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Letter to the Editor

iGLASS: imaging integration into the Glioma Longitudinal Analysis Consortium

The Glioma Longitudinal Analysis (GLASS) consortium is the largest, most comprehensive centralized collection of molecular data from matched paired glioma samples, currently from 35 institutions, enabling investigation of longitudinal molecular trajectories and potential therapeutic vulnerabilities.[1,2] Here, we describe the initiative of integrating imaging into GLASS (iGLASS) for radiogenomic investigation.[3] Specifically, the scope of iGLASS is to identify imaging-phenotypical associations of molecular alterations and longitudinal traits, so-called radiogenomics, thereby contributing to a non-invasive assessment of glioma transformations.

Currently, radiographic imaging in glioma is routinely acquired, often providing the first non-invasive clinical impression (prior to biopsy or excision) and then offering continuous monitoring throughout treatment and follow-up. Although glioma biopsy/excision is standard of care for most patients, such microscopic tissue analysis is not amenable to repeated evaluations during treatment, and invariably assesses only a portion of the tumor, ignoring tumor heterogeneity. Conversely, imaging macroscopically captures the complete tumor extent and, depending on the acquisition protocol, it can capture structural, perfusion, and microstructure characteristics. Following the mounting evidence of radiogenomic biomarkers adding value to tissue assessment,[3] routine longitudinal radiographic acquisition over the course of disease progression presents an opportunity for ample data utilization toward further radiogenomic investigation, contributing to: (i) spatiotemporal tumor heterogeneity assessment, and hence addressing tissue sampling errors by providing a macroscopic overview of the entire tumor; (ii) upfront tumor evaluation, potentially influencing surgical and other treatment decisions, including expedited patient stratification to clinical trials; and (iii) repeated monitoring of treatment response, potentially assisting treatment modification.

The initial goals of iGLASS are based on the imaging timepoints, ie, baseline preoperative and follow-up examinations performed throughout the course of disease. At baseline, iGLASS will investigate (i) distinct spatial tumor distributions of molecular characteristics,[3,4] (ii) mutational burden, and (iii) tumor propensity for hypermutation following DNA-alkylating chemotherapy. Follow-up imaging studies linked to clinical annotation or recurrent tissue samples with molecular profiling will support investigation of (i) radiogenomic biomarkers downstream of treatment, (ii) longitudinal molecular alterations, and (iii) treatment-induced hypermutation changes associated with worse outcome. To achieve these goals, iGLASS focuses on available imaging data corresponding to existing clinical and molecular data of GLASS consortium contributors. Specifically, the imaging data collected are divided into 3 tiers: “Basic” (ie, pre-/post-contrast T1-weighted, T2-weighted, T2-FLAIR), “Advanced” (ie, DSC-MRI, DWI/DTI), and “Supplemental” (eg, DCE-MRI, MRS, CT, PET). Current procedures to preserve patient confidentiality include de-identification of textual data and brain extraction in the acquired cranial scans, preventing facial reconstruction/recognition.[5] Common use of computational toolkits [6] will ensure harmonized processing, as well as standardized radiogenomic biomarker development.[7] Furthermore, the novel paradigm of federated learning will be employed for cases where data cannot be shared by participating institutions,[8] further strengthening the current confidentiality procedures. In summary, protected health information will not be shared under any circumstances and the subjects will not be identified by name or linked with histopathologic/genetic results, except in a strictly de-identified manner, following the GLASS consortium’s research identifier.

In conclusion, radiogenomics is an emerging field with the potential to make a substantial contribution to the non-invasive assessment, prediction, and management of glioma patients. The GLASS consortium offers a unique collaborative effort for integration across genomics, epigenomics, liquid-biopsy, digitized pathology slides, clinical and imaging data, to advance the field of radiogenomics, by specifically adding longitudinal components through iGLASS. This will ultimately advance our understanding of glioma, paving the way for potential reclassification of tumors of the central nervous system with incorporated imaging considerations. *iGLASS* strives toward centralized data storage, as well as immediate availability of all result outcomes (eg, developed computational tools, imaging features, tumor annotations) for the entire consortium and eventually the community.

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