Perfusion MRI accurately guides the biopsy of tumor-rich tissue during Stereotactic Biopsy

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PURPOSE: We report the accuracy of a novel Perfusion MRI (pMRI) thresholding technique, implemented into a clinical neuro-navigational platform, to guide the stereotactic biopsy and collection of tumor-rich material in recurrent high-grade glioma.

INTRODUCTION: Histologic and molecular tissue analyses currently govern the clinical diagnosis and management of high-grade glioma (HGG). These techniques enable accurate grading, prognostication, and assessment of treatment response, but rely critically on the adequacy of tumoral content within surgical biopsy samples.[1,2] Although this is usually not an issue in treatment-naive tumors, the post-treatment setting presents a much greater challenge to isolating tumor-rich specimens, due to common histologic admixture between HGG recurrence and non-tumoral treatment-related inflammation known as post-treatment radiation effect (PTRE). Surgical biopsy is currently guided by Contrast-enhanced MRI (CE-MRI), which cannot reliably differentiate HGG from PTRE, leading to biopsy sampling errors and lack of sufficient tumoral content for tissue analysis.[3,4] There is a critical need for a reliable imaging method by which to guide the collection of tumor-rich tissue, which is necessary for accurate diagnosis and treatment planning in recurrent HGG. Previous work developed the Perfusion MRI (pMRI) Fractional Tumor Burden (FTB) method, which uses relative cerebral blood volume (relCBV) thresholding to classify enhancing CE-MRI lesion voxels as either HGG or PTRE, thereby enabling localization and quantification of voxels predictive of HGG subcomponents;[5] however, the pMRI-FTB method has not yet been prospectively validated as a method to guide stereotactic biopsy. The purpose of the current work is to report the accuracy of pMRI-FTB maps, implemented into a neuronavigational platform, to guide the prospective collection of tumor-rich material in a cohort of recurrent HGG patients.

METHODS: With Institutional Review Board approval, we recruited recurrent HGG patients undergoing surgical re-resection of new CE-MRI enhancing lesions. Preoperative 3T imaging (General Electric, Waukesha WI), included pMRI (gradient echo EPI; TR/TE/flip angle 2000 ms/20 ms/60°; FOV 24 x 24 cm; matrix 128x128; 5-mm sections; no gap; 0.1 mmol/kg i.v.,preload dose; 0.05mmol/kg Gd-DTPA i.v. injection at 3-5 cc/sec) and pre- and post-contrast stereotactic T1W spoiled gradient-refocused-echo MRI (TI/TR/TE 300/6.8/2.8 ms; matrix 320x224; FOV 26 cm; section thickness 2 mm).7-11 We used Osirix (v. 3.6.1), IB Neuro (v1.1.430), and IB Suite (v1.0.454) (Imaging Biometrics, Milwaukee, WI) to create pMRI-FTB maps, whereby all enhancing CE-MRI lesion voxels were classified as either HGG (relCBV > 1.0) or PTRE (relCBV ≤ 1.0). Prior to surgery, we imported FTB maps into the STEALTH (Medtronic, Denver CO) neuronavigational platform, enabling display of tumor voxels as color overlays on stereotactic CE-MRI data sets. Based on feasibility during stereotactic biopsy, neurosurgeons identified and documented (with screen capture images) the three types of pMRI-FTB targets, based on 'high' (≥ 75%), 'medium' (25-75%), or 'low' (≤ 25%) percentage of HGG voxels at the biopsy site. Figure 1 shows two examples of screen capture images of 'high' and 'low' pMRI-FTB targets. A neuropathologist evaluated all biopsy samples and recorded the relative volume of tumor and PTRE elements as histologic tumor fraction (HTF). We classified all specimens as having 'high' (HTF ≥ 75%), 'medium' (HTF 25-75%), or 'low' (HTF ≤ 25%) tumoral content. We compared tissue analysis with pMRI-FTB target classifications, defined within a 3x3 voxel region of interest (ROI) at corresponding coregistered biopsy locations. We calculated percent agreement, sensitivity, and specificity, with 95% confidence intervals (95%CI) for pMRI-FTB targets to predict tumor content, and correlated the percentage of HGG voxels at the biopsy site with HTF using Pearson.

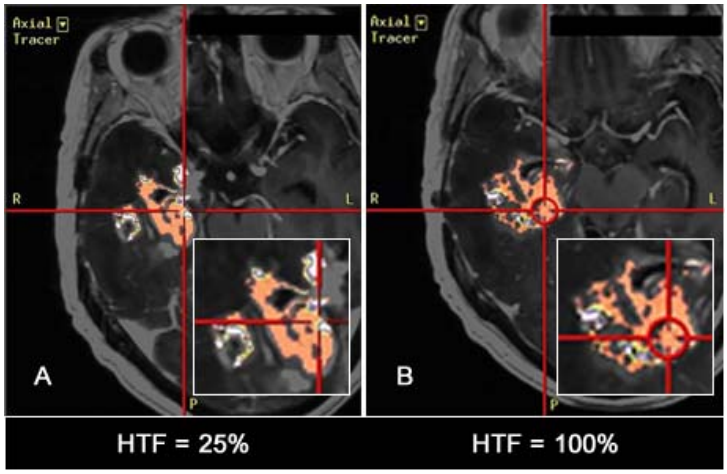

Figure 1: Two representative screen capture images with FTB maps depicting tumor (orange) and PTRE (white) subregions. (LEFT) image shows a 'LOW' FTB target, with corresponding biopsy HTF of 25%. (RIGHT) image shows a 'HIGH' FTB target with biopsy HTF of 100%.

RESULTS: We collected 26 separate biopsies in 12 recurrent HGG patients. There were 10 'High', 5 'Medium', and 11 'Low' pMRI-FTB targets. Of the tissue samples, there were 12 'High', 1 'Medium', and 13 'Low' in tumor content. When considering 'High' vs. 'Medium' vs. 'Low', the overall agreement between FTB and HTF was 22/26 (85%) (95%CI: 65%-96%); with a weighted kappa of 0.84 (95%CI: 0.70-0.99). When using FTB to predict 'High' vs. 'Medium/Low' based on HTF as the gold standard, the sensitivity was 83% (95%CI: 52%-98%), specificity was 100% (95%CI: 77%-100%), positive predictive value was 100% (95%CI: 69%-100%), and negative predictive value was 88% (95%CI: 62%-98%). Pearson correlation between FTB and HTF was 0.90 ($p<0.001$).

DISCUSSION: The pMRI-FTB method provides an accurate method to guide stereotactic biopsy in recurrent HGG patients. By directing the collection of tumor-rich tissue in the setting of histologic heterogeneity, pMRI-FTB-guided biopsy will improve the accuracy of clinical diagnosis and increase the likelihood that tissue samples will contain adequate tumor content for analyses such as molecular profiling.[1-4] Continued work is necessary to understand the factors that cause potential disagreement between FTB and HTF, which may be in part due to misregistration error, brain shift during biopsy, or selection of targets within regions of high histologic heterogeneity.

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