Fusion Radiomics Features from Conventional MRI Predict MGMT Promoter Methylation Status in Lower Grade Gliomas
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Introduction-Glioma

- **CGCG:**
  - WHO Grade II glioma, mOS 78.1m
  - WHO Grade III glioma, mOS 37.6m
  - WHO Grade IV glioma, mOS 14.4m

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**Fig. 2.** Treatment approach for gliomas based on clinical and molecular information. Figure revised from refs [58], [66], [79].
Introduction-MGMT

- MGMT removes the guanine-alkyl group induced by alkylating agent—DNA repair
- MGMT promoter methylation status predict the prognosis of glioma patients

Prognostic value of MGMT in WHO Grade II glioma patients

Prognostic value of MGMT in WHO Grade III glioma patients

Introduction-Radiomics

• Radiomics is defined as the quantitative mapping
• Extraction, analysis and modelling of many medical image features in relation to prediction targets, such as clinical end points and genomic features.

Method

- Patients: Primary LGG patients
- MGMT promoter methylation testing: Pyrosequencing
- MRI data acquisition: 3D-T1-CE image, T2-weighted image
- Image segmentation: Manual
- Post-processing: Resampled to original resolution; brightness normalization
- Feature extraction: Pyradiomics
- Feature selection and model construction: Lasso
- Model validation: TCGA LGG dataset
Method-Co-registration

3D T1

Affine matrix

-0.0183 0.0030 0.9998 42.7896
-0.9998 -0.0036 -0.0183 239.5965
0.0036 -1.0000 0.0031 167.8447
0.0000 0.0000 0.0000 1.0000

Mask

2D T2
# Method-Radiomics Features

<table>
<thead>
<tr>
<th>Feature Class</th>
<th>Name</th>
<th>Count</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shape</td>
<td></td>
<td>13</td>
<td>Represents the spatial characters of the tumor's shape</td>
</tr>
<tr>
<td>First Order</td>
<td></td>
<td>18</td>
<td>Voxel alone based statistical features</td>
</tr>
<tr>
<td>Texture</td>
<td>GLCM</td>
<td>23</td>
<td>Gray-Level Co-occurrence Matrix, represents the relationship of</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>adjacent voxels</td>
</tr>
<tr>
<td></td>
<td>GLRLM</td>
<td>16</td>
<td>Gray Level Run Length Matrix, shows the consecutive voxels with</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>same gray level values</td>
</tr>
<tr>
<td></td>
<td>GLSZM</td>
<td>16</td>
<td>Gray Level Size Zone Matrix, quantifies gray level zones</td>
</tr>
<tr>
<td></td>
<td>GLDM</td>
<td>14</td>
<td>Gray Level Dependence Matrix, exhibits the gray level dependencies</td>
</tr>
<tr>
<td></td>
<td>NTGDM</td>
<td>5</td>
<td>Neighbouring Gray Tone Difference Matrix, quantifies the difference</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>between a gray value and the average gray value of its neighbours</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>within a defined distance</td>
</tr>
<tr>
<td>Wavelet</td>
<td></td>
<td>8x92</td>
<td>Three dimensional frequency filtering are applied to X, Y and Z with</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>wavelet (coif1), each dimensions were separated into 2 part: the</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>high frequency and the low frequency. The six groups of features</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>described above are calculated in each of the eight new spaces.</td>
</tr>
</tbody>
</table>
Result

- Patient characteristics: $p=0.222-0.678$
- Feature selection: 15 feature selected
- Five radiomics models
  - 3D-CE-T1-weighted single radiomics model
  - T2-weighted single radiomics model
  - Fusion radiomics model
  - Linear combination radiomics model
  - Clinical integrated model
- Prediction model performance (fusion model)
  - Training cohort: se 0.883  sp 0.926  auc 0.970  acc 0.839
  - Validation cohort: se 0.821  sp 0.857  auc 0.898  acc 0.886
## Result-Patients

208 patients have pathologically confirmed WHO grade II and III glioma from 2010.8 to 2018.3

199 patients with WHO grade II and III glioma are included in TCIA dataset

107 patients have pre-operative 3D-T1-CE and T2-weighted MRI sequence with good quality

94 patients have single lesion and no therapy or biopsy or CNS tumor history prior to MRI scan

87 patients have adequate frozen tumor tissues and acquired MGMT methylation status

35 primary glioma patients with pre-operative 3D-T1-CE and T2-weighted MRI sequence and MGMT methylation status are randomly selected

Included as training dataset

Included as validation dataset

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>PUMCH</th>
<th>TCGA-LGG</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>43 49.43%</td>
<td>19 54.29%</td>
<td>0.631</td>
</tr>
<tr>
<td>Female</td>
<td>44 50.57%</td>
<td>16 45.71%</td>
<td></td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>45.4</td>
<td>44.2</td>
<td>0.678</td>
</tr>
<tr>
<td><strong>MGMT Promoter</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methylated</td>
<td>60 68.97%</td>
<td>28 80.00%</td>
<td>0.222</td>
</tr>
<tr>
<td>Unmethylated</td>
<td>27 31.03%</td>
<td>7 20.00%</td>
<td></td>
</tr>
<tr>
<td><strong>WHO Grade</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>48 55.17%</td>
<td>22 62.86%</td>
<td>0.442</td>
</tr>
<tr>
<td>III</td>
<td>39 44.83%</td>
<td>13 37.14%</td>
<td></td>
</tr>
</tbody>
</table>
Result-Model Construction

• Five radiomics models were built.
• The fusion radiomics model have the best performance.

<table>
<thead>
<tr>
<th>Models</th>
<th>PUMCH</th>
<th>TCGA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ACC</td>
<td>AUC</td>
</tr>
<tr>
<td>3D-T1-CE Single Model</td>
<td>0.839</td>
<td>0.873</td>
</tr>
<tr>
<td>T2-weighted Single Model</td>
<td>0.805</td>
<td>0.879</td>
</tr>
<tr>
<td>Linear Combined Model</td>
<td>0.805</td>
<td>0.881</td>
</tr>
<tr>
<td>Fusion Radiomics Model</td>
<td><strong>0.839</strong></td>
<td><strong>0.970</strong></td>
</tr>
<tr>
<td>Clinical Integrated Model</td>
<td>0.839</td>
<td>0.969</td>
</tr>
</tbody>
</table>
Result-ROC Curve

PUMCH

TCIA
Result-Bar Chart (Fusion Model)

Prediction on PUMCH LGG

Prediction on TCGA LGG
Conclusion

• Conventional MRI radiomics models are reliable for predicting the MGMT promoter methylation status in LGG patients.

• The fusion of radiomics features from different imaging series may increase the prediction performance.

• Prediction model performance (fusion model)

• Validated in multi-center data with different equipment under various conditions

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