IMT Atlantique
Bretagne-Pays de la Loire
École Mines-Télécom

Internship offer 2022

CHU de Poitiers

Inserm

Predicting the efficacy of immunotherapy in gastric cancer using deep learning

Clinical context

Immunotherapy is a treatment used in many cancers to stimulate the immune system to attack the cancer. Cancer cells express negative molecules, called **immune checkpoints**, which block the action of the immune system, especially lymphocytes. Immunotherapy works by freezing these negative immune checkpoints. The efficacy of immunotherapy is being evaluated in **digestive cancers**, especially for gastric cancers. In particular, one can rely on **inhibitors** of the immune checkpoints referred to as programmed cells death-1 (PD-1) and death-ligand 1 (PD-L1).

Metastatic **gastric cancer** remains a frequent and poor prognosis disease treated with palliative chemotherapy. Recent studies suggest that the combination of chemotherapy and immunotherapy may be more effective than chemotherapy alone in advanced gastric cancer. The presence of PD-L1 in gastric cancers is considered as a factor in the response to immunotherapy. Several other tumor parameters (genetic abnormalities, presence of certain viruses...) have been identified as predictors of response to immunotherapy. Moreover, the efficacy of immunotherapy depends on the infiltration of tumors by lymphocytes. However, these parameters are under-studied in gastric cancers.

The density of **tumor-infiltrating lymphocytes**, especially CD8+ cells, is an important prognostic factor in gastric cancers according to several studies [1]. This **infiltrate** has been mainly studied in the context of operated gastric cancers, on surgical specimens. Only one study [2] suggests the **prognostic value** of this infiltrate on biopsies, as analyzed by immunohistochemistry in a population of metastatic gastric cancers. However, this study relies on expert pathologists which does not guarantee the reproducibility of this criterion.

Internship topic

The development of non-invasive imaging technologies over the last decades has opened new horizons in studying the **digestive anatomy**. Computational analysis from computed tomography (CT) images has become a crucial task for many applications : computer-assisted diagnosis, treatment planning, surgery planning, image-guided interventions... An emerging field deals with **radiomics** which has the potential to uncover tumoral patterns and characteristics that fail to be appreciated by the naked eye (Fig.1). In particular, it could establish **correlations between imaging and lymphocyte infiltrate** [3]. The radiomic score is a quantitative score derived from multi-parametric image analysis, including density and gray level information on an investigator-defined volume of interest. This score would be able to classify tumors with a low versus high CD8+ infiltrate on CT and therefore predict the response to immunotherapy in **gastric adenocarcinoma**.

Recently, the performance of **deep learning** has been intensively demonstrated in medical image analysis [4]. Convolutional neural networks (CNN) can be employed into current radiomics models by extracting deep features from hidden layers. Compared to handcrafted features, deep features contain more representative and high-level medical image information and provide more predictive patterns. In this direction, the goal of the internship will be to develop a **deep radiomics** pipeline [5] and to evaluate its ability to identify immune infiltrate from pre-therapeutic CT of gastric adenocarcinomas, before any systemic treatment. More globally, the identification of a **universal biomarker** to select patients with advanced gastric adenocarcinoma, eligible for immunotherapy, would constitute a major and relevant innovation for the management of such poor prognosis disease.

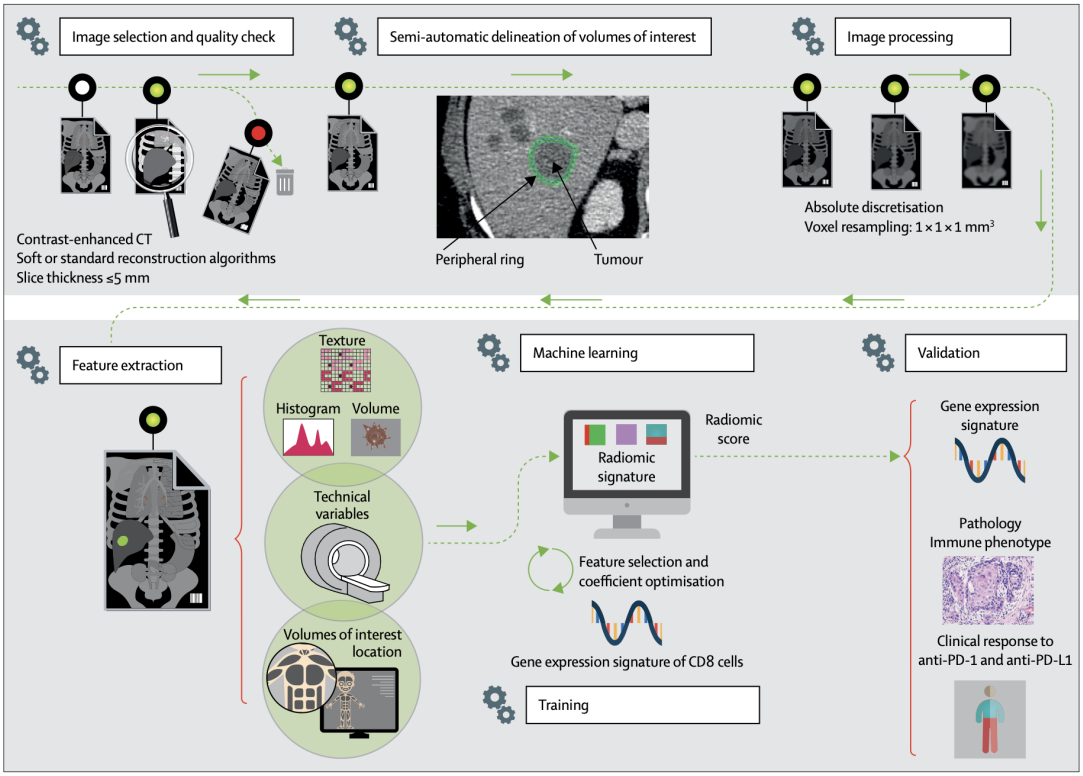

FIGURE 1 – Radiomics workflow, as illustrated in [3].

Candidate profile

We are looking for a M2 student motivated by image analysis with a particular interest in DL applications. A background in biomedical or medical imaging and an experience with Python programming language and Pytorch package are a plus. Good communication and team working skills are also required as the intern will work in collaboration with clinicians. A good ability to communicate in English as well as a fluent English for reading and writing scientific articles are also required.

Internship information

- 6-month internship starting from January to March 2022
- Location : LaTIM laboratory[1], 22 avenue Camille Desmoulins, Brest, France
- Advisors : P.-H. Conze (IMT Atlantique[2], LaTIM) and D. Visvikis (LaTIM, Inserm)
- Collaborators : D. Tougeron (CHU Poitier), J.-P. Tasu (CHU Poitiers, LaTIM)
- Applications by email to P.-H. Conze (`pierre-henri.conze@imt-atlantique.fr`) and D. Visikis (`visvikis@univ-brest.fr`) including full curriculum vitæ, cover letter stating your motivation, latest grade transcripts and recommendation letters or contacts from former teachers/advisors.

Bibliography

[1] C. Tian et al., *Prognostic role of tumour-infiltrating lymphocytes assessed by HE-stained section in gastric cancer : a systematic review and meta-analysis.* BMJ, 2021.

[2] S. Pernot et al., *Infiltrating and peripheral immune cell analysis in advanced gastric cancer according to the Lauren classification and its prognostic significance.* Gastric Cancer, 2020.

[3] R. Sun et al., *A radiomics approach to assess tumour-infiltrating CD8 cells and response to anti-PD-1 or anti-PD-L1 immunotherapy : an imaging biomarker, retrospective multicohort study.* The Lancet Oncology, 2018.

[4] G. Litjens et al., *A survey on deep learning in medical image analysis.* Medical Image Analysis, 2017.

[5] A. Chaddad et al., *Deep radiomic signature with immune cell markers predicts the survival of glioma patients.* Neurocomputing, 2021.

1. Laboratoire de Traitement de l'Information Médicale, `http://latim.univ-brest.fr`
2. `https://www.imt-atlantique.fr/`