Offer for a PhD preparation

Development of multi-omics models
for personalized medicine in follicular lymphoma
U1288 Inserm, Institut Curie
www.lito-web.fr/en

Background

In vivo positron emission tomography (PET) scans have already been shown to be useful in predicting progression free survival (PFS) and overall survival (OS) in lymphoma patients of various types. In particular, the total metabolic tumor volume measurable from whole-body 18F-Fluorodeoxyglucose (FDG) PET scans has been shown to be a prognostic biomarker (1), as has disease dissemination (2,3) and tumor site localization (4). While PET imaging information undeniably contributes to refining the prognosis of patients, studies reported in other contexts suggest that combining information from medical images, anatomopathological slides, clinical records and biological samples improves the accuracy of predictions obtained with a single type of data (5).

The thesis hypothesis is that combining information from medical images, pathological slides, clinical records and biological samples will improve the prognosis of follicular lymphoma patients with either high or low tumor burden.

Objective

The aim of the thesis is to propose multi-omic models, integrating radiomic, clinical, pathomic and genomic characteristics, to predict the two-year outcome of patients with follicular lymphomas with high or low tumor burden. The project is part of the national BIDIFLY collaboration, supported by the American IFLI Foundation (https://cdn.prod.website-files.com/65bff97f5937b9ad7c79af66/66620d53e1f56059eeac3ac9_LYSA-LYSARC%20%26%20IFLI%20BIDIFLY-Press%20Release.pdf) and Inserm (Data-Fol project https://iresp.net/wp-content/uploads/2023/05/AAP-MESSIDORE-2023_Liste-des-laureats.pdf).

Methods

Thanks to a collaboration with LYSARC (https://www.lysa-lymphoma.org), we already have a database of over 1,000 patients with follicular lymphoma of high or low tumor burden, for whom multi-omics and follow-up data are available. Each type of data is analyzed by a team of the BIDIFLY collaboration with expertise in the type of data concerned. These analyses are performed on the Lymphoma Data Hub, and the features identified as relevant for each type of data will be made available to our team and to the PhD student in charge of the multi-omics integration work.

As the laboratory is an expert in the analysis of PET/CT images of lymphoma patients, it already has methods for extracting radiomic features relevant to these patients (https://github.com/Lrebaud/exhaustive_radiomics, https://github.com/Lrebaud/robi) and models capable of integrating different radiomic and clinical features (https://github.com/Lrebaud/ICARE, a MICCAI challenge winning model (6)).

Finally, we have multi-omics data integration pipelines, developed in the context of creating prognostic models in lung cancer patients treated with immunotherapy (https://www.medrxiv.org/content/10.1101/2024.06.27.24309583v1 and https://github.com/ncaptier/multipit).

The project will thus involve:

- Optimizing the extraction of radiomic features from PET/CT images, based on the laboratory's experience (1,2,3).
- Developing, testing and characterizing the performance of several multimodal integration schemes, including early, intermediate and late integration.

- Ultimately producing the best parsimonious model that can be deployed in prospective studies to predict disease progression at 24 months, which is known to be strongly correlated with long-term progression.

Supervision

Day-to-day supervision will be provided by Irène Buvat (DR CNRS), thesis supervisor, and Clémentine Sarkozy (MD, PhD, hematologist), co-supervisor. In particular, the work will benefit from close collaboration with Thomas Walter (U900 Inserm, Professor at Ecole des Mines, Institut Curie, PSL), an expert in anatomopathological image analysis using deep learning, and with Bruno Tesson (LYSARC), an expert in genomic data analysis. The PhD student will be heavily involved in the BIDIFLY consortium, interacting with specialists in different types of data.
The student will attend weekly lab meetings to keep abreast of the progress of work being carried out in the lab on related topics, and will be expected to present his/her results on a regular basis. He/she will also take part in the laboratory's journal club.

Scientific, material (specific security conditions) and financial conditions of the research project

The PhD student will work using the LITO and Institut Curie computing servers, as well as directly on the Lymphoma Data Hub in the Azure Machine Learning environment (Microsoft).
Funding will be provided by the BIDIFLY and Data-Fol contracts, and the employer will be the Institut Curie Research Center.

Objectives for promoting the doctoral student's research work: dissemination, publication and confidentiality, intellectual property rights, etc.

The PhD student will present his/her work at national and international conferences in the fields of medical imaging (RSNA), oncology and hematology (SNMMI meeting, EANM Conference, ASH), and data science (eg, MICCAI, ICML). He or she will publish results in international peer-reviewed journals.

International outlook

The Unit collaborates on lymphoma research with many international players (7), and the PhD student will have the opportunity to get involved in these collaborations as well.

Contact

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Bibliographical references

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(7) Boellaard R, Buvat I, Nioche C, Ceriani L, Cottereau AS, Guerra L, Hicks RJ, Kanoun S, Kobe C, Loft A, Schöder H, Versari A, Voltin CA, Zwezerijnen GJC, Zijlstra JM, Mikhaeel NG, Gallamini A, El-Galaly TC, Hanoun C, Chauvie S, Ricci R, Zucca E,

Meignan M, Barrington SF. International Benchmark for Total Metabolic Tumor Volume Measurement in Baseline 18F-FDG PET/CT of Lymphoma Patients: A Milestone Toward Clinical Implementation. J Nucl Med. jnumed.124.267789, 2024. doi: 10.2967/jnumed.124.267789 (sous presse).