IN PARTNERSHIP WITH:
CNRS

INSERM

Université Rennes 1

Activity Report 2016

Project-Team VISAGES

Vision, Action and information manaGement System in health

IN COLLABORATION WITH: Institut de recherche en informatique et systèmes aléatoires (IRISA)

RESEARCH CENTER
Rennes - Bretagne-Atlantique

THEME
Computational Neuroscience and Medecine

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Creation of the Project-Team: 2005 July 04

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1. Members

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2. Overall Objectives

2.1. Overall objectives

Medical Imaging, Neuroinformatics, Neuroimaging, Medical Image Computing, Modeling of normal and pathological behavior of the human brain, e-health & HealthGrids

The Unit/Project VISAGES U746 is a research team jointly affiliated to INSERM (National Institute of Health and Scientific Research), Inria (National Institute of Research in Computer Sciences and Automation) and IRISA / UMR CNRS 6074, University of Rennes I. We are located in Rennes, France on both medical and sciences campus. The team has been created in 2005. Our ambition is to set up a multidisciplinary team merging researchers in image processing and medical doctors. The goal of VISAGES is to constitute a multidisciplinary team. Even though, research in medical imaging could find motivation and recognition based on methodological breakthroughs alone, the ultimate goal, when dealing with medical imaging research, is to make the clinical practice benefit from the basic and applied research, while keeping the excellence of the methodological research. This objective entails the creation of teams encompassing clinical and scientific researchers to design and conduct research projects together. Our aim through the past period was to build a research team able to perform a research going from a novel and basic stage to original clinical experimentation with clear medical impact.

Our research activities are focused on the research and development of new algorithms in medical imaging in the context of the pathologies of the central nervous system. In this context, we are addressing the general problems of the better understanding of normal and pathological brain organs and systems behavior, at different scales, and the promotion and the support of Virtual Organizations of biomedical actors by means of healthgrid's technologies. The medical application objectives are focused on pathologies of the central nervous system, with a particular effort on extraction of new imaging biomarkers for brain pathologies (e.g. Multiple Sclerosis, neuropaediatrics, strokes, psychiatry, ...). More generally, our application objectives concern the following diseases: Multiple sclerosis, epilepsy, dementia, neuro-degenerative brain diseases, brain vascular diseases.

3. Research Program

3.1. Research Program

The scientific foundations of our team concern the development of new processing algorithms in the field of medical image computing : image fusion (registration and visualization), image segmentation and analysis, management of image related information. Since this is a very large domain, which can endorse numerous types of application; for seek of efficiency, the purpose of our methodological work primarily focuses on clinical aspects and for the most part on head and neck related diseases. In addition, we emphasize our research efforts on the neuroimaging domain. Concerning the scientific foundations, we have pushed our research efforts:

- In the field of image fusion and image registration (rigid and deformable transformations) with a special emphasis on new challenging registration issues, especially when statistical approaches based on joint histogram cannot be used or when the registration stage has to cope with loss or appearance of material (like in surgery or in tumor imaging for instance).
- In the field of image analysis and statistical modeling with a new focus on image feature and group analysis problems. A special attention was also to develop advanced frameworks for the construction of atlases and for automatic and supervised labeling of brain structures.
- In the field of image segmentation and structure recognition, with a special emphasis on the difficult problems of *i*) image restoration for new imaging sequences (new Magnetic Resonance Imaging protocols, 3D ultrasound sequences...), and *ii*) structure segmentation and labelling based on shape, multimodal and statistical information.
- Following the Neurobase national project where we had a leading role, we wanted to enhance the development of distributed and heterogeneous medical image processing systems.

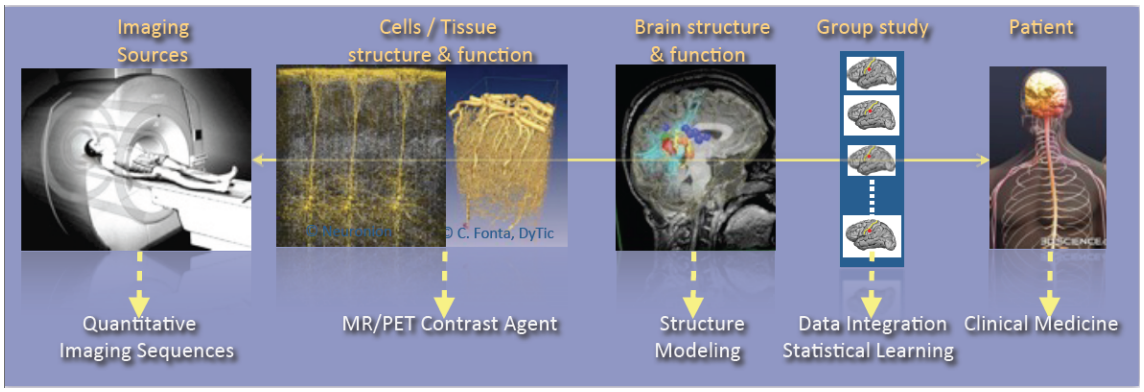

Figure 1. The major overall scientific foundation of the team concerns the integration of data from the Imaging source to the patient at different scales: from the cellular or molecular level describing the structure and function, to the functional and structural level of brain structures and regions, to the population level for the modelling of group patterns and the learning of group or individual imaging markers.

As shown in Fig. 1, research activities of the VISAGES U746 team are tightly coupling observations and models through integration of clinical and multi-scale data, phenotypes (cellular, molecular or structural patterns). We work on personalized models of central nervous system organs and pathologies, and intend to confront these models to clinical investigation studies for quantitative diagnosis, prevention of diseases, therapy planning and validation. These approaches are developed in a translational framework where the data integration process to build the models inherits from specific clinical studies, and where the models are assessed on prospective clinical trials for diagnosis and therapy planning. All of this research activity is conducted in tight links with the Neurinfo imaging platform environments and the engineering staff of the platform. In this context, some of our major challenges in this domain concern:

- The elaboration of new descriptors to study the brain structure and function (e.g. variation of brain perfusion with and without contrast agent, evolution in shape and size of an anatomical structure in relation with normal, pathological or functional patterns, computation of asymmetries from shapes and volumes).
- The integration of additional spatio-temporal imaging sequences covering a larger range of observation, from the molecular level to the organ through the cell (Arterial Spin Labeling, diffusion MRI, MR relaxometry, MR cell labeling imaging, PET molecular imaging, ...). This includes the elaboration of new image descriptors coming from spatio-temporal quantitative or contrast-enhanced MRI.
- The creation of computational models through data fusion of molecular, cellular, structural and functional image descriptors from group studies of normal and/or pathological subjects.
- The evaluation of these models on acute pathologies especially for the study of degenerative, psychiatric or developmental brain diseases (e.g. Multiple Sclerosis, Epilepsy, Parkinson, Dementia, Strokes, Depression, Schizophrenia, ...) in a translational framework.

In terms of methodological developments, we are particularly working on statistical methods for multidimensional image analysis, and feature selection and discovery, which includes:

- The development of specific shape and appearance models, construction of atlases better adapted to a patient or a group of patients in order to better characterize the pathology;
- The development of advanced segmentation and modeling methods dealing with longitudinal and

multidimensional data (vector or tensor fields), especially with the integration of new prior models to control the integration of multiscale data and aggregation of models;

- The development of new models and probabilistic methods to create water diffusion maps from MRI;
- The integration of machine learning procedures for classification and labeling of multidimensional features (from scalar to tensor fields and/or geometric features): pattern and rule inference and knowledge extraction are key techniques to help in the elaboration of knowledge in the complex domains we address;
- The development of new dimensionality reduction techniques for problems with massive data, which includes dictionary learning for sparse model discovery. Efficient techniques have still to be developed to properly extract from a raw mass of images derived data that are easier to analyze.

4. Application Domains

4.1. Neuroimaging

One research objective in neuroimaging is the construction of anatomical and functional cerebral maps under normal and pathological conditions. Many researches are currently performed to find correlations between anatomical structures, essentially sulci and gyri, where neuronal activation takes place, and cerebral functions, as assessed by recordings obtained by the means of various neuroimaging modalities, such as PET (Positron Emission Tomography), fMRI (Functional Magnetic Resonance Imaging), EEG (Electro-EncephaloGraphy) and MEG (Magneto-EncephaloGraphy). Then, a central problem inherent to the formation of such maps is to put together recordings obtained from different modalities and from different subjects. This mapping can be greatly facilitated by the use of MR anatomical brain scans with high spatial resolution that allows a proper visualization of fine anatomical structures (sulci and gyri). Recent improvements in image processing techniques, such as segmentation, registration, delineation of the cortical ribbon, modeling of anatomical structures and multi-modality fusion, make possible this ambitious goal in neuroimaging. This problem is very rich in terms of applications since both clinical and neuroscience applications share similar problems. Since this domain is very generic by nature, our major contributions are directed towards clinical needs even though our work can address some specific aspects related to the neuroscience domain.

4.2. Multiple sclerosis

Over the past years, a discrepancy became apparent between clinical Multiple sclerosis (MS) classification describing on the one hand MS according to four different disease courses and, on the other hand, the description of two different disease stages (an early inflammatory and a subsequently neurodegenerative phase). It is to be expected that neuroimaging will play a critical role to define in vivo those four different MS lesion patterns. An in vivo distinction between the four MS lesion patterns, and also between early and late stages of MS will have an important impact in the future for a better understanding of the natural history of MS and even more for the appropriate selection and monitoring of drug treatment in MS patients. MRI has a low specificity for defining in more detail the pathological changes which could discriminate between the different lesion types. However, it has a high sensitivity to detect focal and also widespread, diffuse pathology of the normal appearing white and gray matter. Our major objective within this application domain is then to define new neuroimaging markers for tracking the evolution of the pathology from high dimensional data (e.g. nD+t MRI) in the brain and the spinal cord. In addition, in order to complement MR neuroimaging data, we ambition to perform also cell labeling neuroimaging (e.g. MRI or PET) and to compare MR and PET data using standard and experimental MR contrast agents and radiolabeled PET tracers for activated microglia (e.g. USPIO or PK 11195). The goal is to define and develop, for routine purposes, cell specific and also quantitative imaging markers for the improved in vivo characterization of MS pathology.

4.3. Modeling of anatomical and anatomo-functional neurological patterns

The major objective within this application domain is to build anatomical and functional brain atlases in the context of functional mapping and for the study of developmental, neurodegenerative or even psychiatric brain diseases (Multiple sclerosis, Epilepsy, Parkinson, Dysphasia, Depression or even Alzheimer). This is a very competitive research domain; our contribution is based on our previous works in this field, and by continuing our local and wider collaborations.

An additional objective within this application domain is to find new descriptors to study the brain anatomy and/or function (e.g. variation of brain perfusion, evolution in shape and size of an anatomical structure in relation with pathology or functional patterns, computation of asymmetries ...). This is also a very critical research domain, especially for many developmental or neurodegenerative brain diseases.

5. Highlights of the Year

5.1. Highlights of the Year

5.1.1. Awards

- In 2015, the Neurinfo platform obtained an “Emergence” label from the IBISA agency, this label has been upgraded in 2016 as a “platform of Excellence” and sustained by IBISA in 2016 and onward. The IBISA label is a national label for technological platforms awarded by the GIS IBISA on an annual basis.

6. New Software and Platforms

6.1. Anima

KEYWORDS: Filtering - Medical imaging - Diffusion imaging - Registration - Relaxometry
SCIENTIFIC DESCRIPTION: Anima is a set of libraries and tools developed by the team as a common repository of research algorithms. As of now, it contains tools for image registration, statistical analysis (group comparison, patient to group comparison), diffusion imaging (model estimation, tractography, etc.), quantitative MRI processing (quantitative relaxation times estimation, MR simulation), image denoising and filtering, and segmentation tools. All of these tools are based on stable libraries (ITK, VTK), making it simple to maintain.

- Participants: Olivier Commowick, Rene-Paul Debroize, Florent Leray and Renaud Hédouin
- Contact: Olivier Commowick
- APP number: IDDN.FR.001.460020.000.S.P.2015.000.31230
- URL: https://github.com/Inria-Visages/Anima-Public/wiki

6.2. MedInria

KEYWORDS: Segmentation - Health - DWI - Visualization - Medical imaging
SCIENTIFIC DESCRIPTION: It aims at creating an easily extensible platform for the distribution of research algorithms developed at Inria for medical image processing. This project has been funded by the D2T (ADT MedInria-NT) in 2010 and renewed in 2012. The VisAGeS team leads this Inria national project and participates in the development of the common core architecture and features of the software as well as in the development of specific plugins for the team’s algorithm.

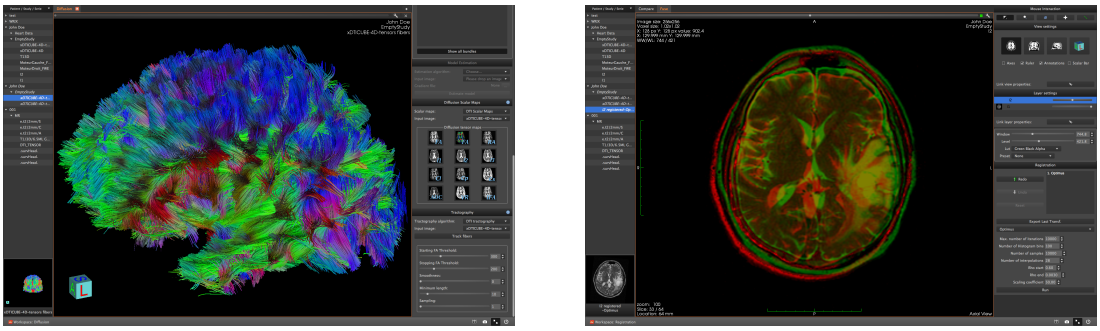

Figure 2. The medInria software platform: Tractography overlapped with 3D image (left), and Fused view of registered images (right).

FUNCTIONAL DESCRIPTION: MedInria is a free software platform dedicated to medical data visualization and processing as illustrated in Fig. 2.

- Participants: Olivier Commowick and Rene-Paul Debroize
- Partners: HARVARD Medical School - IHU - LIRYC - IHU - Strasbourg - NIH
- Inria structures involved : ASCLEPIOS, ATHENA, PARIETAL, VISAGES
- Contact: Olivier Commowick
- URL: http://med.inria.fr
- APP number: IDDN.FR.001.130017.000.S.A.2012.000.31230

6.3. Shanoir

SHAring NeurOImaging Resources
KEYWORDS: Shanoir - Webservices - Data base - Biology - Health - DICOM - Neuroimaging - Medical imaging - PACS - Nifti - Data Sharing - Web Application
FUNCTIONAL DESCRIPTION: SHAring NeurOImaging Resources (Shanoir, Previously InriaNeuroTk) is an open source software platform designed to structure, manage, archive, visualize and share neuroimaging data with an emphasis on multi-centric collaborative research projects. It provides common features of neuroimaging data management systems along with research-oriented data organization and enhanced accessibility (see Fig. 3).

Shanoir is a secured J2EE application running on a JBoss server, reachable via graphical interfaces in a browser or by third party programs via web services. It behaves as a repository of neuroimaging files coupled with a relational database hoding meta-data. The data model, based on OntoNeurolog, an ontology devoted to the neuroimaging field, is structured around research studies where of involved patients have examinations which either produce image acquisitions or clinical scores. Each image acquisition is composed of datasets represented by their acquisition parameters and image files. The system only keeps anonymous data.

Image files imports are possible from various sources (DICOM CDs, PACs, image files in NIfTI / Analyze format) using either online wizards, with completions of related meta-data, or commande line tools. Once de-identified during the import phase, DICOM header's customizable feature. Shanoir can also record any executed processing allowing to retrieve workflows applied to a particular dataset along with the intermediate data.

The clinical scores resulting from instrument based assessments (e.g. neuropsychological tests) can also be entered and easily retrieved and exported in different formats (Excel, CSV, Xml). Scores and image acquisitions are bound together which makes relationship analysis possible. The instrument database is scalable an new measures can be added in order to meet specific project needs, by use of intuitive graphical interfaces.

Using cross-data navigation and advanced search criteria, the users can quickly point to a subset of data to be downloaded. Client side applications have as well been developed to illustrate how to locally access and exploit data through the available web services. With regards to security, the system requires authentication and user rights are tunable for each hosted studies. A study responsible can thereby define the users allowed to see, download or import data into his study or simply make it public.

Shanoir serves neuroimaging researchers in organizing efficiently their studies while cooperating with other laboratories. By managing patient privacy, Shanoir allows the exploitation of clinical data in a research context. It is finally a handy solution to publish and share data with a broader community.

Shanoir integrates the enterprise search platform, Apache Solr, to provide the users a vast array of advanced features such as near real-time indexing and queries, full-text search, faceted navigation, autosuggestion and autocomplete.

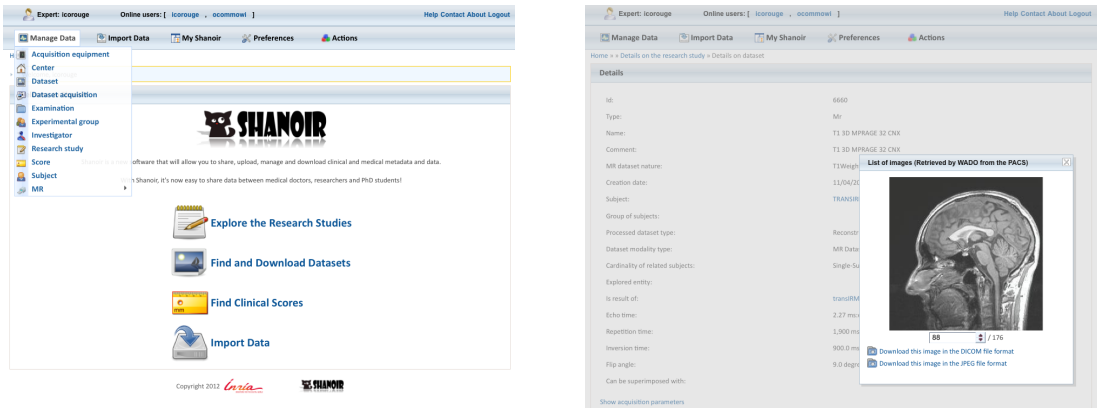

Figure 3. The SHANOIR software is a web application to share, archive, search and visualize neuroimaging data.

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- Partners: CNRS - INSERM - Université de Rennes 1
- Contact: Christian Barillot
- URL: http://shanoir.gforge.inria.fr
- APP number: IDDN.FR.001.520021.003.S.A.2008.000.31230 (2014/08/20)

6.4. QtShanoir

KEYWORDS: Shanoir - Qt - Webservices - Soap - C++ - Health - DICOM - Plug-in - Medical imaging - Nifti

SCIENTIFIC DESCRIPTION: QtShanoir is based on Qt/C++ librairie. It interacts with the Shanoir server using SOAP web services provided. This application queries the server and displays hierarchical data extracted in tree view. Data could also be easily downloaded or uploaded on the server. In order to extend the Shanoir environment, QtShanoir is developed to contain two shared libraries:

- "GUI" that represents all user interfaces.
- "DAO" that takes in charge the data model. This library assures the connection to the server and provides all QtShanoir services : research, download and upload of Processed Dataset (NIfTI).

QtShanoir dynamic libraries are already reused and integrated in other projects: in the software medInria and in an under development command line program.
FUNCTIONAL DESCRIPTION: QtShanoir is a graphical client application of the medical imaging database Shanoir. This application provides various functionalities to satisfy researchers' needs. It allows users to:

- explore neuroimaging data derived from multicenter research trials. Through an intuitive user interface, users could easily visualize voluminous amount of structured data: studies, patients and datasets extracted from Shanoir
- download and to upload data from the server.

This application is available on Windows, UNIX, MacOs X. It is integrated as a plugin in medInria, a multi-plateform for medical image processing and visualization.

- Participants: Olivier Commowick and Florent Leray
- Contact: Christian Barillot
- URL: http://qtshanoir.gforge.inria.fr
- APP number: IDDN.FR.001.130017.000.S.A.2012.000.31230 (2012/02/08)

6.5. ShanoirUploader

KEYWORDS: Shanoir - Webservices - Java - Biology - Health - DICOM - Neuroimaging - Medical imaging - PACS
SCIENTIFIC DESCRIPTION: ShanoirUploader is a desktop application on base of JavaWebStart (JWS). The application can be downloaded and installed using an internet browser. It interacts with a PACS to query and retrieve the data stored on it as illustrated in Fig. 4. After this ShanoirUploader sends the data to a Shanoir server instance in order to import these data. This application bypasses the situation, that in most of the clinical network infrastructures a server to server connection is complicated to set up between the PACS and a Shanoir server instance.
FUNCTIONAL DESCRIPTION: ShanoirUploader is a Java desktop application that transfers data securely between a PACS and a Shanoir server instance (e.g., within a hospital). It uses either a DICOM query/retrieve connection or a local CD/DVD access to search and access images from a local PACS or the local CD/DVD. After having retrieved the data, the DICOM files are locally anonymized and then uploaded to the Shanoir server. A possible integration of a hash creation application for patient identifiers is provided as well. The primary goals of that application are to enable mass data transfers between different remote server instances and therefore reduce the waiting time of the users, when importing data into Shanoir. Most of the time during import is spent with data transfers.

- Participants: Michael Kain, Inès Fakhfakh and Christian Barillot
- Contact: Christian Barillot
- URL: http://shanoir.gforge.inria.fr
- APP number: IDDN.FR.001.380026.000.S.P.2015.000.31230 (2015/09/11)

6.6. iShanoir

KEYWORDS: Shanoir - Biology - Health - Neuroimaging - Mobile application - Medical imaging - Biomedical imaging

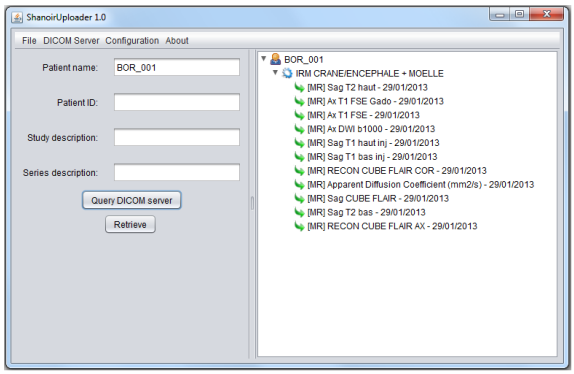

Figure 4. The ShanoirUploader software is a desktop application designed to interact with a PACS to query and retrieve the data stored on any PACS.

FUNCTIONAL DESCRIPTION iShanoir is an iOS application, designed for iPhone and iPad. On base of this application a Shanoir server can be accessed as illustrated in Fig. 5. For this the Shanoir SOAP web-services are called. iShanoir can be used to access and navigate in the data tree structure, stored on a Shanoir server. iShanoir displays as well additional meta data corresponding to the data entities in the tree structure. On base of these informations image files (NIfTI and DICOM) can be selected and downloaded on a local iPhone/iPad in a temporary cache. From this cache the files can be opened and displayed with a corresponding viewer, the user already has to have installed on his device.

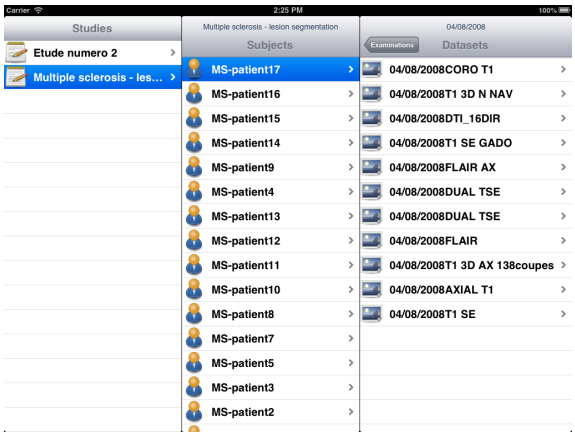

Figure 5. The iShanoir interface, showing the browsing tabs within the research studies stored in the Shanoir database.

- Participants: Michael Kain and Christian Barillot
- Contact: Christian Barillot
- URL: http://shanoir.gforge.inria.fr

6.7. autoMRI

KEYWORDS: FMRI - MRI - ASL - FASL - SPM - Automation
SCIENTIFIC DESCRIPTION: Automri is an analysis pipeline to process morphological, perfusion, BOLD fMRI, relaxometry and neurovascular data. This software is highly configurable in order to fit to a wide range of needs. Pre-processing includes segmentation of anatomical data, as well as co-registration, spatial normalization and atlas building of all data types. The analysis pipelines perform either within-group analysis or between-group or one subject-versus-group comparison and produce statistical maps of regions with significant differences. These pipelines can be applied to structural data to exhibit patterns of atrophy or lesions, to ASL (both pulsed or pseudo-continuous sequences) or PET data to detect perfusion or metabolic abnormalities, to relaxometry data to detect deviations from a template, to functional data - either BOLD or ASL - to outline brain activations related to block or event-related paradigms. In addition to the standard General Linear Model approach, the ASL pipelines implement an a contrario approach and, for patient-specific perfusion study, an heteroscedastic variance model. Besides, the vascular pipeline processes 4D MRA data and enables accurate assessment of hemodynamic patterns.
FUNCTIONAL DESCRIPTION: Based on MATLAB and the SPM8 toolbox, autoMRI provides complete pipelines to pre-process and analyze various types of images (anatomical, functional, perfusion, metabolic, relaxometry, vascular).

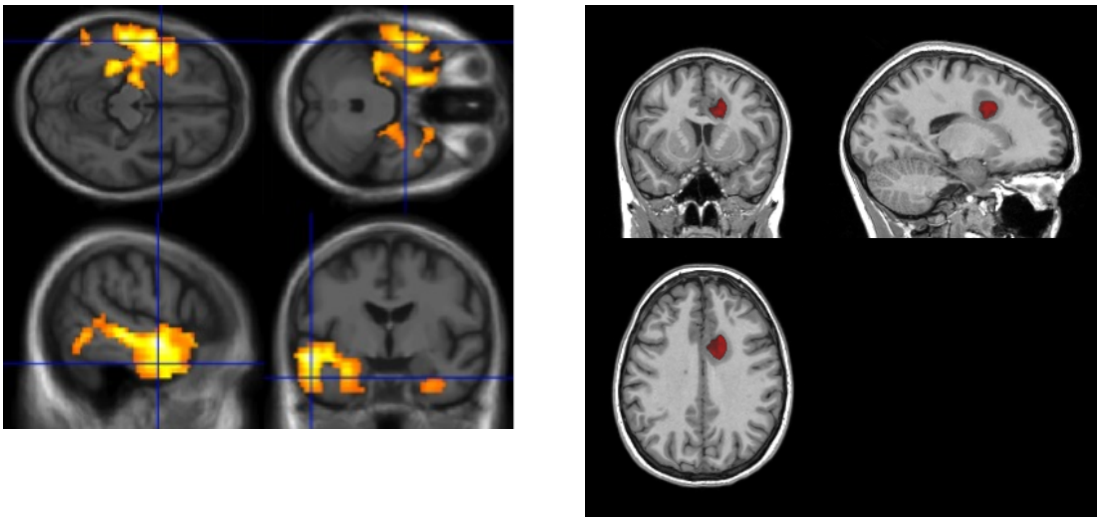

Figure 6. Illustrations of results obtained with autoMRI: Conjunction map showing areas of hypoperfusion and hypometabolism in semantic dementia (left) and detection of relaxometry defect in an MS patient (right).

- Participants: Isabelle Corouge, Quentin Duché, Cédric Meurée, Pierre Maurel and Élise Bannier.
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- URL: http://www.irisa.fr/visages/
- APP number: Part in IDDN.FR.001.130017.000.S.A.2012.000.31230

6.8. Integration of EEG and fMRI

KEYWORDS: medical imaging - EEG - fMRI

FUNCTIONAL DESCRIPTION: Related to the project Hemisfer there have been development of new functions, scripts and demos for the acquisition and processing of the EEG and fMRI data in Real-time. These include:

- Functions for fMRI header info reader, volume reader, motion correction, slice time correction nifty output conversion, real time fMRI initialization, real time fMRI processing, z-score calculation, volume smoother, alignment, etc., functions for real time EEG data acquisition, filtering, power calculation and display.
- Scripts for various protocols used in offline fMRI experiments, real time processing loop for EEG and fMRI.
- Demo for real time acquisition of the EEG and fMRI data, demo for real time processing efficiency of the fMRI data, demo for the real time processing of EEG data, real time z-Score for fMRI data.
- Several small aux functions for I/O interfaces (e.g. com, serial)

In the current stage the prototype also relies on various other free toolboxes (e.g. SPM, pnet).

- Participants: Marsel Mano, Lorraine Perronnet, Anatole Lecyuer, Christian Barillot.
- Contact: Marsel Mano
- International Patent Number: PCT/EP2016/1652279

6.9. Platforms

6.9.1. The Neurinfo Platform

VisAGeS is the founding actor of an experimental research platform which was installed in August 2009 at the University Hospital of Rennes. The University of Rennes 1, Inria, Inserm for the academic side, and the University Hospital of Rennes and the Cancer Institute "Eugene Marquis" for the clinical side, are partners of this neuroinformatics platform called Neurinfo [1]. This platform has been supported under the "Contrat de Projets Etat-Région" (Christian Barillot is the PI) and has received a total amount of 4.01 M€ for the period 2007–2014. European (FEDER), National (through Ministry of research, Inria, Inserm and ANR) and local councils (Brittany Region, Ille et Vilaine, and Rennes Metropole) have joined their effort to support this operation for a total amount of 4 010 k€ (600 k€ for the infrastructures, 2 850 k€ for the equipments and 560 k€ for the functioning). This application was set up through the Regional PIMATGI initiative coordinated by INSERM in Brittany (C. Roux). The overall PIMATGI initiative served for the financing of three distinct, but complementary, platforms: Neurinfo, TheraFONC as a technical platform dedicated to therapy guided by functional imaging especially in the oncology domain (Inserm U650 - LaTIM, Dir. Ch. Roux, Brest), and TherA-Image as a platform dedicated to image guided mini-invasive surgery and therapy especially in the domain of cardio-vascular diseases (U642 -LTSI, Dir. L. Senhadji, Rennes).

Concerning the Neurinfo Platform, the activity domain is a continuum between methodological and technological research built around specific clinical research projects. The ambition is to do innovation in science, technology and medical technology transfer for the implementation on the clinical field. On the medical field, the translational research domain mainly concerns medical imaging and more specifically the clinical neurosciences. Among them are multiple sclerosis, epilepsy, neurodegenerative, neurodevelopmental and psychiatric diseases, surgical procedures of brain lesions, neuro-oncology and radiotherapy planning. Beyond these CNS applications, the platform is also open to alternative applications. Neurinfo ambitions to support the emergence of research projects based on their level of innovation, their pluri-disciplinarity and their ability to foster collaborations between different actors (public and private research entities, different medical specialties, different scientific profiles).

[1] http://www.neurinfo.org

In this context, a new research 3T MRI system (Siemens Verio system) was acquired in summer 2009 in order to develop the clinical research in the domain of morphological, functional, structural and cellular in-vivo imaging. In 2014 a new equipment for simultaneous recording of EEG and MRI images has been acquired from Brain Product. In 2015, a mock scanner for experimental set-up has been acquired as well as a new High Performance Computing environment made of one large computing cluster and a data center that is shared and operated by the Inria center at IRISA (UMR CNRS 6074). The computation cluster (240 cores) and the data center (up to 50 TB) are dedicated to host and process imaging data produced by the Neurinfo platform, but also by other research partners that share their protocols on the Neurinfo neuroinformatics system (currently more than 30 sites).

VisAGeS and its partners in the Neurinfo project are committed to use this new research platform for developing new regional, national and international collaborations around fundamental and applied clinical research projects dealing with in-vivo medical imaging.

In 2016, VisAGeS has been awarded by IBISA as a “Plateforme d’excellence”.

7. New Results

7.1. Image Computing: Detection, Segmentation, Registration and Analysis

7.1.1. Quantitative analysis of T2/T2 relaxation time alteration*

Participants: Benoit Combès, Anne Kerbrat, Olivier Commowick, Christian Barillot.

T2 and T2* relaxometric data [2] becomes a standard tool for the quantitative assessment of brain tissues and of their changes along time or after the infusion of a contrast agent. Being able to detect significant changes of T2/T2* relaxation time is an important issue. Generally, such a task is performed by comparing the variability level in the regions of interest to the variability in the normal appearance white matter. However, in the case of T2 and T2* relaxometry, this solution is highly problematic. Indeed the level of noise in the normal appearance white matter is significanlty smaller than the level of noise in more intense region (e.g. MS lesions). Our aim is to provide a Bayesian analysis of T2/T2* relaxometry estimation and alteration. More specifically, we build posterior distributions for the relaxation time and the relaxation offset by elucidating the dedicated Jeffreys priors. Then the resulting posterior distributions can be evaluated using a Monte Carlo Markov Chain algorithm. Such an analysis has three main advantages over the classical estimation procedure. First it allows in a simple way to compute many estimators of the posterior including the mode, the mean, the variance and confidence intervals. Then, it allows to include prior information. Finally, becauce one can extract confidence interval from the posterior, testing properly whether the true relaxometry time is included within a certain range of value given a confidence level is simple. This work was published as a conference paper in MICCAI 2016 [22].

7.1.2. Block-Matching Distortion Correction of Echo-Planar Images with Opposite Phase Encoding Directions

Participants: Renaud Hédouin, Olivier Commowick, Élise Bannier, Christian Barillot.

By shortening the acquisition time of MRI, Echo Planar Imaging (EPI) enables the acquisition of a large number of images in a short time, compatible with clinical constraints as required for diffusion or functional MRI. However such images are subject to large, local distortions disrupting their correspondence with the underlying anatomy. The correction of those distortions is an open problem, especially in regions where large deformations occur. We have proposed a new block-matching registration method to perform EPI distortion correction based on the acquisition of two EPI with opposite phase encoding directions (PED). It relies on new transformations between blocks adapted to the EPI distortion model, and on an adapted optimization scheme to ensure an opposite symmetric transformation. We have produced qualitative and quantitative results of the block-matching correction using different metrics on a phantom dataset and on in-vivo data. We have shown the ability of the block-matching to robustly correct EPI distortion even in strongly affected areas. This work has been accepted for publication in IEEE Transactions in Medical Imaging 2017.

[2] https://en.wikipedia.org/wiki/Relaxation_(NMR)

7.1.3. An a contrario approach for the detection of patient-specific brain perfusion abnormalities with arterial spin labelling

Participants: Pierre Maurel, Jean-Christophe Ferré, Christian Barillot.

In this work, we introduce a new locally multivariate procedure to quantitatively extract voxel-wise patterns of abnormal perfusion in individual patients. This a contrario approach uses a multivariate metric from the computer vision community that is suitable to detect abnormalities even in the presence of closeby hypo- and hyper-perfusions. This method takes into account local information without applying Gaussian smoothing to the data. Furthermore, to improve on the standard a contrario approach, which assumes white noise, we introduce an updated a contrario approach that takes into account the spatial coherency of the noise in the probability estimation. Validation is undertaken on a dataset of 25 patients diagnosed with brain tumors and 61 healthy volunteers. We show how the a contrario approach outperforms the massively univariate General Linear Model usually employed for this type of analysis. This work as been published in Neuroimage [14].

7.1.4. Dictionary Learning for Pattern Classification in Medical Imaging: Why Does Size Matter?

Participants: Hrishikesh Deshpande, Pierre Maurel, Christian Barillot.

Sparse representation based dictionary learning (DL) technique has proved to be an effective tool for image classification. While standard DL methods are effective in data representation, several discriminative DL methods have been proposed for learning dictionaries better suited for classification. Majority of these methods, in pattern recognition applications, learn the dictionaries for each class and com- pare the error terms of sparse reconstruction for each dictionary. However this raises a question that is still an open problem in the sparsity community: What role does the size of each dictionary play in the classification process? In this work, we prove that this parameter is pivotal, especially in cases where there are variability differences between classes. We illustrate our assertion on standard and discriminative DL techniques in two applications: Lips detection in face images and the classification of multiple sclerosis lesions in multi-channel brain MR images.

7.2. Image processing on Diffusion Weighted Magnetic Resonance Imaging

7.2.1. Maximum Likelihood Estimators of Brain White Matter Microstructure

Participant: Olivier Commowick.

Diffusion MRI is a key in-vivo non invasive imaging capability that can probe the microstructure of the brain. However, its limited resolution requires complex voxelwise generative models of the diffusion. Diffusion Compartment (DC) models divide the voxel into smaller compartments in which diffusion is homogeneous. We developed a comprehensive framework for maximum likelihood estimation (MLE) of such models that jointly features ML estimators of (i) the baseline MR signal, (ii) the noise variance, (iii) compartment proportions, and (iv) diffusion-related parameters. ML estimators are key to providing reliable mapping of brain microstructure as they are asymptotically unbiased and of minimal variance. We compare our algorithm (which efficiently exploits analytical properties of MLE) to alternative implementations and a state-of-the-art strategy. Simulation results show that our approach offers the best reduction in computational burden while guaranteeing convergence of numerical estimators to the MLE. In-vivo results also reveal remarkably reliable microstructure mapping in areas as complex as the centrum semiovale. Our ML framework accommodates any DC model and is available freely for multi-tensor models as part of the ANIMA software. This work was published as a conference paper in MICCAI 2016 [24].

7.3. EEG and MR Imaging

7.3.1. Multi-Modal EEG and fMRI Source Localization using Sparse Constraints

Participants: Saman Noorzadeh, Pierre Maurel, Christian Barillot.

In this work a multi-modal approach is introduced to estimate the brain neuronal sources based on EEG and fMRI. These two imaging techniques can provide complementary information about the neuronal activities of the brain. Each of these data modalities are first modeled linearly based on the sources. The sources are then estimated with a high spatio-temporal resolution based on a symmetrical integrated approach of these models. For a better estimation, a sparse constraint is also applied to the method based on the physiological knowledge that we have about the brain function. The results which are validated on the real data, shows the reconstruction of neuronal sources with the high spatio-temporal resolution. This is a joint work with Remi Gribonval.

7.3.2. Unimodal versus bimodal EEG-fMRI neurofeedback of a motor imagery task

Participants: Lorraine Perronnet, Marsel Mano, Élise Bannier, Christian Barillot.

In the context of the HEMISFER project, we proposed a simultaneous EEG-fMRI experimental protocol in which 10 healthy participants performed a motor-imagery task in unimodal and bimodal neurofeedback conditions. With this protocol we were able to compare for the first time the effects of unimodal EEG-neurofeedback and fMRI-neurofeedback versus bimodal EEG-fMRI-neurofeedback by looking both at EEG and fMRI activations. We also introduced a new feedback metaphor for bimodal EEG-fMRI-neurofeedback that integrates both EEG and fMRI signal in a single bi-dimensional feedback (a ball moving in 2D). Such a feedback is intended to relieve the cognitive load of the subject by presenting the bimodal neurofeedback task as a single regulation task instead of two. Additionally, this integrated feedback metaphor gives flexibility on defining a bimodal neurofeedback target. Participants were able to regulate activity in their motor regions in all neurofeedback conditions. Moreover, motor activations as revealed by offline fMRI analysis were stronger during EEG-fMRI-neurofeedback than during EEG-neurofeedback. This result suggests that EEG-fMRI-neurofeedback could be more specific or more engaging than EEG-neurofeedback. Our results also suggest that during EEG-fMRI-neurofeedback, participants tended to regulate more the modality that was harder to control. Taken together our results shed light on the specific mechanisms of bimodal EEG-fMRI-neurofeedback and on its added-value as compared to unimodal EEG-neurofeedback and fMRI-neurofeedback.

This work was done in collaboration with the Inria Hybrid and Athena teams. Experiments were conducted at the Neurinfo MRI research facility from University of Rennes 1. This was presented during the poster session of the 2016 Organization for Human Brain Mapping (OHBM) conference.

7.3.3. Brain training with Neurofeedback

Participants: Lorraine Perronnet, Christian Barillot.

We published a book chapter called Brain training with Neurofeedback in the book “Brain Computer Interfaces 1: Methods and Perspectives” (published in French and English) [26]. The first section of the chapter defines the concept of neurofeedback and gives an overall view of the current status in this domain. The second section describes the design of a NF training program and the typical course of a NF session, as well as the learning mechanisms underlying NF. The third section retraces the history of NF, explaining the origin of its questionable reputation and providing a foothold for understanding the diversity of existing approaches. The fourth section discusses how the fields of NF and BCIs might potentially overlap in future with the development of "restorative" BCIs. Finally, the fifth and last section presents a few applications of NF and summarizes the state of research of some of its major clinical applications.

7.3.4. Design of an Experimental Platform for Hybrid EEG-fMRI Neurofeedback Studies

Participants: Marsel Mano, Élise Bannier, Lorraine Perronnet, Christian Barillot.

During a neurofeedback (NF) experiment one or more brain activity measuring technologies are used to estimate the changes of the acquired neural signals that reflect the changes of the subject’s brain activity in real-time. There exist a variety of NF research applications that use only one type of neural signals (i.e. uni-modal) like EEG or fMRI, but there are very few NF researches that use two or more neural signals (i.e. multi-modal). This is primarily because of the associated technical burdens.

We have developed, installed and successfully conducted used a hybrid EEG-fMRI platform for bi-modal NF experiments, as part of the project Hemisfer. Our system is based on the integration and the synchronization of an MR-compatible EEG and fMRI acquisition subsystems. The EEG signals are acquired with a 64 channel MR-compatible solution from Brain Products and the MR imaging is performed on a 3T Verio Siemens scanner (VB17) with a 12-ch head coil. We have developed two real-time pipelines for EEG and fMRI that handle all the necessary signal processing, the Joint NF module that calculates and fuses the NF and a visualize module that displays the NF to the subject. The control and the synchronization of both subsystems with each-other and with the experimental protocol is handled by the NF Control.

Our platform showed very good real-time performance with various pre-processing, filtering, and NF estimation and visualization methods. The entire fMRI process from acquisition to NF takes always less than 200ms, well below the TR of regular EPI sequences (2s). The same process for EEG, with NF update cycles varying 2-5Hz, is done in virtually real time (50Hz). Various NF tasks scenarios for regulating the measured brain activity were tested with subjects. In particular, the platform was used for a NF study on 10 subjects with over 50 sessions using three NF protocols based on motor imagery related brain activity: a) fMRI-NF, b) EEG-NF and c) EEG and fMRI-NF; and two online brain activity regulating protocols without NF. Our hybrid EEG-fMRI NF platform has been a very reliable environment for the NF experiments in our project. Its modular architecture is easily adaptable to different experimental environments, and offers high efficiency for optimal real-time NF applications.

7.4. Applications in Neuroradiology and Neurological Disorders

7.4.1. Imaging biomarkers in Multiple Sclerosis: from image analysis to population imaging

Participants: Christian Barillot, Gilles Edan, Olivier Commowick.

The production of imaging data in medicine increases more rapidly than the capacity of computing models to extract information from it. The grand challenges of better understanding the brain, offering better care for neurological disorders, and stimulating new drug design will not be achieved without significant advances in computational neuroscience. The road to success is to develop a new, generic, computational methodology and to confront and validate this methodology on relevant diseases with adapted computational infrastructures. This new concept sustains the need to build new research paradigms to better understand the natural history of the pathology at the early phase; to better aggregate data that will provide the most complete representation of the pathology in order to better correlate imaging with other relevant features such as clinical, biological or genetic data. In this context, one of the major challenges of neuroimaging in clinical neurosciences is to detect quantitative signs of pathological evolution as early as possible to prevent disease progression, evaluate therapeutic protocols or even better understand and model the natural history of a given neurological pathology. Many diseases encompass brain alterations often not visible on conventional MRI sequences, especially in normal appearing brain tissues (NABT). MRI has often a low specificity for differentiating between possible pathological changes which could help in discriminating between the different pathological stages or grades. The objective of medical image analysis procedures is to define new quantitative neuroimaging biomarkers to track the evolution of the pathology at different levels. We have published a position paper in Medical Image Analysis [2] that illustrates this issue in one acute neuro-inflammatory pathology: Multiple Sclerosis (MS). It exhibits the current medical image analysis approaches and explains how this field of research will evolve in the next decade to integrate larger scale of information at the temporal, cellular, structural and morphological levels.

7.4.2. Multiple Sclerosis lesion segmentation using an automated multimodal Graph Cut

Participants: Jérémy Beaumont, Olivier Commowick, Christian Barillot.

In this work, we present an algorithm for Multiple Sclerosis (MS) lesion segmentation. Our method is fully automated and includes three main steps: 1. the computation of a rough total lesion load in order to optimize the parameter set of the following step; 2. the detection of lesions by graph cut initialized with a robust Expectation-Maximization (EM) algorithm; 3. the application of rules to remove false positives and to adjust the contour of the detected lesions. This work was part of the FLI 2016 MSSEG challenge data organized at MICCAI 2016 [25].

7.4.3. Automatic Multiple Sclerosis lesion segmentation from Intensity-Normalized multi-channel MRI

Participants: Jérémy Beaumont, Olivier Commowick, Christian Barillot.

In the context of the FLI MICCAI 2016 MSSEG challenge for lesion segmentation, we present a fully automated algorithm for Multiple Sclerosis (MS) lesion segmentation. Our method is composed of three main steps. First, the MS patient images are registered and intensity normalized. Then, the lesion segmentation is done using a voxel-wise comparison of multi-channel Magnetic Resonance Images (MRI) against a set of controls. Finally, the segmentation is refined by applying several lesion appearance rules. This work was part of the FLI 2016 MSSEG challenge data organized at MICCAI 2016 [21].

7.5. Management of Information in Neuroimaging

Participants: Michael Kain, Olivier Commowick, Élise Bannier, Inès Fakhfakh, Justine Guillaumont, Florent Leray, Yao Chi, Christian Barillot.

The major topic that is addressed in this period concern the sharing of data and processing tools in neuroimaging (through the “Programme d’Investissement d’Avenir” project such as OFSEP and FLI-IAM) which led to build a suitable architecture to share images and processing tools, started from the NeuroBase project (supported by the French Ministry of Research). Our overall goal within these projects is to set up a computer infrastructure to facilitate the sharing of neuroimaging data, as well as image processing tools, in a distributed and heterogeneous environment. These consortium gathered expertise coming from several complementary domains of expertise: image processing in neuroimaging, workflows and GRID computing, ontology development and ontology-based mediation. This enables a large variety of users to diffuse, exchange or reach neuroimaging information with appropriate access means, in order to be able to retrieve information almost as easily as if the data were stored locally by means of the "cloud computing" Storage as a Service (SaaS) concept As an example, the Shanoir environment has been succesfully deployed to the Neurinfo platform were it is routinely used to manage images of the research studies. It is also currently being deployed for two large projets: OFSEP ("Observatoire Français de la Sclérose en Plaques") where up to 30000 patients will be acquired on a ten years frame, and the Image Analysis and Mangment (IAM) node of the France Life Imaging national infrastructure (FLI-IAM). Our team fulfills multiple roles in this nation-wide FLI project. Christian Barillot is the chair of the IAM node, Olivier Commowick is participating in the working group workflow and image processing and Michael Kain is the technical manager of the node. Apart from the team members, software solutions like medInria and Shanoir are part of the final software platform.

8. Bilateral Contracts and Grants with Industry

8.1. Bilateral Contracts with Industry

8.1.1. Siemens

duration: 5 years from 2011/10/26, extended until end of 2017.
In the context of the Neurinfo imaging platform, a partnership between Siemens SAS - Healthcare and University of Rennes 1 was signed in October 2011 for 5 years. This contract defines the terms of the collaboration between Siemens and the Neurinfo platform. The Neurinfo platform has received work in progress (WIP) sequences from Siemens in the form of object code for evaluation in the context of clinical research. The Neurinfo platform has also received source code of selected MRI sequences. This is a major advance in the collaboration since it will enable the development of MRI sequences on site.

8.2. Bilateral Grants with Industry

8.2.1. MEDday

As part of its activities, MEDday led the final testing phase on patients diagnosed from Multiple Sclerosis in order to find treatment of progressive multiple sclerosis. This is done in partnership with several hospitals in France. The goal is to achieve an effective treatment for this disease. The role of the team in this industrial grant is to develop new algorithms to perform the processing and the analysis of the images from this study.

9. Partnerships and Cooperations

9.1. Regional Initiatives

9.1.1. Biogenouest

The VisAGeS team and the Neurinfo platform integrated the Biogenouest "Groupement d'Intérêt Scientifique (GIS)" in 2012. Biogenouest is a Western France life science and environment core facility network. Research programmes are undertaken in the fields of Marine biology, Agriculture/Food-processing, Human health, and Bioinformatics. Set up in keeping with the inter-regional principle of complementarity, Biogenouest coordinates over twenty technological core facilities in both the Brittany and Pays de la Loire regions.

9.1.2. Projet Fondation de France: PERINE

Participants: Élise Bannier, Isabelle Corouge, Olivier Commowick, Jean-Christophe Ferré, Christian Barillot.

This study evaluates the effect of prenatal exposure to neurotoxicants on the developing brain. Following previous studies in the PELAGIE cohort this MRI study involves ASL, Diffusion and working memory as well as motor inhibition BOLD fMRI together with neuropsychological tests in children. Inclusions have started in November 2014 and lasted for 2 years. The MRI acquisitions of the PERINE projects have all been performed and 101 children included. A post-doc will start in April 2017 to process the diffusion MRI and ASL data of this project.

9.1.3. Fondation de l'Avenir - Stroke, rehabilitation and fMRI

Participants: Élise Bannier, Isabelle Bonan, Isabelle Corouge, Jean-Christophe Ferré, Christian Barillot, Jean-Yves Gauvrit.

duration: 12 months from November 2012. Project extended in 2015.
A complementary funding (20 000€) was obtained to support a new research project on rehabilitation of stroke patients. The fMRI tasks were setup and validated on healthy controls (paper ready for submission). The project was extended in 2014 to recruit more patients.

9.1.4. Projet Fondation de France: EPMR-MA

Participants: Pierre-Yves Jonin, Élise Bannier, Christian Barillot, Isabelle Corouge, Quentin Duché, Jean-Christophe Ferré.

This project evaluates memory effects in healthy adults and in patients presenting cognitive impairments using BOLD fMRI and diffusion MRI. A pilot study has been completed in 2015 in order to optimize the experimental design. The inclusions of patients started in 2016 and are ongoing. A Post Doc was recruited to work on fMRI and DTI processing.

9.1.5. Allocation d'Installation Scientifique – Rennes Métropole

Participant: Emmanuel Caruyer.

Diffusion MRI has been a tremendous tool for the diagnosis of a number of brain pathologies such as abnormal development, neuro-degenerative or inflammatory disorders or brain tumors. Typical resolution in diffusion MRI is about 2mm – this suggests that in white matter, any volume element may contain millions of axons. Although currently we can characterize molecular diffusion, recent developments in diffusion MRI have shown the possibility to quantify more specifically some physical tissue parameters in white matter, such as axonal density and diameter: this means that we can retrieve information from a much smaller scale than the typical imaging resolution.

Acquisition time for this kind of measurements remains long and largely incompatible with in vivo application in humans. This projects aims at developing novel signal processing and acquisition methods for the reconstruction of microstructural informations in a reasonable acquisition time. We will study how sparse representations can be applied to the diffusion signal, in order to enable microstructure information reconstruction. In conjunction with this, we will develop acquisition sequences adapted to these sparse represnetations, in order to reconstruct the diffusion signal from fewer measurements, using results from the compressive sensing theory.

9.2. National Initiatives

9.2.1. ANR

9.2.1.1. ANR "MAIA", 2015 generic projects program

Participants: Maia Proisy, Pierre Maurel, Antoine Legouhy, Olivier Commowick, Isabelle Corouge, Jean-Christophe Ferré, Christian Barillot.

Each year in France, 55 000 children are born prematurely, i.e., before the 37th week of gestation. Long-term studies of the outcome of prematurely born infants have clearly documented that the majority of such infants may have significant motor, cognitive, and behavioral deficits.

However, there is a limited understanding of the nature of the cerebral abnormality underlying these adverse neurologic outcomes. In this context, the emergence of new modalities of 3D functional MRI, e.g., Arterial Spin Labeling (ASL), or optical imaging technologies, e.g., Near InfraRed Spectroscopy (NIRS), brings new perspectives for extracting cognitive information, via metabolic activity measures. Other classical technics devoted to cerebral signal measurement, such as ElectroEncephaloGraphy (EEG), provide cognitive information at the cortical level. Each of these various non-invasive imaging technologies brings substantial and specific information for the understanding of newborn brain development.

This project aims at developing innovative approaches for multi-image / multi-signal analysis, in order to improve neurodevelopment understanding methods. From a fundamental point of view, mathematics and computer science have to be considered in association with imaging physics and medicine, to deal with open issues of signal and image analysis from heterogeneous data (image, signal), considered in the multiphysics contexts related to data acquisition (magnetic, optic, electric signals) and biophysics modeling of the newborn brain. A sustained synergy between all these scientific domains is then necessary.

Finally, the sine qua non condition to reach a better understanding of the coupled morphological- cognitive development of premature newborns, is the development of effective software tools, and their distribution to the whole medical community. The very target of this project will be the design of such software tools for medical image / signal analysis, actually operational in clinical routine, and freely available. Academic researchers and industrial partners will work in close collaboration to reach that ambitious goal.

9.2.2. Competitivity Clusters

9.2.2.1. The HEMISFER Project

Participants: Élise Bannier, Jean-Marie Batail, Isabelle Bonan, Isabelle Corouge, Jean-Christophe Ferré, Jean-Yves Gauvrit, Pierre Maurel, Lorraine Perronnet, Christian Barillot.

The HEMISFER project ("Hybrid Eeg-MrI and Simultaneous neuro-FEedback for brain Rehabilitation") will be conducted at Inria Rennes with the support of the Cluster of Excellence "CominLabs" [3]. The goal of HEMISFER is to make full use of the neurofeedback paradigm in the context of rehabilitation and psychiatric disorders. The major breakthrough will come from the use of a coupling model associating functional and metabolic information from Magnetic Resonance Imaging (fMRI) to Electro-encephalography (EEG) to "enhance" the neurofeedback protocol. We propose to combine advanced instrumental devices (Hybrid EEG and MRI platforms), with new man-machine interface paradigms (Brain computer interface and serious gaming) and new computational models (source separation, sparse representations and machine learning) to provide novel therapeutic and neuro-rehabilitation paradigms in some of the major neurological and psychiatric disorders of the developmental and the aging brain (stroke, attention-deficit disorder, language disorders, treatment-resistant mood disorders, ...). This project will be conducted with the HYBRID and PANAMA Teams from Inria Rennes, the EA 4712 team from University of Rennes I and the ATHENA team from Inria Sophia-Antipolis. This work will benefit from the research 3T MRI and MRI-compatible EEG systems provided by the NeurInfo in-vivo neuroimaging platform on which these new research protocols will be set up. A budget of 500keuros will be provided by the CominLabs cluster in the next 3 years to support this project (through experimental designs, PhDs, Post-docs and Expert Engineers).

9.2.2.2. France Life Imaging (FLI)

Participants: Christian Barillot, Olivier Commowick, Michael Kain, Florent Leray, Julien Louis, Aneta Morawin, Mathieu Simon, Yao Chi.

France Life Imaging (FLI) is a proposed large-scale research infrastructure project aimed at establishing a coordinated and harmonized network of biomedical imaging in France. This project was recently selected by the call “Investissements d’Avenir - Infrastructure en Biologie et Santé”. One node of this project is the node Information Analysis and Management (IAM), a transversal node build by a consortium of teams that will contribute to the construction of a network for data storage and information processing. Instead of building yet other dedicated facilities, the IAM node will use already existing data storage and information processing facilities (LaTIM Brest; CREATIS Lyon; CIC-IT Nancy; VisAGeS U746 Inria Rennes; CATI CEA Saclay; LSIIT/ICube Strasbourg) that will increase their capacities for the FLI infrastructure. Inter-connections and access to services will be achieved through a dedicated software platform that will be developed based on the expertise gained through successful existing developments. The IAM node has several goals. It aims first at building a versatile facility for data management that will inter-connect the data production sites and data processing for which state-of-the-art solutions, hardware and software, will be available to infrastructure users. Modular solutions are preferred to accommodate the large variety of modalities acquisitions, scientific problems, data size, and adapted for future challenges. Second, it aims at offering the latest development that will be made available to image processing research teams. The team VisAGeS fulfills multiple roles in this nation-wide project. Christian Barillot is the chair of the node IAM, Olivier Commowick is participating in the working group workflow and image processing and Michael Kain the technical manager. Apart from the team members, software solutions like medInria and Shanoir will be part of the final software platform.

9.2.2.3. OFSEP

Participants: Justine Guillaumont, Élise Bannier, Christian Barillot, Olivier Commowick, Gilles Edan, Jean-Christophe Ferré, Michael Kain, Inès Fakhfakh.

The French Observatory of Multiple Sclerosis (OFSEP) is one of 10 projects selected in January 2011 in response to the call for proposal in the “Investissements d’Avenir - Cohorts 2010” program launched by the French Government. It allows support from the National Agency for Research (ANR) of approximately € 10 million for 10 years. It is coordinated by the Department of Neurology at the Neurological Hospital Pierre Wertheimer in Lyon (Professor Christian Confavreux), and it is supported by the EDMUS Foundation against multiple sclerosis, the University Claude Bernard Lyon 1 and the Hospices Civils de Lyon. OFSEP is based on a network of neurologists and radiologists distributed throughout the French territory and linked to 61 centers. OFSEP national cohort includes more than 50,000 people with Multiple Sclerosis, approximately half

[3] https://iww.inria.fr/cominlabs-newsletter/april-2013-four-projects-selected/#hemisfer

of the patients residing in France. The generalization of longitudinal monitoring and systematic association of clinical data and neuroimaging data is one of the objectives of OFSEP in order to improve the quality, efficiency and safety of care and promote clinical, basic and translational research in MS. For the concern of data management, the Shanoir platform of Inria has been retained to manage the imaging data of the National OFSEP cohort in multiple sclerosis.

9.2.2.4. PHRC EMISEP: Evaluation of early spinal cord injury and late physical disability in Relapsing Remitting Multiple Sclerosis

Participants: Élise Bannier, Christian Barillot, Emmanuel Caruyer, Benoit Combès, Olivier Commowick, Gilles Edan, Jean-Christophe Ferré, Anne Kerbrat, Haykel Snoussi.

Multiple Sclerosis (MS) is the most frequent acquired neurological disease affecting young adults (1/1000 inhabitants in France) and leading to impairment. Early and well adapted treatment is essential in patients presenting aggressive forms of MS. This PHRC project focusses on physical impairment and especially on the ability to walk. Several studies, whether epidemiolgic or based on brain MRI, have shown that several factors were likely to announce aggressive development of the disease, such as age, number of focal lesions on baseline MRI, clinical activity. However, these factors only partially explain physical impairment progression, preventing their use at the individual level. Spinal cord is often affected in MS, as demonstrated in postmortem or imaging studies. Yet, early radiological depiction of spinal cord lesions is not always correlated with clinical symptoms. Preliminary data, on reduced number of patients, and only investigating the cervical spinal cord have shown that diffuse spinal cord injury, observed via diffusion or magnetisation transfer imaging, would be correlated with physical impairment as evaluated by the EDSS score. Besides, the role of early spinal cord affection (first two years) in the evolution of physical impairment remains unknown.

In this project, we propose to address these different issues and perform a longitudinal study on Relapsing Remitting Multiple Sclerosis (RRMS) patients, recruited in the first year of the disease. Our goal is to show that diffuse and focal lesions detected spinal cord MRI in the first 2 years can be used to predict disease evolution and physical impairment at 5 years. Twelve centers are involved in the study to include 80 patients.

To date, 65 of the 80 subjects have been included. H. Snoussi is working in the scope of his PhD thesis on diffusion imaging in the spinal cord and has dedicated his first year to literature review and definition of methodological aspects to tackle starting with distortion correction. B. Combès started as a post doc in November 2016 to process the EMISEP imaging data, starting with morphological data processing (registration, segmentation) and magnetization transfer data processing.

9.3. European Initiatives

9.3.1. FP7 & H2020 Projects

9.3.1.1. EuroBioimaging

Type: CAPACITIES

Challenge: Provide access and training in imaging technologies, and share the best practice and image data in order to make Euro-BioImaging an engine that will drive European innovation in imaging research and technologies

Instrument: Combination of COLLABORATIVE PROJECTS and COORDINATION and SUPPORT ACTIONS

Objective: Euro-BioImaging is a large-scale pan-European research infrastructure project on the

European Strategy Forum on Research Infrastructures (ESFRI) Roadmap.

Duration: December 2010 - 2016

Coordinators: Jan Ellenberg (EMBL) and Oliver Speck (University of Magdeburg)

Partner: EMBL (Germany); Erasmus Medical Center (Netherlands) for WG11

Inria contact: C. Kervrann, Christian Barillot

Abstract: Euro-BioImaging is a pan-European infrastructure project whose mission is to build a distributed imaging infrastructure across Europe that will provide open access to innovative biological and medical imaging technologies for European researchers. The project is funded by the EU and currently the consortium is finalizing the basic principles for the operation of future Euro-BioImaging organisation.

Euro-BioImaging will be governed by representatives of the European countries that will join Euro-BioImaging (Euro-BioImaging member states).

The infrastructure established by Euro-BioImaging will consist of a set of geographically distributed but strongly interlinked imaging facilities (Euro-BioImaging Nodes), which will be selected among the leading European imaging facilities based on an independent evaluation process.

Inria and the VisAGeS team is involved through the FLI national infrastructure and contributes to the WG11 Working Group on Data Storage and Analysis. This WG performs a series of tasks to define a European Biomedical Imaging Data Storage and Analysis infrastructure plan for the construction phase.

9.3.1.2. H2020 OpenAire-Connect

Program: E-INFRA

Topic: EINFRA-22-2016

Type of Action: RIA

Project acronym: OpenAIRE-Connect

Project title: OpenAIRE - CONNECTing scientific results in support of Open Science

Acceptation date: 01/09/2016

Open Science is around the corner. Scientists and organizations see it as a way to speed up, improve quality and reward, while policy makers see it as a means to optimize cost of science and leverage innovation. Open Science is an emerging vision, a way of thinking, whose challenges always gaze beyond its actual achievements. De facto, today's scientific communication ecosystem lacks tools and practices to allow researchers to fully embrace Open Science. OpenAIREConnect aims to provide technological and social bridges, and deliver services enabling uniform exchange of research artefacts (literature, data, and methods), with semantic links between them, across research communities and content providers in scientific communication. It will introduce and implement the concept of Open Science as a Service (OSaaS) on top of the existing OpenAIRE infrastructure, delivering out-of-the-box, on-demand deployable tools. OpenAIRE-Connect will adopt an end-user driven approach (via the involvement of 5 prominent research communities), and enrich the portfolio of OpenAIRE infrastructure production services with a Research Community Dashboard Service and a Catch-All Notification Broker Service. The first will offer publishing, interlinking, packaging functionalities to enable them to share and re-use their research artifacts (introducing methods, e.g. data,software, protocols). This effort, supported by the harvesting and mining "intelligence" of the OpenAIRE infrastructure, will provide communities with the content and tools they need to effectively evaluate and reproduce science. OpenAIRE-Connect will combine dissemination and training with OpenAIRE's powerful NOAD network engaging research communities and content providers in adopting such services. These combined actions will bring immediate and long-term benefits to scholarly communication stakeholders by affecting the way research results are disseminated, exchanged, evaluated, and re-used.

In this project VisAGeS is acting, through CNRS, as the French coordinator to develop the link with the Neuroimaging research community. This will be performed in the context of the FLI-IAM national infrastructure

9.3.2. Collaborations in European Programs, Except FP7 & H2020

9.3.2.1. Kic-EIT-eHealth

Program: KIC-EIT: European Institute of Innovation and Technology

Project acronym: e-Health

Project title: Innovation for healthy living and active ageing

Acceptation date: 01/12/2014

website: http://eithealth.eu/about-us/

EIT Health aims to promote entrepreneurship and develop innovations in healthy living and active ageing, providing Europe with new opportunities and resources. EIT Health will enable citizens to lead healthier and more productive lives by delivering products, services and concepts that will improve quality of life and contribute to the sustainability of healthcare across Europe. EIT Health is a strong, diverse and balanced partnership of best-in-class organisations in education, research, technology, business creation and corporate and social innovation. EIT Health intends to foster cooperation and unlock Europe's innovation and growth potential – developing and retaining the best talents, creating high-quality jobs and boosting the global competitiveness of European industry. VisAGeS is involved in this project through the Inserm and Inria institutions. Christian Barillot is representing Inria as one expert in the dedicated WG "Healthy Brain". VisAGeS is also concerned by the WG "big data".

9.4. International Initiatives

9.4.1. Inria Associate Teams Not Involved in an Inria International Labs

9.4.1.1. BARBANT

Title: Boston and Rennes, a Brain image Analysis Team

International Partner (Institution - Laboratory - Researcher):

Harvard University (United States) - Mathematics Department - Simon K. Warfield

Start year: 2015

See also: https://team.inria.fr/barbant/

BARBANT is an Inria associate team shared between Inria VisAGeS research team and the Computational Radiology Laboratory at the Boston Children's hospital (Harvard Medical School). This associate team aims at better understanding the behavior of normal and pathological Central Nervous System (CNS) organs and systems. Pathologies of particular interest to us are multiple sclerosis, psychiatric, and pediatric diseases such as pediatric multiple sclerosis or tuberous sclerosis. A major challenge is to characterize the future course of the pathological processes in each patient as early as possible in order to predict the progression of the disease and/or adverse neurological outcomes, and to develop better techniques for both monitoring response to therapy and for altering therapy (duration, dose and nature) in response to patient-specific changes in imaging characteristics. At term, this project will allow to introduce objective figures to correlate qualitative and quantitative phenotypic markers coming from the clinic and image analysis, mostly at the early stage of the pathologies. This will allow for the selection or adaptation of the treatment for patients at an early stage of the disease.

9.4.1.2. Informal International Partners

- Collaboration with Sherbrooke University (Sherbrooke, Canada): From Jun to Aug 2016, Michael Paquette, PhD student from Sherbrooke supervised by Maxime Descoteaux, visited the VisAGeS team to collaborate with Emmanuel Caruyer on the development on new analysis techniques for the structural brain connectome. This visit was funded by a MITACS/Inria scholarship.
- Collaboration with LTS5, EPFL (Lausanne, Switzerland) and Computer Science department, University of Verona (Verona, Italy): Alessandro Daducci, Gabriel Girard and Jean-Philippe Thiran visited the VisAGeS team for a 2 days workshop on the development of novel validation methods for the human brain connectome using software generated phantoms.

- Collaboration with the Mathematics department, Politecnico di Milano (Italy): Olivier Commowick and Christian Barillot visited the department for the annual meeting of the Italian statistical society and collaborated with Aymeric Stamm and Simone Vantini.
- Collaboration with the Microstructure Imaging Group, UCL (London, UK): Christian Barillot, Emmanuel Caruyer, Olivier Commowick and Sudhanya Chatterjee visited the group of Daniel Alexander for a workshop on "MRI based Virtual Histology: Meeting Tomorrow's Healthcare Challenges Today"
- visit of Tobias Kober and Bénédicte Maréchal from the ACIT Siemens research group in Lausanne [4] to discuss potential collaborations on the MP2Rage sequence and other brain MR imaging topics

9.5. International Research Visitors

9.5.1. Visits of International Scientists

- Simon Warfield and Benoit Scherrer, Harvard University, visited the VisAGeS team for the annual seminar on Jun 9-10 2016.
- From Jun to Aug 2016, Michael Paquette, PhD student from Sherbrooke supervised by Maxime Descoteaux, visited the VisAGeS team to collaborate with Emmanuel Caruyer on the development on new analysis techniques for the structural brain connectome. This visit was funded by a MITACS/Inria scholarship.
- Alessandro Daducci, Gabriel Girard and Jean-Philippe Thiran visited the VisAGeS team for a 2 days workshop on the development of novel validation methods for the human brain connectome using software generated phantoms.

9.5.2. Visits to International Teams

- Sudhanya Chatterjee visited the Computational Radiology Lab, Boston Children's Hospital, Harvard University for 3 weeks in Oct-Nov 2016. This stay was funded by the international program of University of Rennes 1. Christian Barillot, Emmanuel Caruyer and Olivier Commowick visited the same lab for a 3 days workshop in the context of the Associate Team.
- Christian Barillot, Emmanuel Caruyer, Olivier Commowick and Sudhanya Chatterjee visited the Microstructure Imaging Group, UCL (London, UK) of Daniel Alexander for a workshop on "MRI based Virtual Histology: Meeting Tomorrow's Healthcare Challenges Today"
- Olivier Commowick and Christian Barillot visited the Mathematics department, Politecnico di Milano (Italy) for the annual meeting of the Italian statistical society and collaborated with Aymeric Stamm and Simone Vantini.

10. Dissemination

10.1. Promoting Scientific Activities

10.1.1. Scientific Events Organisation

10.1.1.1. General Chair, Scientific Chair

- Olivier Commowick was General Chair of the "Multiple Sclerosis Lesions Segmentation Challenge", MICCAI 2016.

10.1.1.2. Member of the Organizing Committees

- Olivier Commowick, Michael Kain, Florent Leray, Jean-Christophe Ferré, Anne Kerbrat, Mathieu Simon and Christian Barillot organized the "Multiple Sclerosis Lesions Segmentation Challenge", MICCAI 2016.

[4] http://w1.siemens.ch/home/ch/de/healthcare/produkte/ACIT/Pages/ACIT.aspx

- Christian Barillot is member of the Board of Directors of IPMI conference series (Information Processing in Medical Imaging)

10.1.2. Scientific Events Selection

10.1.2.1. Chair of Conference Program Committees

- Christian Barillot was area chair of SPIE Medical Imaging 2016
- Christain Barillot was area chair of IEEE ISBI 2016

10.1.2.2. Member of the Conference Program Committees

- Christian Barillot was TPC Member of PatchMI-2016, MICCAI-MCV2016
- Emmanuel Caruyer was Program Committee member of the CDMRI MICCAI workshop.

10.1.2.3. Reviewer

- ISBI (Emmanuel Caruyer, Olivier Commowick), ISMRM (Élise Bannier), MICCAI (Emmanuel Caruyer, Olivier Commowick).

10.1.3. Journal

10.1.3.1. Member of the Editorial Boards

- Christian Barillot is member of Editorial Boards of Medical Image Analysis, Current Medical Imaging Reviews, ISRN Signal Processing
- Christian Barillot is Editor-in-Chief of Frontiers in ICT: Computer Image Analysis.

10.1.3.2. Reviewer - Reviewing Activities

- Am J Neuroradiol (Élise Bannier), Comput Biol Med (Christian Barillot), Comput Meth Prog Bio (Christian Barillot), Front Neurosc (Pierre Maurel), Hum Brain Mapp (Emmanuel Caruyer), IEEE TMI (Pierre Maurel, Olivier Commowick), Med Image Anal (Olivier Commowick), Med Phys (Christian Barillot) Neuroimage (Christian Barillot, Isabelle Corouge, Emmanuel Caruyer, Olivier Commowick), Pattern Recog Lett (Christian Barillot).

10.1.4. Invited Talks

- Gilles Edan gave an invited keynote at the world 2016 ECTRIMS conference (London, UK)
- Christian Barillot published an invited position paper for the 20th anniversary of Medical Image Analysis
- Christian Barillot gave an invited lecture at the 25ème COLLOQUE DE LA CONFÉRENCE NATIONALE DES COMITÉS DE PROTECTION DES PERSONNES (CNCP)
- Christian Barillot gave an invited lecture at the Global Bioimaging Training Program, Eurobioimaging ESFRI program, EMBL, Germany
- Christian Barillot gave an invited lecture at the Miccai-BrainLes Workshop 2016, Athenes, GR
- Christian Barillot gave an invited lecture at the Maria de Maeztu Strategic Research Program; Department of Information and Communication Technologies, UPF, Barcelona, Spain
- Christian Barillot gave an invited lecture at the RIR 2016 - Emerging challenges in neuroscience, neurology & psychiatry, Paris, France
- Christian Barillot gave an invited lecture at the Biomedical Imaging Seminar, Erasmus MC, Rotterdam
- Christian Barillot gave an invited lecture at the FCRIN day on “Specificities of clinical research in imaging”
- Christian Barillot, Emmanuel Caruyer and Olivier Commowick gave an invited talk at the “MRI based Virtual Histology: Meeting Tomorrow’s Healthcare Challenges Today” workshop, University College London, May 26-27th.

10.1.5. Leadership within the Scientific Community

- Gilles Edan was elected Fellow of the European Academy of Neurologie. Member of the EAN teaching committee in 2015
- Christian Barillot is member of the Scientific Council of the INS2I [5] Institute of CNRS since 2011 and is Chairman of the Board since 2015
- Christian Barillot is member of the C3N committee (CNRS)
- Christian Barillot is member of the scientific board of "GIS France Grilles"

10.1.6. Scientific Expertise

- Christian Barillot provided an expertise for the Royal Netherlands Academy of Arts and Sciences (KNAW)
- Christian Barillot provided expertise for the EPSRC, UK
- Christian Barillot provided an expertise for ANRT
- Christian Barillot provided expertise for the Assistant professor committee for the University of Paris Sud
- Emmanuel Caruyer provided expertise for the Inria Associate Team program.

10.2. Teaching - Supervision - Juries

10.2.1. Teaching

Master SIBM, University of Angers-Brest-Rennes

Christian Barillot, Élise Bannier, Emmanuel Caruyer, Olivier Commowick, Isabelle Corouge, Jean-Yves Gauvrit, Sylvain Prima, 3D medical imaging – visualization, segmentation, fusion, management, normalization (26h)

Sylvain Prima, Master 1 SIBM, University of Rennes (5h)

Christian Barillot is responsible for one semester

Jean-Yves Gauvrit is the coordinator for the Master

École Supérieure d'Ingénieur de Rennes (ESIR): Pierre Maurel, General image processing (60h), Algorithmics and complexity (60h), Medical imaging (60h)

ENS Rennes: Pierre Maurel, Introduction to image processing (24h)

ISTIC – Université of Rennes 1: Emmanuel Caruyer, Software Engineering (12h)

10.2.2. Supervision

PhD: Hrishikesh Deshpande, "Dimensionality Reduction and Statistical Learning for Computational Modeling of Natural Evolution of Brain Pathologies", Inria, Jun 2012, Christian Barillot, Pierre Maurel.

PhD in progress: Sudhanya Chatterjee, "Image-based Tissue Compartment Characterization of Neural Circuits with in-vivo MRI", Inria, from Nov 2015, Christian Barillot, Olivier Commowick, Jean-Christophe Ferré, Simon Warfield.

PhD in progress: Renaud Hédouin, "Biomarker discovery in brain imaging by using diffusion MRI", Inria/Inserm, from November 2013, Christian Barillot, Olivier Commowick.

PhD in progress: Cédric Meurée, "Quantitative Analysis Of Arterial Spin Labeling MRI For Robust Parametric Information Of Perfusion Maps", Inria / Siemens, from Mar 2014, Christian Barillot, Pierre Maurel.

[5] http://csins2i.irisa.fr

PhD in progress: Corentin Vallée, “Joint estimation of neuronal activation, resting-state and basal metabolism from Arterial Spin Labeling”, Christian Barillot, Isabelle Corouge, Pierre Maurel.

PhD in progress: Antoine Legouhy, “Analyse IRM multimodale pour l’e´tude du de´veloppement ce´re´bral chez le pre´mature´”, from Nov 2016, Christian Barillot, Olivier Commowick, François Rousseau.

PhD in progress: Lorraine Perronnet, “Neurofeedback Using Virtual Reality And Combining Eeg-Mri For Brain Rehabilitation”, Inria/CominLabs Hemisfer project, from Dec 2013, Christian Barillot, Maureen Clerc (Inria Sophia-Antipolis), Anatole Lecuyer (HYBRID project), Fabien Lotte (Inria Bordeaux)

PhD in progress: Haykel Snoussi, “Diffusion MRI detection of early occurring spine lesions in relapsing-remitting multiple sclerosis with late physical impairment”, from Nov 2015, Christian Barillot, Gilles Edan, Emmanuel Caruyer

PhD in progress: Pierre-Yves Jonin, “Relationships between context-free and context-rich memory: cognitive and neural subtrates”, Inria/Inserm/CNRS from Oct 2014, Christian Barillot (co-supervisor)

PhD in progress: Maia Proisy, “Perfusion in neonates and in pediatric diseases”, Univ. Rennes 1/CHRU Rennes, from Oct 2014, Jean-Christophe Ferré (supervisor)

PhD in progress: Anne Kerbrat, “Quantitative MR imaging in MS for Brain and Spine”, Univ. Rennes 1/CHRU Rennes, from Oct 2014, Gilles Edan (supervisor)

10.2.3. Juries

- Pierre Maurel, PhD committee Hrishikesh Despande, Inria, Rennes July 2016.
- Christian Barillot, PhD committees: Hrishikesh Despande, Inria, Rennes July 2016.
- Christian Barillot, PhD reviewer: Mehdi Hadj-Hamou, Inria, Sophia; Dec 2016; Ester Bron, Erasmus MC, NL, March 2016

10.3. Popularization

- Inria demonstration stand, Journées Françaises de Radiologie.

11. Bibliography

Publications of the year

Articles in International Peer-Reviewed Journals

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[2] C. BARILLOT, G. EDAN, O. COMMOWICK. *Imaging biomarkers in Multiple Sclerosis: from image analysis to population imaging*, in "Medical Image Analysis", 2016 [*DOI :* 10.1016/J.MEDIA.2016.06.017], https://hal.inria.fr/hal-01333583

[3] L. BEUZIT, P.-A. ELIAT, V. BRUN, J.-C. FERRÉ, Y. GANDON, E. BANNIER, H. SAINT-JALMES. *Dynamic contrast-enhanced MRI: Study of inter-software accuracy and reproducibility using simulated and clinical data*, in "Journal of Magnetic Resonance Imaging", 2016, vol. 43, n^{o} 6, pp. 1288-300 [*DOI :* 10.1002/JMRI.25101], https://hal-univ-rennes1.archives-ouvertes.fr/hal-01255866

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[5] P.-M. DAVID, N. ICARD, J.-Y. GAUVRIT, M. VÉRIN, F. LE JEUNE. *Interest of multi-modal imaging in bilateral lesions of basal ganglia: A case report of a post-anoxic dystonia*, in "European Journal of Nuclear Medicine and Molecular Imaging", October 2016, vol. 43, n^{o} 11, pp. 2098–2099 [*DOI :* 10.1007/s00259-016-3413-6], https://hal-univ-rennes1.archives-ouvertes.fr/hal-01371659

[6] R. H. FICK, D. WASSERMANN, E. CARUYER, R. DERICHE. *MAPL: Tissue Microstructure Estimation Using Laplacian-Regularized MAP-MRI and its Application to HCP Data*, in "NeuroImage", July 2016, vol. 134, pp. 365–385 [*DOI :* 10.1016/j.neuroimage.2016.03.046], https://hal.inria.fr/hal-01291929

[7] R. GONSETTE, M. DEBOUVERIE, C. SINDIC, J.-C. FERRÉ, G. EDAN. *Pixantrone: a B-cell-depleting immunosuppressant for multiple sclerosis patients with active disease*, in "Multiple Sclerosis Journal", May 2016, vol. 22, n^{o} 6, pp. 817–821 [*DOI :* 10.1177/1352458515601902], https://hal-univ-rennes1.archives-ouvertes.fr/hal-01324700

[8] R. HÉDOUIN, O. COMMOWICK, E. BANNIER, B. SCHERRER, M. TAQUET, S. K. WARFIELD, C. BARILLOT. *Block-Matching Distortion Correction of Echo-Planar Images With Opposite Phase Encoding Directions*, in "IEEE Transactions on Medical Imaging", 2017, 10 p. , Accepted for publication, available on line [*DOI :* 10.1109/TMI.2016.2646920], https://hal.inria.fr/hal-01436561

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[27] L. PERRONNET, A. LÉCUYER, F. LOTTE, M. CLERC, C. BARILLOT. *Entraîner son cerveau avec le neurofeedback*, in "Les interfaces cerveau-ordinateur 1", M. CLERC, L. BOUGRAIN, F. LOTTE (editors), ISTE editions, July 2016, pp. 277-292, https://hal.inria.fr/hal-01413408

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