Post-doc offer:

Signatures of resistance and response to immunotherapy in advanced pancreatic cancer

U1288 Inserm, Institut Curie
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Background
The PRODIGE TEDOPAM (NCT03806309) and MAZEPPA (NCT04348045) clinical trials are two academic, national, multicenter, randomized, controlled phase II trials that evaluated two immunotherapy strategies in patients with advanced pancreatic cancer. As part of these clinical trials, a tumor, blood and imaging dataset was collected to analyze biological and radiomic biomarkers associated with response or resistance to treatment. Both clinical trials have been completed, and clinical data are available, along with tumor, blood and imaging data.

Objectives
The aim of the project is to analyze computed tomography (CT) images from patients enrolled in the TEDOPAM and MAZEPPA studies to identify predictive biomarkers and signatures of resistance/response to two immunotherapy-based maintenance strategies: (i) a vaccine-based approach (TEDOPAM) and (ii) an immunochemotherapy-based approach (MAZEPPA).

Methods
Each of the two studies led to the acquisition of a cohort of 100 patients. Of the 200 patients, around 20% were "long survivors", while 20% experienced rapid disease progression. All patients underwent longitudinal CT scans: before treatment, and then every 8 weeks. The aim is to create models that can predict whether patients belong to one of the two categories (long survivor or rapid progressor), based on radiomic characteristics extracted from CT scans.

The originality of the study is that not only tumor radiomic features will be considered, but also characteristics reflecting body composition. Indeed, various host-related elements can influence the response to immunotherapies and lead to the emergence of hyperprogression, such as age, gender, number of metastases, cachexia or sarcopenia. Although most patients with advanced pancreatic cancer are sarcopenic, the link between sarcopenia and response to immunotherapies has been little explored.

With regard to tumor radiomics, all tumor foci observed on the CT scan will be segmented semi-automatically by an expert radiologist. Based on this segmentation, and after image harmonization (1), local and global tumor characteristics robust to differences in image quality will be calculated, such as individual and total tumor volumes, metastatic tumor volume, tumor shape, intra- and inter-tumor heterogeneity, and tumor dissemination index. The laboratory has all software available to perform these calculations (eg, 2, 3). Univariate and multivariate analyses will be performed to characterize the predictive value of radiomic tumor characteristics.

For body composition, a deep learning algorithm (Tomovision's Slice O Matic® software) will be used to segment muscles, subcutaneous and visceral fat, and deduce body composition characteristics. Measurements will be carried out in 2 or 3 dimensions, using TotalSegmentator already deployed in the laboratory (4). Using the volume, density and shape (where appropriate) of spleen, liver, psoas, pancreas, subcutaneous fat, visceral fat and muscle, univariate and multivariate analyses will be carried out to identify features likely to have an impact on survival and response to immunotherapy.

Finally, a model involving both tumor and host characteristics can be built, to determine the respective contributions of each component and, hopefully, improve predictive accuracy.

Original developments are particularly expected to integrate the longitudinal dimension into the models, as each patient will have several CT scans including a baseline scan and several follow-up scan during treatment.

Scientific environment

The Laboratoire d'Imagerie Translationnelle en Oncologie (LITO) specializes in the production and analysis of medical images, in particular metabolic and functional images (PET and MRI). It is a broadly multidisciplinary team of some forty physicists, engineers, radiologists, nuclear physicians, biologists, oncologists, doctoral students and post-doctoral fellows. Based at the Institut Curie Research Center and working closely with the Institut Curie Hospital, it benefits from an environment that is particularly well suited to projects involving the advanced analysis of medical images using state-of-the-art radiomics and artificial intelligence techniques.

Financial terms and conditions

Funding will be provided by the ImmunoPanc-Sign contract, and the employer will be the Institut Curie Research Center, for a 16-month fixed-term contract. Salary will depend on the candidate's experience. This contract may be extended.

Research valorization objectives: dissemination, publication and confidentiality, intellectual property rights, etc.

The post-doctoral fellow will have the opportunity to present his or her work via papers at national and international conferences in the fields of medical imaging (RSNA), oncology (ASCO, ESMO), and data science (eg, MICCAI, ICML). He or she will publish results in international journals.

Skills required

- Radiology, radiomics, image analysis
- Statistics, learning methods
- Programming

Contact

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References

1. Orlhac F, Frouin F, Nioche C, Ayache N, Buvat I. Validation of A Method to Compensate Multicenter Effects Affecting CT Radiomics. Radiology. 2019 Apr;291(1):53-59.
2. Nioche C, Orlhac F, Boughdad S, Reuzé S, Goya-Outi J, Robert C, Pellot-Barakat C, Soussan M, Frouin F, Buvat I. LIFEx: A Freeware for Radiomic Feature Calculation in Multimodality Imaging to Accelerate Advances in the Characterization of Tumor Heterogeneity. Cancer Res. 2018 Aug 15;78(16):4786-4789.
3. https://github.com/Lrebaud/exhaustive_radiomics
4. Wasserthal J, Breit HC, Meyer MT, Pradella M, Hinck D, Sauter AW, Heye T, Bol DT, Cyriac J, Yang S, Bach M, Segeroth M. TotalSegmentator: Robust Segmentation of 104 Anatomic Structures in CT Images. Radiology: Artificial Intelligence, 5 : e230024, 2023.