Neuroimaging Predictors of Survival, Pathology and Molecular Profiles in TCGA Glioblastomas

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Emory University¹, Thomas Jefferson University²
In Silico research using public data

Integrated Analysis

Histology

Radiology

Molecular

Clinical/pathology

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
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<tbody>
<tr>
<td>1</td>
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<td>Gender</td>
<td>Survival</td>
<td>Disease</td>
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<td>OLIGODENDROI</td>
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<td>GBM</td>
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<td>GBM</td>
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<tr>
<td>8</td>
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<td>ASTROCYTOMA</td>
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Glioblastoma Multiforme (GBM)

- Most common form of primary brain tumor
- Grade IV Astrocytoma
- 14 month median survival
- First tumor in NCI’s *The Cancer Genome Atlas* (TCGA)
  - 500 patients from participating hospitals
  - mRNA transcription, CGH, sequence, DNA methylation
  - Neuroimaging
  - Whole slide pathology images
General Methodology Employed in our In Silico Center

- Goal is to develop human and/or machine based assessments of image features
- A standardized imaging imaging feature (dubbed VASARI) was developed
- Feature set consists of 30 features that describe the size, location and appearance of the MRI image set
- MRI image provides a global view of the tumor
  - Small tumor adjacent to motor area (e.g. eloquent cortex) has vastly different outcome than a small tumor in frontal lobe
Examples of the feature set

f7 – Proportion Necrosis

(2) None

(3) < 5%

(4) 6-33%

(5) 34-67%

Visually, when scanning through the entire tumor volume, what proportion of the tumor is estimated to represent necrosis. Necrosis is defined as a region within the tumor that does not enhance or shows markedly diminished enhancement, is high on T2W and proton density images, is low on T1W images, and has an irregular border. (Assuming that the entire abnormality may be comprised of: (1) an enhancing component, (2) a non-enhancing component, (3) a necrotic component and (4) a edema component.)
Proportion Enhancing Tumor

1-5%  68-95%
Capturing structured annotations and markups
AIM Data Service
Systematic assessment of tumor imaging properties

Data was obtained from the Cancer Imaging Archive http://cancerimagingarchive.net

• Current data set is from 72 patients
• Data is now available from ~125 GBM patients that were part of the TCGA data collection
• Each case was reviewed and scored independently by 3 neuroradiologists
• Consensus measures were obtained and used for this analysis
# Imaging Predictors of Survival

<table>
<thead>
<tr>
<th>Neuroimaging Feature</th>
<th>p value</th>
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<tr>
<td>Edema</td>
<td>0.48</td>
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<tr>
<td>Contrast Enhancing Tumor</td>
<td><strong>0.004</strong></td>
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<tr>
<td>Necrosis</td>
<td>0.37</td>
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<tr>
<td>Non-contrast Enhancing Tumor</td>
<td>0.83</td>
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<table>
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<tr>
<th>Variable</th>
<th>Hazard Ratio (95% Confidence Limits)</th>
<th>p value</th>
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<tr>
<td>Karn Score</td>
<td>0.955 (0.933, 0.978)</td>
<td><strong>0.0001</strong></td>
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<tr>
<td>Contrast Enhancing Tumor</td>
<td></td>
<td></td>
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<tr>
<td>06-33% vs 0-5%</td>
<td>0.528 (0.196, 1.425)</td>
<td><strong>0.025</strong></td>
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<tr>
<td>34-95% vs 0-5%</td>
<td>1.446 (0.485, 4.312)</td>
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Percent of Contrast Enhancement was significantly associated with shorter survival.
Tumor Subtypes and Imaging Features

Do tumor genotypes “look” different?

- The Mesenchymal subtype were noted to have significantly lower rates of non-contrast enhancement compared to other tumor subtypes (p<0.01).
MR Imaging Results

- The Proneural subtype was associated with a low degree of contrast enhancement (0-5%) (p<0.01).
Image based-features and mutation status

- *EGFR* mutant GBMs (11/49) were *larger* based on the T2-weighted FLAIR images than wild type *EGFR* GBMs (p<0.05).
- *TP53* mutant GBMs (9/49 patients) were *smaller* than those that were wild type (p<0.006)
Conclusions

• Imaging based features can provide important prognostic information, even after accounting for other clinical variables

• Current qualitative work suggests genotypes may be associated with imaging phenotypes

Future Work:

– Increase sample size (in progress)
– Move from ordinal assessments (0-5%, 6-33%, 34-67%) to continuous based assessments of tumor compartments (e.g. volumetrics)
– More sophisticated feature extraction to include texture/size/location and voxel-based assessments
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Northwestern University: Pat Mongkolwat

The TCGA Glioma Research Group

If you have imaging data for TCGA contributed cases available and would like to contribute, please contact kirbyju@mail.nih.gov (Justin Kirby) or John Freymann (john freymannj@mail.nih.gov) as we can help with deidentification and sharing

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