PROJECT

Supervisor:	Prof. Antonella Castellano
Title:	**Radiomics and AI-driven advanced imaging biomarkers to predict glioma growth, recurrence, and treatment response**
Curriculum:	Clinical and Experimental Medicine
Link to the personal page of the University or relevant hospital site website:	https://unifind.unisr.it/get/person/castellano-antonella

Description of the Project (max 3,000 characters including spaces)

Background/gap of knowledge

Monitoring gliomas during treatment with MRI remains challenging due to differences in tumor grade and molecular profiles. In low-grade gliomas (LGGs), irregular shapes, blurred margins, and slow growth can be missed with standard RANO criteria (1). High-grade gliomas, including glioblastomas (GBMs), show marked intra-tumor heterogeneity, often linked to treatment failure.

Advanced MRI techniques improve detection. DTI, for example, can reveal microstructural LGG changes earlier than standard MRI or volumetry (2). APT imaging, which reflects protein levels tied to tumor metabolism, offers a gadolinium-free method for glioma diagnosis, monitoring, and insight into tumor grade, IDH mutation, and MGMT status (3). This could be especially useful for evaluating response to new molecular therapies like IDH inhibitors (4).

In high-grade gliomas, habitat imaging provides in vivo insight into tumor heterogeneity by identifying distinct subregions via advanced MRI, PET, and AI-based modelling (5). These imaging-defined "habitats" may help assess treatment response in GBM, where heterogeneity is a key factor in resistance and poor outcomes.

Rationale and hypothesis

This prospective, observational study has two main hypotheses:

- In LGGs, we hypothesize that DTI and APT imaging can detect early microstructural and metabolic changes in patients with IDH-mutant grade 2 gliomas treated with vorasidenib, a pan-IDH inhibitor, outperforming standard and volumetric MRI.

- In HGGs, AI-driven habitat imaging using advanced MRI and PET may offer a non-invasive biomarker to characterize tumor heterogeneity during treatment, supporting prognostic evaluation and dynamic response monitoring.

Objectives and specific aims

Aim 1: To assess the sensitivity of advanced MRI techniques (DTI and APT imaging) in detecting early microstructural changes in patients with infiltrative IDH-mutant LGGs undergoing vorasidenib therapy, compared to conventional MRI. This includes evaluating inter-reader agreement, tumor growth rate, and estimates of progression-free survival (PFS) and time-to-next-intervention (TTNI).

Aim 2: To implement and validate an AI-based habitat imaging approach combining advanced MRI and amino acid PET in GBM patients during follow-up, to non-invasively assess intra-tumoral heterogeneity, predict response to standard radio-chemotherapy (RT/CT), and differentiate true progression from treatment-related changes.

Expected outcomes

This project aims to establish new standards for monitoring IDH-mutant LGGs undergoing IDH-inhibitor therapy, addressing current gaps in response assessment criteria and improving evaluation of treatment effectiveness in LGG clinical trials to guide future therapies. In HGGs, it will define novel biomarkers from AI-driven habitat imaging to quantify GBM heterogeneity and track its evolution during treatment, evaluating their predictive value for response and prognosis.

Skills that the student should acquire (max. 600 characters including spaces):

The PhS student will actively engage in patient enrollment, data collection, analysis, feature extraction, and genomic profiling. The PhS will develop skills in:
- Pre-processing conventional and advanced brain MRI, with feature extraction using machine and deep learning.
- Developing predictive models for personalized treatments based on clinical and imaging data.
- Using specialized software for image pre-processing, radiomics, and statistical analysis.
- Collaborating within a multidisciplinary team and effectively communicating research findings.

References (max. 15)

1. Wen PY, van den Bent M, Youssef G, Cloughesy TF, Ellingson BM, Weller M, et al. RANO 2.0: Update to the Response Assessment in Neuro-Oncology Criteria for High- and Low-Grade Gliomas in Adults. J Clin Oncol. 2023;41(33):5187-99.

2. Castellano A, Donativi M, Rudà R, De Nunzio G, Riva M, Iadanza A, et al. Evaluation of low-grade glioma structural changes after chemotherapy using DTI-based histogram analysis and functional diffusion maps. Eur Radiol. 2016;26(5):1263-73.

3. Sotirios B, Demetriou E, Topriceanu CC, Zakrzewska Z. The role of APT imaging in gliomas grading: A systematic review and meta-analysis. Eur J Radiol. 2020;133:109353.

4. Mellinghoff IK, van den Bent MJ, Blumenthal DT, Touat M, Peters KB, Clarke J, et al. Vorasidenib in IDH1- or IDH2-Mutant Low-Grade Glioma. N Engl J Med. 2023;389(7):589-601.

5. Bailo M, Pecco N, Callea M, Scifo P, Gagliardi F, Presotto L, et al. Decoding the Heterogeneity of Malignant Gliomas by PET and MRI for Spatial Habitat Analysis of Hypoxia, Perfusion, and Diffusion Imaging: A Preliminary Study. Front Neurosci. 2022;16:885291.