Leveraging Unlabeled Data for Glioma Molecular Subtype and Survival Prediction

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Overview

• Setting
  • Genomic biomarkers define brain cancer subtypes which stratify patient survival
  • However, obtaining biomarker status requires invasive surgery
  • Imaging is a non-invasive method that has been used to infer biomarker status
  • Unlabeled imaging data (MRI) is relatively abundant and underutilized

• Questions
  • Can we leverage unlabeled imaging data to better predict these biomarkers (subtypes)?
  • Can we incorporate genomic data, when available, in these models?
  • Subtypes are surrogates for survival—can we predict survival directly?

• Datasets
  • 2018 Brain Tumor Segmentation (BraTS) Challenge: magnetic resonance imaging (MRI)
  • The Cancer Genome Atlas (TCGA): somatic copy number alteration (SCNA)
Glioma

- 80% of primary malignant brain tumors in adults
- Biomarkers: IDH1/2 mutation, 1p/19q co-deletion

**WHO 2016 molecular-based glioma classification**

**Magnetic resonance imaging (MRI)**

**Somatic copy number alteration (SCNA)**

*Menze et al., IEEE transactions on medical imaging 2014, Bakas et al., Scientific Data 2017, Bakas et al., arXiv 2018*
MRI inputs

- All Modalities
  - (4 x 144 x 144 x 144)

- All Modalities (cropped)
  - (4 x 64 x 64 x 64)

- Single Modalities (cropped)
  - (64 x 64 x 64)

- T1ce-T1 Subtraction Map
  - (64 x 64 x 64)
MTL network, glioma subtype classification

We use tumor segmentation as an auxiliary learning task.

(A) We assign weak segmentation labels to MRI samples without segmentation labels.

(B) We train our MTL model to learn glioma subtype jointly with tumor segmentation. For samples without subtype labels, we only take the segmentation loss.
Subtype prediction results

- MTL offers biggest boost to 4-channel, whole brain input
- 1p/19q co-deletion prediction is significantly improved
- T1ce-based modalities are the best predictors of IDH1/2 mutations; these models focus on tumor enhancement

<table>
<thead>
<tr>
<th>Input Modalities</th>
<th>IDH1/2 Mutation (AUC)</th>
<th>1p/19q Co-deletion (AUC)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CNN</td>
<td>MTL (MR)</td>
</tr>
<tr>
<td>All (Whole Brain)</td>
<td>0.669</td>
<td>0.846</td>
</tr>
<tr>
<td>All (Cropped)</td>
<td>0.872</td>
<td>0.894</td>
</tr>
<tr>
<td>T1ce (Cropped)</td>
<td>0.893</td>
<td>0.884</td>
</tr>
<tr>
<td>FLAIR (Cropped)</td>
<td><strong>0.778</strong></td>
<td>0.690</td>
</tr>
<tr>
<td>T1 (Cropped)</td>
<td>0.731</td>
<td><strong>0.738</strong></td>
</tr>
<tr>
<td>T2 (Cropped)</td>
<td><strong>0.778</strong></td>
<td>0.732</td>
</tr>
<tr>
<td>T1ce-T1 (Cropped)</td>
<td><strong>0.895</strong></td>
<td>0.861</td>
</tr>
</tbody>
</table>

4-channel, whole brain input

T1ce modality

Integrated gradients visualization of a IDH1/2 wildtype prediction

Ring enhancement
MTL network, survival prediction

1. We pretrain our MTL models on the IDH1/2 mutation classification task (both using only MRI and MRI + SCNA).

2. We use the last-layer embeddings of the classification branch in these MTL models to train linear Cox proportional-hazards models.

Note: We do not learn survival concurrently with subtype and tumor segmentation, because the CPH loss function requires large batch sizes that far exceed GPU memory given the size of 3D MRI data.
Survival prediction results

<table>
<thead>
<tr>
<th>Input Modalities</th>
<th>All Subtypes (C-index)</th>
<th>1p/19q Co-deleted (C-index)</th>
<th>IDH1/2 Mutant, 1p/19q Intact (C-index)</th>
<th>IDH1/2 Wildtype (C-index)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All (Whole Brain)</td>
<td>0.587</td>
<td>0.723</td>
<td>0.714</td>
<td>1.000</td>
</tr>
<tr>
<td>All (Cropped)</td>
<td>0.697</td>
<td>0.732</td>
<td>0.607</td>
<td>0.964</td>
</tr>
<tr>
<td>T1c (Cropped)</td>
<td>0.719</td>
<td>0.735</td>
<td>0.821</td>
<td>0.786</td>
</tr>
<tr>
<td>FLAIR (Cropped)</td>
<td>0.565</td>
<td>0.731</td>
<td>0.607</td>
<td>0.964</td>
</tr>
<tr>
<td>T1 (Cropped)</td>
<td>0.645</td>
<td>0.728</td>
<td>0.643</td>
<td>0.893</td>
</tr>
<tr>
<td>T2 (Cropped)</td>
<td>0.690</td>
<td>0.718</td>
<td>0.679</td>
<td>0.500</td>
</tr>
<tr>
<td>T1c-T1 (Cropped)</td>
<td>0.707</td>
<td>0.723</td>
<td>0.821</td>
<td>0.857</td>
</tr>
<tr>
<td>SCNA (PCA = 5)</td>
<td>0.724</td>
<td></td>
<td>0.929</td>
<td></td>
</tr>
</tbody>
</table>

- C-index measures how well model orders survival
- MRI + SCNA is better than MRI or SCNA on their own in most categories
- Models predict survival best in patients with 1p/19q co-deletions
- Survival prediction is difficult for patients with IDH1/2 wildtype tumors
Conclusion

• Unlabeled MRI data can be used to improve glioma subtype predictions, especially those defined by 1p/19q co-deletions
• MRI and SCNA mostly improve survival prediction beyond MRI or SCNA on their own
• MTL models associate tumor enhancement with IDH1/2 wildtype tumors
Acknowledgments

The University of Washington
- Linda Shapiro
- Beibin Li
- Mehmet Saygin Seyfioglu
- Sachin Mehta

Fred Hutch
- Eric Holland
- Sonali Arora

University of Washington Medical Center
- PJ Cimino

This material is based upon work supported by the National Science Foundation under Grant DGE-1762114.