Correlation of Microvascularity Identified within Human Gliomas on High Resolution 8T Gradient Echo MRI and Directed Biopsy

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Introduction

Heterogeneity within human gliomas can result in underestimating tumor grade by only sampling foci of lower grade within the tumor bed. Directing biopsies to regions of higher microvascular density (MVD) may help optimize tumor sampling. Ultra high field (UHF) 8 Tesla magnetic resonance imaging (MRI) provides high resolution (HR) images (in plane resolution around 200 µm) with improved signal to noise ratio (SNR). Microvasculature as small as 100 microns in diameter can be visualized in vivo using 8T gradient echo (GRE) sequence within both normal brain and brain tumors (1,2). This study sought to determine whether microvascularity identified within gliomas using HR GRE MRI at 8 Tesla correlates with directed biopsies on histopathology.

Materials and Methods

Subjects:

A total of 35 subjects bearing biopsy proven gliomas were included in the study. World Health Organization (WHO) classification grades included: WHO grade I – 5 subjects, WHO grade II – 11 subjects, WHO grade III – 9 subjects and WHO grade IV – 10 subjects.

Imaging:

UHF 8T high resolution MR images were acquired on an 8 T/80cm MRI system (Magnex-GE, Abingdon, UK) equipped with a Bruker AVANCE console (Bruker, Billerica, MA) interfaced with Techron (Crown International, Elkhart, IN) gradient amplifiers using a custom-built radio-frequency front end. A modified two-port quadrature transverse electromagnetic (TEM) coil was tuned to the head of each subject at 340 MHz. A conventional two-dimensional T2* weighted GRE sequence was used (TR 600-750 msec, TE 10 msec, flip angle 22.50, matrix 1024×1024, FOV 20 cm, slice thickness/gap 2/3 mm). Eighteen to twenty cross-section slices covering the region of tumor were acquired in 12 minutes with an in-plane resolution at 195 µm. These parameters were derived from Bloch equations for the spoiled gradient echo sequence and from preliminary 8T relaxation parameter estimates.

Assessment of microvascular density:

After viewing the high resolution 8T GRE image, 1 to 10 regions of interest (ROI)s were identified within the tumor bed of each subject. The MVD of each ROI was ranked on a semi-quantitative 3-tier scale (high, medium and low) based on vessel size and density relative to cortical penetrating veins. ROIs identified on 8T MRI were then co-registered to 1.5T MR images used for stereotactic guidance using a frameless navigation system. Directed biopsies were obtained from the ROIs. Biopsy specimens from ROIs were evaluated using reticulin stains. Tumoral microvascularity on histopathology was graded as high, medium or low by comparison to normal white matter ad gray matter by an experienced neuropathologist.

Statistics:

Contingency analyses were performed. MVD assessed on HR 8T GRE MRI was compared to MVD assessed on directed biopsy specimens and WHO classification grade. Discrepancies between 8T and histopathology assessment of MVD were identified and analyzed in order to help explain the discrepancies.

RESULTS:

Haphazardly arranged serpiginous low signal structures associated with areas of low signal within the tumor bed on 8T GRE UHF MRI were presumed to be related to microvascularity (figure 1). This low signal was most likely related to susceptibility effect from endogenous paramagnetic material –deoxyhemoglobin within venous structures. There was correlation between WHO classification tumor grade and : 1) number of foci of microvascularity within the tumor bed on 8T MRI ($p<0.0011$) and 2) size of abnormal vessels within the tumor bed relative to normal brain on 8T MRI ($p<0.01$). There was a concurrence in 82% of 115 biopsy samples ($p<0.001$; Pearson) between histopathologic and 8T MRI assessment of microvascularity. Analysis of discrepancies between biopsy samples and 8T GRE assessement of MVD suggested that differences may be explained by: 1) co-existence of radiation induced microvascular change (figure2), 2) low signal to noise on the 8T image as a result of artifact, and 3) normal microvasculature mimicking tumoral microvasculature at the edge of the tumor. Finally, radiation induced morphological change, such as necrosis and hemosiderin deposition, were sometimes difficult to distinguish from microvascularity on 8T GRE MRI.

CONCLUSION:

HR 8T GRE imaging provides a unique detailed view of the cerebral microvasculature and shows promise as a marker for tumoral microvascularity. HR 8T GRE MRI could potentially allow differentiation of high from low-grade gliomas and help direct biopsy. Potential pitfalls in analyzing these images include radiation necrosis, normal anatomy mimicking microvascularity and artifact. Further improvements in image quality may help overcome these problems.

REFERENCES:

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Figure 1: Axial HR 8T GRE MRI of a pilocytic astrocytoma from a 55 year-old female, demonstrates high MVD within the region of interest depicted within the square. This patient's tumor went on to rapidly enlarge and within 3 months the patient died as a result of this tumor.

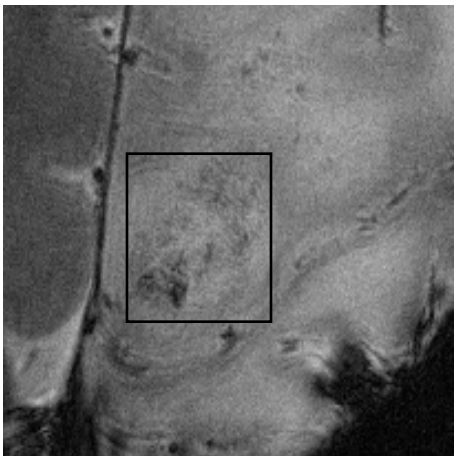

Figure 2: Axial 8T GRE through a recurrent glioblastoma in a patient who underwent radiation therapy. The ROI depicted by the square was considered as high MVD on HR 8T GRE UHFMRI. Histopathology demonstrated radiation induced microvascular hyalinization within recurrent tumor.