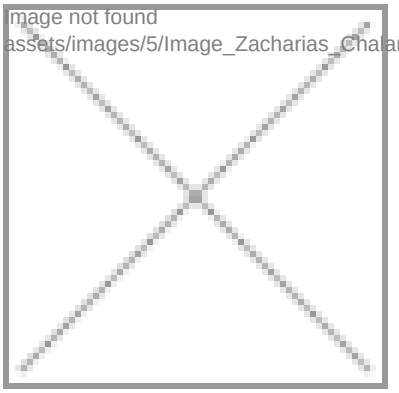
Whole-body parametric PET/MR imaging for improved therapy response assessment in metastatic diseases

HOST INSTITUTION: *The French Alternative Energies and Atomic Energy Commission (CEA)*

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 in Orsay, South of Paris, 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 candidate is registered to the Paris Saclay University EOBE doctoral school.



DESCRIPTION OF THE PROJECT (ESR4 - Zacharias Chalampalakis)

Context. Positron Emission Tomography (PET) and hybrid PET/Magnetic Resonance Imaging (MRI) are able to provide whole-body image information of patients in the context of cancer imaging and screening for metastatic disease. Standard clinical PET and PET/MRI protocols entail the computation of relative quantification parameters (e.g. SUV in PET), based on simplifying assumptions, and derived from a single pass whole-body acquisition. However, these assumptions are not always valid and several studies have shown the benefit of using absolute quantitation for the prediction and assessment of response to therapy. The computation of these quantitative parameters with a direct physiological interpretation is based on a pharmacokinetic analysis of the PET data and is usually limited by the axial field-of-view, and, thus, to a single localisation (e.g. the primary tumour). Input data for the pharmacokinetic analysis are derived from a dynamic PET acquisition over this single “bed position”. However, a more complete re-/staging of cancer patients would benefit from applying such a pharmacokinetic analysis to the whole-body.

Objective. The ESR will develop and evaluate a new data processing algorithm for the estimation of a tri-dimensional (3-D) in vivo map of a pharmacological parameter over the whole body of the patient. The data will be acquired during a dynamic whole-body Positron Emission Tomography (PET) scan with a tracer probing the pharmacological parameter of interest. Magnetic Resonance (MR) images will be acquired simultaneously to the PET data thanks to an integrated PET-MR imaging system. These complementary MR images will guide the estimation of the pharmacological parametric map. The patient data collection and the evaluation of the processing algorithm will be part of two biomedical research protocols, aiming at better understanding and predicting the therapeutic effect of pharmaceutical drugs.

Methodology. At first, a pharmacokinetic model linking the data acquired during the dynamic PET scan to the pharmacological parameter of interest will be defined. Then, an optimisation algorithm will be derived to invert the pharmacokinetic model and reconstruct the parametric map directly from the PET data. This inverse problem faces three major difficulties: (i) The problem is intrinsically ill-posed (projection tomography), hence very sensitive to the stochastic noise (Poisson process) in the PET data; (ii) The high dimensionality of the problem: a few tens of millions of parameters to be estimated for a few hundreds of millions of recorded events; (iii) Missing data: because of the limited axial aperture of the integrated PET-MR system (25 cm long), the whole body cannot be scanned simultaneously. The majority of the dynamic data are not recorded. The novelty of the research project is threefold: (i) The direct estimation of the pharmacological parameter of interest from the acquired data. Usually, it is a twostep process. First, a series of dynamic images of the PET tracer distribution within the body is reconstructed. Then, the pharmacological parameter is estimated from these dynamic images. The goal of the PhD project is to merge these two steps into a single one. (ii) The estimation of the pharmacological parameter of interest over the entire human body. Usually, this estimation is limited to a single anatomical localisation entirely covered by the scanner field-of-view. Thus, there are no missing dynamic data. (iii) The use of simultaneous MR data to help in the estimation of the pharmacological parameter of interest. Usually, PET data only are used.

Within the course of this project, secondments to GE Healthcare (Milwaukee, U.S.A.), the Medical University of Vienne (Austria) and the University Medical Center Groningen (The Netherlands) are planned.