TRIMAGE

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A dedicated trimodality (PET/MR/EEG) imaging tool for schizophrenia

TRIMAGE in brief

TRIMAGE aims to create a trimodal, cost-effective imaging tool consisting of PET/MR/EEG using cutting edge technology with performance beyond the state of the art. The tool is intended for broad distribution to enable effective early diagnosis of schizophrenia and possibly other mental health disorders.

Schizophrenia is a severe mental disorder, characterised by profound disruptions in thinking, affecting language, perception, and the sense of self. It often includes psychotic experiences, such as hearing voices or delusions. Schizophrenia disorders manifest themselves early in life during very active life periods of education and productive work and can impair functioning through the loss of an acquired capability to earn a livelihood, or the disruption of studies. This causes a high social and economic burden on European societies. In most of the cases, if correctly diagnosed, schizophrenia can be treated, and people who are affected can lead a productive life and be integrated in society.

Schizophrenia is usually studied using a translational approach: psychological, social and biological parameters are acquired and analysed together, but the early diagnosis still remains a critical challenge. The clinical impact of conventional off-line combination of data acquired separately with different modalities is limited, because several correlated patient-specific signals may vary over time, thus making the biomarkers elusive. Moreover, schizophrenic patients are not suited for long and repeated diagnostic sessions, thus making “one stop shop” solutions highly demanded.

TRIMAGE covers the need for a new imaging tool that facilitates the diagnosis of schizophrenia early during the development. By fully integrating different diagnostic modalities into a seamless clinical tool, it allows the application of multi-parametric measurements on a routine basis in all schizophrenia patients. In addition, the TRIMAGE system could be used for the simultaneous PET/MR study of other mental health disorders and brain diseases in general, including cancer.

The Consortium

The project is coordinated by the department of physics of the University of Pisa and it is run by a European consortium of five universities, two research institutes and four small and medium enterprises:

- Department of Physics of the University of Pisa (Italy)
- Technological Educational Institute of Athens (Greece)
- Forschungszentrum Juelich GmbH (Germany)
- JARA BRAIN, Department of Psychiatry, Psychotherapy and Psychosomatics, RWTH, Aachen (Germany)
- Technische Universität Munich (Germany)
- Department of Psychiatry, Psychotherapy and Psychosomatics, University of Zurich (Switzerland)
- Istituto Nazionale di Fisica Nucleare, Sezione di Torino (Italy)
- AdvanSiD (Italy)
- WeeROC (France)
- Raytest GmbH (Germany)
- RS2D (France)
Objectives

The main objectives of this project are:

A. To build and optimise an integrated diagnostic solution including a molecular imaging tool based on simultaneous Positron Emission Tomography (PET), Magnetic Resonance (MR) and Electroencephalography (EEG);

B. To install the PET/MR/EEG system in a clinical facility. The selected location is Pisa where the installation will be done during 2018 at the AUOP (Azienda Universitaria Ospedaliera Pisana).

C. To validate the new tool with a pilot study including patients affected by various brain disorders. To study specific biomarkers for detecting characteristic patterns in asymptomatic and at-risk schizophrenic patients so as to corroborate the validity of the tri-modality approach.

D. To provide a cost-effective imaging tool for broad distribution for diagnosis of mental and

Preliminary results

MRI - The system integration along with the cryogen-free 1.5 T magnet has been completed and tested. The MRI pulse sequence and protocol are currently under construction.

PET - Monte Carlo simulations of the system have been performed and design is finalised - First results with brain phantoms achieved.

Attenuation and motion corrections are completed. PET image reconstruction, partial volume and scatter corrections, kinetic analysis and parametric reconstruction are about to be completed.

PRELIMINARY CLINICAL STUDY - Recruitment of subjects and testing the new paradigms on existing systems have been performed: 62 subjects (38 schizophrenic patients/24 controls) have been scanned with a Siemens mMR at the Technische Universitat Munich and their data are being analysed. The examination software has been developed to include patient data, study information, PET control, pre-processing and acquisition parameters and reconstruction parameters.

The figure to the right shows a reconstructed PET image (65-70 min.) overlaid on T1w (top) and net influx rate (min⁻¹) parametric map overlaid on T1w (bottom) with [18F]-FDOPA-PET.

The TRIMAGE project will be completed in November 2018.
Key technological advances

TRIMAGE introduces scientific advances in several fields and has produced series of cutting-edge technologies that were specifically developed for this project.

1. First 1.5 T cryogen-free MRI scanner large enough to scan a human head.
2. First fully integrated brain imaging PET scanner which doubles the sensitivity of state of the art clinical PET/ MRI systems, 2 mm spatial resolution and DOI capability.
3. First commercial application of the custom developed 64 channels TRIROC ASICs for SiPM readout.
4. First fully digital PET front-end able to sense directly coupled LYSO crystals with individual SiPMs.
5. First frequency selective RF shields to minimise interferences between PET and MRI.

IP portfolio

During the development of TRIMAGE, particular attention has been paid on exploiting the most valuable intellectual properties available to the Consortium. At the same time, most of the intellectual property value used in the TRIMAGE project comes from the Consortium itself through proprietary sensors, electronics and software tools. Having the full control of the used technologies, the Consortium is able to offer a dedicated imaging product with a very high added value. In addition, having in-depth knowledge of all the development and implementation details, the Consortium can guarantee long term plans for further improvements and product evolution and maintenance.

Applications

Neurology

With three modality in one, a more complete view of brain functionality and anatomy can be obtained in a fraction of the time. Clinical applications on neurology of the TRIMAGE scanner include early diagnosis of neurodegenerative diseases (Alzheimer, Parkinson etc.) and mental disorders (depression, schizophrenia, etc.). With such an instrument patients can be more carefully selected for treatment and longitudinal studies can be done to monitor the clinical outcome of the therapy.

Oncology

With its superior performance, the application of TRIMAGE to clinical oncology could favour an earlier diagnosis and better staging of solid brain tumours. For the lower dose to the patient with respect to standard PET/CT systems, more frequent patient scans are possible with crucial benefits during treatment planning and follow up, especially for brain tumours in children.

Research

The multimodality allows to directly and simultaneously investigate the activity of neurotransmitters along with the activity and connectivity of a brain region. This combined assessment will open new understandings of brain function in both healthy and mental ill persons. The directly combined application of new PET molecular probes with fMRI measuring brain function to map the distribution and synergic function of receptors will form the basis of a new area of research in today’s rapidly increasing insight in brain function.
Clinical benefits

The clinical impact derived from the combination of molecular imaging with anatomic imaging is clearly superior to the simple arithmetic sum of the two separate components. In addition to conventional PET/CT solutions, PET/MRI allows for: a) less dose/less scan time for a given image quality; b) better soft tissue contrast (critical for brain studies).

TRIMAGE provides unique clinical advantages also within the field of PET/MRI imaging: a) PET has twice the sensitivity of state of the art alternatives, hence it further reduces the administered dose and/or scan time; b) it is less claustrophobic (i.e., a critical issue in schizophrenic patients); c) it uses no cryogenic liquids, thus allowing for multimodal PET/MRI imaging in a conventional nuclear medicine facility and in general easing installation and maintenance.

The reduced production and installation cost make the TRIMAGE system the most cost-effective diagnosis tool for brain disorders at the state of the art and makes it also economically sustainable for the hospital centres.

Market opportunities

The worldwide nuclear medicine imaging market for PET and SPECT equipment is on track to produce $2.2 billion in revenues by 2020, with larger growths expected in far eastern countries. The SPECT and SPECT/CT markets are still larger than the PET, PET/CT, and PET/MRI markets mainly because these scanners are cheaper, and their use has become routine for a wide range of indications. However, physicians believe that many SPECT techniques will ultimately be replaced by PET procedures. Developments in hybrid PET/MR imaging are also expected to increase demand in the near future, especially in the brain domain.

The PET/MRI market is largely dominated by big players (Siemens, GE, Philips), who offer general purpose whole-body solutions. However, the specificity of PET/MR imaging makes brain imaging one of the the major applications. TRIMAGE aims at taking advantage of this scenario by providing a unique technological solution dedicated to the brain, thus cutting the production, installation, maintenance and exploitation costs, in the interest of patient diagnosis, prognosis and care.

Scientific Coordinator: Prof. Alberto DEL GUERRA, University of Pisa, alberto.delguerra@df.unipi.it
Project Office: trimage_po@df.unipi.it  Web site: www.trimage.eu