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Activity Report 2014

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
Medicine**

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Project-Team VISAGES

Keywords: Medical Images, Image Processing, Neuroimaging, Statistical Methods, Sparse Representations, Data Assimilation, Computer Vision

Creation of the Project-Team: 2005 July 04.

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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 basic science 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.

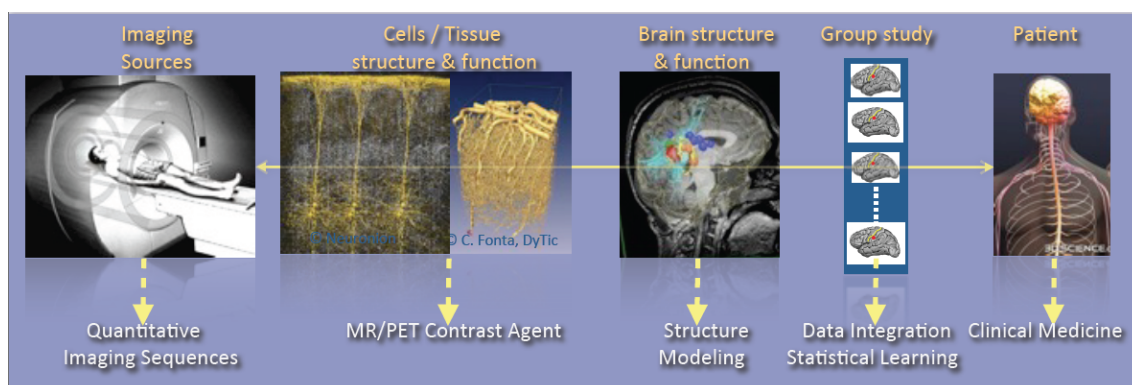


Figure 1. The major overall scientific foundation of the team concerns the integration of data from the Imaging source to the patient at different scales : from the cellular or molecular level describing the structure and function, to the functional and structural level of brain structures and regions,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

As shown in figure 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

neuroimaging, clinical neuroscience, multiple sclerosis, multispectral MRI, brain atlas

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 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. New Software and Platforms

5.1. Shanoir

Participants: Justine Guillaumont, Michael Kain, Yao Yao, Christian Barillot.

Shanoir (Sharing NeuroImaging Resources) is an open source neuroinformatics platform designed to archive, structure, manage, visualize and share neuroimaging data with an emphasis on multi-centric collaborative research projects (Figure 2). It provides a user-friendly interface, a secure web access and offers an intuitive workflow to facilitate the collecting and retrieving of neuroimaging data from multiple sources and a wizard to make the completion of metadata easy. Shanoir comes along many features of neuroimaging data management systems along with research-oriented data imaging organization and enhanced data accessibility, support multi-centers clinical studies on subjects or group of subjects and other functionalities such as anonymization of data. For a better distribution/replication of stored data on a Shanoir server an export and import function on base of XML has been developed for the usage of server administrators.

Shanoir APP registration number is: IDDN.FR.001.520021.003.S.A.2008.000.31230

See also the web page <http://www.shanoir.org>

- Keywords: neuroimaging, ontology, sharing neuroimages
- Version: 0.5
- Software benefit: full featured neuroimaging management system with additionnal web services
- APP: IDDN.FR.001.520021.000.S.P.2008.000.31230
- License: Licence QPL
- Type of human computer interaction: Online web application, web service (SOAP messages based)
- OS/Middleware: Windows, Mac et Linux.
- Required library or software: Java 1.6, JBoss server, JBoss Seam, JSF, JPA Hibernate, EJB, Rich-faces, Faceless, Ajax4JSF, Dcmtk, Dcm4chee.
- Programming language: Java / J2EE
- Documentation: see the website

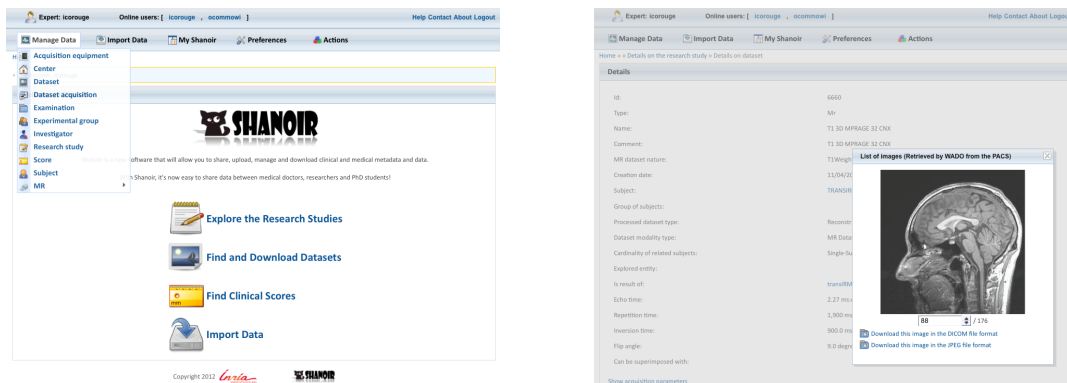


Figure 2. The SHANOIR software is a web application to share, archive, search and visualize neuroimaging data.

5.2. ShanoirUploader

Participants: Justine Guillaumont, Michael Kain, Christian Barillot.

The ShanoirUploader (Fig. 3) 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 any PACS. After this the ShanoirUploader sends the data to a Shanoir server instance to import these data into a Shanoir server instance. 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.

An APP registration is in progress. See also the web page <http://shanoir.gforge.inria.fr> as the ShanoirUploader documentation is integrated on this page.

- Keywords: neuroimaging, ontology, sharing neuroimages
- Version: 0.1
- Software benefit: offers a great solution to query a PACS server, download the data and send the data to a Shanoir server
- License: no defined license for the moment
- Type of human computer interaction: desktop application on base of JavaWebStart (JWS), web service (SOAP messages based)
- OS/Middleware: Linux, Windows and Mac
- Required library or software : Java SDK, installed on client machine
- Programming language: Java
- Documentation : see the website

5.3. iShanoir

Participants: Michael Kain, Christian Barillot.

iShanoir (Fig. 4) is an iOS application, designed for iPhone and iPad. On base of this application a Shanoir server can be accessed. 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. This project is the result of the internship of H el ene G erome in the team. An APP registration is in progress.

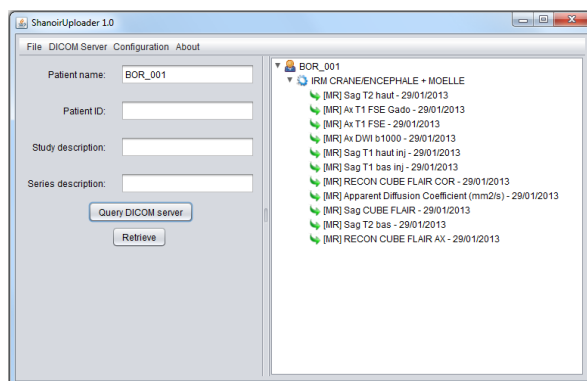


Figure 3. The ShanoirUploader software is a desktop application designed to interact with a PACS to query and retrieve the data stored on any PACS.

See also the web page <http://shanoir.gforge.inria.fr> as the iShanoir documentation is integrated on this page.

- Keywords: neuroimaging, ontology, sharing neuroimages
- Version: 0.1
- Software benefit: offers access to data stored on a Shanoir server from native iOS devices, like iPhones and iPads
- License: no defined license for the moment
- Type of human computer interaction: mobile iOS Cocoa Touch application with web service connection
- OS/Middleware: iOS
- Required library or software: none
- Programming language: Objective-C
- Documentation : see the website

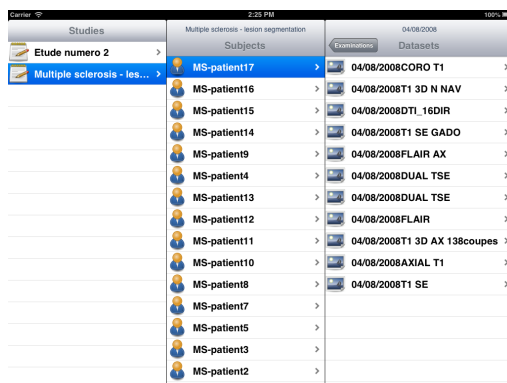


Figure 4. The iShanoir software is a desktop application designed to...

5.4. AutoMRI

Participants: Fang Cao, Isabelle Corouge, Pierre Maurel, Elise Banner.

AutoMRI 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). 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 (Figure 5).

- Keywords: fMRI, MRI, ASL, fASL, SPM, automation
- Software benefit: Automatic MRI data analysis based on SPM. Once the parameters are set, the analysis is performed without human interaction.
- APP: Part in IDDN.FR.001.130017.000.S.A.2012.000.31230
- License: Part under CeCILL
- Type of human computer interaction: Matlab function (script, no GUI)
- OS/Middleware: Windows, OS X, Linux
- Required library or software: Matlab, SPM, SPM toolboxes : Marsbar, LI-toolbox, NS
- Programming language: Matlab
- Documentation: available at <https://gforge.inria.fr/projects/autofmri/> and <https://gforge.inria.fr/projects/asl/>

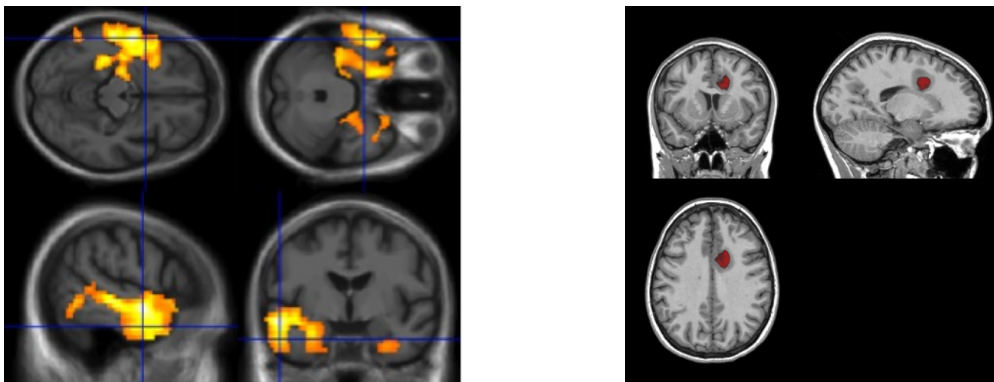


Figure 5. Illustrations of results obtained with autoMRI: Conjunction map showing areas of hypoperfusion and hypometabolism in semantic dementia (right), Detection of relaxometry defect in an MS patient (left).

5.5. medInria

Participants: René-Paul Debroize, Guillaume Pasquier, Laurence Catanese, Olivier Commowick.

medInria is a national Inria project shared between 4 Inria teams (Asclepios, Athena, Parietal and Visages). 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. medInria 2.2.1 has been released in September 2014 for the main distribution platforms. medInria core API source code is also released under a BSD license.

See also Figure 6 and the web page <http://med.inria.fr>

- Keywords: medical imaging, diffusion imaging, registration, filtering, user-friendly interface
- Software benefit: user-friendly interface to cutting-edge research tools for research clinicians. Straightforward to add functionalities through plugins.
- License: core: BSD, plugins: choice of each team.
- Type of human computer interaction: Qt-based GUI
- OS/Middleware: Windows, Mac et Linux.
- Required library or software : Qt, DTK, ITK, VTK.
- Programming language: C++

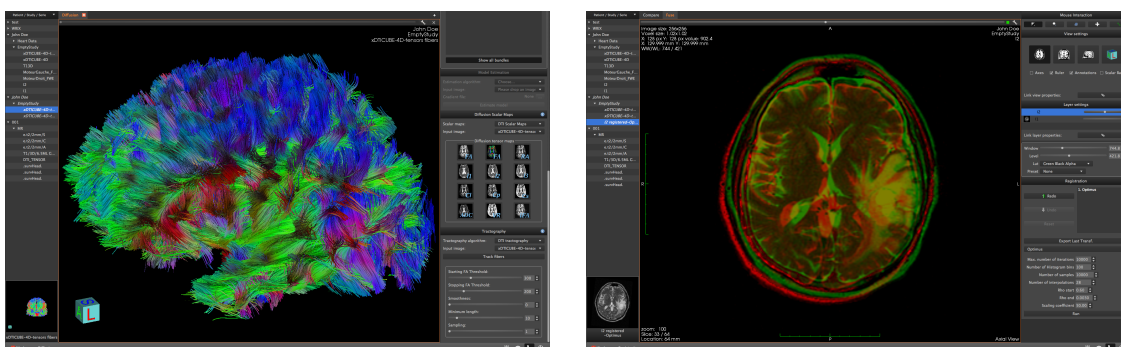


Figure 6. The medInria software platform: Fused view of registered images (right), Tractography overlapped with 3D image (left)

5.6. Anima

Participants: Fang Cao, Laurence Catanese, Olivier Commowick, René-Paul Debroize, Florent Leray, Renaud Hédouin, Guillaume Pasquier.

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.

- Keywords: medical imaging, diffusion imaging, registration, filtering, relaxometry
- Software benefit: New methodological image processing, common place for team code
- Type of human computer interaction: C++ API
- OS/Middleware: Windows, Mac and Linux.
- Required library or software : ITK, VTK.
- Programming language: C++

5.7. Integration of EEG and fMRI

Participants: Marsel Mano, Lorraine Perronnet.

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)

- Keywords: medical imaging, EEG, fMRI
- Software benefit: integration of EEG and fMRI processing
- Type of human computer interaction: C++ API, shell scripts
- OS/Middleware: Windows, Mac and Linux.
- Required library or software : SPM, pnet.
- Programming language: C++, shell scripts

5.8. Platforms

5.8.1. The Neurinfo Platform

VISAGES is the founding actor of a new 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 (<http://www.neurinfo.org>). This platform has been supported under the “Contrat de Projets Etat-Région” (C. Barillot is the PI) and has received a total amount of 5.1 Meuros for the period 2007–2013. European (FEDER), National (through Ministry of research, Inria, Inserm and ANR) and local councils (Brittany Region, Ille et Vilaine, and Rennes Metropolis) have joined their effort to support this operation for a total amount of 5070 keuros (600keuros for the infrastructures, 3670keuros for the equipments and 800keuros 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 U 650 - 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 (U 642 -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). 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. 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 2014, the two engineers running the platform (Elise Bannier and Isabelle Corouge), members of the Visages team, moved from temporary employment contracts to open-ended research engineers contracts.

6. New Results

6.1. Highlights of the Year

Dr Camille Maumet was awarded by the French Society of Magnetic Resonance in Biology and Medicine (SFRMBM) for her PhD Thesis on analysis of neuroimaging data including images from functional Magnetic Resonance Imaging (fMRI) and Arterial Spin Labeling <http://www2.warwick.ac.uk/fac/sci/wmg/idh/idhnews/?tag=Neural+Engineering>.

Dr Americ Stamm was awarded by the Univ. of Rennes I foundation as the best PhD thesis in Math, Computer Sciences and Electrical Engineering. This award is dedicated for the PhDs having the highest potential for innovation and technological transfer <https://fondation.univ-rennes1.fr/les-prix-de-thèses-de-la-fondation>.

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

6.2.1. *A Mathematical Framework for the Registration and Analysis of Multi-Fascicle Models for Population Studies of the Brain Microstructure*

Participant: Olivier Commowick.

Diffusion tensor imaging (DTI) is unable to represent the diffusion signal arising from multiple crossing fascicles and freely diffusing water molecules. Generative models of the diffusion signal, such as multi-fascicle models, overcome this limitation by providing a parametric representation for the signal contribution of each population of water molecules. These models are of great interest in population studies to characterize and compare the brain microstructural properties. Central to population studies is the construction of an atlas and the registration of all subjects to it. However, the appropriate definition of registration and atlas methods for multi-fascicle models have proven challenging. This paper proposes [24] a mathematical framework to register and analyze multi-fascicle models. Specifically, we define novel operators to achieve interpolation, smoothing and averaging of multi-fascicle models. We also define a novel similarity metric to spatially align multi-fascicle models. Our framework enables simultaneous comparisons of different microstructural properties that are confounded in conventional DTI. The framework is validated on multi-fascicle models from 24 healthy subjects and 38 patients with tuberous sclerosis complex, 10 of whom have autism. We demonstrate the use of the multi-fascicle models registration and analysis framework in a population study of autism spectrum disorder. This work was performed in close collaboration with the Children's Hospital Boston.

6.2.2. *Longitudinal Intensity Normalization in Multiple Sclerosis Patients*

Participants: Yogesh Karpate, Olivier Commowick, Christian Barillot, Gilles Edan.

In recent years, there have been many Multiple Sclerosis studies using longitudinal MR images to study and characterize the MS lesion patterns. The intensity of similar anatomical tissues in MR images is often different because of the variability of the acquisition process and different scanners. We proposed [29] a novel methodology for a longitudinal lesion analysis based on intensity standardization to minimize the inter-scan intensity difference. The intensity normalization maps parameters obtained using a robust Gaussian Mixture Model (GMM) estimation not affected by the presence of MS lesions. Experimental results demonstrated that our technique accurately performs the task of intensity standardization. We show consequently how the same technique can improve the results of longitudinal MS lesion detection.

6.2.3. *Simultaneous Estimation of T1, T2 and B1 Maps From Relaxometry MR Sequences*

Participants: Fang Cao, Olivier Commowick, Elise Banner, Christian Barillot.

Interest in quantitative MRI and relaxometry imaging is rapidly increasing to enable the discovery of new MRI disease imaging biomarkers. While DESPOT1 is a robust method for rapid whole-brain voxelwise mapping of the longitudinal relaxation time (T1), the approach is inherently sensitive to inaccuracies in the transmitted flip angles, defined by the B1 inhomogeneity field, which become more severe at high field strengths (e.g., 3T). We have proposed [26] a new approach for simultaneously mapping the B1 field, M0 (proton density), T1 and T2 relaxation times based on regular fast T1 and T2 relaxometry sequences. The new method is based on the intrinsic correlation between the T1 and T2 relaxometry sequences to jointly estimate all maps. It requires no additional sequence for the B1 correction. We evaluated our proposed algorithm on simulated and in-vivo data at 3T, demonstrating its improved accuracy with respect to regular separate estimation methods.

6.2.4. *Quantitative Relaxation Templates for the Human Brain at 3T*

Participants: Fang Cao, Olivier Commowick, Christian Barillot.

Quantitative MRI (qMRI) templates of relaxation times and proton density can be of particular interest for dedicated clinical applications such as characterizing brain tissue abnormalities, as well as general research purposes. We have developed in [27] 3D qMRI statistical templates consisting of T1, T2, T2* and ρ^* maps from the human brain at 3T. The qMRI templates were built from a population of 20 normal controls, for which individual maps were estimated in a robust manner, accounting for acquisition artifacts and expected relationships between the relaxometry parameters. For validation, we fed the qMRI templates into a realistic MRI simulator to synthesize MR-weighted images, and compared these images with the real MR acquisitions. High correlation coefficients (>0.80) show that the developed qMRI templates can be used as input dataset for MRI simulation community, which may be of great interest to clinical neuroscience field.

6.2.5. *Myelin Water Fraction Imaging in Multiple Sclerosis patients*

Participants: Olivier Commowick, Elise Banner, Christian Barillot.

Multi-echo T2 relaxometry is a relevant imaging method for Myelin Water Fraction (MWF) quantification in the study of multiple sclerosis (MS). However, to ensure accurate estimation, a large number of echoes are still required that can drive to very long acquisitions. In practice, 32 echo times (TE) ranging from 10 ms to 320 ms and an echo spacing (ESP) of 10 ms are used. Analysis of the decay curve of the consecutive echoes allows the estimation of the T2 spectrum. The proposed approach makes use of recent spatial regularization methods for MWF estimation from clinically compatible acquisitions (typically 11 echoes acquired within 6 minutes with $TE_1=ESP=8.4$ ms). The algorithms were evaluated on both synthetic and clinical data, illustrating the ability to compute accurate MWF maps from a low number of echoes. The 2 methods used a priori information as well as conventional and fast algorithm (NNLS), and a cross-validation strategy. Based on simulated and clinical data results, the nlsrNNLS estimation is more accurate and less penalizing than srNNLS. This regularization provides an efficient way to circumvent an ill-posed problem aspect, in particular with a reduced number of echoes for clinically acceptable acquisition times, allowing for accurate MWF estimation. This work, performed in the master internship of Lucas Soustelle, was accepted as a conference abstract at SFRMBM 2015, and is submitted to ISMRM.

6.3. Image processing on Diffusion Weighted Magnetic Resonance Imaging

6.3.1. *Fast Identification of Optimal Fascicle Configurations from Standard Clinical Diffusion MRI Using Akaike Information Criterion*

Participants: Olivier Commowick, Christian Barillot.

Analytic multi-compartment models have gained a tremendous popularity in the recent literature for studying the brain white matter microstructure from diffusion MRI. This class of models require the number of compartments to be known in advance. In the white matter however, several non-collinear bundles of axons, termed fascicles, often coexist in a same voxel. Determining the optimal fascicle configuration is a model selection problem. We have proposed [30], [33] a novel approach to identify such a configuration from clinical diffusion MRI where only few diffusion images can be acquired and time is of the essence. Starting from a set of fitted models with increasing number of fascicles, we use Akaike information criterion to estimate the probability of each candidate model to be the best Kullback-Leibler model. These probabilities are then used to average the different candidate models and output an MCM with optimal fascicle configuration. This strategy is fast and can be adapted to any multi-compartment model. We illustrate its implementation with the ball-and-stick model and show that we obtain better results on single-shell low angular resolution diffusion MRI, compared to the state-of-the-art automatic relevance detection method, in a shorter processing time.

6.3.2. Tracking the Cortico-Spinal Tract as a Multi-Modal Distribution of Streamlines from Local White Matter Microstructure Models

Participant: Olivier Commowick.

We have presented [31] a pipeline to reconstruct the corticospinal tract (CST) that connects the spinal cord to the motor cortex. The proposed method combines a new white matter microstructure model coined Diffusion Directions Imaging and a new tractography algorithm based on a particle filter adapted for approximating multi-modal distributions. In this paper, we put the computation time and accuracy of our pipeline to the test in the context of the MICCAI 2014 DTI challenge, which aims to provide fast and accurate reconstructions of the CST for presurgical planning of brain tumor extraction. These two key performance metrics are expected in such a situation where time is of the essence and the quality of the data is dependent on the patient's health condition and ability to cooperate. In no more than 1.5 hours per patient, we successfully provide accurate CSTs of 2 very collaborative patients who underwent a diffusion MRI protocol that included 69 diffusion-sensitizing gradients spread over 4 different shells ranging from $b = 200$ to $b = 3000$ s/mm^2 .

6.3.3. Model selection improvement with non-central chi estimation of multi-compartment models

Participant: Olivier Commowick.

Diffusion images are known to be corrupted with a non-central chi (NCC)-distributed noise. There has been a number of proposed image denoising methods that account for this particular noise distribution. However, to the best of our knowledge, no study was performed to assess the influence of the noise model in the context of diffusion model estimation. In particular, multi-compartment models are an appealing class of models to describe the white matter microstructure but require the optimal number of compartments to be known a priori. Its estimation is no easy task since more complex models will always better fit the data, which is known as over-fitting. However, MCM estimation in the literature is performed assuming a Gaussian-distributed noise. We have shown in a preliminary study [32] that using the appropriate NCC distribution for modeling the noise model reduces significantly the over-fitting, which could be helpful for unraveling model selection issues and obtaining better model parameter estimates.

6.3.4. Symmetric Block-Matching Registration for the Distortion Correction of Echo-Planar Images

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

We have introduced a new approach to correct geometric and intensity distortion of Echo Planar Images (EPI) from images acquired with opposite phase encoding directions. A new symmetric block-matching registration algorithm has been developed for this purpose relying on new adapted transformations between blocks and a symmetric optimization scheme to ensure an opposite symmetric transformation. We present results of our algorithm showing its ability to robustly recover EPI distortion while obtaining sharper results than the popular TOPUP algorithm. This work was performed in close collaboration with the Children's hospital in Boston.

6.4. Medical Image Computing in Brain Pathologies

6.4.1. *Adaptive Dictionary Learning for Competitive Classification of Multiple Sclerosis Lesions*

Participants: Hrishikesh Deshpande, Pierre Maurel, Christian Barillot.

The manual delineation of Multiple Sclerosis (MS) lesions is a challenging task pertaining to the requirement of neurological experts and high intra- and inter-observer variability. It is also time consuming because large number of Magnetic Resonance (MR) image slices are needed to obtain 3-D information. Over the last years, various models combined with supervised or unsupervised classification methods have been proposed for segmentation of MS lesions using MR images. Recently, signal modeling using sparse representations (SR) has gained tremendous attention and is an area of active research. SR allows coding data as sparse linear combinations of the elements of over-complete dictionary and has led to interesting image recognition results. In this work, we have proposed to use a sparse representation and an adaptive dictionary learning paradigm to automatically classify Multiple Sclerosis (MS) lesions from MRI. In particular, we investigate the effects of learning dictionaries specific to the lesions and individual healthy brain tissues, which include White Matter (WM), Gray Matter (GM) and Cerebrospinal Fluid (CSF). The dictionary size plays a major role in data representation but it is an even more crucial element in the case of competitive classification. We present an approach that adapts the size of the dictionary for each class, depending on the complexity of the underlying data. The proposed algorithm is evaluated on 3-D multi-channel MR images demonstrating improved classification.

6.4.2. *Predictive Value of Imaging Markers at Multiple Sclerosis Disease Onset Based on Gadolinium- and USPIO- Enhanced MRI and Machine Learning*

Participants: Olivier Commowick, Jean-Christophe Ferré, Elise Bannier, Gilles Edan, Christian Barillot.

A novel characterization of Clinically Isolated Syndrome (CIS) patients according to lesion patterns has been proposed in [13]. More specifically, patients are classified according to the nature of inflammatory lesions patterns. It is expected that this characterization can infer new prospective figures from the earliest imaging signs of Multiple Sclerosis (MS), since it can provide a classification of different types of lesions across patients. The method is based on a two-tiered classification. Initially, the spatio-temporal lesion patterns are classified. The discovered lesion patterns are then used to characterize groups of patients. The patient groups are validated using statistical measures and by correlations at 24-month follow-up with hypointense lesion loads. The methodology identified 3 statistically significantly different clusters of lesion patterns showing p-values smaller than 0.01. Moreover, these patterns defined at baseline correlated with chronic hypointense lesion volumes by follow-up with an R^2 score of 0.90. The proposed methodology is capable of identifying three major different lesion patterns that are heterogeneously present in patients, allowing a patient classification using only two MRI scans. This finding may lead to more accurate prognosis and thus to more suitable treatments at early stage of MS.

6.4.3. *Robust detection of multiple sclerosis lesion from intensity-normalized multi-channel MRI*

Participants: Yogesh Karpate, Olivier Commowick, Christian Barillot.

Multiple sclerosis (MS) is a disease with heterogeneous evolution among the patients. Better understanding of the disease will lead to improved patient-adapted therapeutic strategies. We propose a novel paradigm to detect MS lesions based on a statistical framework which consists of detection based on differences between multi-channel MRI of patients and controls. This framework fused with intensity standardization was applied to the study of MS and highlighted the great interest of quantitative MRI measurements for a better characterization of MS. Experimental results demonstrate that our technique accurately detects significant differences in lesions consequently improving the results of MS lesion detection. This work has been accepted to SPIE Medical Imaging 2015.

6.4.4. Multiple Sclerosis Lesions Recognition: One Class Learning Approach

Participants: Yogesh Karpate, Olivier Commowick, Christian Barillot, Gilles Edan.

We have developed an automatic algorithm for the detection of multiple sclerosis lesions (MSL) from multi-sequence magnetic resonance imaging (MRI). We build a probabilistic classifier that can recognize MSL as a novel class, trained only on Normal Appearing Brain Tissues (NABT). Patch based intensity information of MRI images is used to train a classifier at the voxel level. The classifier is in turn used to compute a probability characterizing the likelihood of each voxel to be a lesion. This probability is then used to identify a lesion voxel based on simple Otsu thresholding. This work has been submitted to ISBI 2015.

6.5. Vascular Imaging and Arterial Spin Labeling

6.5.1. Peripheral angiography and neurovascular imaging

Participants: H el ene Raoult, Jean-Yves Gauthier, Elise Bannier, Pierre Maurel, Christian Barillot, Jean-Christophe Ferr e.

Work-in-progress Non contrast enhanced MR angiography sequences were optimized on phantom as well as healthy volunteers and evaluated on patients presenting arterio venous malformations (AVM). High temporal resolution (70ms) images were obtained and compared to the gold standard Digital Subtraction Angiography. Results showed that Time-resolved SL MR angiographic imaging over two cardiac cycles is a reliable clinical tool for cerebral AVM characterization, yielding very good to excellent agreement with DSA. This work was published in Radiology late 2013. This data was also post processed to obtain hemodynamics maps (time to peak, wash-in, wash out and mean transit time) and discriminate among different AVM components to relate hemodynamic patterns with rupture risk. This work was published in Stroke [23].

6.5.2. Robust perfusion maps in Arterial Spin Labeling by means of M-estimators

Participants: Pierre Maurel, Jean-Christophe Ferr e, Christian Barillot.

Non-invasive measurement of Cerebral Blood Flow (CBF) is now feasible thanks to the introduction of Arterial Spin Labeling (ASL) Magnetic Resonance Imaging (MRI) techniques. To date, due to the low signal-to-noise ratio of ASL, a single acquisition (pair of control/label scans) is not sufficient to estimate perfusion reliably. Instead, the acquisition is usually repeated several times and the perfusion information is calculated by averaging across the repetitions. However, due to its zero breakdown point, the sample mean is very sensitive to outliers. We have proposed [18] to compute ASL CBF maps using Huber's M-estimator, a robust statistical function that is not overly impacted by outlier. This work was part of the PhD thesis of Camille Maumet.

6.5.3. Brain perfusion gender difference study using MRI in young adults

Participants: L ea Itmi, Pierre Maurel, Christian Barillot.

The usage of population models is becoming increasingly important in cerebral imaging, particularly in ASL. Therefore, it is important to check the limits of the models before applying them, to guarantee the reliability of the results. It is now well-known that brain perfusion changes with the age, and this effect is taken into account when evaluating brain perfusion images. But gender differences have not been well studied yet. It is known for a long time that female brain perfusion is higher than male brain perfusion, but few studies have investigated whether some regional perfusion differences exist or not. We evaluate whether, as for the age, gender differences should be taken into account when analyzing brain perfusion images. We focus on young adults subjects and studied, at the region level and the voxel level if gender differences exist and how it differs. The overall and regional differences were analyzed and then we also investigated the perfusion asymmetries in the brain (left hemisphere versus right hemisphere).

6.6. EEG and MR Imaging

6.6.1. Feasibility and specificity of simultaneous EEG and ASL MRI at 3T

Participants: Elise Bannier, Marsel Mano, Isabelle Corouge, Lorraine Perronnet, Christian Barillot.

Brain functional imaging can be performed using several approaches, including EEG, BOLD and ASL MRI. The Neurinfo platform has acquired an EEG MR compatible 64ch device over the summer to perform joint EEG and BOLD or ASL fMRI. To date, only a few studies have addressed the issue of connecting EEG signal to ASL perfusion. The aim of this study was to assess ASL-EEG at 3T in terms of safety as well as EEG and MR signal quality. The temperature measurements, specific absorption rate, and signal to noise ratio experiments have shown that ASL EEG can be safely performed using the parameters presented above. However, residual gradient artifacts in the PASL-EEG data have to be considered. Further research is needed to understand the artifact variability and to develop an appropriate correction strategy. This study is performed as part of the HEMISFER project in close collaboration with the involved teams.

6.6.2. Neurofeedback using Virtual Reality and Hybrid EEG-MRI for Brain Rehabilitation

Participants: Lorraine Perronnet, Marsel Mano, Christian Barillot.

We have conducted a thorough state-of-the-art of Neurofeedback (NF) and restorative Brain Computer Interfaces (BCI) under EEG and fMRI modality as well as of EEG-fMRI integration, with a particular focus on applications in depression and motor rehabilitation. This enabled us to build a theoretical comparison of EEG- and fMRI-NF methodology that will be helpful in designing NF protocols combining both modalities. In this perspective, we are currently designing a NF protocol based on motor imagery that will be compatible with EEG and fMRI, and running preliminary recordings of motor execution and motor imagery. Besides, we are writing a book chapter about NF and BCI that is intended to disambiguate the existing definitions and to present basic knowledge about NF principles and applications to naive readers. This is a joint work with Anatole Lécuyer team (Hybrid), in the frame of the Hemisfer project.

6.6.3. Symmetrical EEG and fMRI Imaging by Sparse Regularization

Participants: Thomas Oberlin, Pierre Maurel, Christian Barillot.

This work considers the problem of brain imaging using simultaneously recorded electroencephalography (EEG) and functional magnetic resonance imaging (fMRI). To this end, we introduce a linear coupling model that links the electrical EEG signal to the hemodynamic response from the blood-oxygen level dependent (BOLD) signal. Both modalities are then symmetrically integrated, to achieve a high resolution in time and space while allowing some robustness against potential decoupling of the BOLD effect. The novelty of the approach consists in expressing the joint imaging problem as a linear inverse problem, which is addressed using sparse regularization. The sparsity prior naturally reflects the fact that only few areas of the brain are activated at a certain time, and it is easily implemented through efficient so-called proximal algorithms. The significance of the method and the effectiveness of the algorithms are demonstrated through numerical investigations on a simplified head model and simulated data on a realistic brain model. This is a joint work with Remi Gribonval team (Panama), in the frame of the Hemisfer project.

7. Bilateral Contracts and Grants with Industry

7.1. Bilateral Contracts with Industry

7.1.1. Siemens

duration: 5 years from 2011/10/26

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.

7.2. Bilateral Grants with Industry

7.2.1. 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.

8. Partnerships and Cooperations

8.1. Regional Initiatives

8.1.1. 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.

8.1.2. COREC projects

COREC is the "COMité de REcherche Clinique" of the University Hospital of Rennes. This comity proposes an annual project funding in the limit of 30k€ per project. In 2014, the Neurinfo platform as an incitative action for clinical research project emergence accompanied the COREC call by financially supporting the imaging part of the projects up to 50 MRI hours, i.e. 30k€. Two projects including brain MRI were selected. The EPMR-MA project led by the neuropsychologist Pierre-Yves Jonin, and co-funded by Fondation de l'avenir in 2014, will evaluate memory effects in healthy adults and in patients presenting cognitive impairments using BOLD fMRI, ASL and Diffusion MRI. The second project is a complementary funding for the project led by Dr Fabienne Pelé (see below).

8.1.3. *Projet Fondation de France : PERINE*

Participants: Elise 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 will continue over 2 years.

8.1.4. *Fondation de l'Avenir - Depression, suicide and fMRI*

Participants: Elise Bannier, Isabelle Corouge, Jean-Christophe Ferré, Christian Barillot.

initial duration: 12 months from November 2012. Project extended in 2014.

In collaboration with EA 4712 "Comportement et Noyaux Gris Centraux" of the University of Rennes I, a complementary funding (20 000€) was obtained to support an ongoing fMRI research project on emotions, impulsivity and suicide. The study protocol and the fMRI task was finalized. Inclusions started in early 2013. The project was extended in 2014 to recruit more patients.

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

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

duration: 12 months from November 2012. Project extended in 2014.

A complementary funding (20 000€) was obtained to support a new research project on rehabilitation of stroke patients. The fMRI protocol was setup, the task developed and validation on volunteers is ongoing. Patient inclusions started in spring 2013. This project was also extended to 2014 to recruit more patients. Group analysis on the control group was performed and a paper will be submitted soon.

8.2. National Initiatives

8.2.1. ANR

8.2.1.1. ANR “Neurological and Psychiatric diseases” NUCLEIPARK

Participants: Christian Barillot, Sylvain Prima.

NucleiPark project: In the context of the ANR-09-MNPS-016 Nucleipark project we develop a pipeline for detecting shape changes in Parkinson and Paralysis Supranuclear Progressive (PSP) diseases. The pipeline is based on the previous work of Benoit Combès et al. [35]. The pipeline was first validated on controlled synthetic data. For Parkinson disease, a total of 16 patients and 11 healthy controls were evaluated. The structures analyzed were: PPN, GPe, GPi, Caudate, Putamen, SN, STN, RN. Differences (uncorrected $P < 0.001$) were found in the right putamen and caudate structures. And slight difference (uncorrected $P < 0.05$) in the right GPe. No significant correlation was found in PPN, GPi, SN, STN, and RN structures. In the case of PSP disease, a total of 10 patients and 11 healthy controls were evaluated. the structures analyzed were: PPN, GPe, GPi, Caudate, Putamen, SN, STN, RN. Differences (uncorrected $P < 0.001$) were found in the left caudate structure. No significant correlation was found in PPN, GPe, GPi, Putamen, SN, STN, and RN structures. This project involves three partners: NeuroSpin, Inria (Athena and Visages) and UPMC (University Pierre and Marie Curie, Paris) including Inserm U678 and the CENIR.

In the context of this project, we propose a statistical data analysis pipeline that uses the apparent diffusion coefficient (ADC) as biomarker. The ADC is computed considering the diffusion weighted signal as a scalar field on a 5-D manifold. This consideration allows to keep the information about direction of the ADC. We have tested the proposed pipeline on synthetic dataset with promising results. Other contributions were the implementation and minimization, in the 5-D non-euclidean space, of the total variation (in its dual formulation) inpainting problem as interpolation method used in the statistical pipeline.

8.2.1.2. TRANSLATE-MS-REPAIR

Participants: Laurence Catanese, Olivier Commowick, Isabelle Corouge, Jean-Christophe Ferré, Elise Bannier, Gilles Edan, Christian Barillot.

It is now commonly admitted that MS is not only an inflammatory disease but a neurodegenerative disease as well. This project is devoted to show that the olesoxime molecule is not only neuroprotective, but it has the ability to promote the maturation of oligodendrocyte progenitor cells (OPCs) into myelinating oligodendrocytes. However, before considering a large-scale clinical trial to assess efficacy. An important aspect is that to date, no treatment for neuroprotection / remyelination has reached the stage of clinical proof of concept that aims Trophos company who is leading this project. It appears that the best criteria for assessing neuroprotective/remyelinating effect of the drug candidate, are MRI criteria. However, these imaging criteria have not yet been validated for use in multicentre trials - so we will also check the feasibility of such measures under this condition. In addition to Trophos company, the partners of this project are AP-HM/CNRSCEMEREM-CRMBM, CHU Rennes, CHU Reims, and Inria-VISAGES.

8.2.2. Competitivity Clusters

8.2.2.1. The HEMISFER Project

Participants: Elise Bannier, 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"¹. 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).

8.2.2.2. France Life Imaging (FLI)

Participants: Christian Barillot, Olivier Commowick, Florent Leray, Michael Kain, Yao Yao.

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; LSIT/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.

8.2.2.3. OFSEP

Participants: Justine Guillaumont, Elise Bannier, Christian Barillot, Olivier Commowick, Gilles Edan, Isabelle Corouge, Jean-Christophe Ferré, Michael Kain.

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 35,000 people with Multiple Sclerosis, approximately half of the patients residing in France. The generalization of longitudinal monitoring and systematic association

¹<https://www.inria.fr/cominlabs-newsletter/april-2013-four-projects-selected/#hemisfer>

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.

8.2.3. Collaboration with the CEA (Commissariat à l'Energie Atomique) : Imaging data quality control in the context of dementia

Participants: Elise Bannier, Christian Barillot, Isabelle Corouge, Jean-Christophe Ferré, Cédric Meurée.

duration: 12 months from September 2014.

Dementia, in particular Alzheimer Disease (AD), affects about 900,000 people in France. As an early and reliable diagnosis remains a difficult task, neuroimaging plays a crucial role in assisted-diagnosis by analyzing structural and functional brain abnormalities associated with the disease. The "Centre pour l'Acquisition et le Traitement des Images (CATI)" has created a national network of neuroimaging centers in order to promote clinical research on MA using advanced imaging techniques. Visages and the Neurinfo platform are recognized in the CATI for their expertise in Arterial Spin Labeling, both on the acquisition and the post-processing sides. In this context and in the frame of the Alzheimer plan, a collaboration contract was signed between Inria and CEA, the coordinator for the CATI, in order to host an engineer at Inria for a year. This engineer develops control quality tools and advanced post-processing techniques for ASL to be used in nation-wide clinical studies coordinated by the CATI.

8.3. European Initiatives

8.3.1. FP7 & H2020 Projects

8.3.1.1. EuroBioimaging

Type: CAPACITIES

Defi: 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, C. 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.

8.3.2. Collaborations in European Programs, except FP7 & H2020

Program: COST

Project acronym: AID (oc-2010-2-8615)

Project title: Arterial spin labeling Initiative in Dementia

Acceptation date: 18/05/2011

Coordinator: X. Golay, UCL, London, UK

Other partners: Ghent University (BE), Liege University (BE), Hospital Cantonal de Geneve (CH), Fraunhofer MEVIS (D), Freiburg University (D), Max Planck Institute for Human Cognitive & Brain Sciences (D), Glostrup Hospital (DK), Hospital Santa Creu I Sant Pau (ES), Universidad Rey Juan Carlos (ES), University of Navarra (ES), INSERM U836 Grenoble (FR), University of Rennes I (FR), Centro San Giovanni di Dio - Fatebenefratelli (IT), Fondazione Istituto Neurologico Besta (IT), Leiden University Medical Center (NL), UMC Utrecht (NL), VU University Medical Centre (NL), Instituto Superior Técnico (PT), University of Porto (PT), Lund University Hospital (SE), Uppsala University Hospital (SE), Skane University Hospital (SE), Bogazici University (TR), King's College London (UK), University College London (UK), University of Nottingham (UK), University of Oxford (UK)

Abstract: Dementia is a major clinical challenge with care costs approaching 1% of global GDP. Recent estimates suggest that delaying disease onset by 5 years would halve its prevalence. As new disease-modifying treatments will be specific to causative diseases, expensive and bear significant side effects, early diagnosis of dementia will be essential. Current diagnostic criteria include the use of image-based biomarkers using radiotracers. The AID Action aims at coordinating the development of an alternative and cost-effective tool based on an MRI technique, Arterial Spin Labeling (ASL), to obtain reproducible brain perfusion measurements in dementia patients by bringing together scientists and clinicians from across Europe through the flexibility of the COST mechanism. The scientific program is centered around four work packages and three workgroups aiming at developing standards, improving the reliability of the technique and as establishing it as a possible clinical trial outcome measure. Development of MRI methods, post-processing tools, protocols of cross-validation, statistical analyses and launch of clinical and comparative studies will be undertaken. The main benefit of this Action will be to provide a cost-effective alternative to radiotracer-based biomarkers, and help care providers throughout Europe balancing the need for early diagnosis of dementia with the necessary healthcare cost containment. The Visages team is involved in the workgroups ASL data acquisition (E. Bannier), ASL data analysis (C. Barillot, I. Corouge, P. Maurel) and clinical validation of ASL in cognitive impairment (J.-C. Ferré).

8.4. International Initiatives

8.4.1. Inria Associate Teams

8.4.1.1. BARBANT

Title: Boston and Rennes, Brain image Analysis Team

International Partner (Institution - Laboratory - Researcher):

Boston Children's Hospital (ÉTATS-UNIS)

Duration: 2012 - 2014

See also: <http://team.inria.fr/barbant/>

This associated team is shared between Inria Visages team and the Computational Radiology Laboratory of the Children's hospital Boston at Harvard Medical School. We will address the topic of better understanding the behavior and evolution of neurological pathologies (such as neurodevelopmental delay or multiple sclerosis) at the organ and local level, and the modeling of normal and pathological groups of individuals (cohorts) from image descriptors. 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. In 2014, two workshops were organized (one in Rennes, one in Boston), and several publications were accepted /submitted in diffusion imaging. An extension for three more years has been applied for in December 2014.

8.5. International Research Visitors

8.5.1. Visits of International Scientists

- Within the BARBANT associate team, P. Simon K. Warfield, Dr. Benoit Scherrer and Dr. Maxime Taquet (Computational Radiology Laboratory, Harvard Medical School) visited us for a workshop on multiple sclerosis and diffusion image processing.

8.5.2. Visits to International Teams

- Several members of the Visages team (Christian Barillot, Olivier Commowick, Renaud Hédouin, Yogesh Karpate) visited the Computational Radiology Laboratory (Harvard Medical School) for an associate team (BARBANT) meeting to discuss new research topics.
- From November 2014 to February 2015, Hrishikesh Deshpande visits Duke University (in Durham, North Carolina, United States) to collaborate with Professor Guillermo Sapiro on classification using Dictionary Learning. This visit was partially founded by a mobility grant from the doctoral school MATISSE.
- Maia Proisy was co-supervised by UCL and Visages (Pr Jean-Christophe Ferré), during her 6 months visit at UCL for her master research work. In this collaboration was investigated and implemented a pCASL sequence at 3T for measuring brain CBF in neonates at risk of hypoxic-ischemic encephalopathy. This work was also designed to establish a pCASL protocol for further study. Arterial Spin Labelling was a part of an ongoing study (The UCH Baby Brain Study - London), led by Prof Nicola Robertson and Dr Cristina Uria-Avellanal. Imaging data acquisition and processing was made by scientist from the UCL Institute of Neurology - London (Magdalena Sokolska and Prof Xavier Golay).

9. Dissemination

9.1. Promoting Scientific Activities

9.1.1. Scientific events organisation

9.1.1.1. General chair, scientific chair

- C. Barillot co-Chair of Miccai 2014, Boston MA - Sept 14-18 2014

9.1.2. Scientific events selection

9.1.2.1. Chair of conference program committee

- C. Barillot Program Committee Chair of Miccai 2014, Boston MA - Sept 14-18 2014

9.1.2.2. Member of the conference program committee

- C. Barillot was area chair of SPIE Medical Imaging: Image Processing, IEEE ISBI, TPC member of ESMRMB.

9.1.2.3. Reviewer

- O. Commowick was TPC member of MICCAI'2014, IEEE ISBI'2014.

9.1.3. Journal

9.1.3.1. Member of the editorial board

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

9.1.3.2. Reviewer

- IEEE TIP (CB), IEEE TMI (OC, PM), Medical Image Analysis (CB, SP, OC), NeuroImage (CB, OC), Neuroimage clinical (CB), Computer Methods and Programs in Biomedicine (CB), Comput. Med Im & Graph (CB), Comp Meth & Prog in Biomed (CB), IEEE Signal Proc. Let. (CB), Sensors (CB), Magnetic Resonance in Medicine (EC), Plos-ONE (CB, EC), IJICT (CB), IJSISE (CB), IJCVR (CB), Journal of Mathematical Imaging and Vision (PM), Neurobiology of Aging (IC).

9.2. Teaching - Supervision - Juries

9.2.1. Teaching

Teaching on 3D Medical Imaging (visualization, segmentation, fusion, management, normalization) in the following tracks:

Master 2 SIBM, University of Angers-Brest-Rennes: 26h (C. Barillot, O. Commowick, S. Prima, I. Corouge, E. Bannier, J.-Y. Gauvrit):

C. Barillot is responsible for one semester.

J.-Y. Gauvrit is the coordinator for the Master.

Master 1 SIBM, University of Rennes: 5h (S. Prima)

Ecole Supérieure d'Ingénieur de Rennes (ESIR): 60h in medical imaging (P. Maurel)

Other topics:

Ecole Supérieure d'Ingénieur de Rennes (ESIR): 60h in general image processing (P. Maurel) and 60h in algorithmics and complexity (P. Maurel)

ENS Cachan-Bretagne: 24h in introduction to image processing (P. Maurel)

9.2.2. Supervision

PhD Hrishikesh Deshpande, Dimensionality Reduction and Statistical Learning for Computational Modeling of Natural Evolution of Brain Pathologies, Inria, from December 2012, Christian Barillot, Pierre Maurel

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

PhD Yogesh Karpate, Quantitative analysis of MRI in Multiple Sclerosis in the context of the clinically isolated syndrome, INSERM, from December 2011, Christian Barillot, Olivier Commowick

PhD Lea Itmi, Quantitative Analysis Of Arterial Spin Labeling MRI For Robust Parametric Information Of Perfusion Maps, Inria / Siemens, from Mar 2014, Christian Barillot, Pierre Maurel

PhD 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 Hélène Raoult, "Angio-RM morphologique et dynamique sans injection de produit de contraste dans l'exploration des pathologies neurovasculaires", CHRU Rennes, Nov. 2011, defended in October 2014, Elise Bannier, Jean-Yves Gauvrit

9.2.3. Juries

- C. Barillot: PhD, Reviewer, Maxime Taquet, University of Louvain, Jan 2014

- C. Barillot: PhD, President, Celine Louarpe, Univ. Pierre et Marie Curie, Jan 2014
- C. Barillot: PhD, Reviewer, Viviana Siless, Université Paris Sud, July 2014
- C. Barillot: HDR, President, François Rousseau, June 2014
- C. Barillot: PhD, Reviewer, Zehan Wang, Imperial College, London, Nov. 2014
- C. Barillot: PhD, Reviewer and President, Erin Stretton, Mines Paris-Tech, Nov. 2014
- C. Barillot: PhD, President, Aurélie Emilien, Univ. of Bordeaux, Dec. 2014

9.3. Popularization

- Conférence/débat public "Le partage de données d'imagerie en santé: Noeud FLI-IAM", Journées Françaises de Radiologie
- Conférence/débat public "Les biomarqueurs d'imagerie" Collège de France
- Conférence/débat public Technoférence "E-santé", Pôle Image et Réseaux
- Exposition Stand démonstration Inria, Journées Françaises de Radiologie
- Presse écrite "Equipe de recherche Visages et ses projets innovants", Revue CAPITAL
- Site web de vulgarisation "Projet Hemisfer", lettre d'information Emergences Inria
- Site web de vulgarisation : reportage photo Serimedix/inserm
- Site web de vulgarisation Emergence Inria: <http://emergences.inria.fr/emergences-2014/newsletter-n30/L30-SHANOIR>

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- [6] D. GARCÍA-LORENZO, S. PRIMA, L. ARNOLD, D. COLLINS, C. BARILLOT. *Trimmed-likelihood estimation for focal lesions and tissue segmentation in multisequence MRI for multiple sclerosis*, in "IEEE Transactions on Medical Imaging", August 2011, vol. 30, n^o 8, pp. 1455-67 [DOI : 10.1109/TMI.2011.2114671], <http://www.hal.inserm.fr/inserm-00590724>

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