MRI Radiomic Analysis for Survival Prediction in Diffuse Midline Glioma

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Background

- Diffuse midline glioma (DMG), formerly diffuse intrinsic pontine glioma (DIPG), is a pediatric brain tumor that presents as an expansive lesion in the pons.
- Presenting symptoms include cranial nerve palsies, hemiparesis, gait disturbances, and headaches.
- Given the infiltrative nature, radiation therapy is the mainstay of treatment, with little role for surgery.
- Presently, magnetic resonance imaging (MRI) is the mainstay of disease diagnosis and surveillance.
- Currently, prognosis is dismal; median survival from time of diagnosis is approximately one year.

Objective

- To identify prognostic imaging based radiomic biomarkers of DMG and compare their performance to standard clinical variables at presentation.

Methods

- We retrospectively analyzed 104 treatment naïve children with DMG from five centers including Stanford, Seattle, Indiana, Dayton, and London, UK (Table 1).
- Quality control of all MRI and clinical data was performed to confirm image quality (Figure 1) and treatment naïve status.
- Tumor volumes were manually segmented in 3D using ITK-Snap on the diagnostic contrast-enhanced T1-weighted post-contrast (T1) and T2-weighted (T2) MR sequences (Figure 2).
- High-dimensional feature extraction was performed using PyRadiomics[1] on the original, wavelet, and Laplacian of Gaussian (LoG) filtered images.
- 900 features defined by Imaging Biomarker Standardization Initiative (IBSI)[2] were extracted including first-order statistics, size, shape, and texture-based features.
- Overall survival (OS) was our outcome of interest.
- 10-fold cross-validation of least absolute shrinkage and selection operator (LASSO) Cox regression was used to select the top radiomic features to predict OS (*glmnet* package in R version 3.4.3 (Vienna, Austria))[3].

Methods

- From these identified features, we built and compared univariable and multivariable Cox proportional hazard models and the performance of each Cox model was assessed using the concordance (C) index.
- We compared model performance using clinical variables only (age at diagnosis and sex), radiomics only, and radiomics plus clinical variables.

Results

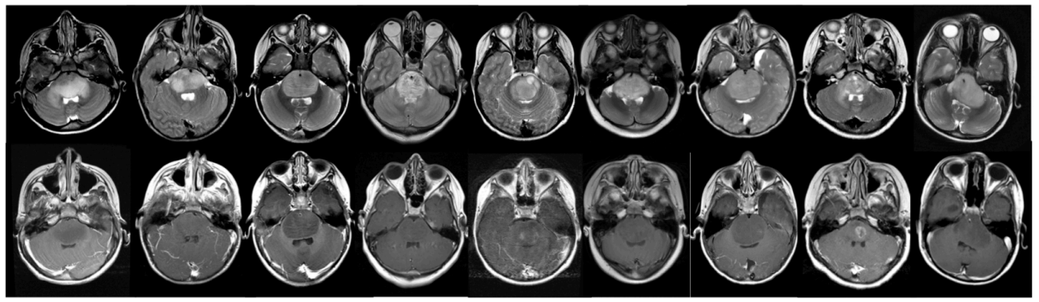

Figure 1: Examples of the various imaging features of nine pontine-origin DMGs at diagnosis on contrast-enhanced T1-weighted MRI

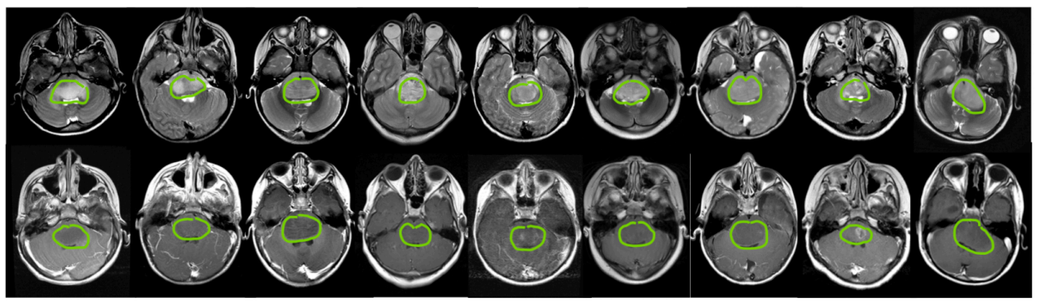

Figure 2: Example of slice-by-slice manual annotation of the nine tumors from Figure 1 using ITK-SNAP.

Table 1: Patient demographics (n=104)

Hospital	
Stanford	41 (39%)
Seattle	35 (34 %)
Indiana	18 (17%)
Dayton	3 (3%)
London, UK	7 (7%)
Sex	
Male	46 (44%)
Female	58 (56%)
Age (median [range])	6.5 years [1.5-19]
Median OS [range]	11 months [1-51]

Table 2: Nine radiomic features selected by 10-fold cross-validation of LASSO Cox regression

Image	Filter	Feature Type	Feature Name
T1	Wavelet (LHH)	GLCM	Cluster Shade
T1	Wavelet (HHL)	GLCM	Maximal Correlation Coefficient
T2	LoG Sigma (5mm)	GLSZM	Grey Level Non-Uniformity
T2	Original	First-Order	Skewness
T2	Wavelet (HHH)	First-Order	Mean
T2	Wavelet (LHL)	First-Order	Mean
T2	Wavelet (HHL)	First-Order	Mean
T2	Wavelet (LLL)	First-Order	Skewness
T2	Wavelet (LLL)	GLSZM	Zone Entropy

*Grey-level co-occurrence matrix (GLCM), grey-level size zone matrix (GLSZM)

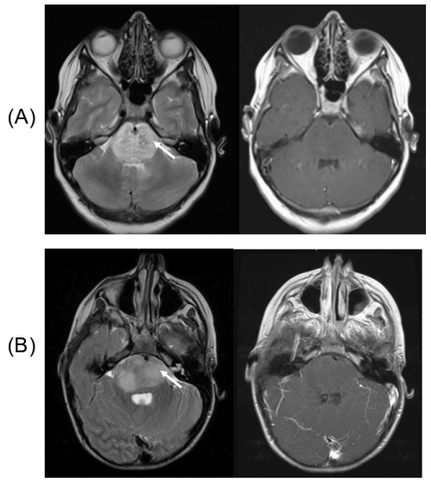

Figure 3: A visual example of MRI radiomics. Example axial T2 (left) and T1 (right) MRI for two children. (A) A patient who survived 20 months demonstrates a more heterogeneous and hyperintense tumor (white arrow) on T2 compared to (B), a patient who survived only 4 months. The T1 post-contrast MRI demonstrates limited qualitative characteristics, consistent with only 2 of 9 features selected from T1 images.

Results

- The radiomics based model significantly outperformed traditional clinical features used for prognosis (C: 0.68 vs. 0.59, p<0.001).
- Adding clinical features to the radiomics model did not significantly improve performance (C: 0.70 vs. 0.68, p=0.06).

Discussion

- This preliminary study has demonstrated the potential of MRI based radiomics and machine learning to predict OS in children with DMG.
- Limitations of this study include manual segmentations of the tumor and a relatively small dataset from only five centers.
- This study also lacks external validation of the results; however refinement and validation of the model is ongoing with a dataset consisting of images from 11 centers.

Conclusions

- There is a potential role for MRI-based radiomics and machine learning for risk stratification of children diagnosed with pontine-origin DMGs.
- Given the poor prognosis and overall survival in these patients, this radiomics model may assist clinicians in deciding when and how to optimally treat each patient.

References

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