Radiomic and genomic approaches to survival stratification in adult-type diffuse glioma

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Adult-type diffuse glioma

- Most common primary adult malignant brain tumor
- Generally regarded as incurable
- Survival ranges from 12-15 months (glioblastoma) to nearly 10 years (oligodendroglioma)
What makes adult-type diffuse glioma so difficult to treat?

Tumor molecular heterogeneity

- Even “effective” treatments do not work on all cells
- Treatment resistant cells drive tumor recurrences

Drug delivery

- Drugs are ineffective if they cannot reach tumor cells

Clinical trial failure

Unknown biomarkers can lead to:
- Phase 2 success for ineffective therapies
- Phase 3 failure for beneficial therapies
Survival stratification helps balance clinical trials
Types of adult-type diffuse glioma

- Glioblastoma, IDH-wildtype
  - 1p/19q-codeletion: Yes → Glioblastoma, IDH-wildtype
  - 1p/19q-codeletion: No → Oligodendroglioma, IDH-mutant & 1p/19q-codeleted
- Astrocytoma, IDH-mutant
  - 1p/19q-codeletion: Yes → Astrocytoma, IDH-mutant
  - 1p/19q-codeletion: No → Oligodendroglioma, IDH-mutant & 1p/19q-codeleted

Survival:
- Glioblastoma, IDH-wildtype (1.2 years)
- Astrocytoma, IDH-mutant (6.7 years)
- Oligodendroglioma, IDH-mutant & 1p/19q-codeleted (11.2 years)
PhD trajectory

1. Tumor segmentation tool

2. Classify tumors by type (IDH, 1p/19q)
   - From imaging data
     - Nuechterlein et al., ICPR, 2021
   - From old genomic data
     - Nuechterlein et al., AANP, 2021
     - Nuechterlein et al., Acta Neuro Com, 2023

3. Find high-risk IDH-wildtype glioblastoma patients
   - From imaging data
     - Nuechterlein et al., SNO, 2020
   - From genomic data
     - Nuechterlein et al., Neuro-Onc Adv, 2021
     - Nuechterlein et al., In Preparation

4. Find low-risker patients in IDH-mutant tumors
   - Find gene *(HOXD12)* in oligodendroglioma
     - Nuechterlein et al., SNO, 2022
     - Nuechterlein et al., In Preparation
   - Extend findings to all IDH-mutant tumors
     - Postdoc work
Radiogenomic modeling predicts survival-associated prognostic groups in glioblastoma

Neuro-oncology advances, 2021
Problem motivation

Background

- Binary classification ≈ short-term survivors vs. long-term survivors
- Patients with second resections survive longer
- Patients with second resections are associated with a copy number signature

Motivation

Acquisition of MRI data is non-invasive and routinely collected

Upfront clinical trials are needed for highest-risk patients

Question

Is MRI data predictive of GBM prognostic copy number signatures?

Approach

Radiomic analysis

- Segment tumor
- Extract radiomic features
- Feature selection
- Predict survival class

Magnetic resonance imaging (MRI)

Magnetic Resonance Imaging (MRI)

255 x 255 x 155 x 4
(> 40 M voxels)

Standard-of-care, fast, non-invasive, repeatable
Method

Radiomic Pipeline

Radiomic Feature
Feature selection

1. MRI
   - Feature extraction

2. LASSO
   - Random 80% of training set
   - Bag of features
   - Select frequent features
   - Generate features from selected components
   - PCA

3. Feature Selection

4. MRI sequence
5. tumor region
6. transformation
7. texture feature
Results: comparisons to other feature selection methods
Where should we look, and what should we look for?
Take aways

- Novel feature selection method tailored for radiomic features
- Promising results, but not ready for clinical adaptation
- MRI has significant limitations
- Genomic approaches
  - Surgical resection is always attempted
  - Unavoidable noise
  - Imaging features are too far “downstream”
  - Biological validation (in vitro, in vivo)
  - Complementary data modalities
  - Superior tumor characterization
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