (GBM°IV) were investigated. All diagnoses have been confirmed by histology. Dynamic perfusion measurements were performed during a constant intravenous gadolinium contrast bolus injection at 4 ml/s of 0.1 mmol/kg body weight. The data acqusition was performed using a multiecho EPI sequence (TE_{GE} = 23ms, TE_{SE} = 95 ms, TR = 1800 ms), giving rise to a GE and SE map of the brain at a resolution of 64x64x16 voxels every 1.8 seconds. The long TR strongly damps T1 saturation effects as often found in solid tumors where leakage occurs. VSI-maps were calculated based on the different transverse relaxation rates of vessels in spin-echo (T2) versus gradient-echo (T2*) measurements during the first bolus passage of contrast as published previously (3,4). Region of interest (ROI) analyses were performed of contralateral normal appearing white matter, thalamus, tumor edge and the center of the tumor. The tumor edge was defined as the area of rim-like contrast enhancement on T1w images, or in case of a non-enhancing tumor the outer edge of the high signal lesion on T2w images. To test for significant differences of the mean VSI in the tumor edge among groups, a Students *t*-Test was performed. Significance was assumed when p was < 0.05. One patient (GBM) had to be excluded because of poor anatomical image quality.

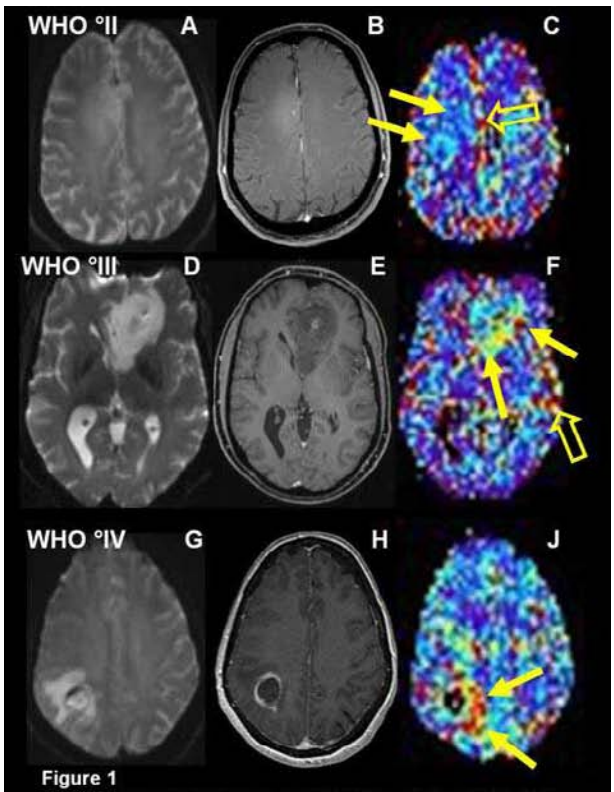

Figure 1
A-C: Corresponding images (EPI-T2w, ceT1w, VSI) of an astrocytoma WHO°II; D-F, oligoastrocytoma WHO°III; G-J, glioblastoma WHO°IV. Closed arrows: VSI in tumor, open arrows: VSI corresponding to large vessels.

Results The mean vessel size index differed among different grades of human glial brain tumors as expected (Figure 2). In accordance to histopathological findings the mean VSI in grade °II tumors was clearly lower than in grade °IV tumors and intermediate in grade °III tumors. Grade °III tumors showed a wide 95%-confidence-interval as compared to the prior groups. Only in the very small group of oligodendrogliomas, no remarkable differences could be identified between °II and °III, being attributed to the sample size of n=3. Students *t*-Test revealed significant differences ($p<0.05$) globally between all WHO°II versus all WHO°III-°IV tumors, as well as between astrocytomas °II and oligoastrocytomas °II compared to astrocytomas °III or glioblastomas °IV (figure 2). Moreover, as shown in Figure 1 G-J, high VSI is visible outside the rim of contrast enhancement (arrows).

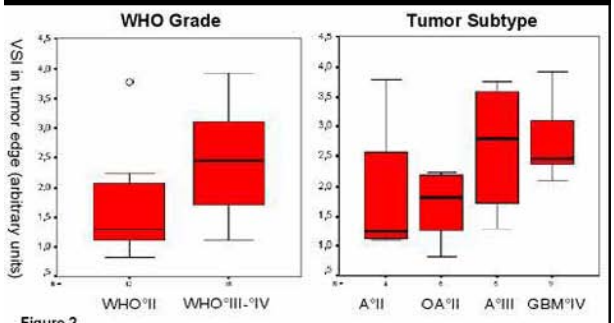

Figure 2
Boxplots with 95%-confidence-intervals and extreme values for all tumors evaluated, according to their WHO grading (left panel) and according to their tumor subtype (right panel). Groups with less than 3 values have been omitted in the right panel, but are included in the left. The difference of the mean values is significant ($p<0.05$) between WHO°II and WHO°III-°IV and between A°II-OA°II versus A°III-GBM°IV.

Discussion In tumor therapy, especially in human glial brain tumors, prognosis and therefore the therapeutic approach differ greatly between low and high grade tumors. Where low grade astrocytomas very often can be followed conservatively over years, high grade tumors require very early and aggressive treatment to seize the little chance of successful curative treatment. On the other hand, low grade tumors tend to progress over time with the ability to further dedifferentiate into higher grade gliomas. Therefore, calculating the vessel size index offers a very promising and valuable noninvasive possibility to increase diagnostic accuracy evaluating glial brain tumors. VSI has shown to be able to detect differences in the mean vessel calibers of tumors in a voxelwise manner. Besides the advantages of having this significant information for noninvasive grading of a tumor, it also allows to spatially differentiate different regions of a single tumor with different grades of dedifferentiation (Figure 1 C, F, J). This allows to guide stereotactic biopsy and to achieve appropriate histology, which still is the gold standard for tumor grading, specifically to areas of a larger vessel calibers most likely reflecting more aggressive areas of the tumor (Figure 1 G-J). The third advantage of the VSI is the possibility to follow-up tumors serially over time, either to early detect further dedifferentiation to change treatment recommendations or to measure the effect of tumor therapy in a certain lesion, especially since latest therapeutic strategies focus on antiangiogenesis.

References (1) Abdulrauf SI et al. J Neurosurg (1998) 88: 513-520. (2) Leon SP et al. Cancer (1996) 77: 362-372. (3) Kiselev VG et al. Magn Res Med (2005) 53: 553-563. (4) Breyer T et al., ISMRM 2006, Seattle (Abstract).