Noninvasive Characterization and Staging of Glioma with MR Elastography - A Pilot Study

Kay Pepin[1], Arvin Arani[2], Nikoo Fattahi[2], Armando Manduca[3], Richard L Ehman[2], John Huston III[2], and Kiaran McGee[2]

[1]*Graduate School, Mayo Clinic, Rochester, Minnesota, United States,* [2]*Radiology, Mayo Clinic, Minnesota, United States,* [3]*Physiology and Biomedical Engineering, Mayo Clinic, Minnesota, United States*

Target Audience: Clinicians and MR scientists interested in brain tumor imaging and MRE applications in cancer.

PURPOSE: Gliomas are the most common form of primary brain tumors. To date no non-invasive technique exists for classification of glioma tumor grade. The current gold standard consists of biopsy followed by pathologic evaluation of the tumor for classification of grade based on the World Health Organization (WHO) grading system [1]. However biopsy can lead to tumor down grading due to the inherent tissue heterogeneity within the tumor. Magnetic resonance elastography (MRE) is a noninvasive imaging technique capable of quantifying tissue stiffness [2]. Previous studies have shown the feasibility of using MRE to characterize both tumors and global brain stiffness with good reproducibility [3-4]. The purpose of this project was to investigate the feasibility of using MRE derived estimates of glioma stiffness as a new, non-invasive biomarker of tumor grade.

METHODS: Ten patients with previously identified gliomas scheduled for resection were recruited for this study. Images were acquired using a 3T MR scanner (GE 14.X Signa, General Electric Healthcare, Waukesha, WI) using a single-shot SE EPI MRE sequence. Shear waves were introduced into the brain using a soft pillow-like vibration source and a pneumatic actuator at a frequency of 60Hz. The following imaging parameters were used: axial slices, TR/TE=3600/62 ms, FOV=24 cm, BW=±250 kHz, 72x72 imaging matrix, 3x ASSET acceleration, 3-mm thick slices, one 40-mT/m 16.7-ms zeroth- and first-order moment nulled motion-encoding gradient on each side of the refocusing RF pulse synchronized to the motion, motion encoding in 6 directions, and 4 phase offsets sampled over one period of the 60-Hz motion. MRE data was processed by calculating the first temporal harmonic of the vector curl of the wave data from the phase images to remove contributions from longitudinal wave propagation and static phase errors [5]. Spatial derivatives were calculated using central differences over a 3x3x3 window. The first-harmonic curl data was then inverted with a 3D direct inversion (DI) algorithm [5]. A tumor region-of-interest (ROI) was manually drawn on each imaging slice containing the tumor, and the mean stiffness was calculated. For comparison, a ROI of equivalent size was drawn on the contralateral side of the brain of the same patient to act as a control.

RESULTS: Figure 1 shows axial magnitude, shear wave and elastogram images of a patient demonstrating the location of the glioma (white dashed ROI). Figure 2 shows the shear stiffness measurements for each patient plotted against the corresponding tumor grade. A single patient was improperly positioned resulting in poor wave motion in the brain and the data was therefore excluded. The average tumor stiffness was 2.2 kPa (range = 1.2-3.0 kPa) while the average stiffness in normal tissue was 3.17 kPa (range = 2.7-3.4 kPa). Five patients had WHO grade II or III tumors that were positive for the IDH1 mutation, and four grade IV (glioblastoma). Tumor shear stiffness values for the glioblastomas were all less than 2.0 kPa and demonstrated an inverse relationship between stiffness and grade (stiffness decreased with increasing grade). In one case, pre-operative radiological assessment and biopsy of the tumor suggested a low grade tumor. However the MRE shear stiffness measurement for this case was 1.7 kPa, consistent with a high grade glioma. Following surgical resection and histopathological assessment, the tumor was reclassified as a grade IV glioblastoma.

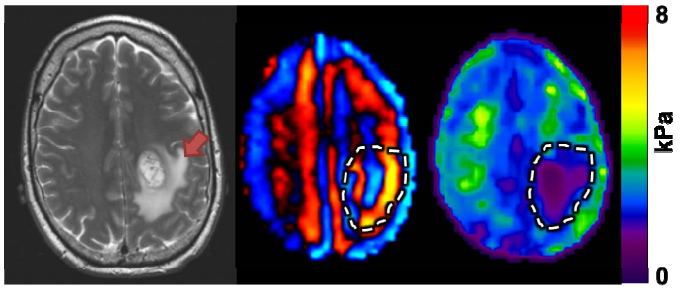

Figure 1: Grade IV – Glioblastoma. (Left) Axial Gadolium-enhanced T2-weighted image. (Middle) MRE wave image. (Right) Elastogram, or stiffness map.

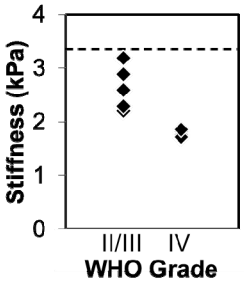

Figure 2: Stiffness vs. tumor grade for n = 5 low grade (II/III) and n = 4 glioblastomas.

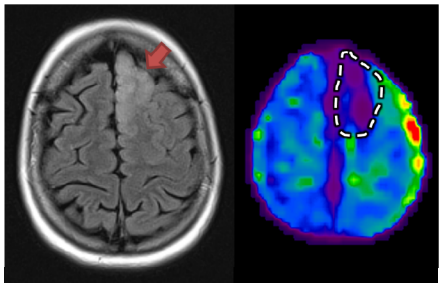

Figure 3: Glioblastoma with a stiffness of 1.7 kPa.

DISCUSSION: In this pilot study, we have shown the feasibility of quantifying shear stiffness in the most common form of malignant brain neoplasm - gliomas. These tumors are softer than the surrounding normal brain tissue and are clearly distinguishable on the elastograms. Higher grade gliomas (glioblastomas) were softer than lower grade gliomas. In this feasibility study, the results suggest that MRE-derived tumor shear stiffness may be correlated with tumor grade in gliomas. Additional volunteers are being identified to confirm this result.

CONCLUSION: Currently, no non-invasive method exists for the grading of gliomas. The potential of MRE as a noninvasive grading metric may improve our ability to accurately diagnose disease state and measure disease progression. The results of this study show the feasibility of using MRE to determine the shear stiffness of gliomas and the potential of using shear stiffness as a biomarker for tumor grade.

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