IN PARTNERSHIP WITH:
CNRS

INSERM

Université Rennes 1

Activity Report 2013

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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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 2006. 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 behaviour, 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.

2.2. Highlights of the Year

- The VISAGES team was awarded by the Brittany INPI Trophee for research and innovation in the *research structure* category (http://www.bretagne-innovation.tm.fr/Temoignages/Laureats-Trophees-INPI-Bretagne-2013-Laboratoire-VisAGeS-Video).
- H. Raoult received a Magna Cum Laude Merit Award at the 21th Annual ISMRM 2013

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 tumour imaging for instance).
- In the field of image analysis and statistical modelling 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 labelling 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.

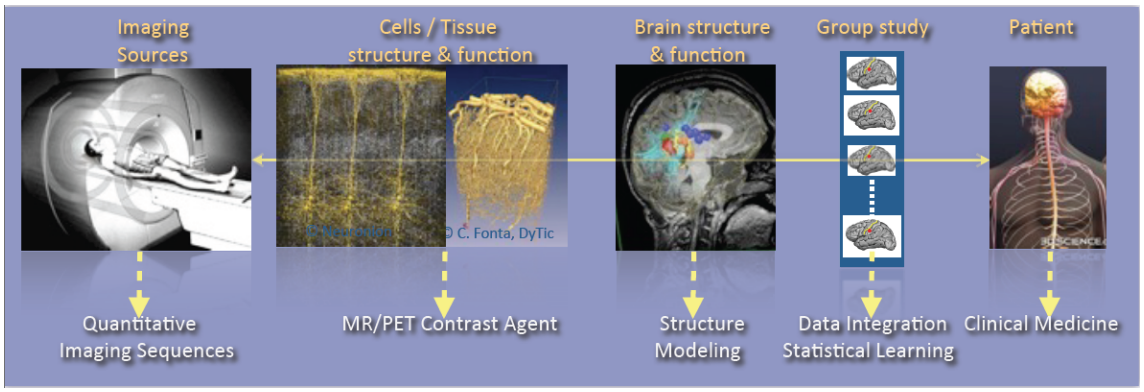

Figure 1. The major overall scientific foundation of the team concerns the integration of data from the Imaging source to the patient at different scales : from the cellular or molecular level describing the structure and function, to the functional and structural level of brain structures and regions, 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. This approaches 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, modelling 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. Since MRI has a low specificity for defining in more detail the pathological changes which could discriminate between the different lesion types, but a high sensitivity to detect focal and also widespread, diffuse pathology of the normal appearing white and grey matter, our major objective within this application domain is 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 labelling 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. Modelling 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. Software and Platforms

5.1. CLARCS: C++ Library for Automated Registration and Comparison of Surfaces

Participants: Juan Francisco Garamendi Bragado, Sylvain Prima.

In collaboration with Benoit Combès (Géosciences Rennes, UMR 6118) and Alexandre Abadie (Inria Saclay Île-de-France), within the 3D-MORPHINE ARC project (http://3dmorphine.inria.fr), we conceived and implemented a C++ library (named CLARCS) for the automated analysis and comparison of surfaces. One of the primary goal of this library is to allow the assessment and quantification of morphological differences of free-form surfaces from medical or paleoanthropological data.

- APP: IDDN.FR.001.130002.000.S.P.2011.000.21000
- Programming language: CC++

CLARCS was presented at the MeshMed MICCAI workshop (http://www2.imm.dtu.dk/projects/MeshMed/2011/index.html) [57] and is to be distributed through a dedicated website (http://clarcs.inria.fr).

We also developed a surface viewer (named 'Surface').

- APP: IDDN.FR.001.110019.000.S.P.2011.000.21000
- Programming language: C++, Python

5.2. Shanoir

Participants: Justine Guillaumont, Michael Kain, Christian Barillot.

Shanoir (Sharing NeurOImaging Resources) is an open source neuroinformatics platform designed to share, archive, search and visualize neuroimaging data. It provides a user-friendly secure web access and offers an intuitive workflow to facilitate the collecting and retrieving of neuroimaging data from multiple sources and a wizzard to make the completion of metadata easy. Shanoir comes along many features such as anonymization of data, support for multi-centres clinical studies on subjects or group of subjects. 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 (Figure 2).

Shanoir APP registration number is: IDDN.FR.001.520021.000.S.P.2008.000.31230

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

- Keywords: neuroimaging, ontology, sharing neuroimage
- 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/Middelware: Windows, Mac et Linux.
- Required library or software: Java 1.6, JBoss server, JBoss Seam, JSF, JPA Hibernate, EJB, Richfaces, Faceless, Ajax4JSF, Dcmtk, Dcm4chee.
- Programming language: Java
- Documentation: see the website

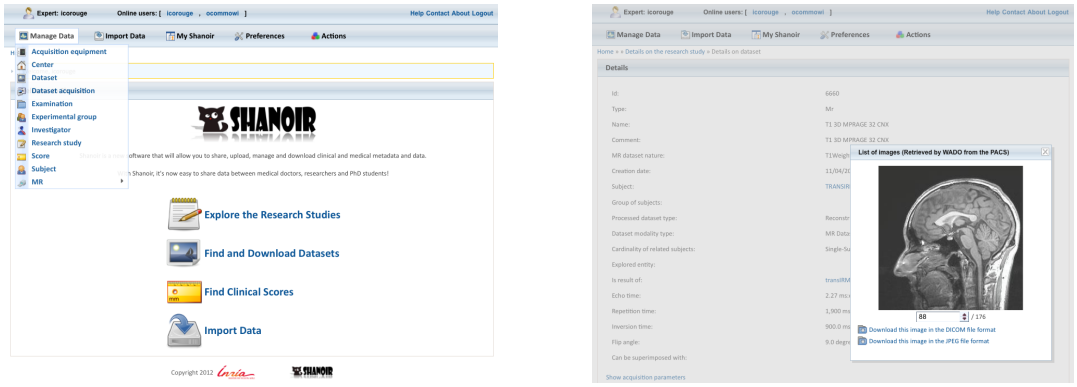

Figure 2. The SHANOIR software is a web application to share, archive, search and visualize neuroimaging data.

5.3. ShanoirUploader

Participants: Justine Guillaumont, Michael Kain.

The ShanoirUploader is a desktop application on base of JavaWebStart (JWS). The app can be downloaded and installed using an internet browser. The app 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 app 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://www.shanoir.org as the ShanoirUploader documentation is integrated on this page.

- Keywords: neuroimaging, ontology, sharing neuroimage
- 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 licence for the moment
- Type of human computer interaction: desktop application on base of JavaWebStart (JWS), web service (SOAP messages based)
- OS/Middelware: Linux, Windows and Mac
- Required library or software : Java SDK, installed on client machine
- Programming language: Java
- Documentation : see the website

5.4. AutoMRI

Participants: Camille Maumet, Isabelle Corouge, Pierre Maurel, Fang Cao, Elise Bannier.

AutoMRI Based on MATLAB and the SPM8 toolbox, autoMRI provides complete pipelines to pre-process and analyze various types of images (anatomical, funcional, 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 normalisation 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 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 3).

- 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/

5.5. Medinria

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

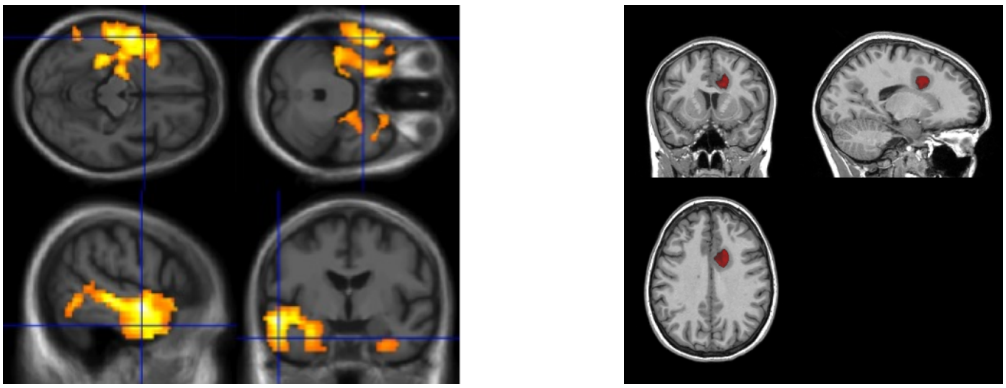

Figure 3. Illustrations of results obtained with autoMRI: Conjunction map showing areas of hypoperfusion and hypometabolism in semantic dementia (right), Detection of relaxometry defect in an MS patient (left).

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 for two years 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 2.1.2 has been released in September 2013 for the main distribution platforms. medInria core API source code has also been released under a BSD license.

See also Figure 4 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/Middelware: Windows, Mac et Linux.
- Required library or software : Qt, DTK, ITK, VTK.
- Programming language: C++

5.6. Anima

Participants: René-Paul Debroize, Guillaume Pasquier, Aymeric Stamm, Fang Cao, Olivier Commowick.

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 simpler 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++

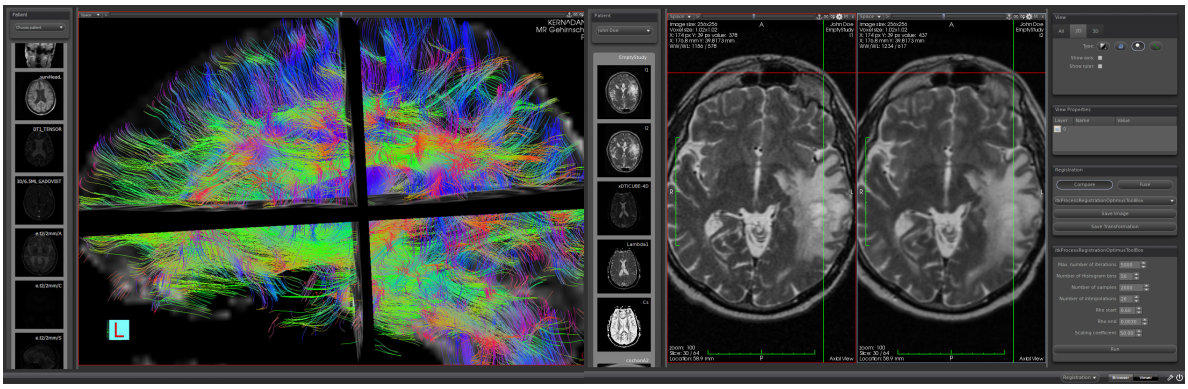

Figure 4. The medInria software platform : Side by side registration using fast algorithms Optimus (right), Tractography overlapped with 3D image (left)

6. New Results

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

6.1.1. 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 atlasing methods for multi-fascicle models have proven challenging. This paper proposes [32] 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.

6.1.2. Multimodal rigid-body registration of 3D brain images using bilateral symmetry

Participants: Sylvain Prima, Olivier Commowick.

In this paper we show how to use the approximate bilateral symmetry of the brain with respect to its interhemispheric fissure for intra-subject (rigid-body) mono- and multimodal 3D image registration. We propose to define and compute an approximate symmetry plane in the two images to register and to use these two planes as constraints in the registration problem. This 6-parameter problem is thus turned into three successive 3-parameter problems. Our hope is that the lower dimension of the parameter space makes these three subproblems easier and faster to solve than the initial one. We implement two algorithms to

solve these three subproblems in the exact same way, within a common intensity-based framework using mutual information as the similarity measure. We compare this symmetry-based strategy with the standard approach (i.e. direct estimation of a 6-parameter rigid-body transformation), also implemented within the same framework, using synthetic and real datasets. We show in [44] our symmetry-based method to achieve subvoxel accuracy with better robustness and larger capture range than the standard approach, while being slightly less accurate and slower. Our method also succeeds in registering clinical MR and PET images with a much better accuracy than the standard approach. Finally, we propose a third strategy to decrease the run time of the symmetry-based approach and we give some ideas, to be tested in future works, on how to improve its accuracy.

6.1.3. Distortion Correction in EPI Diffusion Weighted Images

Participants: Renaud Hedouin, Olivier Commowick.

We have compared and developed several methods which correct distortion of EPI images. The most popular method field map do not give optimal results. We have implemented and improved a method based on reversed phase encoding gradient which give good results. To correct diffusion weighted images this method only need one reversed phase encoding gradient $B0$ image which not need substantial additional acquisition time.

6.1.4. Using bilateral symmetry to improve non-local means denoising of MR brain images

Participants: Sylvain Prima, Olivier Commowick.

The popular NL-means denoising algorithm proposes to modify the intensity of each voxel of an image by a weighted sum of the intensities of similar voxels. The success of the NL-means rests on the fact that there are typically enough such similar voxels in natural, and even medical images; in other words, that there is some self-similarity/redundancy in such images. However, similarity between voxels (or rather, between patches around them) is usually only assessed in a spatial neighbourhood of the voxel under study. As the human brain exhibits approximate bilateral symmetry, one could wonder whether a voxel in a brain image could be more accurately denoised using information from both ipsi- and contralateral hemispheres. This is the idea we have investigated in this paper [45]. We define and compute a mid-sagittal plane which best superposes the brain with itself when mirrored about the plane. Then we use this plane to double the size of the neighbourhoods and hopefully find additional interesting voxels to be included in the weighted sum. We evaluate this strategy using an extensive set of experiments on both simulated and real datasets.

6.1.5. Detection of Multiple Sclerosis Lesions using Dictionary Learning

Participants: Hrishikesh Deshpande, Pierre Maurel, Christian Barillot.

Multiple sclerosis (MS) is a chronic, autoimmune, inflammatory disease of the central nervous system, in which certain areas of brain develop MS lesions, which are characterized by demyelination. Over the last years, various models combined with supervised and unsupervised classification methods have been proposed for detection of MS lesions using magnetic resonance 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. The dictionary used for sparse coding plays a key role in the classification process. In this work, we have proposed to learn class specific dictionaries and develop new classification scheme, to automatically detect MS lesions in 3-D multi-channel magnetic resonance images.

6.1.6. Multiple Sclerosis Lesion Detection in Clinically Isolated Syndromes

Participants: Yogesh Karpate, Olivier Commowick, Christian Barillot.

Quantitative assessment of Multiple Sclerosis Lesions (MSL) in Clinically Isolated Syndromes (CIS) is important, as they are a precursor to subsequent stages of the disease. We address the problem of lesion patch detection with respect to Normally Appearing Brain Tissues (NABT). Our approach consists in learning rotationally invariant MSL and NABT multimodal intensity signatures based on 3D spherical gabor descriptors. This learning step, done once and for all, is followed by a testing step for the patient patches with an exemplar SVM. First, we develop a framework for selecting focused region of interest (fROI) using linear SVM for scoring. This allows an excellent trade-off between speed and accuracy. Second, building rotational invariant and scale independent features for accurate representation of image signatures. The extracted features are sensitive to the orientation of the analyzed image. This is a drawback in classification and retrieval applications. We handle this problem by using shperical Gabor descriptors. And last, we apply max pooling for down sampling of feature vectors. For the classification purpose we use a standard linear Support Vector Machine(SVM). The main contribution of the work is to build binary classifier to discriminate NABTs and MSLs based upon robust image representation. We have validated our approach on synthetic and real patient data. The synthetic lesion data is generated with noise, without noise and with bias field. Further, validation is carried out in three different scenarios. First, we evaluate our classifier using K-fold started with cross validation using NABT from healthy volunteers and MSL from CIS patients, then the detection of NABT and MSL from CIS patients on known patches is performed. The last evaluation concerned the full search algorithm.

6.1.7. Intensity Normalization in Longitudinal MS Patients

Participants: Yogesh Karpate, Olivier Commowick, Christian Barillot.

This work proposes a longitudinal intensity normalization algorithm for multi-channel MRI of brain of MS patient in the presence of lesions, aiming towards stable and consistent longitudinal segmentation. This approach is parametric and developed using two different forms of Robust Expectation Maximization (EM). The first is Spatio-Temporal Robust Expected Maximization (STREM) and other being EM with beta divergence. We validated our method on real longitudinal multiple sclerosis subjects.

6.2. Image processing on Diffusion Weighted Magnetic Resonance Imaging

6.2.1. Statistical Analysis of White Matter Integrity for the Clinical Study of Specific Language Impairment in Children

Participants: Olivier Commowick, Camille Maumet, Aymeric Stamm, Jean-Christophe Ferré, Christian Barillot.

Children affected by Specific Language Impairment (SLI) fail to develop a normal language capability. To date, the etiology of SLI remains largely unknown. It induces difficulties with oral language which cannot be directly attributed to intellectual deficit or other developmental delay. Whereas previous studies on SLI focused on the psychological and genetic aspects of the pathology, few imaging studies investigated defaults in neuroanatomy or brain function. We have proposed [53] to investigate the integrity of white matter in SLI thanks to diffusion Magnetic Res- onance Imaging. An exploratory analysis was performed without a priori on the impaired regions. A region of interest statistical analysis was performed based, first, on regions defined from Catani's atlas and, then, on tractography-based regions. Both the mean fractional anisotropy and mean apparent diffusion coefficient were compared across groups. To the best of our knowledge, this is the first study focusing on white matter integrity in specific language impairment. 22 children with SLI and 19 typically developing children were involved in this study. Overall, the tractography-based approach to group comparison was more sensitive than the classical ROI-based approach. Group differences between controls and SLI patients included decreases in FA in both the perisylvian and ventral pathways of language, comforting findings from previous functional studies.

6.2.2. Adaptive Multi-modal Particle Filtering for Probabilistic White Matter Tractography

Participants: Aymeric Stamm, Olivier Commowick, Christian Barillot.

Particle filtering has recently been introduced to perform probabilistic tractography in conjunction with DTI and Q-Ball models to estimate the diffusion information. Particle filters are particularly well adapted to the tractography problem as they offer a way to approximate a probability distribution over all paths originated from a specified voxel, given the diffusion information. In practice however, they often fail at consistently capturing the multi-modality of the target distribution. For brain white matter tractography, this means that multiple fiber pathways are unlikely to be tracked over extended volumes. We have proposed [51] to remedy this issue by formulating the filtering distribution as an adaptive M-component non-parametric mixture model. Such a formulation preserves all the properties of a classical particle filter while improving multi-modality capture. We apply this multi-modal particle filter to both DTI and Q-Ball models and propose to estimate dynamically the number of modes of the filtering distribution. We show on synthetic and real data how this algorithm outperforms the previous versions proposed in the literature.

6.2.3. Tracking the Cortico-Spinal Tract from Low Spatial and Angular Resolution Diffusion MRI

Participants: Aymeric Stamm, Olivier Commowick, Christian Barillot.

We have participated to the annual MICCAI workshop on DTI tractography [52]. We presented a pipeline to reconstruct the corticospinal tract (CST) that connects the spinal cord to the motor cortex. The proposed method combines a new geometry-based multi-compartment diffusion model coined Diffusion Directions Imaging and a new adaptive multi-modal particle filter for tractography. The DTI Tractography challenge proposes to test our methods in the context of neurosurgical planning of tumor removal, where very low spatial and angular resolution diffusion data is available due to severe acquisition time constraints. We took up the challenge and present our reconstructed CSTs derived from a single-shell acquisition scheme at b = 1000 s/mm2 with only 20 or 30 diffusion gradients (low angular resolution) and with images of 5 mm slice thickness (low spatial resolution).

6.3. Medical Image Computing in Brain Pathologies

6.3.1. Semi-Automatic Classification of Lesion Patterns in Patients with Clinically Isolated Syndrome

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

Multiple sclerosis (MS) is neuro-degenerative disease of the Central Nervous System characterized by the loss of myelin. A Clinically Isolated Syndrome (CIS) is a first neurological episode caused by inflammation/demyelination in the central nervous system which may lead to MS. Better understanding of the disease at its onset will lead to a better discovery of pathogenic mechanisms, allowing suitable therapies at an early stage. We have proposed [37] an automatic segmentation algorithm for two different contrast agents, used within a framework for early characterization of CIS patients according to lesion patterns, and more specifically according to the nature of the inflammatory patterns of these lesions. We expect that the proposed framework can infer new prospective figures from the earliest imaging signs of MS since it can provide a classification of different types of lesions across patients. The lesion detection algorithm based on intensity normalization and subtraction of the used MRI data is a pivotal step, since it avoids the time-demanding task of manual delineation.

6.3.2. Multiple Sclerosis Lesions Evolution in Patients with Clinically Isolated Syndrome

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

Multiple sclerosis (MS) is a disease with heterogeneous evolution among the patients. Some classifications have been carried out according to either the clinical course or the immunopathological profiles. Epidemiological data and imaging are showing that MS is a two-phase neurodegenerative inflammatory disease. At the early stage it is dominated by focal inflammation of the white matter (WM), and at a latter stage it is dominated by diffuse lesions of the grey matter and spinal cord. A Clinically Isolated Syndrome (CIS) is a first neurological episode caused by inflammation/demyelination in the central nervous system which may lead

to MS. Few studies have been carried out so far about this initial stage. Better understanding of the disease at its onset will lead to a better discovery of pathogenic mechanisms, allowing suitable therapies at an early stage. We have proposed [36] a new data processing framework able to provide an early characterization of CIS patients according to lesion patterns, and more specifically according to the nature of the inflammatory patterns of these lesions. The method is based on a two layers classification. Initially, the spatio-temporal lesion patterns are classified using a tensor-like representation. The discovered lesion patterns are then used to identify group of patients and their correlation to 15 months follow-up total lesion loads (TLL), which is so far the only image-based figure that can potentially infer future evolution of the pathology. We expect that the proposed framework can infer new prospective figures from the earliest imaging sign of MS since it can provide a classification of different types of lesion across patients.

6.3.3. Arterial Spin Labeling at 3T in semantic dementia: perfusion abnormalities detection and comparison with FDG-PET

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

Arterial Spin Labeling (ASL) is a non invasive perfusion imaging technique which has shown great diagnosis potential in dementia. However, it has never been applied to semantic dementia (SD), a rare subtype of frontotemporal lobar degeneration characterized by the gradual loss of conceptual knowledge, which is actually explored by a now well established marker of SD: ^{18}fluorodeoxyglucose-positron emission tomography (FDG-PET) imaging. Although ASL and FDG-PET respectively measure perfusion and metabolism, they have been shown to be strongly correlated. In this work, we explore the ability of ASL to detect perfusion abnormalities in SD in comparison with FDG-PET. Using patients and healthy subjects data from an ongoing clinical study, we apply our analysis framework starting with visual comparison of ASL and FDG-PET, and focusing on ASL data preprocessing and statistical analysis at the individual and group level. Preliminary results yield concordant observations between ASL and FDG-PET as well as expected hypoperfusions in SD, namely in the left temporal lobe, thus suggesting the potential of ASL to assess perfusion impairments in SD.

6.4. Vascular Imaging and Arterial Spin Labelling

6.4.1. Patient-specific detection of perfusion abnormalities combining within-subject and between-subject variances in Arterial Spin Labeling.

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

In this paper, patient-specific perfusion abnormalities in Arterial Spin Labeling (ASL) were identified by comparing a single patient to a group of healthy controls using a mixed-effect hierarchical General Linear Model (GLM). Two approaches are currently in use to solve hierarchical GLMs: (1) the homoscedastic approach assumes homogeneous variances across subjects and (2) the heteroscedastic approach is theoretically more efficient in the presence of heterogeneous variances but algorithmically more demanding. In practice, in functional magnetic resonance imaging studies, the superiority of the heteroscedastic approach is still under debate. Due to the low signal-to-noise ratio of ASL sequences, within-subject variances have a significant impact on the estimated perfusion maps and the heteroscedastic model might be better suited in this context. In this paper we studied how the homoscedastic and heteroscedastic approaches behave in terms of specificity and sensitivity in the detection of patient-specific ASL perfusion abnormalities. Validation was undertaken on a dataset of 25 patients diagnosed with brain tumors and 36 healthy volunteers. We showed evidence of heterogeneous within-subject variances in ASL and pointed out an increased false positive rate of the homoscedastic model. In the detection of patient-specific brain perfusion abnormalities with ASL, modeling heterogeneous variances increases the sensitivity at the same specificity level [24].

6.4.2. An a contrario approach for the detection of activated brain areas in fMRI

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

BOLD functional MRI (fMRI) is now a widespread imaging technique to study task-related activity in the brain. However, getting the areas of activation at the individual subject level is still an open issue. The standard massively univariate statistical analysis is usually performed after smoothing the data and makes use of a single p-value for final thresholding of the results [1]. In group fMRI studies, the need for compensation of cross-subjects misregistrations clearly justifies the smoothing. However, at the individual level, where neat delineations of the activated areas are of interest, the use of Gaussian smoothing as a pre-processing step is more questionable. In this paper, we propose to study the ability of an a contrario approach, recently adapted for basal perfusion abnormalities detection [2], to correctly detect areas of functional activity [42].

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

Participants: Camille Maumet, Pierre Maurel, Jean-Christophe Ferré, 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. In this paper, we propose to compute ASL CBF maps using Huber's M-estimator, a robust statistical function that is not overly impacted by outliers. This method is compared to an empirical approach, introduced in [1], based on z-score thresholding [43].

6.4.4. Quantifying CBF from Aterial Spin Labeling via Diverse-TI: sampling diversity or repetitions ?

Participants: Lei Yu, Pierre Maurel, Christian Barillot.

Arterial Spin Labeling (ASL) is a noninvasive perfusion technique which allows the absolute quantification of Cerebral Blood Flow (CBF). The perfusion is obtained from the difference between images with and without magnetic spin labeling of the arterial blood and the captured signal is around 0.5-2% of the magnitude of the labeling images, so the noise is one of the main problems for further data analysis. Classical method, *Mono-TI*, for CBF quantification is averaging repetitions with only one Inversion Time (TI) - the time delay between labeling and acquisition to allow the labeled blood to arrive the imaging slice. It improves the robustness to noise, however, cannot compensate the variety of Arterial Arrival Time (AAT). In this paper, *Diverse-TI* is proposed to exploit different TI sampling instants (sampling diversity) to improve the robustness to variety of AAT and simultaneously average repetitions with each TI (sampling repetitions) to improve the robustness to noise. Generally, the sampling diversity is relatively small and can be considered as compressed measurements, thus the Compressive Matched Filter (CMF) enlightened from sparsity is exploited to directly reconstruct CBF and AAT directly from compressed measurements. Meanwhile, regarding the CBF quantification performance, the compromise between the sampling repetition and sampling diversity is discussed and the empirical protocol to determine the sampling diversity is proposed. Simulations are carried out to highlight our discussions. This is a joint work with Remi Gribonval (Panama Team) [56].

6.4.5. Peripheral angiography and neurovascular imaging

Participants: Hélène Raoult, Jean-Yves Gauvrit, Elise Bannier, Pierre Maurel, Clement Neyton, Christian Barillot, Jean-Christophe Ferré.

Vascular imaging contributions were performed on two different regions during the evaluation period: first on peripheral angiography, then on neurovascular imaging. Arteriography and MR angiography are routinely performed in patients presenting vascular pathologies. Yet, contrast agent injection is contraindicated in patients with renal insufficiency and the underlying risk of developing nephrogenic systemic fibrosis further encourages research on non-contrast enhanced MR angiography techniques (NCE MRA). In this context, we have been working on new MR sequences to reliably detect vascular abnormalities.

A first study [29] was published, where we assessed the feasibility and image quality of an improved non-gated carotid NATIVE TrueFISP NCE MRA sequence providing an extended field of view and a shorter acquisition time as compared to Time-of-Flight (TOF) imaging. A second study [48] was recently accepted for publication in Radiology on intracranial NCE MRA for arteriovenous malformation imaging with a high temporal resolution over 2 cardiac cycles. Combined with image post-processing, it allows improved depiction of venous drainage necessary to evaluate hemorrhagic risk and quantification. This ongoing work was just submitted.

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 a major advance in the collaboration since it will enable the development of MRI sequences on site.

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 2012, 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, ie 30k€. Two projects were selected by the COREC. The MALTA project led by radiologist Jean-Christophe Ferré will compare the ability of functional BOLD MRI and perfusion ASL MRI to detect language areas in patients with brain tumor.

8.1.3. Projet CRITT Santé Bretagne : AfaCorVis3D

Participants: Elise Bannier, Isabelle Corouge, Christian Barillot.

duration: 12 months from November 2011

A research projet in fMRI involving 3D visual stimulation was performed to try and differentiate areas activated by 2D versus 3D visualisation, whether static or dynamic. The task was evaluated on 10 volunteers in the context of the Master Research Projet of Guillaume Koch. Areas activated specifically by 3D visualisation were extracted.

8.1.4. Défis Scientifiques Emergents - Université de Rennes I

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

duration: 22 months from March 2012 (end: December 31, 2013)

The ASLDEM project was partially funded the University of Rennes 1 "Défis Scientifiques Emergents" grant (7000 euros).

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

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

duration: 12 months from November 2012

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 will start early 2013.

8.1.6. 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

A complementary funding (20 000€) was obtained to support a new research project on rehabilation of stroke patients. The fMRI protocol was setup, the task developed and validation on volunteers is ongoing. Patient inclusions will start in spring 2013.

8.1.7. Fondation Planiol

Participants: Elise Bannier, Hélène Raoult, Jean-Yves Gauvrit.

duration: 12 months from November 2012

In the context of a neurovascular imaging research study, funding (13500€) was obtained to perform a phantom study on test objects representing carotid stenosis, with a circulating flow. This project will be performed as part of a collaboration with Dr Cavaro Ménard - Angers (LISA), Dr Langevin - Compiègne (UTC) and Pr Saint Jalmes - PRISM (UR1).

8.2. National Initiatives

8.2.1. ANR

8.2.1.1. ANR "Neurological and Psychiatric diseases" NUCLEIPARK

Participants: Christian Barillot, Sylvain Prima, Juan Francisco Garamendi Bragado.

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. [58]. The pipeline was first validated on controlled synthetic data. For Parkinson disease, a total of 16 patients and 11 healthy controls were evaluated. The structuctures analyzed were: PPN, GPe, GPi, Caudatge, 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.

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. ANR Cosinus VIP

Participants: Fang Cao, Olivier Commowick, Christian Barillot.

VIP is collaborative project supported by ANR "Conception and Simulation"; it was accepted in 2009 (around 1 million euros). VIP aims at building a computing environment enabling multi-modality, multi-organ and dynamic (4D) medical image simulation, using GRID infrastructure. The goal is to integrate proven simulation software of the four main imaging modalities (MRI, US, PET and X-Ray/CT), and to cope interoperability challenges among simulators. The partners are CREATIS in Lyon (main contractor, Principal Investigator: Tristan Glatard), UNS-I3S in Nice, CEA-LETI in Grenoble and MAAT-G Maat G, a spanish company. The role of VISAGES in this project concerns primarily Task 1.1 and Task 3.3, focusing respectively on ontologies development and application to multiple sclerosis images simulation. This grant serves as support for the positions of Olivier Luong (PhD student) and Germain Forestier (post-doc).

8.2.1.3. AINSI Inria joint project

Participants: Christian Barillot, Isabelle Corouge, Pierre Maurel, Jean-Christophe Ferré, Elise Bannier, Camille Maumet.

We have been involved in a 2-year Inria ARC project AINSI (http://thalie.ujf-grenoble.fr/ainsi). AINSI stands for “Modeles statistiques pour l’Assimilation d’Informations de Neuroimagerie fonctionnelle et de perfuSIon cerebrale”. The goal is to propose an innovative statistically well-based solution to the joint determination of neural activity and brain vascularization by combining BOLD constrast images obtained in functional MRI and quantitative parametric images (Arterial Spin Labelling: ASL). The partners involved are the Mistiss project from Inria in Grenoble (Lead F. Forbes) and Parietal in Saclay, the INSERM Unit U594 (Grenoble Institute of Neuroscience) and the LNAO laboratory from CEA NeuroSpin.

8.2.1.4. TRANSLATE-MS-REPAIR

Participants: Fang Cao, 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, Michael Kain.

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.

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://iww.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.

8.3. European Initiatives

8.3.1. FP7 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

Objectif: Euro-BioImaging is a large-scale pan-European research infrastructure project on the European Strategy Forum on Research Infrastructures (ESFRI) Roadmap.

Duration: December 2010 - November 2013

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

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

Inria contact: Ch. Barillot X. Pennec

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

Program: COST

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

Project title: Arterial spin labelling 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 Narvarra (ES), INSERM U836 Grenoble (FR), University of Rennes I (FR), Centro San Giovanni di Dio - Fatebenefratelli (IT), Fondazione Instituto 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 Labelling (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.

8.4. International Initiatives

8.4.1. Inria Associate Teams

8.4.1.1. BARBANT

Title: Boston and Rennes, Brain image Analysis Team

Inria principal investigator: Christian Barillot

International Partner:

Children's Hospital Boston - Harvard Medical School (United States) - Computational Radiology Laboratory - Christian Barillot

Duration: 2012 - 2014

See also: https://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.

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.
- Christian Barillot visited the Information and Communications department at the Graduate School of Information Science of the Nagoya University, Japan in May 2013

9. Dissemination

9.1. Scientific Animation

9.1.1. Editorial board of journals

- C. Barillot is Associate Editor of IEEE Transactions on Medical Imaging (IEEE-TMI).
- C. Barillot is Associate Editor of Medical Image Analysis (MedIA).
- C. Barillot is Associate Editor of ISRN Signal Processing.
- C. Barillot is Associate Editor of Current Medical Imaging Reviews.
- C. Barillot serves in the peer review committee of the Journal of Computer Assisted Tomography.
- C. Barillot serves in the peer review committee of Neuroimage.
- P. Maurel serves in the peer review committee of Frontiers in Neurosciences

9.1.2. Workshop/Symposium Organization

- S. Prima was the co-organiser and chairman (with Antoine Balzeau from CNRS-MNHN, Paris and François Marchal from CNRS, Marseille) of the colloquium "Symmetry and asymmetries in anthropology" which took place on 24 January 2013 during the annual meeting of the Société d'Anthropologie de Paris (http://www.sapweb.fr).
- S. Prima was in the Steering Committeee of the MICCAI workshop on Mesh Processing in Medical Image Analysis (MeshMed 2013), Nagoya, Japan, September 26, 2013 (http://www2.imm.dtu.dk/projects/MeshMed).
- C. Barillot was program co-chair of the Miccai 2013 international conference (http://www.miccai2013.org/organization.html). MICCAI 2013 Proceedings have been published as LNCS series from Springer. The volume numbers are LNCS 8149, 8150 and 8151 (http://www.springer.com/computer/image+processing/book/978-3-642-40810-6).

9.1.3. Peer Reviews of journals

- IEEE TIP (CB), Medical Image Analysis (CB), NeuroImage (CB), Computer Methods and Programs in Biomedicine (CB), Phys. Med. Biol. (CB), Comp. in Biol & Med. (CB), J. of Neuroscience Methods (CB), Image and Vision Computing (CB), JMIV (CB), NeuroBiology of Aging (IC).

9.1.4. Technical Program Committees (TPC) of conferences

- C. Barillot was area chair of Miccai 2012, SPIE 2012, TPC member of MICCAI workshops DCICTIA 2012, ICSS 2012, MBIA 2012, and MCV 2012, TPC member of IEEE CBMS 2012, ICPR 2012, ESMRMb 2012, SFRMBM 2012, ECR/imaGine 2011.
- S. Prima was TPC member of MeshMed'2013.
- P. Maurel was TPC member of MICCAI'2013.

- O. Commowick was TPC member of MICCAI'2013, IEEE ISBI'2013.

9.1.5. Scientific societies

- C. Barillot is member of the Board of Directors of IPMI (Information Processing in Medical Imaging)
- C. Barillot is member of IEEE EMBS
- C. Barillot is senior member of IEEE
- C. Barillot is member of the European Society of Molecular Imaging (ESMI)
- C. Barillot, O. Commowick, P Maurel and S. Prima are members of the MICCAI society
- E. Bannier, C. Barillot and I. Corouge are members of the European Society of Magnetic Resonance in Medicine and Biology (ESMRMb)

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)
- Elise Bannier gave 4-day lecture in fMRI and E-Prime to Emmanuelle Le Bars, MR Physicist from the University Hospital of Montpellier (February 2012, Rennes, France). This training was funded by Siemens.
- 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 Modelling of Natural Evolution of Brain Pathologies, Inria, December 2012, Christian Barillot, Pierre Maurel
- PhD Renaud Hedouin, Biomarker discovery in brain imaging by using diffusion MRI, Inria/Inserm, November 2013, Christian Barillot, Olivier Commowick
- PhD Yogesh Karpate, Quantitative analysis of MRI in Multiple Sclerosis in the context of the clinically isolated syndroma, INSERM, December 2011, Christian Barillot, Olivier Commowick
- PhD Camille Maumet, From Group to Patient-Specific Analysis of Brain Function in Arterial Spin Labelling and BOLD Functional MRI, University of Rennes I, defended April 2013, 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, Elise Bannier, Jean-Yves Gauvrit

- PhD Aymeric Stamm, Diffusion Directions Imaging: High resolution reconstruction of white matter fascicles from low angular resolution diffusion MRI, University of Rennes I, defended Nov. 2013, Christian Barillot, Patrick Perez (Technicolor)

9.2.3. Juries

- C. Barillot: PhD reviewer, Andrea Valsecchi, University of Oviedo, Spain, Dec. 2013
- C. Barillot: PhD reviewer, Maxime Taquet, Université Catholique de Louvain, Belgium, Nov. 2013
- C. Barillot: PhD, Solveig Badillo, University Paris Sud, Orsay, Nov. 2013
- C. Barillot: PhD, Thomas Samaille, University PIERRE ET MARIE CURIE, Paris, June 2013
- C. Barillot: PhD reviewer, Sylvain Merlet, University of Nice-Sophia Antipolis, Nice, Sept. 2013
- C. Barillot: PhD reviewer, Stefano Baraldo, Department of Mathematics, Politechnico di Milano, Italia, June 2013
- C. Barillot: PhD, president, Tao LI, University of Rennes I, Rennes, Feb. 2013
- C. Barillot: HDR, Olivier Coulon, University of Aix-Marseille, Marseille, Sept. 2013
- C. Barillot: HDR president, Alexandre Krupa, University of Rennes I, Marseille, Dec. 2012

9.3. Popularizationn

- Inria Emergence, ”Une plateforme de Neuroimagerie pour la sclerose en plaque”
- Serimedis/inserm Multimedia report (http://www.serimedis.inserm.fr/fr/spotlight/6203/visages-vision-action-et-gestion-d-informations-en-sante/page/1/SN/techno)
- Video production for INPI Trophee of 2013 (http://www.bretagne-innovation.tm.fr/Temoignages/Laureats-Trophees-INPI-Bretagne-2013-Laboratoire-VisAGeS-Video).
- Ouest Inria: ”La fabuleuse histoire de Shanoir ”
- Emergences Inria: ”Un cloud pour l’imagerie médicale” (http://emergences.inria.fr/2012/newsletter_24/L22-IRT)

10. Bibliography

Major publications by the team in recent years

[1] C. CIOFOLO, C. BARILLOT. *Atlas-based segmentation of 3D cerebral structures with competitive level sets and fuzzy control*, in "Medical Image Analysis", 2009, vol. 13, n^{o} 3, pp. 456–470

[2] P. COUPÉ, P. HELLIER, C. KERVRANN, C. BARILLOT. *NonLocal Means-based Speckle Filtering for Ultrasound Images*, in "IEEE Transactions on Image Processing", 2009

[3] P. COUPÉ, P. YGER, S. PRIMA, P. HELLIER, C. KERVRANN, C. BARILLOT. *An Optimized Blockwise Non Local Means Denoising Filter for 3D Magnetic Resonance Images*, in "IEEE Transactions on Medical Imaging", April 2008, vol. 27, n^{o} 4, pp. 425-441, http://hal.inria.fr/inria-00332014/en/

[4] C. DE GUIBERT, C. MAUMET, J.-C. FERRÉ, P. JANNIN, A. BIRABEN, C. ALLAIRE, C. BARILLOT, E. LE RUMEUR. *FMRI language mapping in children: A panel of language tasks using visual and auditory stimulation without reading or metalinguistic requirements*, in "NeuroImage", February 2010, vol. 51, n^{o} 2, pp. 897–909, http://www.hal.inserm.fr/inserm-00461666/en/

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[6] P. JANNIN, X. MORANDI. *Surgical models for computer-assisted neurosurgery*, in "Neuroimage", 2007, vol. 37, n° 3, pp. 783–91

[7] F. LALYS, C. HAEGELEN, J.-C. FERRÉ, O. EL-GANAOUI, P. JANNIN. *Construction and assessment of a 3T MRI brain template*, in "Neuroimage", 2010, vol. 49, n° 1, pp. 345-354 [*DOI :* 10.1016/J.NEUROIMAGE.2009.08.007], http://www.hal.inserm.fr/inserm-00546487/en/

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Publications of the year

Doctoral Dissertations and Habilitation Theses

[11] C. MAUMET. , *Des études de groupe aux analyses individuelles dans l'exploration de la fonction cérébrale en imagerie de perfusion par marquage de spins et en IRM fonctionnelle BOLD*, Université Rennes 1, May 2013, http://hal.inria.fr/tel-00863908

Articles in International Peer-Reviewed Journals

[12] A. BALZEAU, D. GRIMAUD-HERVÉ, F. DÉTROIT, R. HOLLOWAY, B. COMBÈS, S. PRIMA. *First description of the Cro-Magnon 1 endocast and study of brain variation and evolution in anatomically modern Homo sapiens*, in "Bulletins et Mémoires de la Société d'Anthropologie de Paris", April 2013, vol. 25, n° 1-2, pp. 1-18 [*DOI :* 10.1007/S13219-012-0069-Z], http://hal.inria.fr/inserm-00853862

[13] A. ESQUEVIN, H. RAOULT, S. BELLIARD, I. COROUGE, E. BANNIER, F. LEJEUNE, C. BARILLOT, J.-C. FERRÉ, J.-Y. GAUVRIT. *Étude de la perfusion cérébrale par Arterial Spin Labeling : principes et applications en neurosciences cliniques*, in "Revue de Neuropsychologie", 2013, vol. 5, n° 2, pp. 135-141 [*DOI :* 10.1684/NRP.2013.0265], http://hal.inria.fr/inserm-00856795

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