Preliminary Analysis of Contralesional Hemisphere Hippocampal Volume and Cortical Thickness as a Predictor for Survival in a subset of Glioblastoma Multiforme Patients

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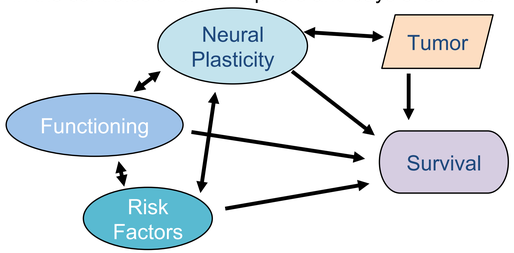
Background

Background: Patients with glioblastoma multiforme (GBM) brain tumors provide a clinical population for studying the brain structural response to a lesion. GBM patients survive a median of 12 months with 3-10% living longer than five years. However, little is known about what brain and tumor factors relate to survival. This study assesses cognitive neural compensation by examining the contralesional hemisphere in GBM patients.

Research Question

In patients with **temporal lobe GBM tumors**, what is the relationship between structural compensation in the contralesional hemisphere and days of survival?



Methods: Patient Demographics

37 left-hemisphere **temporal lobe GBM patients** and 39 right-hemisphere **temporal lobe GBM patients** recruited at Northwestern University, University of Washington, and Columbia University.

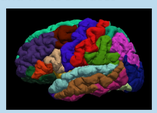
	Left Temporal Lobe Tumors	Right Temporal Lobe Tumors
Number of Patients (m/f)	37 (20/17)	39 (23/16)
Age at diagnosis Mean ± SD [range] (years)	59.1 ± 15.4 [22-84]	62.2 ± 9.3 [47-84]
Overall survival Mean ± SD [range] (days)	814 ± 780 [23-2973]	551 ± 509 [23-2142]
Long survivors Surviving >= 3 years	10	7

Methods: Image and Statistical Analysis

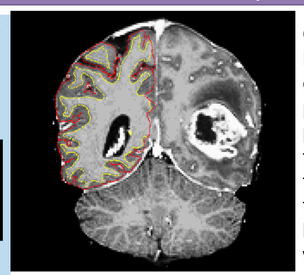
We computed contralesional cortical thickness and subcortical structure volume and shape using **pre-treatment T1 weighted with gadolinium contrast** magnetic resonance imaging (MRI). Patients who lived longer than three years were considered long term survivors. Cortical thickness was determined using Freesurfer. QDEC (Query, Design, Estimate, Contrast) was used to determine differences in average thickness based on days of survival. Hippocampal volume was determined using Freesurfer-Initiated Large-Deformation Diffeomorphic Metric Mapping. These structural measures were categorized as less than or greater than the population median. Days of survival was calculated from date of diagnosis until death. χ^2 and logistic regression analyses were performed in SPSS.

Methods: Contralesional Temporal Lobe Cortical Thickness

- Pial surface = Gray/CSF boundary
- White surface = Gray/White boundary
- Cortical thickness = Distance between pial and white surfaces

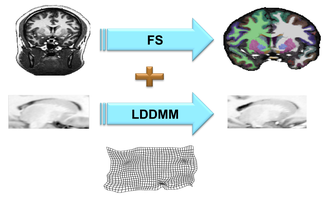


http://freesurfer.net/

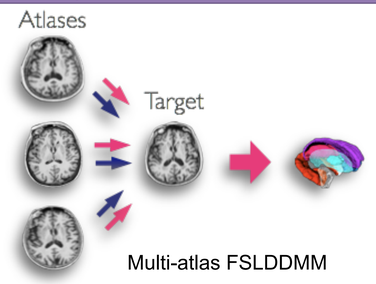


Cortical thickness for the contralesional hemisphere is determined by calculating the distance between the pial and white surfaces. Freesurfer pipelines were modified to only analyze the contralesional hemisphere as the tumor would cause the "fix topology" step to fail. Pial surface = red; white/gray boundary matter = yellow. Tumor is bright white spot enhanced by the gadolinium.

Methods: Hippocampal Volume

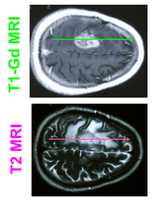


FSLDDMM

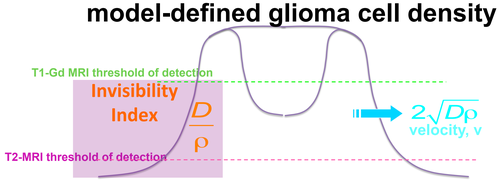


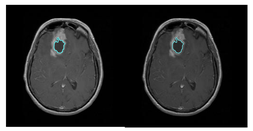
Multi-atlas FSLDDMM

Methods: Tumor Kinetics



Proliferation-Invasion model-defined glioma cell density





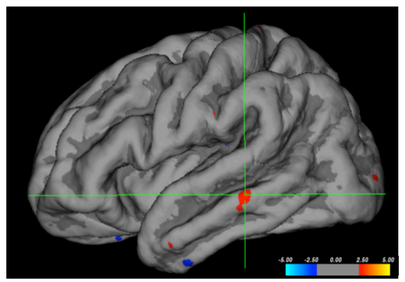
Tumor volume = Σ (area measured on each slice x thickness of each slice)

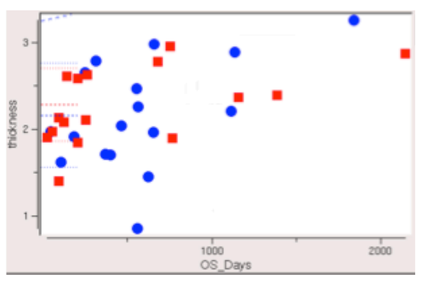
c = tumor cell density
D = motility coefficient
ρ = net proliferation rate
K = cell carrying capacity

$$\delta c/\delta t = \nabla[D(x)\nabla c] + \rho c(1-\frac{c}{K})$$

Rate of change of glioma cell density | Net dispersal of glioma cells | Net proliferation of glioma cells

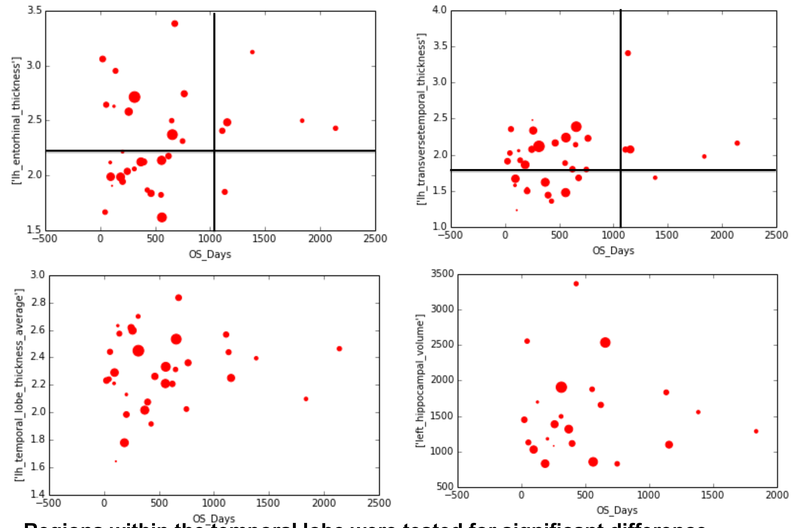
Results: Cortical Thickness in Contralesional Temporal Lobe is Correlated with Days of Survival (Right Temporal Lobe GBM)





Vertex-wide whole brain analysis: Is there a region in the brain where the correlation between thickness and days of survival is significant after controlling for tumor volume and average at diagnosis?
Left figure: In patients with right temporal lobe tumors, there is a cluster in the middle temporal lobe that displays a significant positive correlation between cortical thickness and days of survival. Scale bar: value = -log10(p) . All significant clusters shown have p-values <0.01 .
Right figure: In this cluster in the middle temporal lobe, cortical thickness is positively correlated with days of survival (red square represent female patients; blue circles male)

Results: Long-term survivors have greater contralesional entorhinal and transverse temporal cortical thickness



Regions within the temporal lobe were tested for significant difference between long-term survivors and short-term survivors
Scatterplots of cortical thickness of regions within the temporal lobe and hippocampal volume of right temporal lobe tumor patients. Filled circles are scaled to tumor size. Vertical line separates short-term and long-term survivors (1095 days). Horizontal line indicates ROI-specific median thickness. Top left: entorhinal thickness; Top right: transverse temporal thickness; Bottom left: temporal lobe thickness average; Bottom right: hippocampal volume

Limitations

- Challenges of analyzing images with tumors and gadolinium contrast
- Variability of clinical scanners
- Small number of long-term survivors
- Tumor is not localized to one lobe
- Tumor may infiltrate macroscopically normal tissue
- Lead-time bias

Conclusions

- In long-term survivors with GBM, contralesional cortex compensates for tumor effects in right temporal lobe tumors. Work is ongoing to further understand the complex relationship between contralesional brain structural measures and survival, and their relationship with tumor characteristics.

Future Directions

- Future studies will assess tumors as well as structural compensation in other areas of the brain.
- Other tumor factors (diffusion/proliferation, velocity) will be considered.
- Longitudinal clinical imaging for each patient will be analyzed for changes in thickness and volume.
- Structural compensation will be correlated with performance on cognitive and neuropsychology tests.
- Resting-state fMRI will also be analyzed to determine disruptions in networks.

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