PROJECT 1

DoS: Prof.ssa Nicoletta Anzalone

Title: Quantitative imaging and artificial intelligence for prognostic prediction in primary central nervous system lymphoma

Curriculum: Experimental and Clinical Medicine

Link to OSR/UniSR personal page:

https://www.unisr.it/docenti/a/anzalone-nicoletta-emanuela

Project description (*Number of characters*, *including spaces*: 2.000 - 3.000):

Primary Central Nervous System Lymphomas (PCNSL) are an overly aggressive type of Extranodal Non-Hodgkin Lymphoma confined to the central nervous system. Modern treatment of PCNSL includes two phases: induction and consolidation. Joint international efforts have improved patient prognosis in recent years, but nearly 30% of patients still do not respond to the first line induction therapy with high-dose methotrexate-based poly-chemotherapy and ≈20% of patients relapse after consolidation. The mechanisms underlying these events still have to be fully elucidated, but early identification of these non-responding patients is of the uttermost importance, as it may help in driving clinical decision making and in tailoring treatment accordingly. At the present time, our ability to predict outcomes is limited to purely clinical models. Thus, there is an open need to develop improved predictive models for PCNSL to better identify high-risk patients and to foster new therapeutic advances.

Neuroimaging studies, especially magnetic resonance imaging (MRI), are widely performed for diagnosis and evaluation of treatment response in PCNSL. Nowadays, imaging studies are read by neuroradiologists, who reach a diagnostic conclusion based on their subjective expert knowledge and previous experience, but neuroimaging studies may also be a source of additional objective data, if analyzed with novel approaches. Radiomics is a recent field of study with the goal of extracting minable high-dimensional data from clinical images, which may reveal many valuable information regarding the development and progression of cancer.

Radiomics in neuro-oncology already achieved important results in the understanding of the biology and treatment of brain tumors [1]. Recent studies demonstrated the accuracy and reproducibility of radiomics approaches in brain tumor imaging, as well as their ability to differentiate PCNSL from atypical glioblastoma [2]. In this context, Artificial Intelligence (AI) techniques (e.g., deep neural networks) represent a valuable resource to create prognostic models and they have already been effectively applied in many oncological fields. There is a wide potential for deep neural networks to create predictive models of response to cancer therapy, especially with the combination of different sources of data (radiological, clinical, histopathological and molecular).

Our Institute has a long research history in the field of PCNSL and an active fruitful collaboration is already in place between the Neuroradiology, Hematology and Pathology departments, which has already led to several publications using MRI not only for diagnosis but also for monitoring new therapeutic agent effects [3].

Aim of this project is to use quantitative imaging features, combined with clinical and laboratory data to build a prognostic algorithm able to recognize patients with PCNSL at high-risk of not responding to current standard treatment in order to help clinical decision-making.

Skills to be acquired by the student:

The PhD candidate will learn how to collect and organize data, as well as recognize and deal with possible sources of bias, all key skills to build meaningful AI models. One particular challenge will be missing data, a common issue in medicine; the candidate will learn to perform data imputation, and leverage recently developed methods, like generative adversarial networks (GANs), to address this issue. The PhD candidate will also learn how to effectively interpret research results in order to draw meaningful conclusions. The PhD candidate will acquire expertise in statistical analysis, bioinformatics (radiomics and AI techniques) and interpretation of imaging and non-imaging biomarkers. Moreover, the PhD candidate will learn how to generalize the concepts and skills acquired and apply them to other fields (e.g., body imaging, patients' triage and therapeutics). The PhD candidate will learn how to write

research reports/paper and will be encouraged to improve oral communication skills and independent thinking. Multidisciplinary interaction and integration will be encouraged.

References (max. 3)

[1] Zhou M, Scott J, Chaudhury B, Hall L, Goldgof D, Yeom KW, et al. Radiomics in brain tumor: image assessment, quantitative feature descriptors, and machine-learning approaches. American Journal of Neuroradiology. 2018, 39(2):208-216.

[2] Suh HB, Choi YS, Bae S, Ahn SS, Chang, JH, Kang SG, et al. Primary central nervous system lymphoma and atypical glioblastoma: differentiation using radiomics approach. European Radiology. 2018, 28(9):3832-3839.

[3] Ferreri AJM, Calimeri T, Conte GM, Cattaneo D, Fallanca F, Ponzoni M, et al. R-CHOP preceded by blood-brain barrier permeabilization with engineered tumor necrosis factor-α in primary CNS lymphoma. Blood 2019; 134 (3): 252-262.