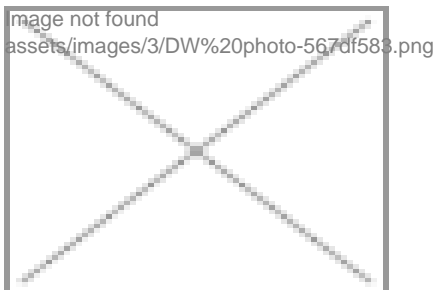


Tumour ID cards for multi-scale characterization of tumour heterogeneity

HOST INSTITUTION: *The French Alternative Energies and Atomic Energy Commission (CEA) - from 01.04.2020: Institut Curie (IC)*

CEA is a French key player in research, development and innovation. It includes 10 research centres among which 51 research units employing 16.000 researchers, engineers, technologists and staff. It is the first French research centre in terms of patents filed (753 in 2015). CEA is very actively involved in the European Research organization, with 438 ongoing European projects in 2015. CEA created 187 start-ups since 1972 in the innovative technologies sector and has an annual budget of 4.1 billion euros. The ESR is affiliated with IMIV, a research unit hosted by CEA and funded by CEA, Inserm, CNRS and Paris South University. This research unit is specialized in Positron Emission Tomography (PET) imaging and is located on the *Service Hospitalier Frédéric Joliot* (SHFJ) premises, which is a historical cradle of PET in France. IMIV currently includes 60 scientists and staff and is organized in 4 groups: the molecular probe group, the biomedical physics group, the experimental imaging group and the clinical investigation group, covering altogether all aspects of PET, from the production of original tracers up to first-in-man studies in volunteers and patients. IMIV benefits from the fully-equipped facility of the nuclear medicine department of SHFJ, including a tracer production unit, quality control labs, and 6 preclinical and clinical PET systems. This intimate link between basic and clinical research using PET imaging is a unique feature of the centre and allows for high standard translational research in PET.

The ESR is registered to the Paris Saclay University EOBE doctoral school.



DESCRIPTION OF THE PROJECT (ESR9 - David Wallis)

In the current healthcare environment, cancer treatment is most often selected based on one or several biopsies within the tumour, from which the anatomopathological characteristics of the tumour are identified and used to determine the best therapeutic strategy. However, due to tumor heterogeneity, more than 60% of the abnormalities present in the cells of the tumour tissue are not found everywhere throughout the tumour and are therefore unlikely to be detected using a single biopsy. Unlike biopsies, medical images provide anatomical, functional and molecular information pertaining to the whole tumour, to all tumour foci, and also to the tumour environment. The computation of biomarkers from different medical images and their analysis to predict the nature of the tumour and its therapeutic response are the subject of an emerging discipline, radiomics, which consists in extracting a large number of features such as intensity, shape, texture, from medical images and to determine if radiomic features, possibly combined with other patient features (omics data, blood biomarkers, etc), can assist patient management. The ESR will identify and investigate robust biomarkers extracted from various kinds of anatomical (MR, CT), functional (PET, MR) and molecular (PET) images in order to characterize at best the complexity of tumours.

Based on these biomarkers, he will determine an image-based tumour phenotype that bears useful prognostic information and will help predict the patient response to therapy, the progression-free survival and the overall survival in different patient cohorts (eg, brain tumours, non-small cell lung cancer).

Methodology. In the past four years, IMIV has been highly involved in the field of radiomics. We have established the complementary or redundant nature of some measurable biomarkers from positron emission tomography (PET) images. The sources of biomarker variability have been identified and robust computational methods have been proposed. Links have been found between some PET radiomic biomarkers and the histological characteristics of the tumours measured *ex vivo*. The evolution of radiomic biomarkers as a function of the macroscopic characteristics of the tumors has also been analyzed. Methods to overcome the variability of biomarkers across medical centres have been proposed. The PhD thesis project will therefore build on this experience and will now focus on: 1) the determination of robust image-based phenotype, or tumour ID card, that is reproducible and explainable; 2) the design and validation of models based on this ID card, possibly combined with other biological, omics, or clinical information, that could predict the patient response to therapy and outcome. The validity of the ID card, that is likely to depend on the cancer type, and the usability of the models for a large variety of imaging devices and imaging protocols will be carefully determined, so that models established in a given centre can be used for data acquired in a different centre.

Within the course of this project, secondments to GE Healthcare (Buc, France), King's College London (UK) and the Eberhard Karls University in Tuebingen (Germany) are planned.

Main bibliographic references of the hosting lab on the PhD thesis topic:

- Orhac et al. Tumor texture analysis in 18F-FDG-PET: relationships between texture parameters, histogram indices, SUVs, metabolic volumes and total lesion glycolysis. *J Nucl Med* 55: 414-422, 2014.
- Buvat et al. Tumor texture analysis in PET: where do we stand? *J Nucl Med* 56: 1642-1644, 2015.
- Orhac et al. 18F-FDG PET-derived textural indices reflect tissue-specific uptake pattern in non-small cell lung cancer. *Plos One* 10(12):e0145063, 2015.
- Orhac et al. Multi-scale texture analysis: from 18F-FDG PET images to pathological slides. *J Nucl Med* 57: 1823-1828, 2016.
- Orhac et al. Understanding changes in tumor textural indices in PET: a comparison between visual assessment and index values in simulated and patient data. *J Nucl Med* 58: 387-392, 2017.
- Reuze et al. Prediction of cervical cancer recurrence using textural features extracted from 18F-FDG PET images acquired with different scanners. *Oncotarget*. 8: 43169-43179, 2017.
- Schernberg et al. A score combining baseline neutrophilia and the SUVpeak of the primary tumor on FDG-PET predicts outcome in locally advanced cervical cancer. *Eur J Nucl Med Mol Imaging* in press doi: 10.1007/s00259-017-3824-z, 2017.