Correlation of MRI Contrast Enhancement in Gliomas with Immuno-histological Vascular Parameters using Image-guided Biopsy Specimens

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Purpose: The purpose of this study was to correlate the status of MRI contrast enhancement with immuno-histological vascular parameters such as microvascular cellular proliferation (MVCP), microvascular density (MVD), VEGFR-2 (vascular endothelial growth factor receptor-2) expression and WHO grade obtained from image-guided biopsy specimens. We also compared perfusion CT (PCT) parameters such as cerebral blood volume (CBV), cerebral blood flow (CBF) and permeability surface area-product (PS) with the presence or absence of contrast enhancement.

Background/Introduction: Gliomas are usually very heterogeneous and presence or absence of contrast enhancement may not always indicate higher grade of the tumor. Previous studies have shown high grade gliomas may not always show contrast enhancement, whereas some of the low grade tumors may show contrast enhancement. However, despite this predicament, resection or biopsy from the contrast enhancing part of the tumor is still the norm, which does lead to errors in diagnosis. Recent literature (1, 2,) has stressed the role of functional imaging techniques in glioma grading and to guide the biopsy so as to obtain the highest grade of the tumor based on metabolic, physiologic or hemodynamic status of the tumor, however, use of some of the advanced neuroimaging techniques is still limited to very few centers. We therefore correlated contrast enhancement with immuno-histological markers as well as CT perfusion parameters to assess the utility of MRI contrast enhancment as a measure of tumor angiogenesis and agressiveness.

Materials and Methods: 27 image-guided biopsy specimens in 17 patients with treatment naive gliomas were obtained from contrast enhancing (CE) and non-enhancing (NE) regions of the glioma and contrast enhancement status was correlated with MVD, MVCP, VEGFR-2 expression and WHO grade as well as with the PCT parameters. Histological sections were stained with hematoxylin and eosin, CD34 and VEGFR-2 and examined under a light microscope.

Table1:Correlation of MRI Contrast Enhancement with Immuno-histological Markers

Immuno-histological Markers		CE samples (N=16)	NE samples (N=11)
MVCP	Positive	9 (56%)	0 (0%)
	Negative	7(44%)	11(100%)
MVD (no of vessels /20x hpf)		138.1± 40.1	81.6 ± 9.0
VEGF-R2 reactivity	Positive	12 (75%)	5 (50%)
	Negative	4(25%)	5(50%)

Table 2: Correlation of MRI Contrast Enhancement with Perfusion CT parameters

CTP Parameter	CE samples (N=16) (Mean ± SD)	NE samples (N=11) (Mean ± SD)	p Value
CBV	2.57 ± 0.93	1.23 ± 0.10	0.117
CBF	71.16 ± 35.39	28.18 ± 5.11	0.212
MTT	4.46 ± 0.80	4.43 ± 0.76	0.951
PS	3.12 ± 1.17	0.46 ± 0.06	***0.008***

Results: Seventeen patients underwent 27 image-guided biopsy specimens using either stereotactic biopsy. or open surgical biopsies. Six patients were diagnosed with low grade gliomas (I=1, II=5) and 11 patients with high grade gliomas (III=4, IV=7) as their final tumor grade. There were 16 CE specimens and 11 NE specimens. The results showing correlation of contrast enhancement and immune-histological Markers is shown in Table 1 and with CT perfusion parameters in Table 2. Out of 16 CE specimens, 10 (62.5%) were high grade (III=3, IV=7) whereas 6 (37.5%) were low grade (II=6). Out of the 11 NE specimens, 10 (91%) were low grade (I=1, II=9) and 1 specimen could not be graded. VEGFR-2 staining was done in 26 specimens. Out of 16 CE specimens, 12 (75%) showed positive VEGFR-2 immuno-reactivity, whereas 4 (25%) CE specimens were VEGFR-2 negative. 16 CE specimens showed much higher number of blood vessels (138.1± 40.1/20x hpf) as compared to 11 NE specimens (81.6 ± 9.0/20x hpf). CE specimens did show higher CBV (p value 0.117), CBF (p value 0.212) and PS (p value 0.008) as compared to NE specimens though only PS values showed a statistically significant correlation.

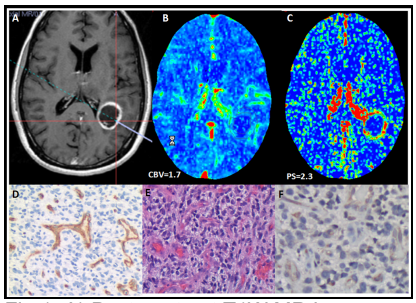

Fig 1. A) Post-contrast T1W MR Image showing biopsy site from a WHO grade IV glioma. B) CBV and C) PS maps with ROI corresponding to the biopsy site showing very high CBV and PS. D) 20x Hematoxylin and eosin, E) CD34 and F) VEGFR-2 stains showing high cellularity (score 3), high MVD (score 3, 263 vessels/20x), MVCP (score 2) and positive VEGFR-2 staining of the endothelial cells in vessel lumen.

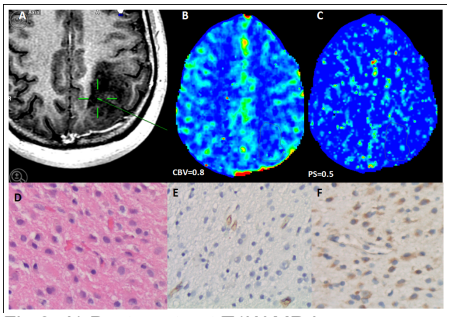

Fig 2. A) Post-contrast T1W MR Image showing biopsy site from non-enhancing WHO grade II glioma. B) CBV and C) PS maps with ROI corresponding to the biopsy site showing low CBV and PS. D) 20x Hematoxylin and eosin, E) CD34 and F) VEGFR-2 stains showing moderate cellularity (score 2), low MVD (score 1, 55 vessels/20x), MVCP (score 0) and negative VEGFR-2 immunoreactivity of the endothelial cells.

Conclusion: Gliomas have complex and heterogeneous tumor vasculature and thus different regions within a tumor may show different grade, aggressiveness and treatment response based on heterogeneity of tumor angiogenesis. Functional imaging like perfusion studies can predict tumor grade and angiogenesis (3). But availability and expertise in interpretation are important limiting factors in their widespread use. Our study shows that MRI contrast enhancement correlates well with various immune-histological markers as well as CT perfusion parameters and can help assess regional heterogeneity of tumor angiogenesis.

References:[1] Ellika SK, Jain R et al. AJNR Am J Neuroradiol 2007:28:1981-87.[2] Law M et al. AJNR Am J Neuroradiol 2004:25:746-55.[3] Jain R, Gutierrez J et al. AJNR Am J Neuroradiol 2010 Nov 11. [Epub ahead of print].