Glioma Imaging Predicts Underlying Genetic Mutations: A Multi-Center Study

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Gliomas

- Gliomas are the most common malignant primary brain tumor in adults impacting ~5 per 100,000 individuals[1]
- Per WHO classification, genomic characterization is necessary for diagnosis and subtyping[2]
- Genetic markers are critical for precision oncology treatment plans and prognostication[3]
- Tumor tissue for this purpose is often obtained via biopsy

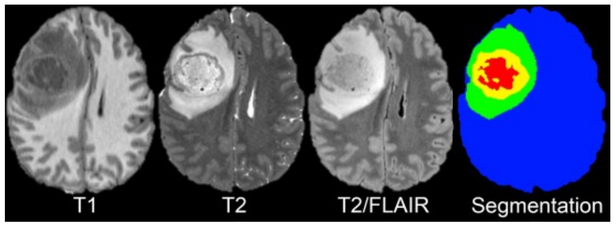
Biopsies Are Not Simple

- Morbidity: estimated at 3 - 13% e.g. neurological impairment, symptomatic hemorrhage, seizures[4]
- Mortality: estimated at 0.7 - 4%[4]
- Financial cost: estimated at ~$40,000 and ~$1,100 in out-of-pocket expenses[5]
- Turnaround times for certain genetic biomarkers can be 2+ weeks and lead to delays in optimal treatment

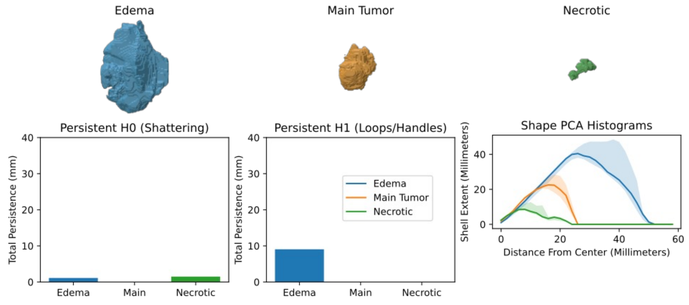
Imaging as a Biopsy

- Liver Imaging Reporting and Data System (LI-RADS): Image-based grading for liver lesions to advance therapy without biopsy[6]
- Initial attempts for CNS tumors have mixed performance[7]
- **Goal: Leverage intrinsic phenotype-genotype relationship to predict biomarkers from pre-resection MRI of gliomas**

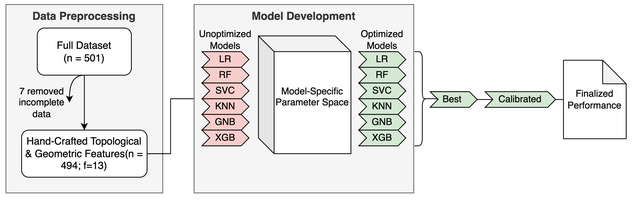
Methods



- Four institutions: Duke, UCSF, Penn, NIH
- 3076 MRIs from unique adult patients with gliomas
- Custom deep learning algorithm to separate enhancing tumor, non-enhancing/necrotic tumor, and surrounding FLAIR abnormality
- Tumors were evaluated for IDH mutations, 1p/19q codeletion and MGMT methylation



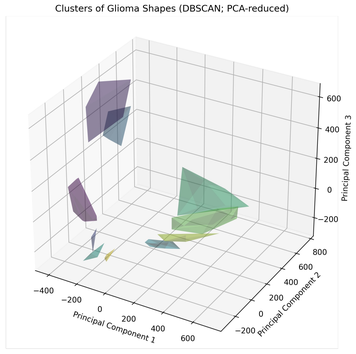
- Segmentation masks were processed to create topological and geometric features describing the tumor's 3D shape
- For example: shape histograms, D2 histograms, shape PCA histograms, connected components, TDA



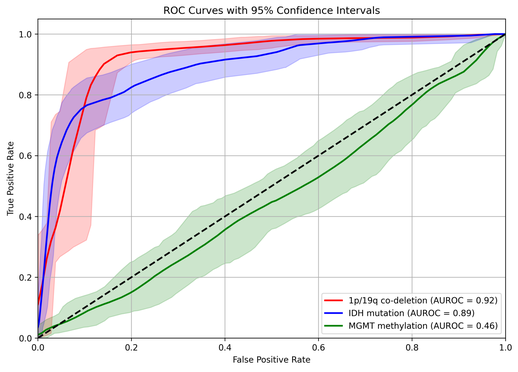
- These features, without other clinical variables, were used in a custom machine learning pipeline to predict the presence of IDH mutations, 1p/19q codeletion, and MGMT methylation.

Results

- Natural sub-groupings emerge from the distribution of tumor shape:



- On the test-subset, using only topological and geometric features:



	IDH mutation	1p/19q codeletion	MGMT methylation
Accuracy	87.2% (83.6%-90.9%)	88.2% (83.6%-92.9%)	42.8% (25.7%-60.0%)
Specificity	90.3% (83.9%-96.6%)	94.5% (84.3%-100%)	76.0% (43.1%-100%)
Sensitivity	75.7% (68.0%-83.3%)	86.6% (79.6%-93.6%)	30.5% (0.0%-66.0%)

Conclusions

1. There appears to be a strong MRI phenotype-genotype relationship for adult gliomas
2. The shape of a tumor is a useful and understudied feature
3. Non-invasive imaging modalities hold promise as potential adjuncts or replacements to tissue biopsies for initial brain tumor management

Future

- Increased sample size with non-glioma controls and increased performance is needed before prospective assessment
- Expand to non-glioma tumors (e.g. meningiomas)
- Predicting alternative outcomes using tumor shape, e.g. risk of recurrence, prognosis

Acknowledgments

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