Quantitative Image-based Response Prediction in Patients Receiving Radiation for Primary Brain Cancer or Intracranial Metastases

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Overview: Patients with primary brain tumors and intracranial metastases represent two distinct populations with overall poor clinical outcomes, though there is potential for more tailored, effective treatments using quantitative image-based analysis. With primary brain tumors such as gliobastoma multiforme (GBM), treatment involves maximal surgical resection followed by adjuvant chemoradiation. A persistent problem is monitoring patients in the post-treatment setting, when treatment-related changes can manifest either as pseudo-progression (an early radiation-induced change) or radiation necrosis (a delayed radiation-induced change). Both these conditions mimic tumor recurrence, both clinically and radiographically, rendering expert diagnosis challenging on routine MR imaging (50-60% accurate). This leads to thousands of unnecessary biopsies annually for pathologic confirmation. There is thus a need to develop non-invasive **post-treatment** biomarkers to identify these tumor-mimicking artifacts. In the setting of brain metastases, a separate but equally perplexing problem is encountered in the pre-treatment setting. In patients with obvious widespread disease, whole brain radiation therapy (WBRT) is offered for palliation, however this confers a well-documented risk of neurocognitive side effects. Patients with limited disease burden (1-3 lesions) are thus offered more local alternatives using resection, stereotactic radiosurgery (SRS), or a combination of the two to remove and/or ablate all visible disease. A known limitation in this scenario is the risk of distant brain metastases (DBMs) in the untreated brain requiring close MRI-based surveillance (a strategy which may ultimately result in salvage WBRT in the end). In those with more significant burden of disease (5-10 lesions or greater), this problem is even more pronounced, however the number of lesions by itself does not always predict for further intracranial progression. There is thus a strong clinical need for an accurate **pre-treatment** predictor of DBMs to determine which combination of treatments may be most optimal for patients with brain metastases. The PI has previously demonstrated that MR-based radiomics can be helpful in both pre- and post-treatment response assessment. Here, we aim to augment this effort by incorporating radiotherapy dose planning information, which has not yet been explicitly studied in this context. This data can be leveraged to identify specific zones of interest for computational analysis and develop more precise predictive biomarkers.

Proposed Approach: The PI has been pioneering the development, application, and validation of "interpretable" radiomic (computerized feature analysis) techniques from routine imaging scans (MRI and CT) for predicting response to treatment (radiation therapy, chemotherapy, and immunotherapy). Furthermore, the PI's collaboration with the department of Radiation Oncology at Stony Brook has enabled the unique analysis of radiotherapy planning data, from which novel treatment-based features might be studied and used to predict outcomes in brain tumor patients. Our approach comprises the following thrusts:

Thrust 1: Develop an enhanced radiomic risk scoring (RRS) system to distinguish brain tumor recurrence from treatment-induced effects on post-treatment imaging in primary brain cancer

Thrust 2: Develop a pre-treatment quantitative imaging predictor of spatial risk of local and regional recurrence in brain metastases using treatment-naive imaging

***Innovation*:** Unlike traditional approaches, the proposed features will capture the spatial heterogeneity of the lesions, as well as the biophysical deformations in the normal surrounding tissue surrounding the tumor. Our approach is also multifaceted, leveraging integration of radiotherapy planning data including physician-annotated structure sets and radiation dose maps. Leveraging cutting edge computational approaches, we will study both "dosiomic" features in addition to features generated via self-supervised learning to further strengthen our models' predictive capabilities beyond what might be achieve using traditional MRI imaging alone. This will be the first integrative pre-treatment predictor of local and regional response in neuro-oncology. The co-PI has curated a large patient cohort (N~200 metastatic patients, N~100 GBM), nearly all with serial pre-treatment and post-treatment imaging in addition to radiation treatment planning data. The algorithms will be trained and validated on this in-house cohort with plans for a broader translational study. Successful development of the proposed methods can ideally lead to more effective multimodality therapy tailored to individualized patient risk.