Highlights CERIMED Newsletter N°6
April 2011

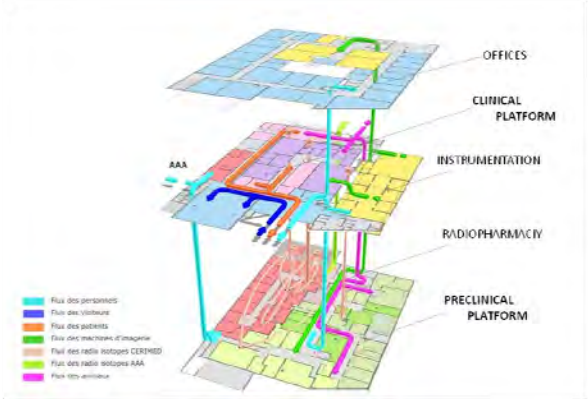
EDITORIAL

The publication of this CERIMED Newsletter n°6 has been delayed for several months. We apologize for this delay related to important recent achievements that we wanted to report on as precisely as possible. Indeed CERIMED has reached now a decisive step at several levels including infrastructure, equipments and structuring. In parallel, CERIMED has carried on its pilot research activities in the technological and clinical sectors.

1. Infrastructure and Equipment

The CERIMED project team has been very busy with the completion of the complex design of the building and the administrative work for legal authorizations. The GFC Construction group, a subsidiary of Bouygues Construction, was selected as the manager for the design-construction consortium of CERIMED that includes two architect offices: Didier Rogeon and Scott Tallon Walker, and Beterem Company for engineering.

Cad view of the CERIMED building
Courtesy of Didier Rogeon, architect



Exploded view of the CERIMED building
Courtesy of GFC

The design-construction of CERIMED is supervised by staff members from the Public Buildings of the University of the Mediterranean: Laure Dumoulin, Christine Blanc, Thierry Barontini, and Sophie-Caroline Petit under the leadership from Elisabeth Goig. Enrico De Maria represents the company Advanced Accelerator Applications (AAA), which has the responsibility to install and run the two cyclotrons and the two radiopharmaceutical laboratories of CERIMED.

The CERIMED infrastructure will be delivered by July 2012, and we hope all platforms of CERIMED to be fully operational by the end of 2012. As described in previous newsletters the CERIMED building is funded by the Public National/Regional Funding Infrastructure Plan 2007-2013 for 11.6 Million Euros. The City Hall of Marseilles (4.0 M. €), the Region (3.0 M €), and Department (2.5 M €), Councils, European Funding for Regional Development (1.6 M €) and French Government (0.5 M €) contribute to this budget.

2. Structuring

A Scientific Interest Group or GIS (Groupement d'Intérêt Scientifique) has been set up between: CNRS, "Ecole Centrale" Engineering School of Marseilles, Paoli-Calmettes Institute, « Assistance Publique Hôpitaux de Marseille » and « Université de la Méditerranée ». The Convention between these five institutions defines the rules for running CERIMED. The different partners contributions to human resources, cost of the experiments (equipments maintenance and amortization), fluids and maintenance of the building is specified in the convention. The partners of this convention are all involved in medical imaging research and development. Other partners are welcome to join the GIS following a simple procedure. The CERIMED project has been supported by two French competitive clusters ("Pôle de Compétitivité"): Optitec and Eurobiomed. CERIMED has been included now in the Centre for Innovation and Users in Health, part of a third cluster: "Solutions Communicantes Sécurisées". This label will give CERIMED an opportunity to act as a National Reference in the guidelines for medical imaging applications in medicine.

3. CERIMED projects on the way

In order to federate an international community of interest around the CERIMED action a number of technological and clinical research projects have been launched since the beginning of this initiative.Among them two technological projects are briefly described in this newsletter. They have been designed in an interdisciplinary, multi-institutional and international spirit.Clinical research in medical imaging is now organized as an axis of the Clinical Investigation Centre (CIC) of Marseilles. Thirteen protocols have been validated by the CIC Technical Committee focusing on oncology, neurosciences, and cardiovascular diseases.

CERIMED THEMATIC WORKSHOPS

1. Metabolic signature of cancers : from laboratory to clinic

Nuclear imaging using in the recent years, 18-Fluorodeoxyglucose positron emission tomography (^{18}F-FDG-PET) has gained an increasing role in the detection and follow-up of cancers. However, despite its clinical relevance, only little is known on the functional significance of this signal. For example, highly aggressive primary adrenocortical carcinomas are as ^{18}F-FDG-avid as benign pheochromocytomas. Two workshops have been organized under the direction of Dr David Taïeb (Department of Nuclear Medicine at Timone Hospital and UMR-S 624) and with the support of Cancéropole PACA.

First workshop on December 18th, 2009 Energy homeostasis is a critical determinant for cell death and survival, including cancer cells. Oxydative phosphorylation (OXPHOS) is the main source of ATP for the eukaryotic cell. By contrast, cancer cell glucose metabolism is characterized by a metabolic switch from OXPHOS to glycolysis (even under conditions of plentiful oxygen) which is far less effective in producing ATP. However, this phenotype provides a selective growth advantage for tumour cells *in vivo.* As cancer cells have very high energy

demands, they must accelerate their rate of glucose uptake. Enhanced glucose uptake can be seen with ^{18}F-FDG-PET imaging. The mechanisms for metabolic programming of cancer cells (cellular stress, acquired mitochondrial impairments and/or genetic defects involving oncogenes and tumour suppressor genes), as well as the biochemical link between glucose metabolism alterations and non-metabolic features of cancer cells such as angiogenesis, have also been discussed.

Second workshop on December 17 th,2010 Focus has been put on cancer research programs using whole-animal imaging modalities and key regulatory proteins involved in cancer-associated energy metabolism reprogramming. Preclinical steps in development of new radiopharmaceuticals and the potential role of drug delivery vehicles has been presented followed by reports on new applications of PET tracers, such as ^{18}F-Dopa in clinic.

2. Advanced Multimodality Endoscopic Instruments in the Detection, Diagnosis, Therapy, and Follow-Up of Diseases – January 14th, 2011

This seminar has been co-organized by CERIMED, Istituto Nazionale di Fiisica Nucleare (INFN) and Istituto Superiore di Sanita (ISS), Italy and West Virginia University, USA, with the additional financial and logistic support from the European Commission, Cancéropole PACA, Medical School of Marseilles and Foundation “Santé, Sport and Développement Durable” .

It took place in Marseilles Timone university hospital on January 13-14, following the FP7 EndoTOFPET-US kickoff meeting (see next paragraph). It was an opportunity for about 50 physicists, clinicians, and surgeons from several European countries and USA to meet and actively discuss about the needs for miniaturized multimodal endoscopic imaging devices for detection, diagnosis, treatment follow-up, and minimally surgery operations. Although addressing a number of clinical cases, the workshop program particularly emphasized the role of endoscopic approaches for prostatic and pancreatic cancers. Besides lively discussions about the impact of recent technological developments in the domain of scintillating crystals, photodetectors, low noise and highly integrated electronics, the increasing importance of functional and molecular imaging has been highlighted to complement the information given by morphological imaging techniques such as ultrasound and OCT (optical coherence tomography) currently in use for endoscopy. As a conclusion, it was stressed that the high sensitivity and spatial resolution from the proximity of the target allowed by endoscopic imaging systems can be seen as a real benefit for the development and validation of new and specific biomarkers for organs accessible by natural tracks.

CERIMED PROJECTS IN INSTRUMENTATION: two examples

EndoTOFPET-US

The CERIMED coordinated project: EndoTOFPET-US submitted in the last Health call of the 7th European Framework Program (HEALTH-FP4-2010-256984) has been approved for funding by the European Commission. The main objective of this project is to address image-guided diagnosis and minimally invasive surgery with a miniaturized bimodal (ultrasound and PET) endoscopic probe. The PET detector head will be a small array of 750 microns diameter heavy crystalline fibers (LuAG: Ce or similar) readout by novel ultrafast and low bias (<30V) photodetector array based on Geiger mode avalanche photodiodes. In close proximity to the organ under study (for instance the prostate, or the pancreas) this detector head, even small, covers a large solid angle and provides therefore a high sensitivity. Background rejection will be obtained by electronic collimation on the few centimeters Region Of Interest (ROI) by challenging Time of Flight (TOF) techniques (with a FWHM coincidence timing precision of 200 ps) between the endoscopic crystal head and an outer crystal array positioned external to the patient (on the belly for prostate exams). The aim is to improve harvesting of tumoural tissue during biopsy by combining the functional biological information of radioactive biomarkers with the morphological information obtained from ultrasound.

This project is coordinated by CERIMED with Prof. R. Laugier from the Timone University Hospital in Marseilles as project coordinator with the following participating institutes : Université de la Méditerranée, Aix-Marseille, France - European Organization for Nuclear Research, Geneva, Switzerland - Cantonal University hospital in Lausanne, Switzerland - Technische Universität München, Germany - University of Heidelberg, Germany - Deutsches Elektronen-Synchrotron in Hamburg, Germany - Technical University of Delft, Holland - University Milano Biccoca, Italy - Laboratório de Instrumentação e Física Experimental de Partículas in Lisbon, Portugal - Surgiceye in München, Germany - Fibercryst company in Lyon, France - Kloe company in Montpelier, France.

This project has been approved by the European Commission with a European grant of of 5.5M€ over a period of 4 years. The kick-off meeting has been organized in Timone Hospital on January 12th 2011.

ClearPEM-Sonic

The project has been fully described in CERIMED Newsletter n°4. The instrument has been set up through in collaboration between Laboratory of Instrumentation and Experimental Particles Physics (LIP), Vrije University of Brussels, University of Milan Biccoca, CERN and the company SuperSonic Imagine. The instrument has been delivered to the Department of Nuclear Medicine in North Hospital in Marseilles. The calibration program will finish by the end of April, and clinicals trials with Clear PEM- Sonic are scheduled on the second trimester of 2011 by Doctor Laurent Tessonnier from Professor Olivier Mundler's department.

CERIMED PUBLICATIONS

1. Performance in recognition memory is correlated with entorhinal / perirhinal interictal metabolism in temporal lobe epilepsy. Guedj E, Barbeau EJ, Liégeois-Chauvel C, Confort-Gouny S, Bartolomei F, Chauvel P, Cozzone PJ, Ranjeva JP, Mundler O, Guye M.
Epilepsy & Behavior. 2010;19:612-7

2. Déjà-vu in temporal lobe epilepsy: metabolic pattern of cortical involvement in patients with normal brain MRI.Guedj E, Aubert S, McGonigal A, Mundler O, Bartolomei F.
Neuropsychologia. 2010;48:2174-81

3. Partially reversible cortical metabolic dysfunction in familial hemiplegic migraine with prolonged aura.Guedj E, Belenotti P, Serratrice J, Ene N, Pineau S, Donnet A, Mundler O, Weiller PJ.
Headache. 2010;50:872-7

4. Could clinical profile influence CSF biomarkers in early onset Alzheimer disease. Koric L*, Félician O, Guedj E, Huvert AM, Mancini J, Boucraut J, Ceccaldi M.
Alzheimer Disease & Associated Disorders. 2010;24:278-83.

5. Shear wave elastography: a new ultrasound imaging mode for the differential diagnosis of benign and malignant thyroid nodules.Sebag F, Vaillant-Lombard J, Berbis J, Griset V, Henry JF, Petit P, Oliver C.
J Clin Endocrinol Metab. 2010 ,95;5281-8;.

6. Long-term consolidation of declarative memory: Insight from temporal lobe epilepsy. Tramoni E, Felician O*, Barbeau EJ, Guedj E, Guye M, Bartolomei F, Ceccaldi M.
Brain. In press**.**

Congratulations to Christian Morel

A multinational collaboration known as OpenGATE has been awarded the 2009 *Physics in Medicine & Biology* (PMB) Citations Prize for the research paper "GATE: a simulation toolkit for PET and SPECT". The annual prize is presented to the authors of the PMB research paper that received the most citations in the preceding five years (according to ISI). The winning article, which has received over 200 citations since its publication in 2004, describes the design and development of GATE – the Geant4 Application for Tomographic Emission. GATE exploits the comprehensive modelling capabilities of the Geant4 package, but adapted specifically for use within nuclear medicine. The result: a modular, scripted toolkit for intuitive configuration of PET and SPECT simulations.

The PMB citations prize was marked with the presentation of the Rotblat medal to Morel. The medal, named in honour of Professor Sir Joseph Rotblat (PMB's second and longest serving editor), was awarded at a recent OpenGATE meeting in Orsay, France. Christian Morel is Professor at the University of Mediterranean Sea, and he is doing his research at the Centre for Particule Physics in Marseilles (UMR 6550). He is very active in the CERIMED project team and he shares with Paul Lecoq the leadership of its Technological sector.

News from the CERIMED Coordination

Mrs Michèle Seyer has joined the CERIMED team on May 2010 as the new assistant manager of CERIMED. She has been recruited at the University after being in charge of the administration of scientific offices in French embassies in Africa. She was in charge of the organization of the second cycles of education in the Medical School.

Mrs Isabelle Halgand, the previous assistant manager of CERIMED, has joined the Foundations teams of our University. We are grateful for the quality of her work and her investment in the management of the CERIMED at its early stages.

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POSITION OPENING

The CERIMED is hiring a top qualified researcher in medical imaging to fill a full first class professor position at the "Université de la Méditerranée". Professorship deals primarily with CERIMED coordination and research/teaching in medical imaging.

- Primary job responsibilities will include

  . Direction of the CERIMED which is composed of four platforms : radiopharmaceutical, (with a convention with Advanced Accelerators Applications), technological, clinical and preclinical imaging.
  . Contribution to significant research/development progress with the Clinical Imaging Departments (CIC) of Marseilles University Hospitals.
  . Teaching in medical imaging (basics and applications).

- Required qualifications

  The candidate must be internationally recognized in her/his medical imaging field.
  . PhD in Physics, Biology or Human Pathology
  . MD or Pharmacists with at least 10 years experience in leading research program in medical imaging.

  Additional salary from the University Hospital may be offered.
  Want to apply job ?, then follow the link below for further instructions.

  Agenda :
  . Deadline for registration : May 24th 2011 (application form on : www.galaxie.enseignementsup-recherche), available from April 28 th 2011

  . Selection and audition of candidate : September 2011.

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