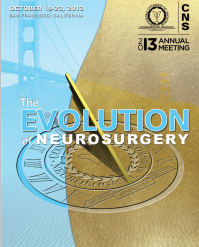


Creating a Radiogenomics Map of Multi-omics and Quantitative Image Features in Glioblastoma Multiforme

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Introduction

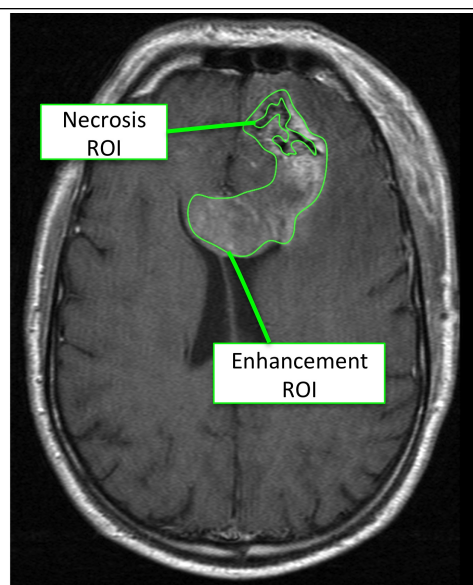
Glioblastoma (GBM) is the most frequent primary malignant brain tumor in adults. Despite decades of research and multimodality treatment with microsurgical resection followed by chemotherapy and radiation therapy, mean survival time is only 12–14 months. The development of a radiogenomic map – a link between image features and underlying molecular data – holds the potential to address the clinical need for surrogate biomarkers that accurately predict underlying tumor biology and therapy response in GBM.

Methods

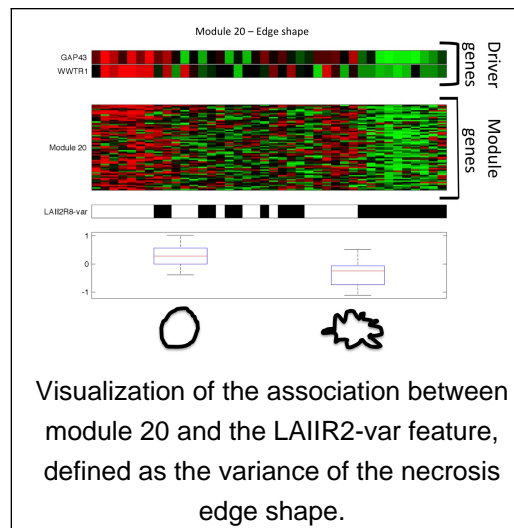
We obtained multi-omics data from 251 patients and MR image data from a subset of 55 patients in the Cancer Genome Atlas (TCGA) and The Cancer Imaging Archive (TCIA) GBM databases. A board certified neuroradiologist traced 2D regions of interest (ROI) around necrotic and enhanced parts of the largest lesion in a selected slice from a T1 post-contrast MR, and around the region of hyperintensity obtained from the enhancement on the matched T2 FLAIR slice. These ROIs were used to compute quantitative image features from their shapes and pixel values. We used a module network algorithm called AMARETTO to integrate copy number, DNA methylation and gene expression data into 100 co-expressed gene modules. We established a radiogenomics map by correlating these modules with the quantitative image features, and used significant module-image feature correlation for survival analysis using Cox proportional hazards modeling.

Results

The majority (63%) of the quantitative image features was robust to intra-reader variation and had meaningful correlations with survival outcomes, VASARI image features, and molecular GBM subtypes. For example, the irregularity of the enhanced tumor edge had the strongest correlation with overall survival and all but one VASARI feature was correlated with at least one quantitative image feature. The radiogenomic map showed intriguing correlations between image features and molecular pathways. For example Module 20's expression signature is correlated to necrosis edge shape. This module is enriched with genes related to neuronal development. Overall, this technique allowed annotation of 82% of quantitative image features with biological pathways.

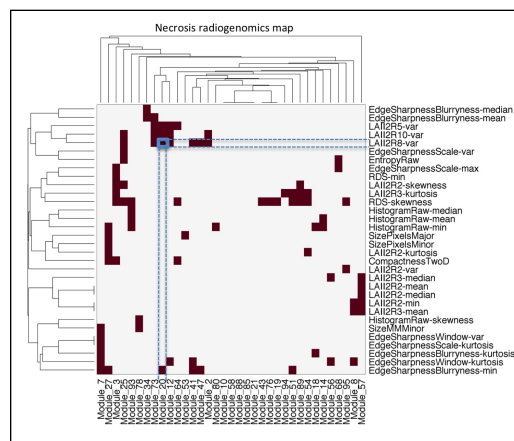


Example of necrosis and enhancement ROI of a poor prognosis patient.



Results Continued

We used AMARETTO to build a module network based on 426 TCGA patients. Next, we created radiogenomic maps by correlating only prognostic modules with quantitative image features. This establishes radiogenomic maps between the quantitative image features and 35 prognostic modules separately for all ROIs. Each map shows several significant associations between modules and image features.



Conclusions

Radiogenomic is rapidly gaining recognition as a powerful new field that has several promising applications, such as non-invasive molecular lesion assessment. If successful image surrogates can be identified that predict relevant molecular aberrations (e.g. mutation in EGFR), the value added by radiogenomic can be easily translated as medical imaging is part of routine management in oncology. In this study, we have shown exploratory results of two extensions to radiogenomic analysis of GBM cases from TCGA. We demonstrated the use of quantitative image features in GBM and reported meaningful correlations with VASARI image features, survival and molecular data. We also show the power of creating radiogenomic maps using AMARETTO, and using the module network to indirectly associate image features with underlying biological processes. Our results demonstrate that building radiogenomic maps with quantitative image features is a promising complementary strategy towards non-invasive management of GBM.

References

- Verhaak RG, et al. Cancer Cell. 2010;17(1):98-110
- Gutman DA, et al. Radiology. 2013 May;267(2):560-9
- Jain R, et al. Radiology 2013 Apr;267(1):212-20.
- Zinn PO, PLoS One. 2011;6(10):e25451
- Gevaert O, Plevritis S. Pac Symp Biocomput. 2013:123-34.
- Gevaert O, et al. Interface Focus. 2013;3:20130013.