PhD thesis proposal: Guiding clinical routine practice decisions using amino-acid PET imaging for neuro-oncology with artificial intelligence

Context

Research context

Brain tumors and central nervous system tumors have an incidence of 24.71 cases per 100,000 people. Meningiomas are the most frequent (39.7%) and gliomas account for approximately 80% of malignant tumors [1]. The latter are associated with a poor prognosis, with a median survival of 15 months for glioblastomas, the most common type of glioma [2]. Due to the high risk and difficulty of invasive procedures, the diagnosis and monitoring of cancer in neuro-oncology rely heavily on medical imaging, such as magnetic resonance imaging (MRI) and positron emission tomography (PET) radiolabeled amino acids like 18F-FDOPA or 18F-FET which are recommended by international groups [3].

Biopsy planning is comprised in these recommendations, as it better delineates the tumor extent compared to conventional MRI. In particular, amino acid PET helps locate the most aggressive part of the lesion and guide the biopsy target, which is crucial for patient prognosis and subsequent treatment. This part is currently determined by the tumor regions with the highest PET uptake [4] while several publications have shown that the kinetics of tumor metabolism during acquisition can provide additional and relevant information at the time of initial diagnosis to identify the most aggressive tumors [5,6] especially when extracted at the voxel level [7–9] and has never been applied to biopsy planning. As early as 2011, a study by Kunz et al. showed that dynamic hotspots could be useful in identifying malignant parts of tumors [10].

Moreover, 18F-FDOPA PET is also recommended by the RANO group in addition to MRI for recurrent gliomas [3] in the differential diagnosis between radionecrosis, a treatment-induced change, and true progression. This is the primary indication for amino acid PET in gliomas, as it has better diagnostic performance than conventional MRI [11]. Numerous studies in the literature have demonstrated the excellent performance of amino acid PET based on simple image analysis [12,13] or more advanced analysis with massive extraction of tumor characteristics coupled with an artificial intelligence model for classification [7]. During the last decade, deep neural network models have been developed to automate certain healthcare-related tasks and assist physicians in their clinical practice. When applied to medical imaging data, such models are often designed for specific tasks, need large amounts of annotated data, and demonstrate little generalization capability. Recently, foundation models have gained prominence for their ability to learn robust and generic latent representations of data in a self-supervised way. However, such models are still very rare for 3D imaging, common in the medical field. In particular, no such model integrates PET imaging. But these models could improve performance on specific subtasks through fine-tuning on a small number of annotated data, which is particularly interesting in the context of rare tumors such as gliomas. Furthermore, despite an exponential number of publications attempting to develop a machine learning model to answer a specific question, only a very small number make it into clinical routine [14], often due to a lack of evaluation in this context and model acceptability. The representations learned by a foundation model being more robust and general, the potential for explainability is greater, and they are therefore more likely to be accepted as tools for clinical decision support.

Research environment

The IADI (Adaptive Diagnostic and Interventional Imaging) laboratory is a joint research unit of the University of Lorraine/INSERM, specializing in medical imaging and developing innovative technologies to improve the quality of medical images and the resulting diagnoses. The nuclear medicine division of the laboratory specializes in processing 18F-FDOPA PET images, developing methods necessary for dynamic analysis at the voxel level and studying the heterogeneity of dynamic behaviors within a tumor. Numerous publications in high-impact international journals have earned the team national and international recognition in the field. Concurrently, the core of the IADI laboratory has focused on developing innovative techniques for imaging moving organs using MRI. Some of these techniques have been developed using diffusion and perfusion sequences, which are particularly relevant in the context of neuro-oncology and could be applied in this setting. The laboratory as a whole has also developed strong competencies in machine learning, with numerous applied projects related to this domain.

A major theme of this PhD work is artificial intelligence applied to medical images. In this regard, the IADI and LORIA laboratories have demonstrated their competencies through numerous projects, with IADI possessing deep knowledge of PET and MRI images for use with deep learning, and LORIA offering a more fundamental understanding of the functioning of these models and the methods to apply, with national recognition in this field. Thereafter the PhD student will be co-supervised by researchers in these two labs.

The thesis supervisor, Pr Antoine VERGER, from IADI lab is also a medical practitioner at Nancy University Hospital. He maintains constant contact with clinical teams involved in the management of glioma patients (nuclear medicine physicians, neurosurgeons, neuro-oncologists, pathologists), enabling the PhD student to consult them with questions, discuss their expectations, or gain a better understanding of the problem.

The thesis co-supervisor, Erwan Kerrien, from LORIA lab, is an Inria researcher who specializes in computer vision and image processing, in particular for neuro-imaging. He will support the PhD student regarding computer science issues, discussing innovations in the computer vision field and connecting with the computerized medical imaging research community.

PhD Project

Objectives

The research project aims to develop machine learning models based on learned features describing the complex relationships between voxels in 18F-FDOPA PET scans in gliomas.

1. Development of a self-supervised deep learning model to learn the representation of both healthy and pathological brains from multimodal PET and MRI images (WP1).

2. Identification of an aggressive subregion within a glioma using the previously constructed latent representation and MRI and PET images to assist in

biopsy planning (WP2).

3. Development of a classification model for differential diagnosis between radionecrosis and true progression, with evaluation in a clinical routine context (WP3).

Method

WP1: Construction of a robust and glioma-specific latent representation in 3D medical imaging

The construction of this model will be analogous to that of a foundation model. Unlike models developed in the field of computer vision, which aim to be highly generalized, we aim to develop a model that is specific and representative of our pathology. It will be trained in a self-supervised manner using a dataset of multimodal MRI and PET images, with the possibility of initialization using a more general foundation model. The dataset will consist of open-source and local datasets. The training of this model will be self-supervised, meaning no external annotation is required. The model architecture will be based on a vision transformer aimed at encoding information from part of the image along with its context, particularly spatial context. The latent representation will be formed by training the model to perform multiple tasks simultaneously, such as inpainting.

WP2: Identification of aggressive subregions using multiparametric dynamic 18F-FDOPA PET and MRI images of gliomas at initial diagnosis for biopsy planning

The model developed in WP1 will serve as a prior to obtain a robust representation of the image in a reduced-dimensional space where areas of the image with similar behavior are close. The features of each patient's image will be grouped to form an image signature for each patient. Association studies will then be conducted between the tumor's image signature and its molecular signature. Once elements of interest are identified in the image signature, the tumor area they characterize will be identified using explainability methods for machine learning algorithms.

WP3: Explainable deep learning model for differentiating between radionecrosis and true progression in clinical routine

To develop our classification model, the model from WP1 can serve as an initialization with the advantage of converging to the solution with less data. The results obtained with this model will be compared to completely supervised CNN classification models trained from scratch and a model based on a radiomics pipeline with traditional machine learning algorithms. The model will be evaluated in terms of diagnostic performance, including precision, sensitivity, and specificity. The model must demonstrate good generalization performance on an external validation dataset. However, this external validation is only a first step; the crucial aspect is proving the added value of the model in a clinical routine context, which will be assessed by doctors from different hospitals. Explainability methods will be integrated into the model to increase its acceptability. Expected impact This project will have a scientific impact towards a more detailed understanding of the presentation of gliomas and their evolution, as well as a practical impact on the management of patients with gliomas in clinical routine. Each WP will lead to the publication of a paper in an international journal with peer review

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Profile and skills required

We are looking for a researcher with a passion for image processing and machine learning to join our team. You will be working on cutting-edge projects to develop innovative solutions to complex problems.

Skills required:

Technical skills :

- Advanced knowledge of image processing (acquisition, filtering, segmentation, object recognition, etc.)
- Advanced knowledge of machine learning (classification, regression, clustering, deep learning, etc.)
- Proficiency in programming languages (Python, C++, etc.)
- Experience with ML libraries (scikit-learn, pytorch, tensorflow, ...)
- Ability to develop and deploy machine learning models
- Ability to work with high-performance computing environments (GPU, etc.)

Behavioural skills :

- Independent and able to work autonomously
- Ability to work in a team and collaborate with experts from other fields
- Thorough and detail-oriented
- Excellent analytical and problem-solving skills
- Ability to communicate clearly and effectively

Education / qualifications :

- Master's degree in computer science, mathematics, engineering or related field

Contact information

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