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Activity Report 2012

# 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 Medicine and Neuro-sciences**

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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:* July 04, 2005 .

# 1. Members

**Research Scientists**

Christian Barillot [Team Leader, Research Director Cnrs, HdR]
Olivier Commowick [Inria Research Scientist]
Sylvain Prima [Inria Research Scientist]

**Faculty Members**

Gilles Edan [PU-PH research scientist, Medical Faculty, University of Rennes 1 and University Hospital of Rennes, neurology Department, HdR]
Jean-Christophe Ferré [PH research scientist, University Hospital of Rennes, neuro-radiology Department]
Jean-Yves Gauvrit [PU-PH research scientist, Medical Faculty, University of Rennes 1 and University Hospital of Rennes, neuro-radiology Department, HdR]
Pierre Maurel [Assistant Professor, University of Rennes 1]

**External Collaborators**

Isabelle Bonan [Associated Faculty, PU-PH, Medical Faculty, University of Rennes 1 and University Hospital of Rennes, Rehabilitation Department]
Patrick Bourguet [Associated Faculty, PU-PH, Medical Faculty, University of Rennes 1 and Nuclear Medicine Department, Cancer Institute of Rennes]
Clément De Guibert [Associated Faculty, Assistant Professor, University of Rennes 2]
Pierre Darnault [Associated Faculty, PU-PH, Medical Faculty, University of Rennes 1 and University Hospital of Rennes, Radiology Department]

**Engineers**

Elise Bannier [Neurinfo technical staff, University of Rennes 1]
Isabelle Corouge [Neurinfo technical manager, University of Rennes 1]
René-Paul Debroize [75% Junior technical staff, from 01/09/20121]
Justine Guillaumont [Inria Junior technical staff, from 01/10/2012]
Clément Philipot [Inria Junior technical staff, IA, until 30/09/2012]
Guillaume Pasquier [Inria technical staff, from 01/10/2012]
Guillaume Renard [Inria Junior technical staff, IA, until 30/04/2012]

**PhD Students**

Camille Maumet [Ph-D student, Neurinfo technical staff, University of Rennes I]
Hrishikesh Deshpande [Ph-D student, Inria, from 15/11/2012]
Yogesh Karpate [Ph-D student, Inserm, from 01/12/2011]
Hélène Raoult [Ph-D student, University Hospital of Rennes]
Aymeric Stamm [Ph-D student, Research Ministry grant]

**Post-Doctoral Fellows**

Fang Cao [Inria VIP project, Post doctoral]
Alessandro Crimi [Inria , Post doctoral, until 01/12/2012]
Juan Francisco Garamendi [Inria, Post doctoral]
Lei Yu [Inria technical staff, Post doctoral]
Brivael Trelhu [ATER University of Rennes 2, from 01/10/2012]

**Administrative Assistants**

Angélique Jarnoux [Administrative assistant, TR Inria, shared with I4S projects, 60%]
Maelle Pegeault [Administrative assistant, AGT University of Rennes 1, 50% from medical faculty, until 30/04/2012]

# 2. Overall Objectives

## 2.1. Overall objectives

*Medical Imaging, Neuroinformatics, Neuroimaging, Data Fusion, Image Processing, Neurological Pathologies, Modelling of normal and pathological behavior of the human brain, e-health, HealthGrids*

In the '70s, the major research advances in biomedical signal and image processing came from the introduction of tomography (literally from (TOMOS) – SECTION and (GRAPHO) – WRITE) which was in some way a revolution compared to the current image standard consisting of projected images (X-ray, scintigraphy ...) Some of these major discoveries include CT scans and, later on, MRI, SPECT or PET scans, complemented by the increasing influence of electrophysiological data (MEG, EEG, ECG ...). This period was the early stage of the in vivo image slices of the human body. Major research advances in the '80s included 3D imaging in the clinical context. The '90s, with the advent of data fusion algorithms (mostly registration) and new sequences of Magnetic Resonance Images – MRI (especially fast and functional sequences), added one or two more dimensions to clinical imaging. Most of our current research challenges follow this evolution by:

- adding new spatio-temporal dimensions to the anatomical and functional data at the acquisition and the analysis level,
- adding new scales of analysis (nano or micro biological and molecular images to macro medical images,
- adding network interconnection between clinical data centers which will extend the corpus of accessible information,

Then, it becomes possible today to acquire anatomical (i.e structural) and physiological information (e.g. functional), which are complementary in the same subject. However, this increase of available information for diagnosis and treatment must be balanced by an equivalent improvement in the quantity of data the user can integrate and interpret. So, the traditional way physicians use these data is often sub optimal implying that today important number of valuable information is still neglected during the medical decision process.

In order to advance, the physician has to consider not only the original biomedical signals but also the processing tools to get an optimal interpretation. Processing biomedical images and signals is still very complex and is not only based on matching these data but also on the knowledge about the observed structures and their interactions, either anatomical, structural or functional in nature. It is clear today that, except the emergence of new acquisition modalities, the advent of new algorithms and new systems, capable to jointly use all these information, will improve patient's care, diagnosis and therapy.

Based on this perspective, the classical way to use medical imaging data, mostly based on subjective human interpretation, becomes increasingly suboptimal. In addition, the pressure from the society for a cost effective use of the equipments on the one hand, and a better traceability and quality assurance of the decision making process on the other hand, strengthened the need of advanced computer assisted biomedical imaging systems.

Besides this evolution regarding acquisition and application of medical images, in parallel, there is an evolution of high band electronic communication systems (e.g. through the Internet). This argues even more strongly to share different resources (medical images, processing algorithms...) between users of the same community sharing a common interest on pathologies, research domains or even education. This explains why recent advances coming from information technologies through GRID infrastructures are becoming an acute issue in clinical medical imaging for assisting medical imaging actors to share their heterogeneous and distributed resources for the purpose of improving their clinical practice, or being more acute (i.e. specific in doing research on pathologies).

Research activities of the VISAGES U746 team follow the global evolution of our domain of activity for the design and development of computational models of living systems to be confronted to biological images/signals/measurements. This translates to better understand the behavior of normal and pathological CNS organs and systems, at different scales, which includes the purpose of imaging the brain pathologies in order to better understand the pathological behavior from the organ level to the cell and the molecule, and the modeling of normal and pathological group of individuals (cohorts) from image descriptors. This includes the challenge of discovery of unlikely facts (e.g. rare events in image series), data mining and knowledge discovery from image descriptors, validation and certification of new drugs from imaging features and more generally the integration of neuroimaging in Neuroinformatics.

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, epilepsy, dementia, neuro-degenerative brain diseases, brain vascular diseases, strokes, neuropaediatrics, psychiatry, ...).

## 2.2. Highlights of the Year

Aymeric Stamm received the Magna Cum Laude Merit Award from the ISMRM organisation for [42] .
BEST PAPER AWARD :
[42] **A new multi-directional fiber model for low angular resolution diffusion imaging in Proc. Intl. Soc. Mag. Reson. Med.**. A. STAMM, P. PEREZ, C. BARILLOT.

# 3. Scientific Foundations

## 3.1. Scientific Foundations

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.

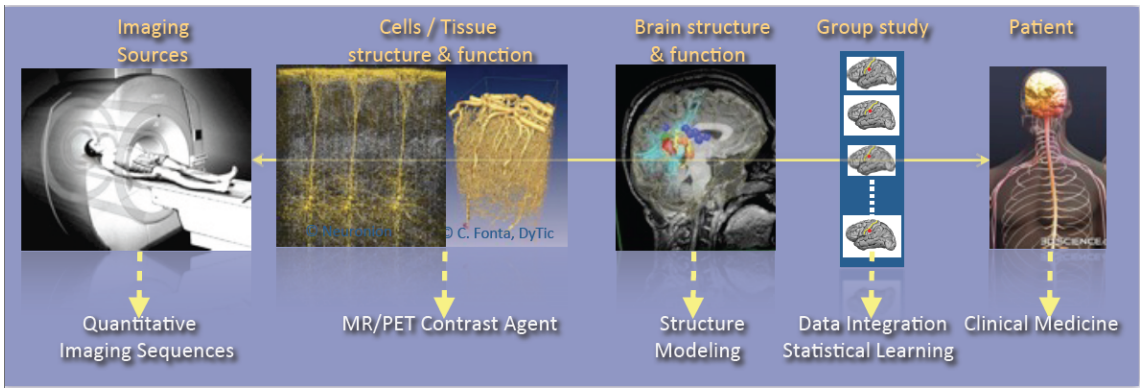



*Figure 1. The major overall scientific foundation of the team concerns the integration of data from the Imaging source to the patient at different scales : from the cellular or molecular level describing the structure and function, to the functional and structural level of brain structures and regions, 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 [52], [54], [53], [55], and by continuing our local and wider collaborations.

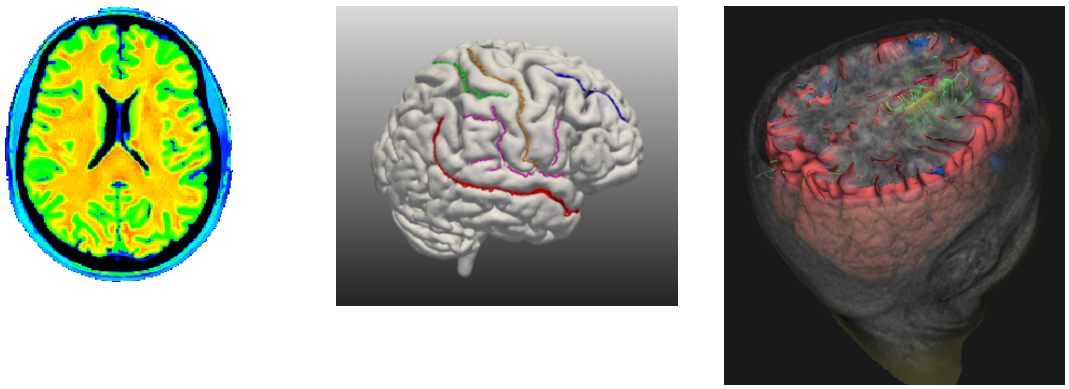
An additional objective within this application domain is to find new descriptors to study the brain anatomy and/or function (e.g. variation of brain perfusion, evolution in shape and size of an anatomical structure in relation with pathology or functional patterns, computation of asymmetries ...). This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

# 5. Software

## 5.1. Vistal

**Participants:** Olivier Commowick, Clément Philipot.

VistaL is a software platform of 3D and 3D+t image analysis allowing the development of generic algorithms used in different contexts (rigid and non-rigid registration, segmentation, statistical modelling, calibration of free-hand 3D ultrasound system and so on, diffusion tensor image processing, tractography). This software platform is composed of generic C++ template classes (Image3D, Image4D, Lattice and so on) and a set of 3D/3D+t image processing libraries. VistaL is a multi-operating system environment (Windows, Linux/Unix...). A web site presenting the project has been developped, precompiled packages and the SDK are now available. VistaL APP registration number is:IDDN.FR.001.200014.S.P.2000.000.21000.
See also the web page http://vistal.gforge.inria.fr.



(a) (b) (c)

*Figure 2. Some ViSTAL results screenshots: a) The ViSTAL Logo, b) ViSTAL Brain surface and sulci modelisation, c) The ROI3D Extraction view*

- Keywords: medical image processing, image analysis, registration, segmentation, denoising
- Software benefit: New methodological image processing, some GPU based algorithms, easy to use C++ library
- APP: IDDN.FR.001.200014.S.P.2000.000.21000

- License: Licence Propriétaire
- Type of human computer interaction: C++ API and less complete Python API
- OS/Middleware: Windows, Mac et Linux.
- Required library or software: CMake (GPL) - ITK (BSD) - VTK (BSD) - Boost (BSD) - Libxml++ (LGPL) - CppUnit (LGPL)
- Programming language: C/C++, Python
- Documentation: Documentation Doxygen, documentation utilisateur.

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

**Participants:** Juan Francisco Garamendi, 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) [49] 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

## 5.3. SUBANA: SUrface-BAsed Neuronavigation on Atlas for TMS

**Participant:** Sylvain Prima.

In collaboration with Charles Garraud (Syneika), Benoit Combès (Géosciences Rennes, UMR 6118) and Pierre Hellier (Technicolor), we developed a software for i) the automated surface reconstruction of the face and skull cap from sparsely acquired points and ii) the automated nonlinear registration of free-form surfaces. The latter step is implemented using the CLARCS library (http://clarcs.inria.fr). The primary goal of this software is the surface-based neuronavigation for transcranial magnetic stimulation. The method was presented at the MeshMed MICCAI workshop (http://www2.imm.dtu.dk/projects/MeshMed/2011/index.html) [50].

- APP: IDDN.FR.001.440010.000.S.P.2010.000.31230
- Patent: was granted, but the reference number is unknown
- Programming language: C++

## 5.4. Shanoir

**Participants:** Guillaume Renard, Justine Guillaumont, 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.

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.001.200014.S.P.2000.000.21000
- 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

## 5.5. QtShanoir

**Participants:** Olivier Commowick, Guillaume Renard.

QtShanoir is a C++ Qt based library for querying data from a Shanoir server. For those who don't know what is shanoir, see the shanoir website at http://shanoir.org. QtShanoir uses the soap based webservices provided by a shanoir server to get and display studies, patients, data with their associated metadata. In QtShanoir, you will find a set of Qt widgets (inherited from a QWidget object) that you can embed in your Qt application.

An APP registration is in progress and the library has been release in october under the LGPL license. See http://qtshanoir.gforge.inria.fr.

- Keywords : medical imaging, dicom
- Software benefit: offers a great solution to query a Shanoir server. Can be easily re used in larger Qt applications
- License: no defined licence for the moment
- Type of human computer interaction: C++ library
- OS/Middelware: Linux, Windows and Mac
- Required library or software : Qt
- Programming language: C++
- Documentation : http://qtshanoir.gforge.inria.fr

## 5.6. AutoMRI

**Participants:** Camille Maumet, Isabelle Corouge, Elise Bannier.

AutoMRI is an SPM-based set of tools to study structural and functional MRI data. This software is currently made up of 9 modules : autofMRI, autoVBM, automorpho, autoASL, autoFASL, autoROI, autoasltemplate, autofmriacontrario and autoNCEMRA. AutofMRI produces statistical maps of activations and deactivations at the group or the subject level based on functional MRI data. It can deal with block or event-related designs and is highly configurable in order to fit to a wide range of needs. autoVBM performs between-group voxel-based morphometric analysis in order to outline regions of grey (or white) matter volume reduction and increase. To further study a morphometric or a functional analysis, regions of interest analysis can be performed with autoROI. This module also provides the user with laterality indexes. Automorpho performs one-versus-many group analysis on anatomical data in order to outline pathological dysplasia or heterotopia. AutoFASL (collaboration with Rémi Dubujet) produces statistical maps of activations and deactivations at the group or the subject level based on functional Arterial Spin Labeling data. AutoASL performs between-group voxel-based morphometric analysis in order to outline regions of reduced (or increased) perfusion. Autoasltemplate focus on patient-specific detection of perfusion abnormalities with a standard massively univariate General Linear Model or with an a contrario approach. Autofmriacontrario provides an alternative

to autofmri to produce statistical maps of activations and deactivations at the subject level using an a contrario approach. autoNCEMRA enables automatic processing of 4D MRA data to remove unwanted signal from the skull, using a mask based on 3D T1w segmentation of grey matter, white matter and CSF. Thus, denoised maximum intensity projections in axial, coronal and sagittal planes can be calculated to enable accurate assessment of hemodynamic patterns, from arterial input to venous drainage (in particular in patients presenting arteriovenous malformations).

- 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
- Type of human computer interaction: Matlab function (script, no GUI)
- OS/Middleware: Linux/Windows
- Required library or software : Matlab, SPM, SPM toolboxes : Marsbar, LI-toolbox, NS
- Programming language: Matlab
- Documentation : Available

## 5.7. Medinria

**Participants:** René-Paul Debroize, Clément Philipot, Guillaume Pasquier, 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 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 2.0.1 has been released in April 2012 for the main distribution platforms. Development of an SDK and of a new verions is underway and should be released in June 2013.

See also 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++

## 5.8. USGraphCut

**Participant:** Christian Barillot.

This software has been developed in collaboration with Jan Petr and Alexandre Krupa during the ANR USComp project. It concerns the segmentation of echographic data by using the graph cut algorithm. It allows the segmentation and the tracking of evolving objects in 2D/3G echographic data in real time thanks to a specific CUDA framework.

## 5.9. CtrlQ - MR Quality Assurance

**Participants:** René-Paul Debroize, Isabelle Corouge, Elise Bannier.

As part of the monitoring of the 3Tesla MR equipment, a quality control consistent with the one recommended by the American College Of Radiology (ACR) is performed weekly. As part of its MRI accreditation program, the ACR standardized a procedure for monitoring quality consisting of a series of measurements performed on a standardized imaging protocol on a test object with known geometry. A robust and intuitive software was developed, with a graphical interface, to ensure the automation of the measurements necessary to the control. The application was developed in C++ using the Qt, ITK, and DCMTK libraries.

## 5.10. SimuBloch

**Participants:** Fang Cao, Olivier Commowick, Elise Bannier, Christian Barillot.

We developed a simulator package *SimuBloch*, which is made for a fast simulation of image sequences based on Bloch equations, which can be run directly from VIP Portal: http://vip.creatis.insa-lyon.fr. The current version is v0.3. The simulator allows to construct 6 different MR pulse sequences:

1. *SimuBlochSE*: Simulation of spin echo sequences.
2. *SimuBlochGRE*: Simulation of gradient echo sequences.
3. *SimuBlochIR-SE*: Simulation of inversion recovery spin echo sequences.
4. *SimuBlochIR-GRE*: Simulation of inversion recovery gradient echo sequences.
5. *SimuBlochSP-GRE*: Simulation of spoiled gradient echo sequences.
6. *SimuBlochCoherentGRE*: Simulation of coherent gradient echo sequences.

# 6. New Results

## 6.1. Image Segmentation, Registration and Analysis

### *6.1.1. Estimating A Reference Standard Segmentation with Spatially Varying Performance Parameters: Local MAP STAPLE*

**Participant:** Olivier Commowick.

We present a new algorithm, called local MAP STAPLE, to estimate from a set of multi-label segmentations both a reference standard segmentation and spatially varying performance parameters. It is based on a sliding window technique to estimate the segmentation and the segmentation performance parameters for each input segmentation. In order to allow for optimal fusion from the small amount of data in each local region, and to account for the possibility of labels not being observed in a local region of some (or all) input segmentations, we introduce prior probabilities for the local performance parameters through a new maximum a posteriori formulation of STAPLE. Further, we propose an expression to compute confidence intervals in the estimated local performance parameters. We carried out several experiments with local MAP STAPLE to characterize its performance and value for local segmentation evaluation. First, with simulated segmentations with known reference standard segmentation and spatially varying performance, we show that local MAP STAPLE performs better than both STAPLE and majority voting. Then we present evaluations with data sets from clinical applications. These experiments demonstrate that spatial adaptivity in segmentation performance is an important property to capture. We compared the local MAP STAPLE segmentations to STAPLE, and to previously published fusion techniques and demonstrate the superiority of local MAP STAPLE over other state-of-the-art algorithms.

This work was done in collaboration with Alireza Akhondi-Asl and Simon K. Warfield [15].

### *6.1.2. Voxel-based quantitative analysis of brain images from F-18 Fluorodeoxyglucose Positron Emission Tomography with a Block-Matching algorithm for spatial normalization*

**Participant:** Olivier Commowick.

Statistical Parametric Mapping (SPM) is widely used for the quantitative analysis of brain images from F-18 fluorodeoxyglucose positron emission tomography (FDG PET). SPM requires an initial step of spatial normalization to align all images to a standard anatomic model (the template), but this may lead to image distortion and artifacts, especially in cases of marked brain abnormalities. This study aimed at assessing a block-matching (BM) normalization algorithm, where most transformations are not directly computed on the overall brain volume but through small blocks, a principle that is likely to minimize artifacts. Large and/or small hypometabolic areas were artificially simulated in initially normal FDG PET images to compare the results provided by statistical tests computed after either SPM or BM normalization. Results were enhanced by BM, compared with SPM, with regard to (i) errors in the estimation of large defects volumes (about 2-fold lower) because of a lower image distortion, and (ii) rates of false-positive foci when numerous or extended abnormalities were simulated. These observations were strengthened by analyses of FDG PET examinations from epileptic patients. Results obtained with the BM normalization of brain FDG PET appear more precise and robust than with SPM normalization, especially in cases of numerous or extended abnormalities.

This work was done in collaboration with Christophe Person, Valérie Louis-Dorr, Sylvain Poussier, Grégoire Malandain, Louis Maillard, Didier Wolf, Nicolas Gilet, Véronique Roch, Gilles Karcher and Pierre-Yves Marie [19].

### *6.1.3. Block-matching strategies for rigid registration of multimodal medical images*

**Participants:** Olivier Commowick, Sylvain Prima.

We propose and evaluate a new block-matching strategy for rigid-body registration of multimodal or multisequence medical images. The classical algorithm first matches points of both images by maximizing the iconic similarity of blocks of voxels around them, then estimates the rigid-body transformation best superposing these matched pairs of points, and iterates these two steps until convergence. In this formulation, only discrete translations are investigated in the block-matching step, which is likely to cause several problems, most notably a difficulty to tackle large rotations and to recover subvoxel transformations. We propose a solution to these two problems by replacing the original, computationally expensive, exhaustive search over translations by a more efficient optimization over rigid-body transformations. The optimal global transformation is then computed based on these local blockwise rigid-body transformations, and these two steps are iterated until convergence. We evaluate the accuracy, robustness, capture range and run time of this new block-matching algorithm on both synthetic and real MRI and PET data, demonstrating faster and better registration than the translation-based block-matching algorithm [28].

### *6.1.4. Automated diffeomorphic registration of anatomical structures with rigid parts: Application to dynamic cervical MRI*

**Participants:** Olivier Commowick, Sylvain Prima.

We propose an iterative two-step method to compute a diffeomorphic non-rigid transformation between images of anatomical structures with rigid parts, without any user intervention or prior knowledge on the image intensities. First we compute spatially sparse, locally optimal rigid transformations between the two images using a new block matching strategy and an efficient numerical optimiser (BOBYQA). Then we derive a dense, regularised velocity field based on these local transformations using matrix logarithms and M-smoothing. These two steps are iterated until convergence and the final diffeomorphic transformation is defined as the exponential of the accumulated velocity field. We show our algorithm to outperform the state-of-the-art log-domain diffeomorphic demons method on dynamic cervical MRI data [27].

### *6.1.5. Computer-assisted paleoneurology*

**Participant:** Sylvain Prima.

In collaboration with Antoine Balzeau and colleagues at the MNHN (http://www.mnhn.fr), we made the first ever description of the “digital” endocranial cast of the Cro-Magnon 1 specimen, discovered in 1868 at the Eyzies-de-Tayac, Dordogne, France [13]. Together with Benoit Combès (Géosciences Rennes, UMR 6118), we were especially involved in the assessment of its endocranial asymmetries, using an algorithm previously developed at VisAGeS [51] in the context of the ARC 3D-MORPHINE coordinated by Sylvain Prima (http://3dmorphine.inria.fr).

## 6.2. Image processing on Diffusion Weighted Magnetic Resonance Imaging

### *6.2.1. Non-Local Robust Detection of DTI White Matter Differences with Small Databases*

**Participants:** Olivier Commowick, Aymeric Stamm.

Diffusion imaging, through the study of water diffusion, al- lows for the characterization of brain white matter, both at the population and individual level. In recent years, it has been employed to detect brain abnormalities in patients suffering from a disease, e.g. from multiple sclerosis (MS). State-of-the-art methods usually utilize a database of matched (age, sex, ...) controls, registered onto a template, to test for differences in the patient white matter. Such approaches however suffer from two main drawbacks. First, registration algorithms are prone to local errors, thereby degrading the comparison results. Second, the database needs to be large enough to obtain reliable results. However, in medical imaging, such large databases are hardly available. In this paper, we propose a new method that addresses these two issues. It relies on the search for samples in a local neighborhood of each pixel to increase the size of the database. Then, we propose a new test based on these samples to perform a voxelwise comparison of a patient image with respect to a population of controls. We demonstrate on simulated and real MS patient data how such a framework allows for an improved detection power and a better robustness and reproducibility, even with a small database [26].

### *6.2.2. Registration and Analysis of White Matter Group Differences with a Multi-Fiber Model*

**Participant:** Olivier Commowick.

Diffusion magnetic resonance imaging has been used extensively to probe the white matter in vivo. Typically, the raw diffusion images are used to reconstruct a diffusion tensor image (DTI). The incapacity of DTI to represent crossing fibers leaded to the development of more sophisticated diffusion models. Among them, multi-fiber models represent each fiber bundle independently, allowing the direct extraction of diffusion features for population analysis. However, no method exists to properly register multi-fiber models, seriously limiting their use in group comparisons. This paper presents a registration and atlas construction method for multi-fiber models. The validity of the registration is demonstrated on a dataset of 45 subjects, including both healthy and unhealthy subjects. Morphometry analysis and tract-based statistics are then carried out, proving that multi-fiber models registration is better at detecting white matter local differences than single tensor registration.

This work was done in collaboration with Maxime Taquet, Benoit Scherrer, Jurriaan Peters, Mustafa Sahin, Benoît Macq and Simon K. Warfield [44].

### *6.2.3. Automated delineation of white matter fiber tracts with a multiple region-of-interest approach*

**Participant:** Olivier Commowick.

White matter fiber bundles of the brain can be delineated by tractography utilizing multiple regions-of-interest (MROI) defined by anatomical landmarks. These MROI can be used to specify regions in which to seed, select, or reject tractography fibers. Manual identification of anatomical MROI enables the delineation of white matter fiber bundles, but requires considerable training to develop expertise, considerable time to carry out and suffers from unwanted inter- and intra-rater variability. In a study of 20 healthy volunteers, we compared three methodologies for automated delineation of the white matter fiber bundles. Using these methodologies, fiber bundle MROI for each volunteer were automatically generated. We assessed three strategies for inferring the automatic MROI utilizing nonrigid alignment of reference images and projection of template MROI. We assessed the bundle delineation error associated with alignment utilizing T1-weighted MRI, fractional anisotropy images, and full tensor images. We confirmed the smallest delineation error was achieved using the full tensor images. We then assessed three projection strategies for automatic determination of MROI in each volunteer. Quantitative comparisons were made using the root-mean-squared error observed between streamline density images constructed from fiber bundles identified automatically and by manually drawn MROI in the same subjects. We demonstrate that a multiple template consensus label fusion algorithm generated fiber bundles most consistent with the manual reference standard.

This work was done in collaboration with Ralph Suarez, Sanjay Prabhu and Simon K. Warfield [23].

#### *6.2.4. Corticospinal tractography with morphological, functional and diffusion tensor MRI: a comparative study of four deterministic algorithms used in clinical routine*

**Participants:** Sylvain Prima, Camille Maumet, Jean-Christophe Ferré.

In collaboration with Romuald Seizeur, Nicolas Wiest-Daesslé and Xavier Morandi, we aimed to compare four deterministic tractography algorithms used in clinical routine for the study of the corticospinal tract (the bundle mediating voluntary movement) in 15 right-handed volunteers. We found no difference between right and left sides of the brain for any of the algorithms [22].

#### *6.2.5. A new multi-directional fiber model for low angular resolution diffusion imaging*

**Participants:** Aymeric Stamm, Christian Barillot.

Diffusion MRI is a tool of choice for the analysis of the brain white matter fiber pathways. When translated to clinics, the short acquisition time leads to low angular resolution diffusion (LARD) images. Fiber pathways are then inferred assuming Gaussian diffusion (a.k.a. DTI) that provides one fiber orientation per voxel. In the past decade, recent researches highlight more intricate intra-voxel fiber configurations using higher angular resolution diffusion images. In collaboration with Patrick Perez (Technocolor), we have proposed a non-Gaussian diffusion model of the white matter fibers able to recover from crossing of fibers even from low angular resolution.This model enables crossing fibers to be theoretically estimated from only 8 diffusion MR images. In particular, this model allows for the retrospective study of DW data sets acquired in the past. [42] [43].

### 6.3. Medical Image Computing in Brain Pathologies

#### *6.3.1. Detection of dysplasia and heterotopia*

**Participants:** Elise Bannier, Camille Maumet, Jean-Christophe Ferré, Christian Barillot.

Focal cortical dysplasia and heterotopias are a recognized cause of epilepsy. Indication for surgery relies on precise localization and delineation. However, visual depiction of focal cortical dysplasia and heterotopias is difficult, time-consuming and reader dependant. Several 3D T1 voxel based morphometry methods have been proposed to automatically identify and suggest potential abnormalities to the reader. Several studies have shown the ability of Double Inversion Recovery imaging to detect intracortical lesions in MS and Epilepsy. In this study we propose to evaluate the ability of Double Inversion Recovery voxel based analysis to detect cortical and juxtacortical lesions in pharmaco resistant epileptic patients. This work was performed in collaboration with Arnaud Biraben, Anca Pasnicu and Eduardo Pasqualini, Béatrice Carsin-Nicol [24].

#### *6.3.2. MRI Estimation of $T_1$ Relaxation Time Using a Constrained Optimization Algorithm*

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

We propose a new method to improve $T_1$ mapping with respect to the popular *DESPOT1* algorithm. A distance function is defined to model the distance between the pure signal and the measurements in presence of noise. We use a constrained gradient descent optimization algorithm to iteratively find the optimal values of $T_1$ and $M_0$. The method is applied to MR images acquired with 2 gradient echo sequences and different flip angles. The performance of $T_1$ mapping is evaluated both on phantom and on in vivo experiments [25].

#### *6.3.3. Characterization and Modeling of Multidimensional MRI signatures in Multiple Sclerosis in clinically isolated syndromes.*

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

Clinically Isolated Syndrome data contribute to critical factors in obtaining meaningful precursor and predictors of Multiple Sclerosis. Current methodologies don't go beyond segmentation and which generalize poorly over multi-modal MRI data. The project objective is to research and develop a framework for characterization and modeling of multidimensional MRI signatures in clinically isolated syndrome(disease's onset),based on earlier and concurrent research and developments in the lab. In on going work an algorithmic framework is being developed to address the MS lesions' classification ,identification and retrieval in USPIO-6 database.

As part of a battery of pre- processing techniques ,the module for intensity normalization of MRI volumes based on Spatio-Temporal Robust Expectation Maximization (STREM) is developed. This work is primarily based on 3 MRI modalities viz T1-w,T2-w and FLAIR. Complementary to this work , an another intensity normalization algorithm is devised based on parametric robust as well as efficient estimation by minimizing a density power divergence (beta divergence).The proposed method is indexed by a single parameter alpha which controls the trade-off between robustness and efficiency. The methodology affords a robust extension of maximum likelihood estimation for which alpha tends to be zero. Choices of alpha near zero afford considerable robustness while retaining efficiency close to that of maximum likelihood.

Moving forward, to facilitate accurate lesion tracking,features must be selected which are robust to photometric and geometric distortions. Energy measures are used to capture lesion's multiscale orientation structure in space.To illustrate utility with respect to a lesion detection, we have developed descriptor like local energy based on 3D steerable wavelets. This will be followed by the rigorous empirical evaluations of the resulting algorithm yielding better lesion identification and retrieval.

### *6.3.4. Multiple Sclerosis Lesions Evolution in Patients with Clinically Isolated Syndrome.*

**Participants:** Alessandro Crimi, Olivier Commowick, 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 in inflammatory disease. At the early stage it is dominated by focal in 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 neurologic episode caused by in 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 propose 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. Our method is based on a two layers unsupervised clustering. 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 one year follow-up total lesion loads, which is so far the only image-based figure that can potentially correlate to 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 [30].

## 6.4. Vascular Imaging and Arterial Spin Labelling

### *6.4.1. Robust Cerebral Blood Flow Map Estimation in Arterial Spin Labeling*

**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, the low signal-to-noise ratio of ASL gives us no option but to repeat the acquisition in order to accumulate enough data to get a reliable signal. Perfusion signal is usually extracted by averaging across the repetitions. However, due to its zero breakdown point, the sample mean is very sensitive to outliers. A single outlier can thus have strong detrimental effects on the sample mean estimate. In this paper, we propose to estimate robust ASL CBF maps by means of M-estimators to overcome the deleterious effects of outliers. The behavior of this method is compared to z-score

thresholding as recommended in [8]. validation on simulated and real data is provided. Quantitative validation is undertaken by measuring the correlation with the most widespread technique to measure perfusion with MRI: Dynamic Susceptibility weighted Contrast (DSC) [37].

### *6.4.2. A comprehensive framework for the detection of individual brain perfusion abnormalities using Arterial Spin Labeling*

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

Arterial Spin Labeling (ASL) enables measuring cerebral blood flow in MRI without injection of a contrast agent. Perfusion measured by ASL carries relevant information for patients suffering from pathologies associated with singular perfusion patterns. However, to date, individual identification of abnormal perfusion patterns in ASL usually relies on visual inspection or manual delineation of regions of interest. In this paper, we introduce a new framework to automatically outline patterns of abnormal perfusion in individual patients by means of an ASL template. We compare two models of normal perfusion and assess the quality of detections comparing an a contrario approach to the Generalized Linear Model (GLM) [33], [35], [36].

### *6.4.3. Using Negative Signal in Mono-TI Pulsed Arterial Spin Labeling to Outline Pathological Increases in Arterial Transit Times*

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

The presence of unexpected negative perfusion estimates has been sparsely discussed in the ASL literature. In the study of perfusion maps extracted from a single inversion time in ASL (mono-TI ASL), it is however common to deal with areas of significant negative signal. This is problematic since performing statistical analysis based on this data might therefore lead to inacurrate results. Though isolated negative values could be attributed to noise, clusters of significant negative signal should be explained by another phenomenon. Following [2], which outlined that negative values might arise due to increased transit times, we investigated this hypothesis based on real clinical datasets including healthy control and patient data [34].

### *6.4.4. 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. 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, to correctly detect areas of functional activity.

### *6.4.5. Compressive Matched Filter for Cerebral Blood Flow Quantification with ASL: sampling diversity or repetition?*

**Participants:** Lei Yu, Pierre Maurel, Christian Barillot.

The Arterial Spin Labeling (ASL) is an MRI (Magnetic Resonance Imaging)-based perfusion technique which uses the magnetically tagged water as a freely diffusible tracer to measure perfusion non-invasively. This blood water is first labeled with a radio-frequency pulse in the neck of the patient. After a delay, called Inversion Time (TI), which allows the labeled blood to arrive in the brain, a labeled image of the brain is acquired. A control image is also acquired without labeling and the CBF (Cerebral Brain Flow) estimation is done on the difference between the control and labeled image. 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 work [45], 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.

The future works will consist in applying the parameter design protocol to guide the Diverse-TI technique in real ASL data acquisitions. Meanwhile, it is possible to extend CMF algorithm by considering additional priors to regularize the CBF estimation problem which might also improve the performance.

This work was done in collaboration with Remi Gribonval (Metiss team) [45].

### *6.4.6. Non-contrast enhanced neurovascular imaging*

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

Detecting internal carotid artery (ICA) stenosis is a main challenge for the prevention of stroke, the third leading cause of death in the developed world. Novel non-contrast-enhanced MRA (NCE MRA) sequences have emerged as an alternative to traditional MRA approaches, especially for patients during pregnancy or with renal insufficiency.

Up to now, the inversion-prepared bSSFP NCE MRA approach has been applied to imaging of renal arteries or kidney transplants and only few studies focused on the ICA, using ECG-gating. The purpose of this first study was to assess the feasibility and image quality of an improved non-gated carotid NATIVE TrueFISP NCE MRA sequence providing an extended field of view as compared to Time-of-Flight (TOF) imaging. Sixteen healthy volunteers were included to evaluate different sequence parameter sets. In comparison to standard TOF, the used NCE MRA sequence offered equivalent to higher image quality along with larger coverage and shorter acquisition times. Improved image quality was achieved without ECG gating, which had been used in previous studies. A Partial Fourier scheme with an early acquisition of k-space center yielded higher image quality and signal intensity compared to a late acquisition.

A second study evaluated the non-contrast-enhanced ECG-gated 4D MRA combining arterial spin labeling (ASL) and bSSFP readout (bSSFP NCE 4D MRA) sequence to non invasively investigate morphological and hemodynamic patterns of cerebral arteriovenous malformations (AVM). Previous studies have shown high temporal resolution (50-100 ms), yet with temporal windows limited to a single cardiac cycle. This precludes the complete venous drainage analysis, which is necessary to evaluate AVM hemorrhagic risk. This study aimed at assessing the feasibility, quality and diagnosis performance of a bSSFP NCE 4D MRA sequence with a large acquisition time window over 2 cardiac cycles (2 RR) without a significant reduction of spatial resolution. Ten patients presenting AVM and referred to digital subtraction angiography (DSA) were included in the study. The 2-RR bSSFP NCE 4D MRA sequence yielded an image quality comparable to that of a corresponding 1-RR acquisition. AVM analysis, however, was improved due to a better depiction of venous drainage necessary to evaluate hemorrhagic risk. The simultaneous high-resolution morphologic and hemodynamic data also offered an especially accurate delineation of the nidus, target of the treatment.

### *6.4.7. ASLDEM : Arterial Spin Labeling At 3t In Semantic Dementia: Perfusion Abnormalities Detection And Comparison With Fdg-pet*

**Participants:** Isabelle Corouge, Jean-Christophe Ferré, Elise Bannier, 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 project, we explore the ability of ASL to detect perfusion abnormalities in SD in comparison with FDG-PET. We apply our analysis framework (implemented as part of the

'autoasl' and 'autoasltemplate' softwares) on patients and healthy subjects data from an ongoing clinical study with a focus 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 [29].

For this work, Aurore Esquevin was awarded the prize "Communication Jeune Chercheur 2012" at the "Journées Françaises de Radiologie (JFR)" conference.

## 6.5. Abnormal functional lateralization and activity of language brain areas in developmental dysphasia

### *6.5.1. Statistical analysis of white matter integrity for the clinical study of specific language impairment in children*

**Participants:** Olivier Commowick, Aymeric Stamm, Camille Maumet, Jean-Christophe Ferré, Clément De Guibert, 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 propose to investigate the integrity of white matter in Specific Language Impairment thanks to diffusion Magnetic Resonance 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. This work was performed in collaboration with Emmanuel Vallée, Clément de Guibert, Catherine Allaire and Elisabeth Le Rumeur.

# 7. Bilateral Contracts and Grants with Industry

## 7.1. 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.

#### *7.1.1.1. TransIRMf project*

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

*duration : 24 months, from 01/10/2010*

The objective of this project is to set up and validate acquisition and data processing pipelines for metabolic and functional MRI. Acquition techniques comprise innovative block design and event related paradigms based on various stimuli (visual, auditive) and use various MRI sequences (BOLD, ASL). Paradigms were selected to cover a large scope of potential applications. The protocol imaging namely includes a BOLD fMRI resting state paradigm, an n-back working memory paradigm for BOLD fMRI, as well as and for the first time, for functional ASL. An emotional prosody recognition task was implemented, also for the first time, in an event related BOLD fRMI context. Data were acquired on 30 healthy subjects. Processing of these data is in progress based on inhouse pipelines (e.g., template construction using DARTEL, PVE correction for ASL data). This grant was awarded in collaboration with Biotrial within the CRITT-Santé Bretagne program.

# 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 first one 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. The second one led by Erwan Donal, physician at CHU-Rennes, will apply advanced MRI acquisition techniques in cardiac pathology.

### *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 monts from March 2012 (end : December 31, 2013)*

The ASLDEM project was partially funded the University of Rennes 1 "Défis Scientifiques Emergents" grant (7000 euros). The ASLDEM project is described in Sect. 6.4.7

### *8.1.5. Fondation de l'Avenir 2012 - 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 2012 - 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 2012*

**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.

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 Benoît Combès et al. [48]. 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, Pierre Maurel, Jean-Christophe Ferré, Elise Bannier, Camille Maumet, Isabelle Corouge.

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 Neuroim- agerie 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.

## 8.3. European Initiatives

### *8.3.1. 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: ChristianBarillot

International Partner (Institution - Laboratory - Researcher):

Children's Hospital Boston - Harvard Medical School (United States) - Computational Radiology Laboratory - Simon K. Warfield

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.

# 9. Dissemination

## 9.1. Animation of the scientific community

### *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.

### *9.1.2. Workshop/Symposium Organization*

- S. Prima was co-chairman of the MICCAI workshop on Mesh Processing in Medical Image Analysis (MeshMed 2012), Nice, France, Oct. 1, 2012 (http://www2.imm.dtu.dk/projects/MeshMed).

### *9.1.3. Peer Reviews of journals*

- IEEE TIP (SP, CB), IEEE TBE (SP), IEEE TITB (SP), Medical Image Analysis (CB, SP), NeuroImage (CB, IC), 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), Machine Vision and Applications (SP), Pattern recognition letters (SP), American Journal of Physical Anthropology (SP), Journal of Anatomy (SP)

### 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 MICCAI'2012, IEEE ISBI'2012, IEEE ICPR'2012, MeshMed'2012.
- I. Corouge was TPC member of the MICCAI 2012 Workshop on Novel Biomarkers for Alzheimer's Disease and Related Disorders.
- P. Maurel was TPC member of MICCAI'2012, IEEE ISBI'2012, MICCAI 2012 Workshop on Novel Biomarkers for Alzheimer's Disease and Related Disorders.
- O. Commowick was TPC member of MICCAI'2012, IEEE ISBI'2012, MICCAI 2012 Workshop on Novel Biomarkers for Alzheimer's Disease and Related Disorders.

### 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, O. Commowick, P Maurel and S. Prima are members of the MICCAI society

## 9.2. Teaching

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

- Master 2 SIBM, University of Angers-Brest-Rennes : 26h (*C. Barillot, O. Commowick, S. Prima, I. Corouge, E. Bannier, JY Gauvrit*)
- C. Barillot is responsible for one semester.
- J-Y. Gauvrit is the coordinator for the Master.
- Sylvain Prima gave two 3-hour lectures as an invited speaker at the SERA summer school (June 5-8, Tampere, Finland, http://www.cs.tut.fi/sera2012)
- 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) and 60h in general Image Processing (P. Maurel)

## 9.3. Participation to seminars, scientific evaluations, awards

- C. Barillot served as expert for the APHP-DHU program 2012
- C. Barillot served as expert for the PHRC national program 2012
- C. Barillot is elected-member of the Scientific Board of CNRS-INS2I
- C. Barillot is permanent member of the Administrative Council of the pôle de compétitivité "Images & Réseaux"
- Sylvain Prima served as expert for The Netherlands Organisation for Scientific Research (NWO)
- Sylvain Prima is a member of the CUMIR committee (Commission des Utilisateurs des Moyens Informatiques pour la Recherche) and of the working group "voyages".

## 9.4. Dissemination toward non specialists

- Sylvain Prima gave a 1-hour lecture on “computer-assisted paleoanthropology” on June 26 at the “Conf’Lunch” monthly seminar organised at Inria.
- Christian Barillot participate to a 1-hour debate on "L’exploration médicale du cerveau : hommage au Voyage fantastique d’Isaac Asimov" during the "UTOPIALES" festival at Palais des Congres, Nantes, Nov. 2012. (http://www.utopiales.org/christian-barillot)
- In collaboration with Biogenouest, Neurinfo organized a user meeting in December 2012. This meeting attended by scientists, students, MRI operators, physicians, ..., gave us the opportunity to present an overwiew of the Neurinfo activities to our user community. Four users presented the research project they have been conducting at Neurinfo.
- In cunjonction with INSERM and ARSEP we organized a Lab visits to the MS population community to disseminate our current work in imaging in Multiple Sclerosis (16th November 2012).

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