INRIA

INSTITUT NATIONAL DE RECHERCHE EN INFORMATIQUE ET EN AUTOMATIQUE

Project-Team Asclepios

Analysis and Simulation of Biomedical Images

Sophia Antipolis - Méditerranée

THEME BIO

Table of contents

1. Team

Head of project-team

Nicholas Ayache [Research Director (DR) Inria, HdR]

Vice-head of project-team

Grégoire Malandain [Research Director (DR) Inria, HdR]

Research Scientists

Hervé Delingette [Research Director (DR) Inria, HdR]
Xavier Pennec [Research Director (DR) Inria, HdR]
Maxime Sermesant [Research Associate (CR) Inria]
Olivier Clatz [Research Associate (CR) Inria]

Research Team Assistant

Isabelle Strobant [TR, Research Team Assistant, Inria]

Engineers

Nicolas Toussaint
Barbara André
Daniel Barbeau

PhD Students [funding, year of defense]

Florence Billet [CardioSense3D, 2009]
Jonathan Boisvert [Funding Ecole Polytechnique Montreal, 2008]
François Chung [Funding 3D Anatomical Human, 2010]
Olivier Commowick [Funding Cifre DOSIsoft, 2007]
Jimena Costa [Funding Maestro EC project, 2008]
Stanley Durrleman [Detached from Corps des Telecom, 2009]
Romain Fernandez [Funding CIRAD-Region Midi-Pyrénées, 2009]
Pierre Fillard [Funding MESR, 2008]
Tristan Glatard [Funding MESR, 2007]
Heike Hufnagel [Funding EC (P&M Curie), 2008]
Ender Konukoglu [Funding INRIA-Region PACA, 2008]
Damien Lepiller [Funding Philips Medical Systems, 2009]
Thomas Mansi [Funding HealthEChild, 2010]
Jean-Marc Peyrat [Funding Siemens, 2008]
Liliane Ramus [Funding Cifre DOSIsoft, 2010]
Jean-Christophe Souplet [Funding Qualicore, 2008]
Tom Vercauteren [Funding Cifre Mauna Kea Technologies, 2008]

Trainee

Sébastien Novellas [Interventional Radiologist, CHU Nice, 2007]

Visitors

William Wells [Associate Professor on sabbatical from 01/08/07 until 20/12/07, from Harvard Medical School]
Boon Thye Thomas Yeo [PhD candidate, visiting scientist from 01/06/07 until 01/09/07, from MIT, Boston]
Darko Zikic [PhD candidate, visiting scientist from 19/11/07 until 23/12/07, Technische Universität München]
Kilian Pohl [Instructor of Radiology, visiting scientist from 20/08/07 until 15/09/07, from Harvard, Boston]
Jean Gallier [Professor, School of Engineering and Applied Science, on sabbatical from 01/09/2006 to 31/07/2007, from University of Pennsylvania]
Guido Gerig [Director of Utah Center for Neuroimage Analysis, Professor of Computer Science on sabbatical from 01/01/07 until 30/04/07, from Utah University]

External Collaborators

Eric Bardinet [CNRS, La Pitié-Salpêtrière Hospital, Paris]
Pierre-Yves Bondiau [Radiotherapist, CAL, Nice]
Miguel-Angel Gonzalez-Ballester [MEM Research Center, University of Bern]
Jacques Darcourt [Nuclear Medicine, CAL, Nice]
Didier Dormont [Neuroradiology, La Pitié-Salpêtrière Hospital, Paris]
Christine Lebrun-Frénay [Neurology, Pasteur Hospital, Nice]
Jean Gallier [UPenn, Philadelphia]
Polina Golland [MIT, Boston]
Reza Razavi [King's College London, Division of Imaging Sciences, St Thomas' Hospital, London]
Robert Howe [Harvard University, Boston]
Johan Montagnat [I3S]
Luc Soler [IRCAD, Strasbourg]
Paul Thompson [LONI, UCLA, Los Angeles]
Simon Warfield [Computational Radiology Laboratory, Boston]

2. Overall Objectives

2.1. Introduction

There is an irreversible evolution of medical practice toward more quantitative and personalized decision processes for prevention, diagnosis and therapy.

This evolution is supported by a constantly increasing number of biomedical devices providing *in vivo* measurements of structures and processes inside the human body, at scales varying from the organ to the cellular and even molecular level. Among all these measurements, biomedical images of various forms play a more central role everyday, as well as the exploitation of the genetic information attached to each patient.

Facing the need of a more quantitative and personalized medicine based on larger and more complex sets of measurements, there is a crucial need for developing

1. advanced image analysis tools capable to extract the pertinent information from biomedical images and signals,
2. advanced models of the human body to correctly interpret this information, and
3. large distributed databases to calibrate and validate the models.

2.2. Highlights of the year

- Olivier Clatz was awarded *Le Monde* Prize for best Ph.D. in Science and Medicine.
- Nicholas Ayache received the *trophée du chercheur de l'année PACA 2007* awared by the *Nouvel Economiste*.
- Nicholas Ayache gave an invited talk the 12th of February 2007 at the Maison des Arts et Métiers in Paris for the Colloquium in memory of Gilles Kahn, and 5 presentations in memory of Gilles Kahn in the USA: Mayo Clinic (June 15th, Rochester) , MIT (Sept 7th, Cambridge), Harvard (Sept 28th, Cambridge), Brigham and Women's Hospital (Oct 1st, Boston) and Martinos Research Center (Oct 10th, Boston).
- The associated team CompuTumor was created on January 1st 2007 (see section 7.4). This project is dedicated to the study of brain tumor models and their confrontation with medical images to better assist diagnosis and therapy. It will strongly enhance the current collaborations between INRIA and a group of world leading teams with complementary technical and clinical expertise on these topics in Boston (MIT, Harvard, Harvard Medical School, CIMIT) and Nice (CHU Nice, Centre Antoine Lacassagne).

- The INRIA Cooperative Research Initiative BrainVar was funded (see section 7.2.6). It aims at understanding and modelling the individual anatomy of the brain and its variability across a population, and federates the efforts of several groups in France (Asclepios, INRIA Sophia Antipolis; LNAO Neurospin, CEA - DSV - DRM- SHFJ; Neurospin, INRIA Futurs; MMiXT, CNRS UPR640 LENA, Pitié-Salpétrière; VisAGeS, IRISA Rennes; LSIS, UMR 6168, LXAO team, Marseille; CMLA, ENS Cachan) to identify the challenges for a future potential neuro-anatomic plateform.
- 12 members of the team attended the MICCAI'07 conference in Brisbane, Australia, to present original contributions (Nicholas Ayache, Jimena Costa, Tom Vercauteren, Heike Hufnagel, Olivier Clatz, Stanley Durrleman, Maxime Sermesant, Nicolas Toussaint, Pierre Fillard, Hervé Delingette, Ender Konukoglu, Xavier Pennec). N. Ayache was Program Chair, G. Malandain and X. Pennec were Program Committee members.
- Maxime Sermesant is a part-time lecturer in the Interdisciplinary Medical Imaging Group, Division of Imaging Sciences, St Thomas' Hospital, King's College London. The XMR facility within this hospital is a unique possibility to validate and exploit the cardiovascular modelling work.

3. Scientific Foundations

3.1. Introduction

Tremendous progress has been made in the automated analysis of biomedical images during the past two decades [114]. Readers who are neophyte to the field of medical imaging will find an interesting presentation of acquisition techniques of the main medical imaging modalities in [105], [101]. Regarding the target applications, a good review of the state of the art can be found in the book *Computer Integrated Surgery* [100], in N. Ayache's article [108] and in the more recent synthesis [114]. The scientific journals *Medical Image Analysis* [103], *Transactions on Medical Imaging* [104], and *Computer Assisted Surgery* [102] are also good reference material. One can have a good vision of the state of the art with the proceedings of the most recent conferences MICCAI'2005 (Medical Image Computing and Computer Assisted Intervention) [97], [98] or ISBI'2004 (Int. Symp. on Biomedical Imaging) [99].

For instance, for rigid parts of the body like the head, it is now possible to fuse in a completely automated manner images of the same patient taken from different imaging modalities (e.g. anatomical and functional), or to track the evolution of a pathology through the automated registration and comparison of a series of images taken at distant time instants [116], [135]. It is also possible to obtain from a Magnetic Resonance Image (MRI) of the head a reasonable segmentation into skull tissues, white matter, grey matter, and cerebro-spinal fluid [139], or to measure some functional properties of the heart from dynamic sequences of Magnetic Resonance [107], Ultrasound or Nuclear Medicine images [117].

Despite these advances and successes, one can notice that statistical models of the anatomy are still very crude, resulting in poor registration results in deformable regions of the body, or between different subjects. If some algorithms exploit the physical modeling of the image acquisition process, only a few actually model the physical or even physiological properties of the human body itself. Coupling biomedical image analysis with anatomical and physiological models of the human body could not only provide a better comprehension of the observed images and signals, but also more efficient tools to detect anomalies, predict evolutions, simulate and assess therapies.

3.2. Medical Image Analysis

The quality of biomedical images tends to improve constantly (better spatial and temporal resolution, better signal to noise ratio). Not only the images are multidimensional (3 spatial coordinates and possibly one

temporal dimension), but medical protocols tend to include multi-sequence (or multi-parametric)[1] and multi-modal images[2] for each single patient.

Despite remarkable efforts and advances during the past twenty years, the central problems of segmentation and registration have not been solved in the general case. It is our objective in the short term to work on specific versions of these problems, taking into account as much *a priori* information as possible on the underlying anatomy and pathology at hand. It is also our objective to include more knowledge on the physics of image acquisition and observed tissues, as well as on the biological processes involved. Therefore the research activities mentioned in this section will incorporate the advances made in Computational Anatomy and Computational Physiology as described in sections 3.4 and 3.5.

We plan to pursue our efforts on the following problems:

1. multi-dimensional, multi-sequence and multi-modal image segmentation,
2. Image Registration/Fusion,

3.3. Biological Image Analysis

In Biology, a huge number of images of living systems are produced every day to study the basic mechanisms of life and pathologies. If some bio-imaging *principles* are the same as the ones used for medical applications (e.g. MR, CT, US, Pet or SPECT), the bio-imaging *devices* are usually customized to produce images of higher resolution[3] for the observation of small animals (typically rodents). In addition, Optical Imaging techniques and biophotonics are developing very fast. This includes traditional or Confocal Microscopy, multi-photon confocal microscopy, Optical Coherent Tomography, near-infrared imaging, diffuse optical imaging, phased array imaging, etc. A very new and promising development concerns micro-endoscopy, which allows cellular imaging at the end of a very small optical fiber [122].

Most of these imaging techniques can be used for *Molecular Imaging*, an activity aiming at the *in vivo* characterization and measurement of biological processes at cellular and molecular level. With optical techniques, molecular imaging makes an extensive use of the fluorescent properties of certain molecules (in particular proteins, e.g. GFP[4]) for imaging of gene expression *in vivo*. With other modalities (like PET, SPECT, MR, CT and even US), molecular imaging can use specific contrast agents or radioactive molecules. For clinical applications, the ultimate goal of molecular imaging is to find the ways to probe much earlier the molecular anomalies that are the basis of a disease rather than to image only its end effects [140].

Some of the recent advances made in Medical Image Analysis could be directly applied (or easily adapted) to Biological Image Analysis. However, the specific nature of biological images (higher resolution, different anatomy and functions, different contrast agents, etc.), requires specific image analysis methods (one can refer

[1] Multisequence (or multiparametric) imaging consists in acquiring several images of a given patient with the same imaging modality (e.g. MRI, CT, US, SPECT, etc.) but with varying acquisition parameters. For instance, using Magnetic Resonance Imaging (MRI), patients followed for multiple sclerosis may undergo every six months a 3-D multisequence MR acquisition protocol with different pulse sequences (called T1, T2, PD, Flair etc): by varying some parameters of the pulse sequences (e.g Echo Time and Repetition Time), images of the same regions are produced with quite different contrasts depending on the nature and function of the observed structures. In addition, one of the acquisition (T1) can be combined with the injection of a contrast product (typically Gadolinium) to reveal vessels and some pathologies. Diffusion tensor images (DTI) can be acquired to measure the self diffusion of protons in every voxel, allowing to measure for instance the direction of white matter fibers in the brain (same principle can be used to measure the direction of muscular fibers in the heart). Functional MR images of the brain can be acquired by exploiting the so-called Bold Effect (Blood Oxygen Level Dependency): slightly higher blood flow in active regions creates subtle higher T2* signal which can be detected with sophisticated image processing techniques.

[2] Multimodal acquisition consists in acquiring on the same patient images from different modalities, in order to exploit their complementary nature. For instance CT and MR may provide information on the anatomy (CT providing contrast between bones and soft tissues, MR providing contrast within soft tissues of different nature) while SPECT and PET images may provide functional information by measuring a local level of metabolic activity.

[3] This is the case with micro-MRI, Micro-CT, Micro-US devices, and to a less extent with Micro-SPECT and Micro-PET devices.

[4] Green Fluorescent Protein.

to the recent tutorial [130] and to the Mouse Brain Atlas Project [106]. This is particularly true when dealing with *in vivo* microscopic images of cells and vessels.

Our research efforts will be focused to the following generic problems applied to *in vivo* microscopic images:

1. quantitative analysis of microscopic images,
2. detection and quantification of variations in temporal sequences,
3. construction of multiscale representations (from micro to macro).

3.4. Computational Anatomy

The objective of Computational Anatomy (CA) is the modeling and analysis of biological variability of the human anatomy. Typical applications cover the simulation of average anatomies and normal variations, the discovery of structural differences between healthy and diseased populations, and the detection and classification of pathologies from structural anomalies[5] [126].

Studying the variability of biological shapes is an old problem (cf. the remarkable book "On Shape and Growth" by D'Arcy Thompson [138]). Significant efforts have been made since that time to develop a theory for statistical shape analysis (one can refer to [113] for a good synthesis, and to the special issue of Neuroimage [137] for recent developments). Despite all these efforts, there is a number of challenging mathematical issues which remain largely unsolved in general. A particular issue is the computation of statistics on manifolds which can be of infinite dimension (e.g the group of diffeomorphisms).

There is a classical stratification of the problems into the following 3 levels [124]: 1) construction from medical images of anatomical manifolds of points, curves, surfaces and volumes; 2) assignment of a point to point correspondence between these manifolds using a specified class of transformations (e.g. rigid, affine, diffeomorphism); 3) generation of probability laws of anatomical variation from these correspondences.

We plan to focus our efforts to the following problems:

1. Statistics on anatomical manifolds,
2. Propagation of variability from anatomical manifolds,
3. Linking anatomical variability to image analysis algorithms,
4. Grid-Computing Strategies to exploit large databases.

3.5. Computational Physiology

The objective of Computational Physiology (CP) is to provide models of the major functions of the human body and numerical methods to simulate them. The main applications are in medicine and biology, where CP can be used for instance to better understand the basic processes leading to the apparition of a pathology, to model its probable evolution and to plan, simulate, and monitor its therapy.

Quite advanced models have already been proposed to study at the molecular, cellular and organic level a number of physiological systems (see for instance [129], [121], [111], [133], [118]). While these models and new ones need to be developed, refined or validated, a grand challenge that we want to address in this project is the automatic adaptation of the model to a given patient by confronting the model with the available biomedical images and signals and possibly also from some additional information (e.g. genetic). Building such *patient-specific models* is an ambitious goal which requires the choice or construction of models with a complexity adapted to the resolution of the accessible measurements (e.g. [134], [125] and the development of new data assimilation methods coping with massive numbers of measurements and unknowns.

[5] The NIH has lauched the Alzheimer's Disease Neuroimaging Initiative (60 million USD), a multi-center MRI study of 800 patients who will be followed during several years. The objective will be to establish new surrogate end-points from the automated analysis of temporal sequences. This is a challenging objective for researchers in Computational Anatomy. The data will be made available to qualified research groups involved or not in the study.

There is a hierarchy of modeling levels for CP models of the human body:

- the first level is mainly geometrical, and addresses the construction of a digital description of the anatomy, essentially acquired from medical imagery;
- the second level is physical, involving mainly the biomechanical modeling of various tissues, organs, vessels, muscles or bone structures;
- the third level is physiological, involving a modeling of the functions of the major biological systems (e.g. cardiovascular, respiratory, digestive, central or peripheral nervous, muscular, reproductive, hormonal, etc.) or some pathological metabolism (e.g. evolution of cancerous or inflammatory lesions, formation of vessel stenoses, etc.);
- a fourth level would be cognitive, modeling the higher functions of the human brain.

These different levels of modeling are closely related to each other, and several physiological systems may interact together (e.g. the cardiopulmonary interaction [123]). The choice of the resolution at which each level is described is important, and may vary from microscopic to macroscopic, ideally through multiscale descriptions.

Building this complete hierarchy of models is necessary to evolve from a *Visible Human* project (essentially first level of modeling) to a much more ambitious *Physiological Human project* (see [120], [121]). We will not address all the issues raised by this ambitious project, but instead focus on topics detailed below. Among them, our objective is to identify some common methods for the resolution of the large inverse problems raised by the coupling of physiological models to biological images for the construction of patient-specific models (e.g. specific variational or sequential methods (EKF), dedicated particle filters, etc.). We also plan to develop a specific expertise on the extraction of geometrical meshes from medical images for their further use in simulation procedures. Finally, computational models can be used for specific image analysis problems studied in section 3.2 (e.g. segmentation, registration, tracking, etc.). Application domains include

1. Surgery Simulation,
2. Cardiac Imaging,
3. Brain tumors, neo-angiogenesis, wound healing processes, ovocyte regulation, ...

3.6. Clinical and Biological Validation

If the objective of many of the research activities of the project is the discovery of original methods and algorithms with a demonstration of feasibility on a limited number of representative examples (i.e. proofs of concept) and publications in high quality scientific journals, we believe that it is important that a reasonable number of studies include a much more significant validation effort. As the BioMedical Image Analysis discipline becomes more mature, this is a necessary condition to see new ideas transformed into clinical tools and/or industrial products. It is also often the occasion to get access to larger databases of images and signals which in turn participate to the stimulation of new ideas and concepts.

4. Software

4.1. MedINRIA

Keywords: *DTI*, *Log Euclidian*, *MRI*, *MS*, *f-MRI*, *fiber tracking*, *image processing*, *medical imaging*, *registration*, *tensor*, *tractography*.

Participants: Pierre Fillard [Correspondant], Nicolas Toussaint, Jean-Christophe Souplet, Maxime Sermesant, Christine Lebrun, Grégoire Malandain.

MedINRIA (http://www-sop.inria.fr/asclepios/software/MedINRIA) is the new front end software for the Asclepios Project. Its development started in 2006 with the venue of Nicolas Toussaint. MedINRIA has grown fast, and is now becoming a reference not only in the medical image processing community, but also in a clinical environment thanks to the efforts we put to develop an intuitive, reactive and easy-to-use user interface. MedINRIA is a collection of softwares with a well defined application. Last year, only two applications were available: "DTI Track" (DT-MRI processing with Log-Euclidean metrics) and "Tensor Viewer" (Tensor field visualization). Among many improvements of these two initial softwares, new applications were released during 2007:

- **Registration Tool** (Fig. 1 top right): Funded by the Health-e-Child European project, RegistrationTool is a general image registration application that proposes, in a few clicks, to register manually or fully automatically two 3D medical images. A non-linear registration algorithm, the diffeomorphic demons by Tom Vercauteren [91], is also available.
- **ImageViewer** (Fig. 1 bottom left and right): This more generic application was missing in the first release of MedINRIA. It allows to visualize 3D images either in 2D (slice mode), or in 3D (using volume rendering or multi-planar reconstruction). Many features are available: possibility to color code images with a lookup table, to manually segment them, and to compare all of them in a preview mode. Moreover, for a better clinical integration, we worked on developing an automatic DICOM importer (DICOM is the file format most often encountered in clinics).
- **Lesions Segmentation Editor/Lesions Segmentation Comparator**: These two applications were developed by Jean-Christophe Souplet and propose manual and semi-automatic segmention methods of multiple sclerosis (MS) lesions. Lesions can be quantified (volume, number, etc.). In the manual mode, the user segments a lesion slice by slice with the mouse. In the semi-automatic mode, the user only needs to spot the lesion and click inside it, and the segmentation is achieved automatically. Automatic segmentation is based on a region growing algorithm acting on both image and image gradient. Different colors can be attributed to each lesions for visual distinction. Obtained segmentation can be visualized in 2D and 3D, they can be saved and statistics can be computed.

In march 2007, MedINRIA was migrated to the INRIA gforge, a complete and performant framework for developers, including a source code manager server, forums, mailing lists and trackers (bugs, patches, etc.). Since then, MedINRIA has been downloaded more than 8500 times (source: October 2006). MedINRIA end-users include: the University of Utah (with Guido Gerig), the Kremlin-Bicêtre Hospital, Paris, and McGill University, Montreal.

The MAC version has been finally released in march 2007. Many medical experts are MAC users, and it was really important to offer to this audience a compatible version of the software. MedINRIA has been also registered on the "Apple Download Center", which helps spreading the software around.

MedINRIA was presented by Nicolas Toussaint at the MICCAI'07 workshop: "Interaction in Medical Image Analysis and Visualization" [87].

4.2. SepINRIA

Keywords: *Multiple Sclerosis*.

Participants: Jean-Christophe Souplet [Correspondant], Pierre Fillard, Nicolas Toussaint, Christine Lebrun, Grégoire Malandain.

SepINRIA (http://www-sop.inria.fr/asclepios/software/SepINRIA) is a specialization of MedINRIA, devoted to the analysis of MR cerebral images of Multiple Sclerosis (MS) patients. It includes several features: an image visualization module which is able to read a large panel of medical image format (DICOM, analyze, ITK MetaImage, etc.); a registration tool; a manual lesion contouring tool, to allow the neurologist to draw ground truth segmentation; and a segmentation comparison tools, to quantify the discrepancy between two segmentations (e.g. the manual ground truth and an automatic segmentation.

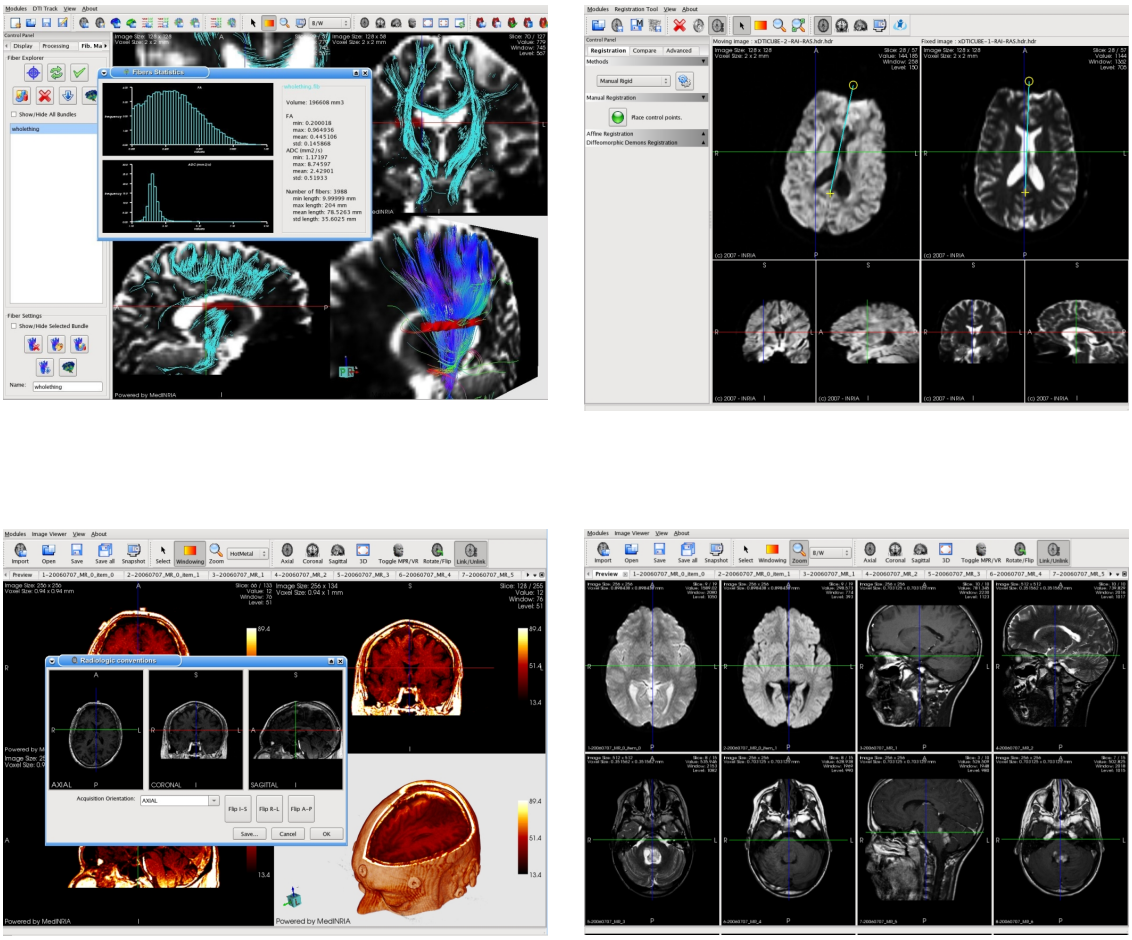


Figure 1. ***Snapshots of MedINRIA.*** *Top left: The "DTI Track" application. Top right: The "Registration Tool". Bottom left: The "Image Viewer". Bottom right: The preview window of the "Image Viewer".*

4.3. CardioViz3D: Cardiac Imaging and Simulation Software

Keywords: *Cardiac Imaging*, *Cardiac Simulation*, *CardioSense3D*, *DICOM*, *KWWidgets*, *Mesh Projection*, *Software*, *Time Sequence*, *vtkINRIA3D*.

Participants: Nicolas Toussaint [Correspondant], Tommaso Mansi, Maxime Sermesant, Herve Delingette.

CardioViz3D (http://www-sop.inria.fr/asclepios/software/CardioViz3D) is a front-end software for cardiac imaging and simulation. It started in October 2006 and is developed in the framework of CardioSense3D National project (see section 7.2.1). It has two main objectives:

- to provide clinicians and industrials with a front-end application highlighting the capacities of CardioSense3D in terms of cardiac simulation.
- to provide researchers with a set of tools for cardiac data processing, simulation and visualization.

CardioViz3D presents a sophisticated "toolbox framework" that helps potential developers to easily plug in their own work into the software. Among all the currently available features (see Fig. 2), several domains of application can be pointed out.

- **Image visualization**: The images are displayed into a tab browsing system (firefox-like). The navigation and all user interactions are fairly simple and intuitive actions. Features such as the visualization of scalar distribution or basic image processing are provided.
- **Mesh Visualization**: Surface and volume meshes can be easily visualized into the previously described tab browsing system. Rendering properties (i.e. color, light, surface interpolation) can be set and the meshes can be projected on 2D slices for a better insight of the object of interest. Scalar and vector fields can be assigned to a mesh object and visualized.
- **Time Support**: Cardiac imaging requires a good handling of time sequences of data. In CardioViz3D either image and mesh sequences can be imported, synchronized, and visualized (in real-time). Movie export is also provided.
- **Cardiac Modelling**: Cardiac models can be generated either out of some anatomical characteristics, or out of some manually defined control points. A semi-automatic process allows to extract cardiac regions from an input image.
- **Cardiac Segmentation**: This CardioViz3D module provides tools to semi-automatically segment the heart on 3D MRI. They are organised as a wizard pipeline to guide the user throughout the different steps of the process.

CardioViz3D was migrated to the INRIA gforge, can be accessed through the INRIA gforge, a complete framework for developers, including a source code manager server, forums, mailing lists and trackers (bugs, patches, etc.). Since October 2007, a beta release is available for download under Windows, Linux and MacOSX at http://www-sop.inria.fr/asclepios/software/CardioViz3D.

4.4. vtkINRIA3D: A VTK Extension for Spatiotemporal Data Synchronization, Visualization and Management

Keywords: *DICOM*, *Data Management*, *Interaction*, *Mesh*, *Spatiotemporal Data*, *Synchronization*, *Time Sequence*, *VTK*, *Visualization*, *medical imaging*.

Participants: Pierre Fillard [Correspondant], Nicolas Toussaint, Maxime Sermesant.

vtkINRIA3D is an open source set of C++ libraries, extending the Visualization ToolKit VTK (http://www.vtk.org). It was initiated to gather the developement efforts in terms of data visualization.

In medical image processing and visualization, one often has to deal with very specific types of data that require specialized visualization and interaction techniques. Moreover, the management of all these data by programmers who want to build a complete processing and visualization system can be a challenging task, due to the various forms they can take, and to the specific visualization strategies they require.

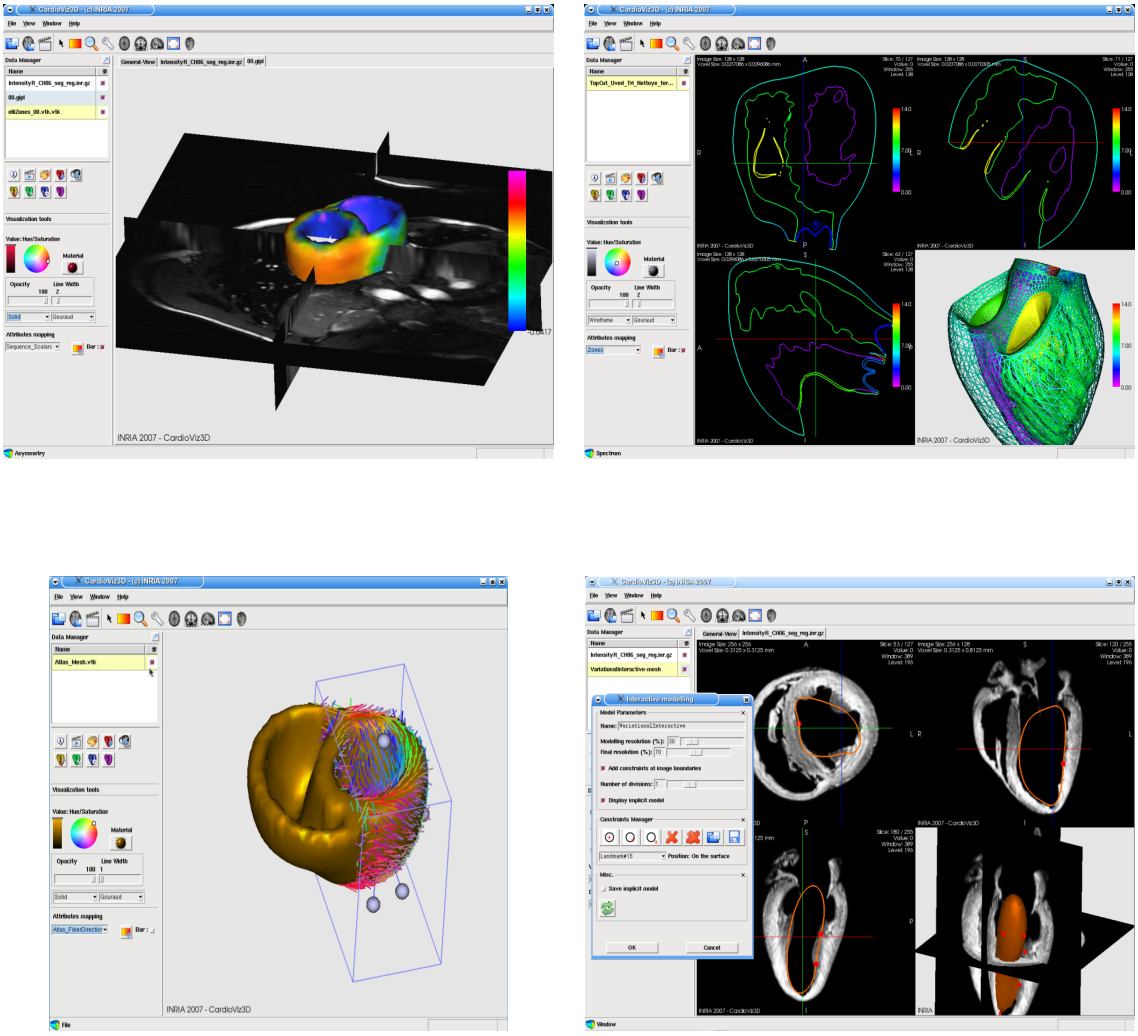


Figure 2. ***Snapshots of CardioViz3D.*** *Top Left: Image and mesh displayed in CardioViz3D interface. The mesh is colored according to the cardiac action potential. Top Right: Surface mesh projected in the 3 orthogonal planes (data provided by the 3D Science project). Bottom Left: Mesh and cardiac fibers are displayed. Fibers are colored with respect to their directions. Bottom Right: Interactive mesh generation from manually defined control points.*

In this context, the aim of vtkINRIA3D is to make available a simple and versatile library providing useful features and allowing developers to build their own software upon it. Several softwares are already using these features: MedINRIA, SepINRIA and CardioViz3D. Among the provided features of vtkINRIA3D, three topics can be highlighted:

- **Synchronization of interactions and visualization.** vtkINRIA3D proposes a group of classes to handle the visualization of medical images, in which an effort has been made to synchronize interactions between several views of the same image. This includes for instance the slice position, the zoom level or the image contrast (see Fig. 3).
- **Adapted manipulation of complex data.** Considering the increasing diversification of the medical information sources, we offer in vtkINRIA3D a framework to facilitate the task of programmers who want to quickly integrate nice visualization and interactions of scientific data into their software. This includes for example the visualization management of several surface meshes, the rendering of DT-MRI tensors into several graphic primitives, or a sophisticated visualization scheme of neural fibers as obtained in DT-MRI (see Fig. 3).
- **Simple and efficient management of spatiotemporal data.** Another feature provided in vtkINRIA3D is the management of several types of datasets, and time sequences of datasets in the same framework. This allows the developer for example to manage, use and display any of these datasets with a minimal effort, have access to each individual dataset, process it and directly observe the results. Time support is also provided, and allows to easily manipulate and visualize several time sequences of any type and synchronize them. Time support represents a very useful feature in some applications such as cardiac simulation.

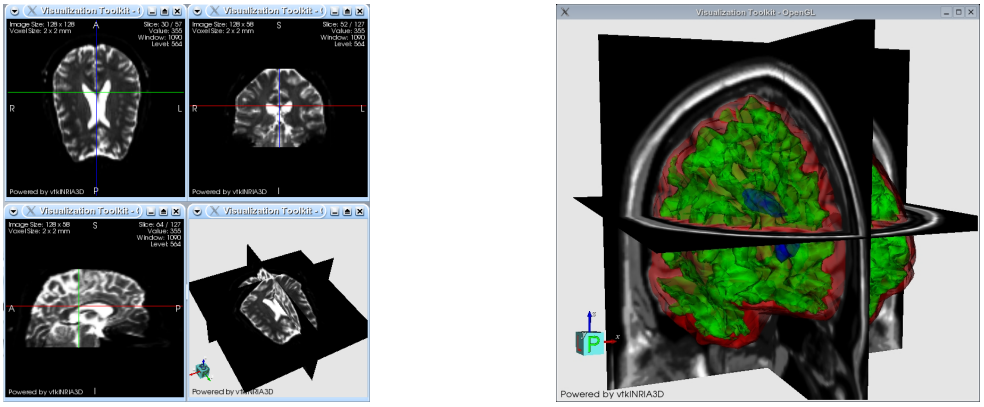


Figure 3. ***Snapshots of vtkINRIA3D.*** *Left: Four views of a 3D brain MR image are shown. Thanks to the vtkINRIA3D synchronization view framework, an interaction in one view (i.e. a change of the slice position, the image contrast or the zoom level) will have the same effect on the other views. Right: In this figure some isosurfaces of brain structure segmentations are visualized on top of an MRI image.*

vtkINRIA3D is compiled with VTK 5.0.3, ITK 3.2.0 (for some optional components), CMake 2.4.6, and is open-source. Source code, doxygen files, dashboard, and examples data can be found at: http://www-sop.inria.fr/asclepios/software/vtkINRIA3D. Pierre Fillard presented vtkINRIA3D at the MICCAI'07 workshop on "Open Source and Open Data for MICCAI" [87].

4.5. Baladin

Keywords: *Multimodal image registration*.

Participant: Grégoire Malandain [Correspondant].

This software allows to register 3-D multimodal medical images with rigid or affine transformations. It is based on the computation of correspondences obtained by registering small sub-images (or blocks) with a local similarity measure (correlation coefficient). As a result, it yields the computed transformation and resampled images.

4.6. smDeform

Participant: Hervé Delingette [Correspondant].

smDeform is a software that allows the interactive segmentation of medical images based on deformable simplex meshes. With such a software, the user can define local and global constraint on the mesh deformation based on a priori knowledge about the shape and appearance of the anatomical structure to be segmented.

4.7. simuDeform

Participant: Hervé Delingette [Correspondant].

simuDeform allows the real-time simulation of soft tissue deformation, especially in the context of surgery simulatiom. This software can handle haptic devices for force-feedback interaction and includes different types of soft tissue models (tensor-mass, non-linear elastic, precomputed elastic) suitable for simulating the deformation and cutting of volumetric materials (parenchymatous organs like the liver or the brain).

4.8. Medical Image Processing Software (MIPS)

Participant: Hervé Delingette [Correspondant].

This library is an effort to gather and capitalize all software developments of the team. It includes mainly YAV++ but also a number of other softwares (EpidaureLib, Baladin, CrestMatch, Demons, Pasha, Yasmina, etc). MIPS is composed of several librairies and executables that allows the visualisation and manipulation of 3-D images and meshes.

4.9. Simulation Open Framework Architecture (SOFA)

Keywords: *medical simulation*, *surgery simulation*.

Participants: Barbara Andrée, Hervé Delingette [Correspondant].

Web site: http://www.sofa-framework.org/ Gforge link: https://gforge.inria.fr/projects/sofa/

SOFA is an Open Source framework for the real-time simulation of deformable structures, particularly for medical simulation and planning. Three INRIA research teams are currently contributing to development of the SOFA platforms: the project team Alcove in Lille, Asclepios in Sophia-Antipolis and Evasion in Grenoble. The simulation group of the CIMIT (affiliated to MIT / Harvard / Massachussets General Hospital) has also strongly supported its development. This international open source platform is mostly intended for the research community to help the development of new algorithms, but it can also be used as a prototyping tool thanks to its modular architecture.

The involvement of the Asclepios team has been mostly focused on a new design that allows each SOFA component to cope with topological changes. Indeed, when simulating the surgical resection or suturing of an organ, it is necessary to update the data structure associated with the mesh of the organ but also the sparse matrices used in the computation of the mass and stiffness of the material. Propagating those topological changes to all components in a modular and generic way is a challenging task but provides a significant added value to all SOFA users.

An additional objective include the definition of scalar fields (like pressure, electric potential fields) on surface or volumetric meshes in order to implement physiological models. Our mid-term goal is to develop in SOFA a real-time simulator of radiofrequency ablation involving haptic devices which is suitable to train cardialogist for this endovascular procedure.

A plenary meeting of the SOFA developers involving 15 people has been organized in Sophia-Antipolis on Sept 11th, 12th and 13th.

4.10. Yasmina

Keywords: *Multimodal image registration*.

Participant: Grégoire Malandain [Correspondant].

This software allows to register 3-D multimodal medical images with rigid or affine transformations. It is based on the minimisation (or maximisation) of global iconic similarity measures (e.g. mutual information, correlation ratio, etc).

4.11. Pasha

Participant: Xavier Pennec [Correspondant].

This software allows advanced nonlinear registration of 3-D images, using both iconic and geometric criteria.

4.12. Runa

Participant: Xavier Pennec [Correspondant].

This software allows advanced nonlinear registration of 3-D images, with a parallel implementation.

4.13. Prospect

Participant: Xavier Pennec [Correspondant].

This software is designed for protein matching, and is based on geometric hashing.

5. New Results

5.1. Introduction

Current research activities are focused on:

- Medical Image Analysis
- Biological Image Analysis
- Computational Anatomy
- Computational Physiology
- Clinical and Biological Validation

5.2. Medical Image Analysis

5.2.1. Segmentation and motion estimation of lower limb structures

Keywords: *biomechanic*, *lower limb*, *motion estimation*, *registration*, *segmentation*.

Participants: Francois Chung, Olivier Clatz, Hervé Delingette.

This works takes place in the work package WT2 of the European Marie Curie project "3D Anatomical Human", whose aim consists in providing a sample stack of musculoskeletal models and motion data from two individuals. The MRI images we used for this task were received from University College London, partner in this project.

As a preprocessing step, in order to perform some low level image processing to improve the signal to noise ratio without loosing structural information, we used bias correction and anisotropic filtering. From dynamic MR images of the lower limb, the motion of each structure can be extracted for further analysis and serve as ground truth for biomechanic simulation. A first approach has been to extract bone motion based on the manual registration of bone structures. Ongoing work is to use automated registration software to estimate this motion.

5.2.2. Segmentation of anatomical structures of the lower abdomen for radiotherapy planning

Keywords: *bladder*, *deformable models*, *lower abdomen*, *prostate*, *radiotherapy planning*, *rectum*, *segmentation*, *simplex meshes*.

Participants: María Jimena Costa, Nicholas Ayache, Hervé Delingette, Grégoire Malandain.

This work is performed in the framework of the european project MAESTRO (Methods and Advanced Equipment for Simulation and Treatment in Radio Oncology), in collaboration with DOSIsoft SA, Cachan.

The main objective of this work is to provide radio-oncology specialists with automatic tools for delineating organs at risk of a patient undergoing a radiotherapy treatment of prostate tumors. In order to achieve this goal, we work with CT scan images. The images are first put in a common frame of reference by means of locally–affine registration based on the pelvic bone structures. A progressive approach consisting of three stages is then applied: the bladder is first delineated, the prostate is later included, and the rectum segmentation is finally integrated.

Given the highly heterogenous nature of the images in our database, our contribution for the segmentation process is centered on *flexibility*.

The bladder is a highly variable structure, both in terms of shape (fillings, compression by surrounding organs) and of intensity levels, the latter due to inhomogeneities caused by the presence or absence (to various levels) of a contrast agent. We propose a segmentation approach that is able to automatically adapt both to the shape and, most remarkably, to the intensity variability.

The prostate shows no distinct "edge" in the image itself; its interface with the bladder is often very difficult (if not impossible) to discern, even for the trained eye of medical experts. We have incorporated anatomical information and taken the intensity similarities into account in our approach to contour this structure. An original non–overlapping constraint optimizes the result in terms of image and shape prior information, in order to avoid ambiguities in the delineation of the common boundaries. If needed, the final automatic result may be manually improved by an expert.

A set of CT images that have been segmented by medical experts were used to validate the method. These hand–made contours act as "ground truth", allowing for an objective evaluation of the performance of the algorithm.

We are now working on the incorporation of the rectum into the segmentation. Different acquisition protocols for the CT scans result in images containing rectums with very different characteristics in terms of shape and intensity (due to filling level and nature, air insufflation, contrast agent, etc.). A flexible method that makes no assumptions about the interior of the structure has been developped and is being tested.

5.2.3. Construction and Use of a Head and Neck Atlas for Radiotherapy

Keywords: *Non-rigid registration*, *atlas*, *head and neck*, *quantitative evaluation*.

Participants: Olivier Commowick, Grégoire Malandain.

In collaboration with DOSIsoft SA, Cachan and Université Catholique de Louvain

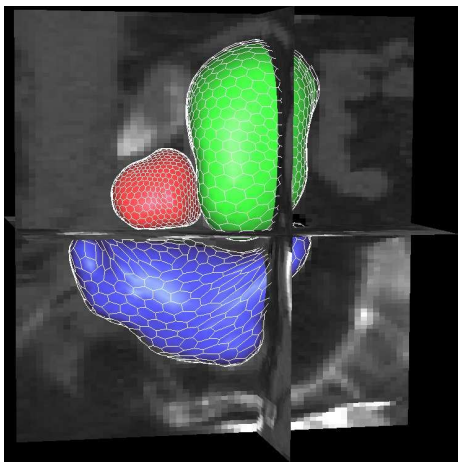
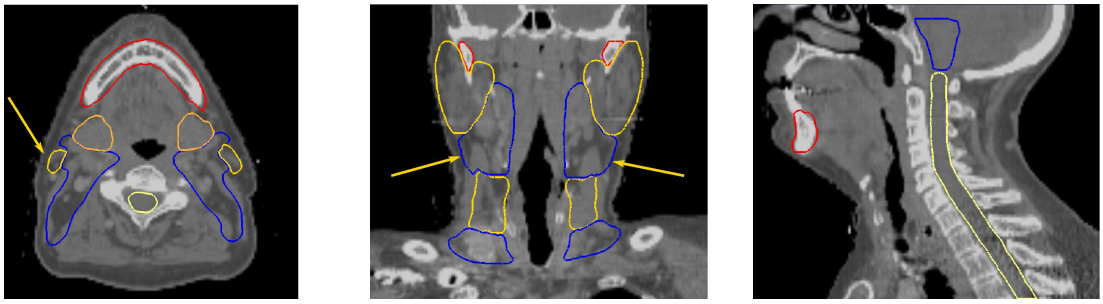


Figure 4. ***Lower abdomen structures segmentation.*** *The prostate (red), the bladder (green) and the rectum (blue) in a CT image.*

Atlas-based segmentation has been shown to be very efficient to delineate brain critical structures. A major localization of cancers is the head and neck region (7 % of all cancers). It is therefore of great interest to have an anatomical atlas of this region to help the clinicians with the delineation of structures of interest in this region.

We have therefore presented in [28] a method to create a symmetric anatomical atlas of the head and neck region from a database of manually delineated patients. We present in Fig. 5 results of the atlas based segmentation, showing qualitatively good segmentation results. The atlas was also quantitatively evaluated using a Leave-One-Out method on a database of 45 patient images provided by Pr. V. Grégoire from the Université Catholique de Louvain.



(a) (b) (c)

Figure 5. ***Illustration of head and neck atlas-based segmentation.*** *Axial, coronal and sagittal views of a patient with the automatic delineations superimposed.*

The atlas-based segmentation of the brain and the head and neck has been implemented as a module in the radiotherapy planning software from Dosisoft S.A. This module is currently used by clinicians for qualitative and quantitative evaluation in the frame of the MAESTRO European project.

5.2.4. Efficient Selection of the Most Similar Image in a Database for Critical Structures Segmentation

Keywords: *Non-rigid registration*, *atlas*, *head and neck*, *quantitative evaluation*.

Participants: Olivier Commowick, Grégoire Malandain.

Head and neck atlas-based segmentation for the automatic delineation of critical structures demonstrated very promising results in [28]. However, the construction of the atlas is very difficult due to the high variability of the anatomies of the patients. This can therefore generate over-segmented structures in the atlas, leading to an over-segmentation of the patient structures.

To overcome this drawback, we have presented in [62] an efficient method to find, in a database, the most similar image to the patient to be delineated. This method is based on the use of the average atlas as an intermediate reference. The transformations from each image of the database to the mean atlas, obtained from the atlas construction, are compared with the one obtained when registering the patient on the atlas. The most similar image is then chosen as the one that minimizes the distance between its transformation and the one of the patient.

We present in Fig. 6 qualitative results obtained by the most similar image based segmentation. The structures obtained by the most similar image based segmentation are visually better and are not oversegmented anymore (see arrows on images (b) and (c)). This was confirmed by a quantitative leave one out study performed on a database of 45 patients, showing a large increase in the specificity of the results.

5.2.5. Efficient Image Registration, Diffeomorphisms and the Demons Algorithm

Keywords: *ESM*, *Image registration*, *demons algorithm*, *diffeomorphisms*.

Participants: Tom Vercauteren, Xavier Pennec, Aymeric Perchant, Nicholas Ayache.

This work is done in collaboration with Mauna Kea Technologies, Paris, France, http://www.maunakeatech.com.

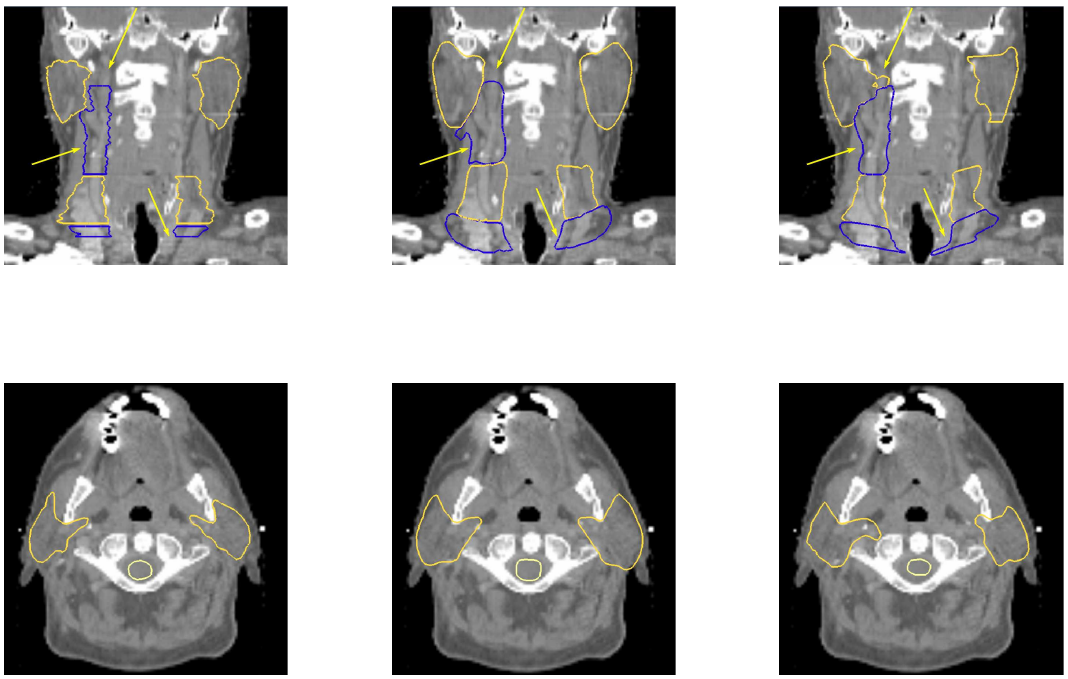
As image registration becomes more and more central to many biomedical imaging applications, the efficiency of the algorithms becomes a key issue. In [90], we showed that some tools that have recently been developed in the field of vision-based robot control can outperform classical image registration solutions used in biomedical image analysis.

The adequacy of these tools for linear image registration led us to revisit non-rigid registration. The insight we gained allows us to provide interesting theoretical roots to the different variants of Thirion's demons algorithm. And more importantly, by casting the non-rigid registration problem into an optimization problem on a Lie Group, we developed in [91] a fast non-parametric diffeomorphic image registration scheme. Our algorithm proved to outperform many existing registration approaches even in 3D. An open-source implementation of our scheme was proposed in [53].

5.2.6. Diffeomorphic Registration of Diffusion Tensor Images with Exact Finite-Strain Differential

Keywords: *Demons*, *Diffusion Tensor Images*, *Log-Euclidean*, *Registration*.

Participants: B.T. Thomas Yeo, Tom Vercauteren, Pierre Fillard, Xavier Pennec, Polina Golland, Nicholas Ayache, Olivier Clatz.



(a) (b) (c)

Figure 6. ***Qualitative atlas and most similar image based segmentation results.*** *(a) Manual segmentation of the patient. (b) Atlas-based segmentation of the patient. (c) Segmentation using the most similar image in the database. Upper line: Coronal slices. Bottom line: Axial slices.*

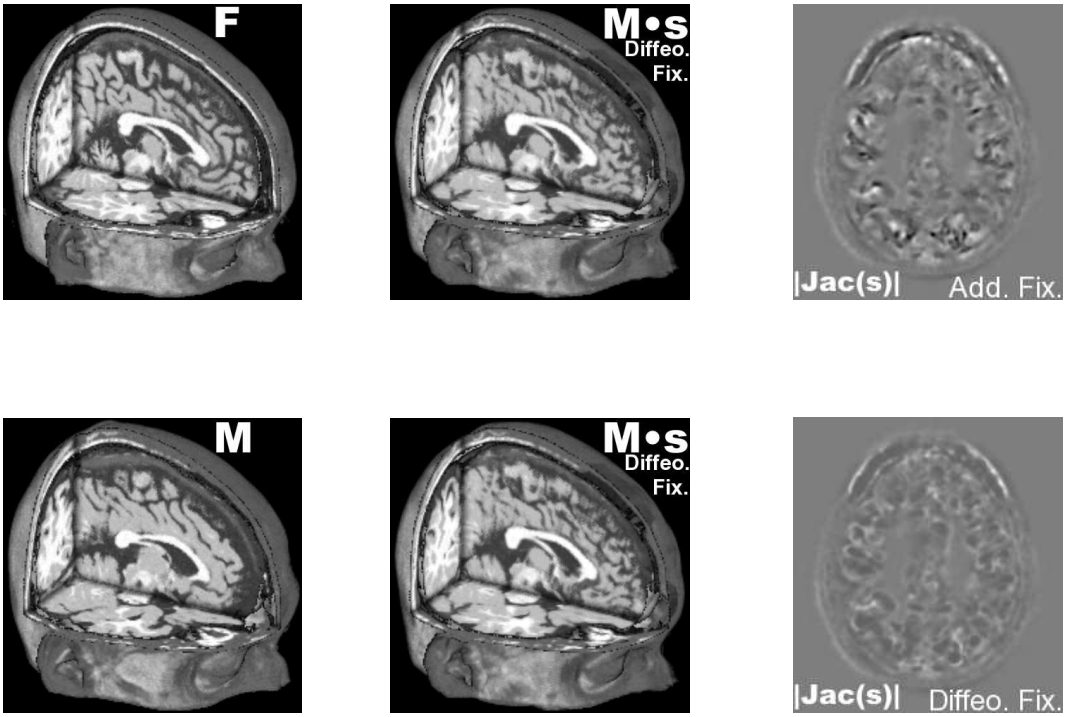
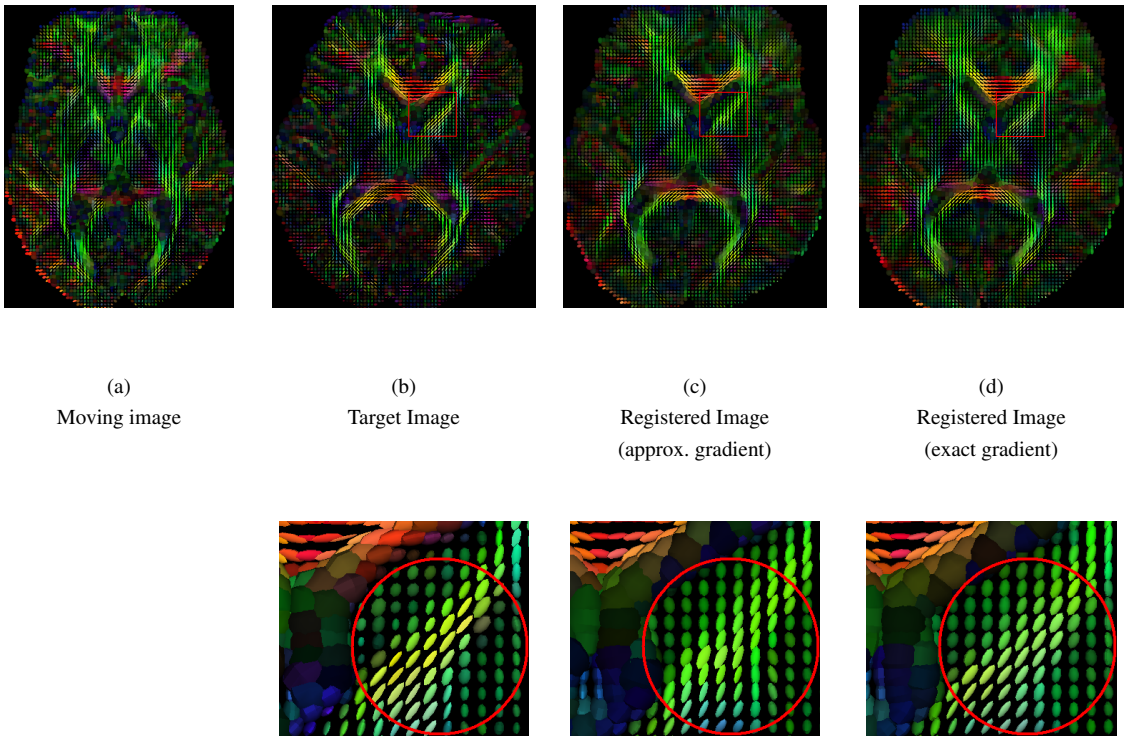


Figure 7. ***Registration of two synthetic T1 MR images of distinct anatomies from BrainWeb.*** *For visually similar results, our diffeomorphic demons algorithm provides smoother and diffeomorphic transformations when compared to the additive demons algorithm.*

In this work, we propose an algorithm for the diffeomorphic non-linear registration of diffusion tensor images. Previous diffusion tensor registration algorithms using full tensor information suffer from difficulties in computing the differential of the Finite Strain (FS) tensor reorientation strategy and therefore the gradient of the objective function. In contrast, we borrow results from the pose estimation literature in computer vision to derive an analytical gradient of the registration objective function. By leveraging on the closed-form gradient and the velocity field representation of the one parameter subgroup of diffeomorphism, the resulting registration algorithm is diffeomorphic and fast. Implemented under the Insight Toolkit (ITK) framework, registration of a pair of 128x128x60 diffusion tensor volumes takes 15 minutes. We compare the algorithm with a classic alternative that does not take into account the reorientation in the gradient computation. We show on 40 pairwise DTI registration that using the exact gradient achieves significantly better registration at the cost of being a few times slower.



(a) Moving image | (b) Target Image | (c) Registered Image (approx. gradient) | (d) Registered Image (exact gradient)

Figure 8. ***Qualitative comparison between the use of exact FS gradient and approximated gradient for registering a pair of subjects (same parameters).*** *Log-Euclidean interpolation and LOG-MSE are used in the objective function. (a) Moving Image (b) Fixed Image (c) Registration result from using approximated FS gradient. (d) Registration result from using exact gradient. Exact gradient achieves better alignment of fiber tracts without disturbing the displacement field.*

5.2.7. Atrophy measurement on magnetic resonance images

Keywords: *Atrophy*, *Multiple Sclerosis*, *Skull-Stripping*.

Participants: Jean-Christophe Souplet, Christine Lebrun [Neurology, Pasteur Hospital, Nice], Nicholas Ayache, Grégoire Malandain.

This work is done in collaboration with the Neurology Department, Pasteur Hospital, Nice.

This work finds a direct application in the Qualicore project (evaluation of cognitive troubles and quality of life of multiple sclerosis patients) and is performed in close collaboration with Christine Lebrun (Neurology Department), at Pasteur Hospital, Nice.

In Multiple Sclerosis (MS) research, lesion load and brain atrophy measurements are currently used. Studies have shown that brain atrophy seems to be better correlated with patients handicap. However, the different actual atrophy measurement method results can be conflicting and there is no reproducible method dedicated to MS magnetic resonance images whereas the lesion presences can impair the measurement.

For each patient, three Magnetic Resonance (MR) sequences (T1, T2 FSE, PD) are available at least at two time points. First, the different sequences are co-registered, intra-image and inter-image intensity inhomogeneities are corrected. A new skull-stripping algorithm presented in [85] is applied. Second, an Expectation-Maximization framework is used to classify brain MRI voxels at each time point. Taking into consideration artifacts presence, the classification is realized into ten classes: White Matter (WM), Gray Matter (GM), Cerebro-Spinal Fluid (CSF) six GM/CSF partial volume (PV) classes and an outlier class. Taking into consideration the proportion of WM, GM or CSF into the different classes, the WM, GM and CSF volumes are computed at each time points. The brain parenchymal fraction (BPF) is computed from these volumes at each time point. Evolution of the BPF between the different time points reflects the brain atrophy.

This method has been first validated on simulated data. The classification algorithm yields correct segmentation on MS BrainWeb images (Similarity Index (SI) > 0.80 for the WM, GM, and CSF segmentation). On other simulated data, the atrophy measurements were strongly correlated to simulated atrophy ($R^2 > 0.99; p < 0.05$). Results on a multi-sites database of brain MRI of 50 MS patients with different exam time points agree with the literature.

5.2.8. *Clinical DT-MRI Estimation, Smoothing and Fiber Tracking with Log-Euclidean Metrics*

Keywords: *DT-MRI*, *DTI*, *Log-Euclidean*, *Rician*, *fiber tracking*, *tensor*, *tractography*.

Participants: Pierre Fillard, Xavier Pennec, Nicholas Ayache.

We proposed a new tensor estimation procedure that is well adapted to acquisitions typical of a clinical environment. The special constraints of the clinical world (short scanning time, rather old scanners), combined with the special requirements of Diffusion Tensor Magnetic Resonance Imaging (DT-MRI) (i.e. acquisition of several images), result in rather low signal-to-noise (SNR) images. In that case, the hypothesis of a Gaussian noise corrupting the measure is not valid anymore, and we need to switch to a Rician noise model. Log-Euclidean metrics allowed us to formalize this problem with an objective function, and to efficiently optimize it. We combined the tensor estimator with a Rician prior to an anisotropic regularization term, which enforces the spatial regularity of the field. Finally, we demonstrate the benefits of using a correct noise model with low SNR images typical of a clinical acquisition (brain and spinal cord DTI). In particular, we show that using a wrong noise model with low SNRs images induces a "shrinking effect": tensors tend to be smaller than they actually are. Using our estimation procedure allows to correctly recover the volume loss, and we showed that even DT-MRI of a poor quality could be used to perform reliable tractography (Fig. 9 and 10).

This work was published in the IEEE-TMI special issue on diffusion tensor MRI [41], and was used to illustrate the concepts of DT-MRI in the book "Voir l'Invisible" [47].

5.3. Biological Image Analysis

5.3.1. *3D segmentation and reconstruction of cellular structures from rice's root meristem multiphoton images*

Keywords: *3D segmentation*, *cells*, *meristem*, *plants modelling*.

Participants: Romain Fernandez, Grégoire Malandain, Christophe Godin [Virtual Plants], Jean-Luc Verdeil [CIRAD].

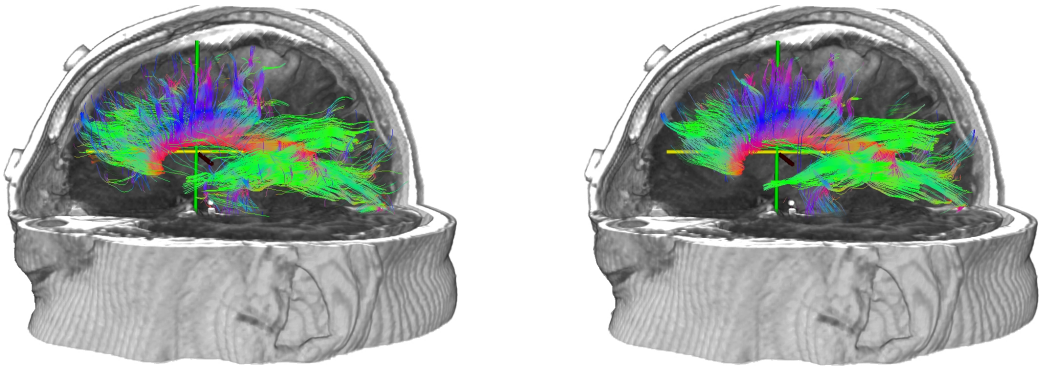


Figure 9. ***Improvement of fiber reconstruction.*** *A seed region was placed inside the corpus callosum. Results of the fiber reconstruction after a classical estimation (**Left**), and after the Rician estimation (**Right**). Fibers are overlapped with a volume rendering of the T1 image.*

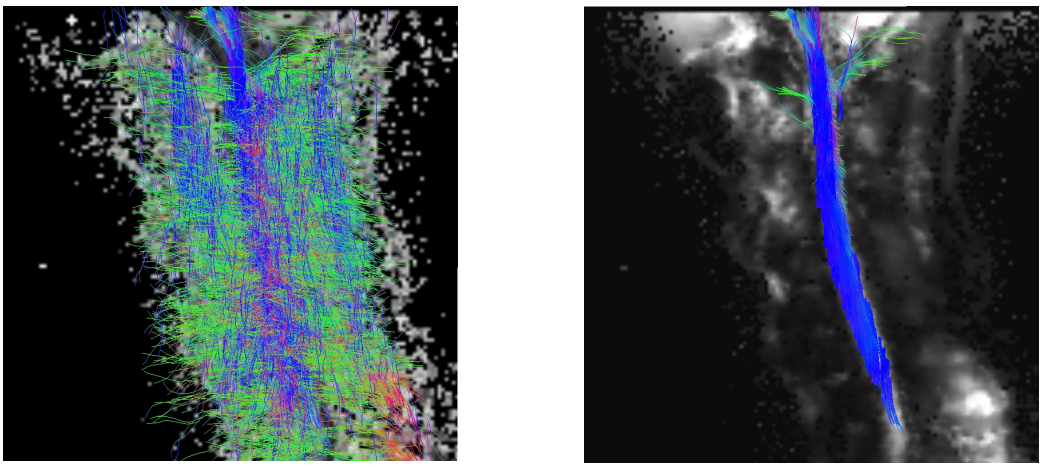


Figure 10. ***Spinal cord fiber tract reconstruction.*** *A region containing the spinal cord was used for the tracking.* ***Left:*** *The spinal cord reconstructed after the Classic estimation.* ***Right:*** *The same tract after our proposed variational framework. Fibers are overlapped with a slice of the FA map.*

In order to extend the insight of the biologists and to improve plant growth models, there is a growing need to design algorithms to process new 3D images of vegetal cells from microscopy. Current geometric models only describe the surface of the meristem [109] and protocols to analyse cellular dynamics in the surface layer during plant development. Here, we try to construct automatically a 3D model of meristem cells from images of Arabidopsis (shoot and root) and rice (root only) meristems. These meristems are collected in-vivo with a confocal microscope at ENS-Lyon or with a multiphoton laser scanning microscope at PHIV (*Plateau d'Histologie et d'Imagerie cellulaire Végétale*, CIRAD, Montpellier), which is the first multiphoton used on vegetal tissues in France, and that allows 3D imaging with deep penetration in the tissue.

Our goal is to achieve automatic segmentation of shoot/root meristem cells during plant growth and to build geometric and topologic models of the meristem structure.

This year, we worked on the customization of acquisition parameters and we designed a method for 3D images processing based on watersheds. Then, we constructed algorithms to build automatically 3D models (abstract simplicial complex or simplex mesh), which will permit simulation of the activity of stem-cells and a better understanding of plants' behaviour.

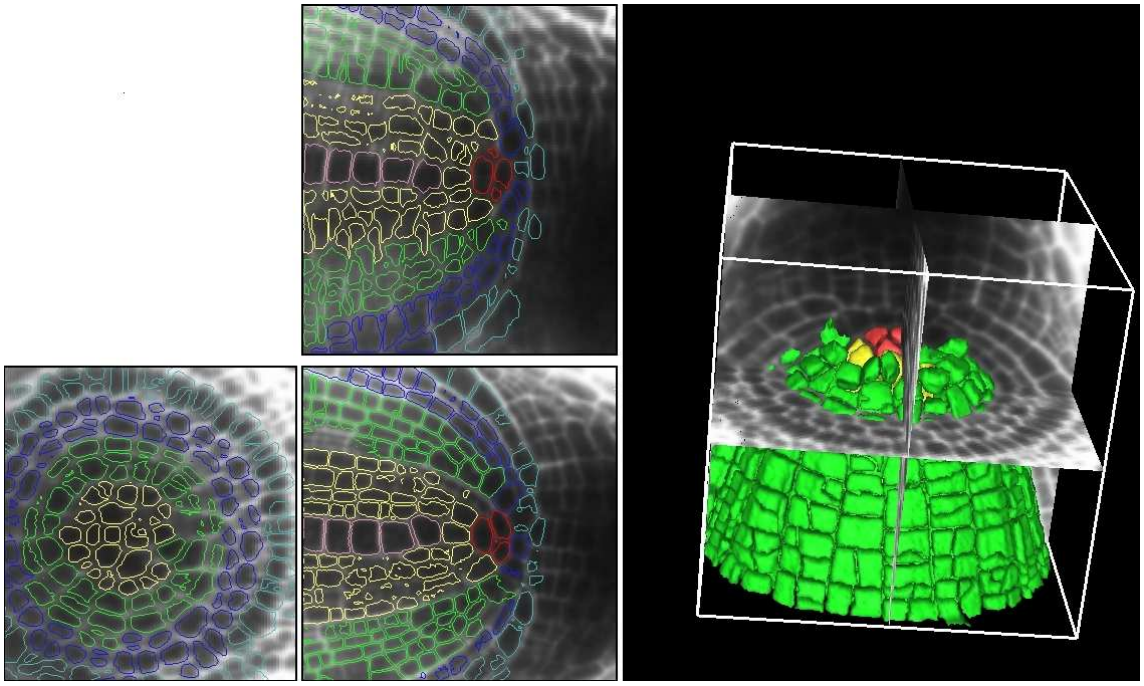


Figure 11. ***Meristem cells segmentation .*** *On the left, the 3 orthogonal views of the 3D optical stack from multiphoton microscope, with the superimposed segmentation of meristem's layers of cells. On the right, the volume rendering of the segmentation.*

5.3.2. Image Registration and Mosaicing for Dynamic In Vivo Microscopy

Keywords: *Cellvizio*, *Mosaicing*, *fibered confocal microscopy*, *image registration*, *tracking*.

Participants: Tom Vercauteren, Aymeric Perchant, Nicholas Ayache.

This work is done in collaboration with Mauna Kea Technologies, Paris, France, http://www.maunakeatech.com

Fibered confocal microscopy (FCM), and especially Cellvizio® by Mauna Kea Technologies, is a potential tool for *in vivo* and *in situ* optical biopsy. We have previously proposed an algorithm using image sequence mosaicing techniques to widen the field of view (FOV) and enhance the possibilities offered by FCM. In 2006, we validated our algorithm from a technical point of view. We have now pushed the evaluation of our mosaicing tool into the clinic [34], [89], [54].

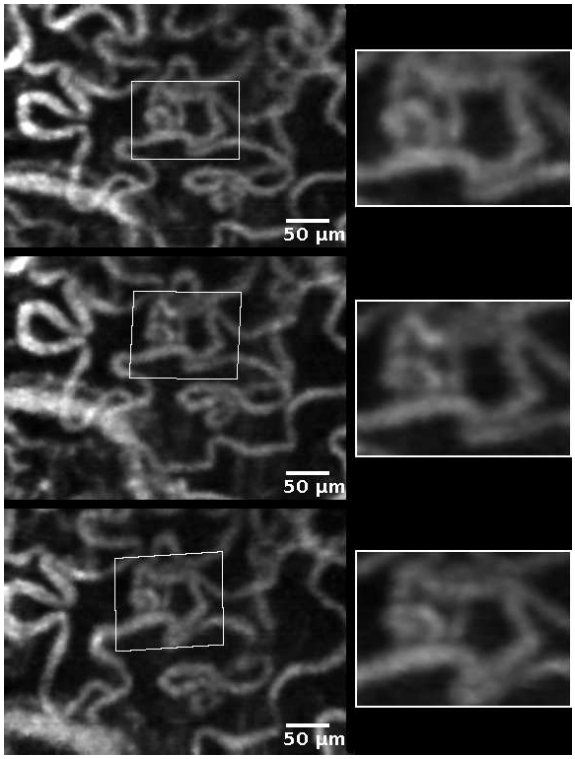


Figure 12. ***Tracking a selected ROI on tumor vasculature acquired in vivo.*** *The upper frame is the reference frame, the other rows represent the frames 11 and 15 at from a 200 frame sequence. The tracked ROIs are shown on the left column with the corresponding warped region on the right column.*

In vivo and *in situ* confocal images are often distorted by motion artifacts and soft tissue deformations. To measure small amplitude phenomena on this type of images, we have to compensate for those artifacts. One way of doing it is by using image registration schemes. In [80], we presented a region of interest tracking algorithm, which is specialized for confocal imaging using a scanning device. One typical application of this tool was developed: the blood velocity estimation inside a capillary on a moving organ. To the best of our knowledge there had been no previous attempt to perform blood flow velocity measurement on a sequence acquired *in vivo* with global tissue motion.

5.4. Computational Anatomy

5.4.1. Spinal Shape Analysis Using Articulated Models

Keywords: *Anatomical Variability*, *Articulated models*, *Orthopedic Treatments*.

Participants: Jonathan Boisvert, Nicholas Ayache, Farida Cheriet, Xavier Pennec.

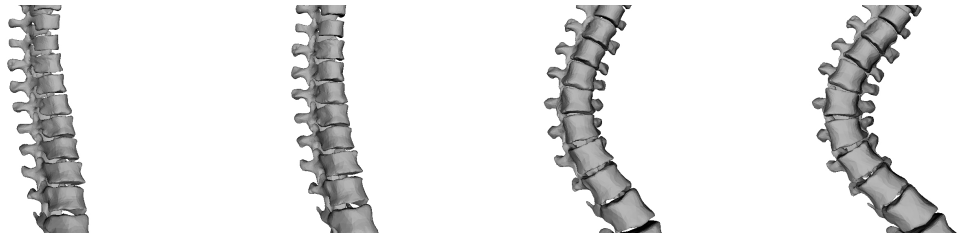
This project is part of a partnership between the Asclepios team, the Montreal's Sainte-Justine hospital and the Polytechnic School of Montreal.

Articulated models are commonly used for recognition tasks in robotics and in gait analysis, but can also be extremely useful to develop analytical methods targeting spinal deformities studies. The three-dimensional analysis of these deformities is critical since they are complex and cannot be reduced to a two-dimensional phenomenon. However, analyzing large databases of 3D spine models is a difficult and time-consuming task.

In this context, we introduced a method to analyze the variability of the spine shape and of its deformations using articulated shape models [36]. The spine shape was expressed as a vector of relative poses between local coordinate systems of neighbouring vertebrae. Spine shape deformations were then modeled by a vector of rigid transformations that transforms one spine shape into another. Because rigid transforms do not naturally belong to a vector space, the Fréchet mean and a generalized covariance were used instead of the conventional ones. The spine shapes of a group of 295 scoliotic patients were quantitatively analyzed as well as the spine shape deformations associated with the Cotrel-Dubousset corrective surgery (33 patients), the Boston brace (39 patients) and the scoliosis progression without treatment (26 patients). Brace and surgery were found to have a significant effect on the Fréchet mean and on the generalized covariance in specific spine regions where treatments modified the spine shape (see Asclepios 2006 activity report).

Then, we proposed a method that automatically extracts the most important deformation modes from sets of articulated spine models [35]. The spine was described with two levels of details. In the first level, the global shape of the spine was expressed using a set of rigid transformations that superpose local coordinates systems of neighboring vertebrae. In the second level, anatomical landmarks measured with respect to a vertebra's local coordinate system were used to quantify vertebra shape. Once again, the Fréchet mean and a generalized covariance were used to construct a statistical shape model of the scoliotic spine. The principal deformation modes were then extracted by performing a principal component analysis (PCA) on the generalized covariance matrix.

The principal deformations modes were computed for a large database of untreated scoliotic patients. The obtained results indicate that combining rotation, translation and local vertebra shape into a unified framework leads to an effective and meaningful analysis method for articulated anatomical structures. The computed deformation modes also revealed clinically relevant information. Other experiments were performed on patients classified by orthopedists with respect to a widely used two-dimensional surgical planning system (the Lenke classification) and patterns relevant to the definition of a new three-dimensional classification were identified. Finally, relationships between local vertebrae shapes and global spine shape (such as vertebra wedging, see Figure 13) were demonstrated using a sample of 3D spine reconstructions with 14 anatomical landmarks per vertebra.



(a) (b) (c) (d)

Figure 13. ***Asymmetrical deformation of a vertebral body located near the apex of a spinal curve*** *(a phenomena also called vertebra wedging) observed in the third principal deformation modes of a group of scoliotic patients which had 14 anatomical landmarks reconstructed on each of their vertebrae. Model reconstructions for* -3σ *(a),* $-\sigma$ *(b),* σ *(c) and* 3σ *(d)*

5.4.2. A Computational Framework for the Statistical Analysis of Cardiac Diffusion Tensors

Keywords: *Atlas*, *DT-MRI*, *DTI*, *cardiac*, *diffusion tensor magnetic resonance imaging*, *fiber architecture*, *heart*, *laminar sheets*, *statistics*.

Participants: Jean-Marc Peyrat, Maxime Sermesant, Xavier Pennec, Hervé Delingette, Chenyang Xu [Siemens SCR, USA], Elliot McVeigh [Lab of Cardiac Energetics, NHLBI, USA], Nicholas Ayache.

This work was funded in part by Siemens Corporate Research (NJ, USA).

Cardiac fiber architecture, a complex arrangement of myofibers bounded to each other to form laminar sheets, plays an essential role in defining the electrical and mechanical behavior of the heart. The study of the cardiac fiber architecture and its variability is important to better understand physiological principles and to construct computational models of the heart. As an extension of a preliminary work [132], a unified computational framework is proposed to build a statistical atlas of the cardiac fiber architecture from diffusion tensor magnetic resonance images (DT-MRIs).

An interactive groupwise registration of the anatomical MRIs is performed to align the different geometries to an average geometry (see Fig. 14). Coacquired with the anatomical MRIs, the DT-MRIs need to be properly transformed into the average geometry. Since the diffusion tensors depend on the space in which they are defined, the transformation of the space implies a transformation of the diffusion tensors. Different methods were proposed: the Finite Strain (FS) and the Preservation of Principal Direction (PPD). We showed (see Fig. 14) that the FS had the property to preserve geometric features of diffusion tensor fields whereas the PPD was modifying them following a mechanical deformation of the underlying microstructure [49]. In the context of intersubject registration, we preferred the FS that preserves geometric features (for instance, the transmural variation of the fiber orientation) to be able to compare them without artificially modifying them. Once DT-MRIs are transformed into the average geometry, we proceed to a statistical analysis of a population of diffusion tensors at each voxel. Then, an average cardiac fiber architecture and a measure of its variability are computed using novel diffusion tensor statistical tools. These tools allow to extract the variability of the eigenvalues and eigenvectors orientation (see Fig. 14) from a covariance matrix of diffusion tensors [49].

This framework was applied to a small database of nine ex vivo canine hearts (see Fig. 14). The resulting statistical analysis confirmed the already established good stability of the fiber orientations and a higher variability of the laminar sheet orientations within a given species. The statistical comparison between the canine atlas and a standard human cardiac DT-MRI showed a better stability of the fiber orientations than their laminar sheet orientations between the two species [81]. The proposed computational framework can be applied to larger databases of cardiac DT-MRIs from various species to better establish intra- and inter-species statistics on the anatomical structure of cardiac fibers.

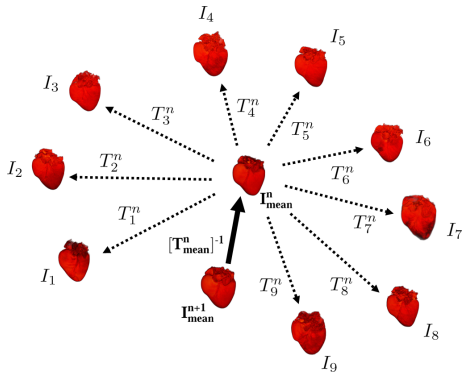
5.4.3. Point-Based Statistical Shape Models Using Correspondence Probabilities

Keywords: *EM-ICP*, *correspondence probabilities*, *statistical shape models*.

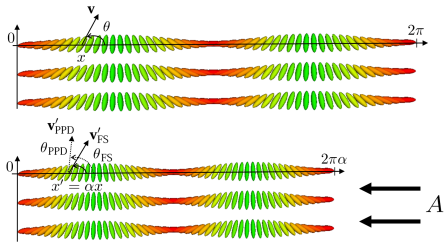
Participants: Heike Hufnagel, Xavier Pennec.

This work takes place in a cooperation with the medical imaging group of the university Hamburg-Eppendorf.

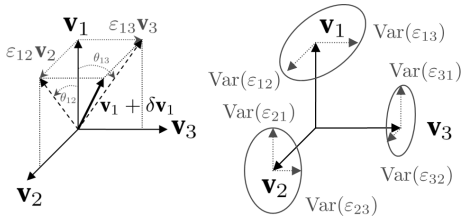
A fundamental problem when computing statistical shape models is the determination of correspondences between the observations of the associated data set. Often, homologies between points that represent the surfaces are assumed which might lead to imprecise mean shape and variability results. Based on [119] we propose an approach where exact correspondences are replaced by evolving correspondence probabilities [72]. This is done by aligning the observations using the Expectation Maximization - Iterative Closest Point (EM-ICP) algorithm which is based on probabilistic correspondences and proved to be robust and fast. These probabilistic correspondences are the basis for a novel algorithm that computes a generative statistical shape model (gSSM). Here, we strictly distinguish between *model parameters* ('mean shape' and 'modes of variation') and *observation or nuisance parameters* ('transformation' and 'deformation coefficients' associated to each observation). To find the optimal model parameters of the gSSM from a set of observations (learning phase) we used a Maximum A Posteriori (MAP) framework which leads to a unique criterion. The



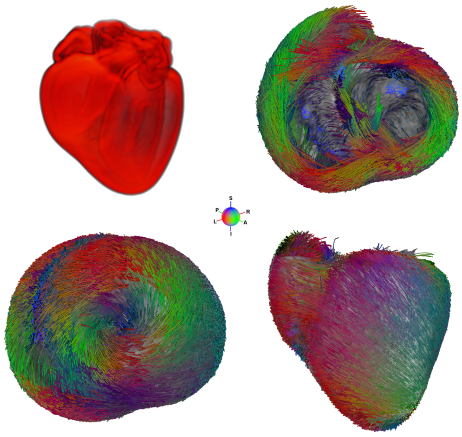
(a) Groupwise registration of the anatomical MRIs.



(b) Comparison of the Finite Strain (FS) and the Preservation of Principal Direction (PPD) when applying a non-uniform scaling.



(c) Eigenvectors variability described by an ellispoidal cone of uncertainty.



(d) Average geometry and fiber tracking on the DT-MRI atlas.

Figure 14. ***Computational Framework for the Statistical Analysis of Cardiac Diffusion Tensors.***

alternated optimization of the MAP explanation with respect to the observation and the generative model parameters leads to very efficient and closed-form solutions for (almost) all parameters [73]. Our gSSM clearly distinguishes the shape variability (encoded in the modes of variation) from the observation noise, contrary to the classical Principal Component Analysis (PCA) which looks for variations in the residual noise after observation alignment.

Experimental results on brain structure data sets demonstrate the efficiency and well-posedness of the approach. A comparison with a statistical shape model which is built using an Iterative Closest Points registration algorithm and a PCA shows the superior performance measures of our method, especially for shapes with different structure details [71].

5.4.4. Efficient Approximations of Sets of Curves and Surfaces seen using Currents

Keywords: *Currents*, *curves*, *greedy approximation*, *matching pursuit*, *surfaces*.

Participants: Stanley Durrleman, Xavier Pennec, Alain Trouvé, Nicholas Ayache, Guido Gerig.

In the field of computational anatomy, an analysis of brain variability often denotes a set of successive processing: atlas formation, atlas-to-subject registrations, measure of the variance of deformations. As shown in Section 5.4.7, such an analysis ends up with a group-wise measure of variability that highly depends on the different assumptions and different parameters used at each step. From a more statistical point of view, we can see an individual observation (like an MRI scan) as a noisy deformation of an unknown template. A statistical inference procedure would therefore estimate at the same time and in a consistent manner: the template (or atlas), the hidden deformations, and the covariance structure of both the deformations and the noise on data. Compared to a pipeline of unconsistent processing, such an integrative framework depends on much fewer priors, leads to less biased results and finally provides a way to automatically set the different parameters via an EM-like procedure for instance.

To achieve this goal, we need to define first a deformation framework and, second, a modeling of the geometrical primitives (here curves and surfaces). The well-posedness and the several mathematical and numerical properties of the diffeomorphic registration scheme (see e.g. Section 5.4.7) makes it particularly well-suited for the first point. To model geometrical primitives, we are using currents. This allows us to consider curves and surfaces as a whole, thus avoiding to reduce them to sets of features. It also provides an efficient way to measure distances between shapes without assuming any point correspondences. We develop matching pursuit algorithms to represent currents more efficiently in terms of combination of simple elements of current. This enables to compute and visualize mean lines or surfaces as well as to perform principal component analysis on dataset of such primitives. This tool was used to compute empirical mean of 66 sulcal lines for 82 subjects (kindly provided by Pr. Paul Thompson, UCLA) as well as mean of 10 subcortical structures for 75 subjects (kindly provided by Pr. Guido Gerig, University of Utah), thus showing the efficiency and the high degree of generality of our approach.

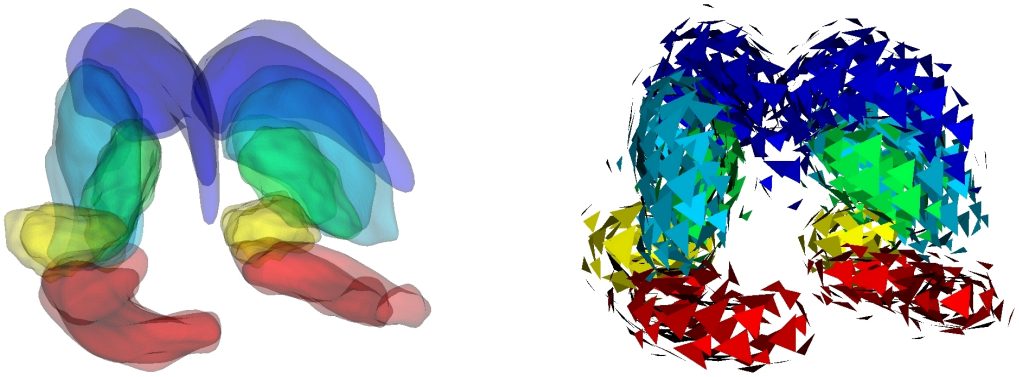
The database of subcortical structures contains two acquisitions of each subject, the first at age 2 and the second at age 4. In the framework of the IP project Health-e-child, we are currently investigating to include the brain maturation information into the geometrical and statistical modelling.

5.4.5. Measuring Anatomical Correlations in the Brain

Keywords: *Log-Euclidean*, *brain*, *computational anatomy*, *correlation*, *tensor*, *variability*.

Participants: Pierre Fillard, Xavier Pennec, Paul M. Thompson, Nicholas Ayache.

Modeling and understanding the degree of correlations between brain structures is a fundamental problem in neuroscience. Correlated anatomic measures may arise from common genetic and trophic influences across brain regions, and may be overlooked if structures are modeled independently. In our previous work, we restricted our analysis to a measure of the individual variability of each cortical positions. In this work, we propose a new method to analyze structural brain correlations based on a large set of cortical sulcal landmarks (72 per brain) delineated in 98 healthy subjects (age: 51.8 +/-6.2 years). First, we evaluate the correlation between any pair of sulcal positions via the total covariance matrix (TCM), a 6×6 symmetric positive-definite



a- Set of 10 meshes for 2 subjects b- Empirical mean of each mesh for 75 subjects

Figure 15. ***Left:*** *set of 10 meshes of subcortical structures for 2 subjects.* ***Right:*** *Representation of the empirical mean of the surfaces seen as currents for 75 subjects. Such a representation consists in a set of small triangles and is computed thanks to a matching pursuit algorithm.*

matrix. As TCMs are tensors, we were able to use the same Log-Euclidean extrapolation of our previous study to obtain a dense information from sparse measures (TCMs are only known along sulci). Second, based on TCMs, we performed canonical correlation analysis (CCA) to statistically evaluate the degree of correlations between any two sulcal positions.

We applied this methodology to six sulcal positions of reference (the starting, middle and ending points of the central and inferior temporal sulci) versus the whole brain, and for each sulcal point position versus its corresponding structures in opposite hemispheres (hemispheric correlations). As expected, results showed a high correlation in a large area around the reference points: points that are anatomically close have a correlated distribution among individuals. More interestingly, correlated regions most often include the structures opposite hemisphere counterparts, but not always: the most inferior position of the central sulcus is not symmetrically correlated, most likely because its variability across subject is very low. Likewise, Broca's and Wernicke's areas, which were already shown to exhibit the greatest asymmetries in variability, do not show correlation with their symmetric counterpart. However, the main striking new result is the observation of long-range asymetric correlation, for instance between the back of the inferior temporal sulcus and the left and right intra-parietal sulci. Although these two distinct areas are widely studied for their hemispheric asymmetry, none or a little was known on their possible correlations.

This work was presented at the MICCAI'07 workshop on statistical pair-wise and group-wise registration [68]. It is also available as an INRIA research report [93]. Finally, our previous work on brain variability modeling has been chosen to take part of a book entitled: "Voir l'Invisible" [48].

5.4.6. Towards Statistical Tensor Atlases of the Brain

Keywords: *DT-MRI*, *DTI*, *Log-Euclidean*, *atlas*, *fiber tracking*, *registration*, *tensor*, *tractography*, *z-score*.

Participants: Pierre Fillard, Denis Ducreux.

In the context of clinical studies, one often needs to compare a single patient's image to a population of controls. On standard scalar images, this comparison is generally done by estimating how far the patient is from an atlas summarizing the reference population using a so called z-score (Mahalanobis distance at each point). Thresholding this distance map points out statistically significant differences (Voxel Based Morphometry). The goal of this work is to extend this methodology to diffusion tensor images (DTI).

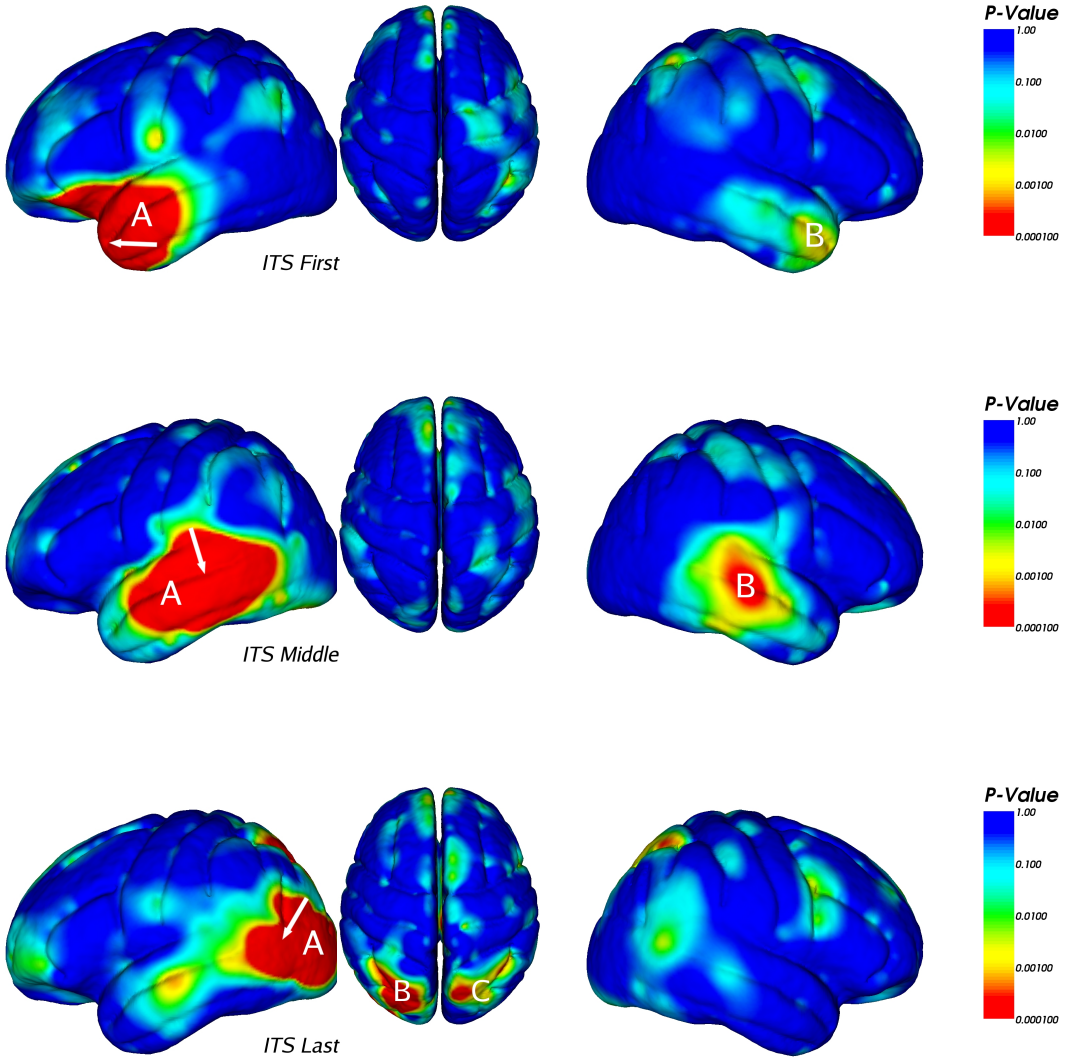


Figure 16. ***Correlation Maps between a Specific Reference Point and Other Brain Regions****. Three positions of the Inferior Temporal Sulcus are analyzed. The first (top row) and middle (second row) positions are symmetrically correlated (marks A and B). The last position (third row) correlates less with its opposite hemisphere counterpart, than with the intra-parietal sulci (marked B and C).*

Thanks to Log-Euclidean (LE) metrics, we are able to efficiently build DTI atlases of a given population. Tensor images are aligned based on the deformation computed between their two b_0 (baseline images) using the diffeomorphic demons algorithm developed by Tom Vercauteren [91]. To obtain an unbiased atlas, the initial reference image is randomly picked within the population, and is iteratively recomputed as the LE average after the alignement of all the images. To warp tensors, we used the finite strain action which rotate the tensor according to the rigid part of the Jacobian of the transformation only. In figure 17, we show a color fractional anisotropy (left) and the fibers extracted from the atlas (right) built from 13 diffusion tensor images (13 iterations were used for the altas construction). The next step will be to compute the covariance matrices such as in [131] and to evaluate the Mahalanobis distance with some pathological images.

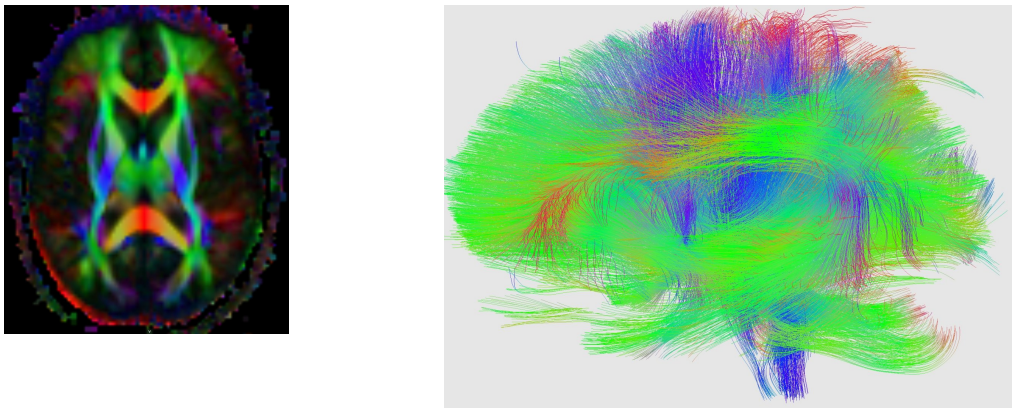


Figure 17. ***DTI Atlas of 13 Normal Controls: Color-FA map (left) and Fiber Atlas (right).*** *Thanks to the non-linear registration algorithm used to build the atlas (13 iterations were used to build the atlas), very small structures are preserved and not smoothed out during the averaging. This is the case, for instance, of the cingulum tract near the splenium.*

5.4.7. Measuring Brain Variability via Diffeomorphic Registrations of Sulcal Lines

Keywords: *diffeomorphic mapping*, *inter-individual variability*, *non linear registration*, *sulcal lines*.

Participants: Stanley Durrleman, Xavier Pennec, Alain Trouvé, Nicholas Ayache, Pierre Fillard, Paul Thompson.

In the framework of the ARC BrainVar, we compared two different methods to measure brain variability from a dataset of sulcal lines. A first method was set up by P. Fillard et al in [115]. Here we measured the variability on the same dataset, but using statistics on large diffeomorphic registrations of lines modeled as currents. This method avoids computing point-to-point correspondences between lines. Moreover, the deformations obtained are defined in the whole space, which avoids the previous extrapolation step to compute the variability at any point in the brain. Thanks to spatial consistence of the statistical model, we could also perform a global PCA analysis which showed the major trend of deformation within the studied population (see Fig. 19). The two methods produce different results (see Fig. 18) although the same original data were used. A deep comparison of both approaches was presented both at the SAMSI workshop *Geometry and Statistics of Shape Spaces* at Chapell Hill (USA) in July 2007 and at the MICCAI Conference in Brisbane (Australia) in October 2007 [66].

5.5. Computational Physiology

5.5.1. Estimation of cardiac function mechanical parameters

Keywords: *data assimilation*, *deformable model*, *electromechanical models*, *heart simulation*.

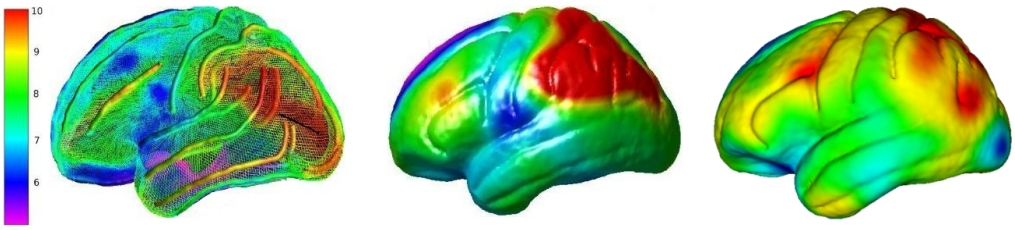


Figure 18. ***Comparison of variability maps obtained by 3 different methods.*** *The scalar value mapped on the mean cortex is the trace of the covariance tensor (the variance). The more red, the more variable within the dataset.* ***Left:*** *variability of the cortex surface in an independent normal sample (15 controls) using a non-linear surface registration algorithm [136].* ***Middle:*** *variability map computed on 34 subjects by extrapolating the covariance matrix along their sulci [115].* ***Right:*** *Variability Map computed from diffeomorphic registrations of the same sulcal lines. Here, the color is the variance of the initial speed vector field of the deformation rather than the variance of the obtained displacement.*

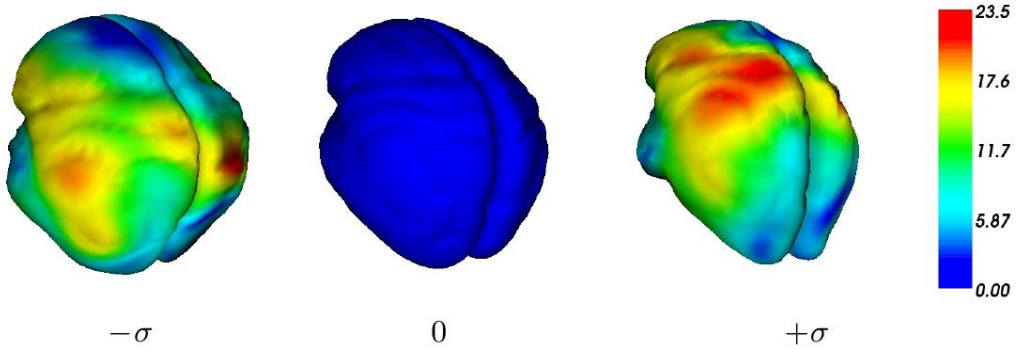


Figure 19. We perform a PCA analysis on the same initial deformation speed as for Fig.18. This figure shows the first mode of deformation applied on a mean surface (middle) at $-\sigma$ (left) and $+\sigma$ (right). This represents the major trend of variation within the studied population. Surfaces are coloured according to the displacement in millimeter. See [66] for details.

Participants: Florence Billet, Maxime Sermesant, Hervé Delingette, Nicholas Ayache.

The aim of this work is to improve diagnosis and therapy planning by estimating local parameters of the cardiac function from images. In order to achieve this, improvements to the current model were first needed.

The electrical wave propagation results in an augmentation of Calcium in the myofibre, which leads to the contraction of the sarcomere. The sliding filament theory of Huxley at the microscopic scale combined to the multi-scale approach of Bestel-Clement-Sorine leads to the modelling of the excitation/contraction coupling at the macroscopic scale. The final constitutive law is based on the Hill-Maxwell scheme, where muscles are represented by a combination of a contractile element and a parallel element, mainly representing the elastic properties of the muscle. The mechanical model used is a simplified one in order to be computationally efficient and with few parameters. We gave a physical signification to some parameters of this simplified law and linked some of these. Then we can better calibrate this model.

This constitutive law is integrated in the dynamic equation which describes the behaviour of the heart. The heart cycle can be divided in four phases: filling, isovolumetric contraction, ejection and isovolumetric relaxation. The dynamics of the heart change with the phase. We introduced the Lagrangian theory in the isovolumetric phases to compute the forces associated to the isovolumetric constraint. This approach allows us to reduce the computation time in a very significant manner. Different outputs of the simulation of heart cycles were presented in figure 20.

The current cycle time simulation (7 min) is very promising for the estimation process.

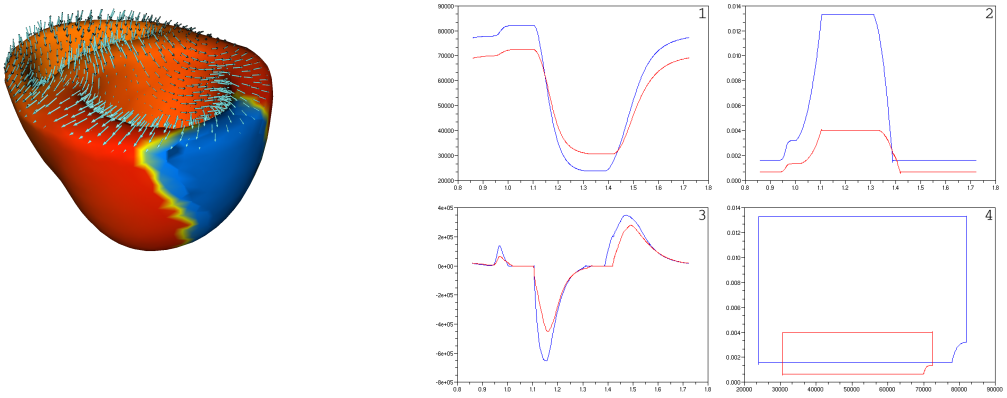


Figure 20. Left: Electromechanical model. Right: Different outputs of the simulation of a heart cycle. In Red: the right ventricles curves. In Blue: the left ventricles curves. (1) volumes (in mm^3). (2) pressures (in MPa). (3) flow curves (in mm^3/s). (4) PV diagram. Time is in seconds.

5.5.2. Parameter estimation for an electrophysiology model of the heart

Keywords: *cardiac resynchronization*, *electrophysiology*, *model adjustment*, *simulation of cardiac pathologies*.

Participants: Damien Lepiller, Maxime Sermesant, Hervé Delingette, Nicholas Ayache.

Last year, we presented a 3D electrophysiology model of the heart ventricles and a simple method to calibrate it from a set of temporal recordings of depolarisation waves. The parameters were adjusted by minimising the differences between depolarisation times and action potential durations from the model and the measures. It showed very promising results on synthetic measures making it possible to test it on real data.

We have improved this method which runs in two steps : an instantaneous calibration of the parameter by fitting a model to the parameter-measure relation, and a simple gradient descent algorithm to refine the solution. We made several tests on the epicardial depolarisation times given by dogs hearts to adjust the apparent conductivity locally. It worked well enough to detect an infarcted area (see Fig.21) though we had to raise the time sampling (and thus the length of computation) to avoid instabilities.

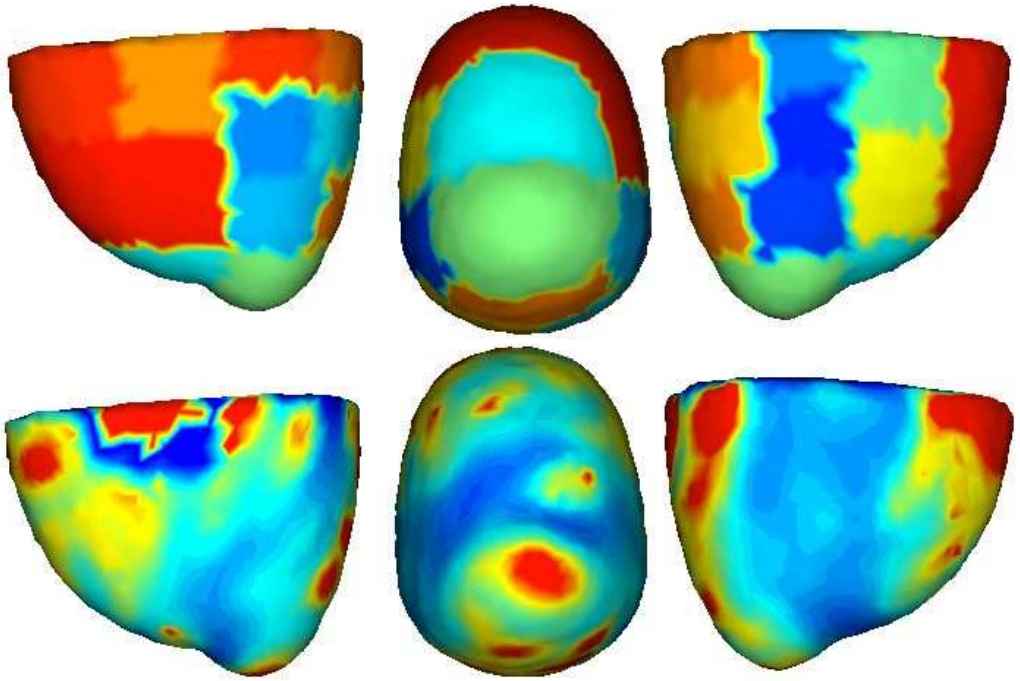


Figure 21. ***Adjustment of conductivity.*** *Above: estimated values of conductivity. Below: depolarisation speed map from measured activation times (red: high value, blue: low value). An infarcted area is located in the low depolarisation speed area.*

Currently, in collaboration with Sunnybrook Health Sciences Center in Toronto, we are trying to run the adjustment methods from visual recordings of electrical waves on pig hearts. A fluorescent dye reacts to the depolarisation and two cameras record the scene, making it possible to reconstruct the heart surface with stereoscopy. We defined the filtering and analysing methods of the videos which now allow the automatic extraction of the depolarisation times. We also made the method to project them to the stereo surface and then to the mesh used for simulation. Adjustment tests are coming next.

5.5.3. Towards a Real-Time Model of Cardiac Electrophysiology

Keywords: *cardiac electrophysiology*, *fast marching method*, *simulation*.

Participants: Maxime Sermesant, Ender Konukoglu, Hervé Delingette, Nicholas Ayache.

A critical point in integrating models within clinical application is to design models whose parameters are observable in clinical data and whose computational time is compatible with clinical constraints.

In order to achieve fast enough simulations of cardiac electrophysiology, and thus be clinically applicable, we worked on a fast model of cardiac electrophysiology, based on the fast marching method. A particular Eikonal equation has been shown to be an approximation of reaction-diffusion electrophysiology models.

But in order to simulate realistically cardiac electrophysiology, in a normal and pathological behaviour, we had to introduce anisotropy and multi-front capabilities into this model. The current implementation is almost real-time, which opens up possibilities for cardiac intervention simulation. Future work includes quantitative comparison with PDE based models.

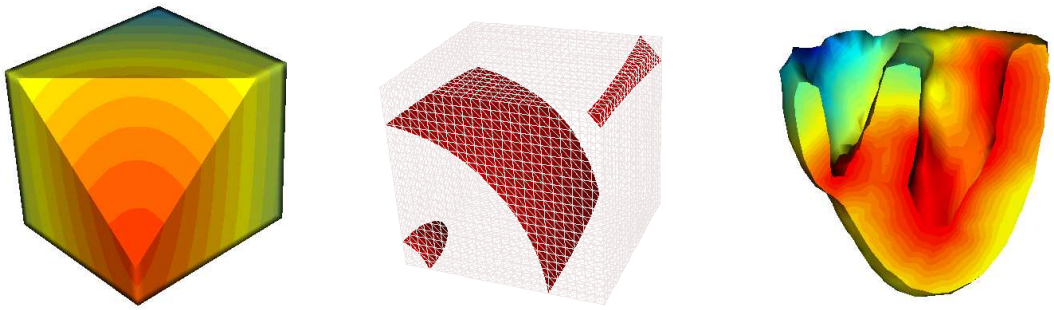


Figure 22. ***Fast Model of Cardiac Electrophysiology.*** *Left: anisotropic fast marching, middle: multi-front propagation, right: resulting isochrones in the myocardium.*

We are also looking into catheter-based intervention simulation in order to train the clinician on patient-specific models. The impact of computational models can be both in diagnosis, where estimation of parameters of cardiac function can improve the decision process, but also in therapy planning, where the clinician can test several interventions on a patient-specific computational model.

5.5.4. Simulation of paediatric cardiac pathologies using an electromechanical model of the heart

Keywords: *electromechanical models*, *health-e-child*, *heart simulation*, *paediatric diseases*.

Participants: Thomas Mansi, Maxime Sermesant, Xavier Pennec, Nicholas Ayache.

Within the framework of the European project Health-e-Child (cf section 6.8), we are adapting the electromechanical model of the heart developed during the last years to simulate three groups of paediatric cardiac pathologies: right-ventricle overload, dilated cardiomyopathies and hypertrophied cardiomyopathies.

As a first stage, we expressed biomedical observations (clinical, cellular, etc.) as macroscopic geometrical and electromechanical parameters to simulate those pathologies.

Simulation parameters were first calibrated by simulating the normal heart in children. A 3D representation of the heart was created by using super-ellipsoidal primitives to get realistic anatomies. Then, electromechanical parameters were set to obtain simulation results consistent with the clinical observations.

Once this calibration process was performed, the three diseases were simulated by modifying the internal parameters according to the medical observations.

To simulate right-ventricle overload due to atrial defects, right-atrial pressure was augmented and the geometry of the right ventricle was slightly stretched to take into account the increased pre-load. Similarly, dilated cardiomyopathies were simulated by dilating the 3D geometry of the normal heart and decreasing the contractility parameters of the biomechanical model (to account for the observed impaired contractility of the myocardium). Finally, hypertrophied cardiomyopathies were simulated by increasing the thickness and the stiffness of the myocardium while decreasing the electrical conductivity.

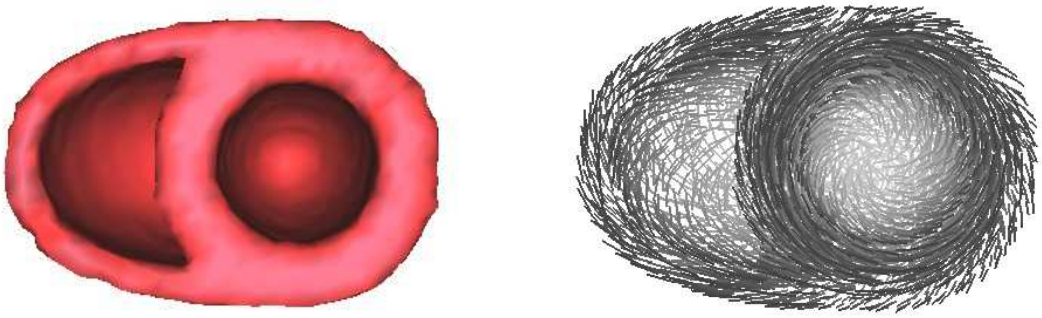


Figure 23. ***3D anatomical model of the heart.*** *Right ventricle is modelled by using a truncated super-ellipsoid. Left: geometry used to simulate the normal heart. Right: simulated cardiac fibres for this geometry.*

The results were discussed and evaluated with the help of the cardiologists involved in the project. This joint work allowed us to improve and validate the simulations, but also to identify new objectives to enrich the models. In this way, current work aims now at adapting these models to each patient by using medical image analysis, and at integrating local and subtle features of each cardiac disease by refining the electromechanical model.

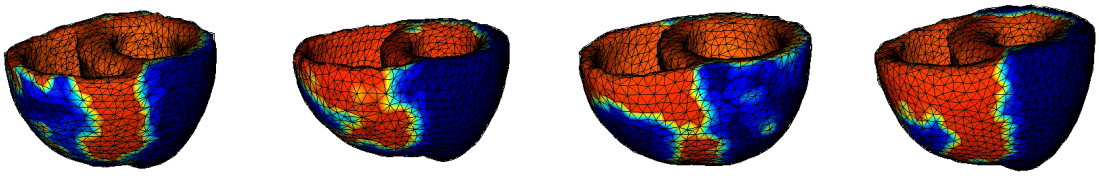


Figure 24. ***Snapshots of heart simulations.*** *From left to right: normal heart, right-ventricle overload, dilated cardiomyopathy, hypertrophied cardiomyopathy.*

The results of the simulations have been published in a deliverable of the Health-e-Child project, presented as a web site[6], containing additional illustrations and animations.

5.5.5. Tumor Growth Modelling

Keywords: *Fisher Kolmogorov*, *Tensors*, *glioblastoma*, *glioma*, *modelling*, *radiotherapy*, *tumor*.

Participants: Ender Konukoglu, Olivier Clatz, Maxime Sermesant, Jean-Marc Peyrat, Pierre-Yves Bondiau, Hervé Delingette, Nicholas Ayache.

Tumor growth modelling mathematically describes the dynamics of the infiltration and expansion of tumors. Over the last decade researchers proposed a variety of different tumor growth models. Different approaches can be coarsely classified into two groups, microscopic and macroscopic models. Microscopic ones try to describe the progression of the tumor in the cellular level in terms of interactions between individual cells and their surrounding. These models are detailed and capture the stochastic nature of tumor growth successfully.

[6] http://www-sop.inria.fr/asclepios/projects/hec/

However, they often include microscopic parameters that are not observable from medical images making it hard to adapt these model to specific patient cases. Macroscopic models on the other hand, describe the average behavior of tumor cells and model the evolution of local tumor cell densities rather than individual cells. Therefore, they cannot capture the stochastic behaviour of tumor growth. On the opposite side, they have fewer equations and parameters which can be derived from medical images making macroscopic models easier to adapt to the patient data.

A macroscopic model which is shown to be capable of being adapted to a specific patient was previously proposed in our group by Olivier Clatz. This model is based on the reaction-diffusion type partial differential equations and uses tissue and structural information of the brain obtained from magnetic resonance (MR) and diffusion-tensor (DT) MR images. By modeling the infiltration of tumor cells through an anisotropic diffusion process and including the DT-MRI, the model is able to capture the differential motility of tumor cells on the white and the grey matter. Through simulations it is also able to demonstrate the effect of this difference on the invasion patterns encountered in gliomas.

Our work this year mainly concentrated on automatically adapting the reaction-diffusion model to specific patient cases through medical images. Our main goal was to find the model parameters and the speed of tumor invasion by fitting the model to the images. For this purpose, we have first proposed to reduce the macroscopic model in order to get rid of the inconsistency between the information required by the model and observed from images. As the reduced model, we have derived an anisotropic Eikonal equation that approximates any front evolution which is described by a reaction-diffusion model. Such a reduced model is much easier to adapt to the clinical information we obtain from medical images than the reaction-diffusion models, see Figure 25.

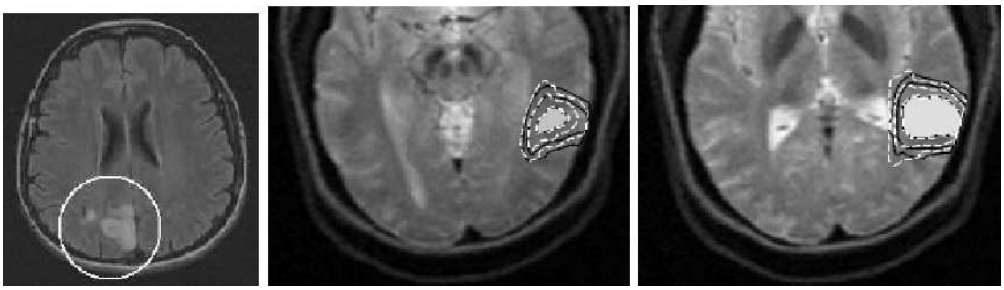


*Figure 25. Left: The figure illustrates the type of images we obtain from patients. We observe that only an enhanced region is available in this case showing the tumor front. Middle and Right: Figures illustrate in black the iso-cell density contours of a tumor grown artificially using the **full** reaction-diffusion model which would be inconsistent with the observations obtained from images like the one on the left. The white dashed curves show the same iso-density contours obtained using the reduced model. We see that the reduced model indeed captures the dynamics of the full one.*

Together with the idea of reducing the model we have proposed an accurate and efficient algorithm to solve anisotropic Eikonal equations [76], see Figure 26.

We have also applied the same idea of model reduction and our fast-solver to the problem of simulating cardiac electrophysiology [84]. Based on our work on model reduction and the fast numerical method, we attacked the problem of model parameter identification from medical images. We have proposed a formulation and a minization scheme which would estimate the average speed of tumor invasion between two images taken from the same patient at different times [75]. We demonstrated the applicability of the model in our preliminary experiments, see Figure 27.

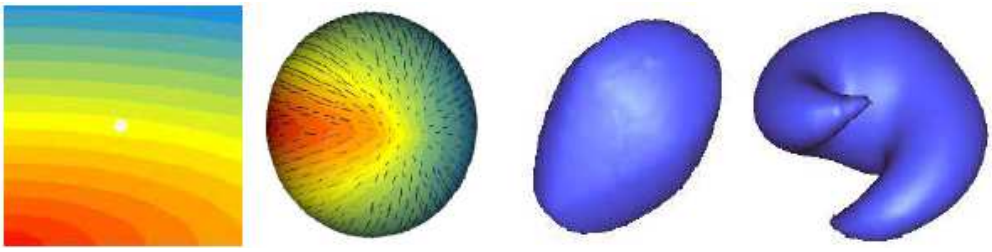


Figure 26. ***Artificial results of anisotropic distances obtained using the recursive fast marching method proposed in [76].*** *As the examples demonstrate the algorithm works equally well on surface meshes, volumetric data and in planar meshes.*

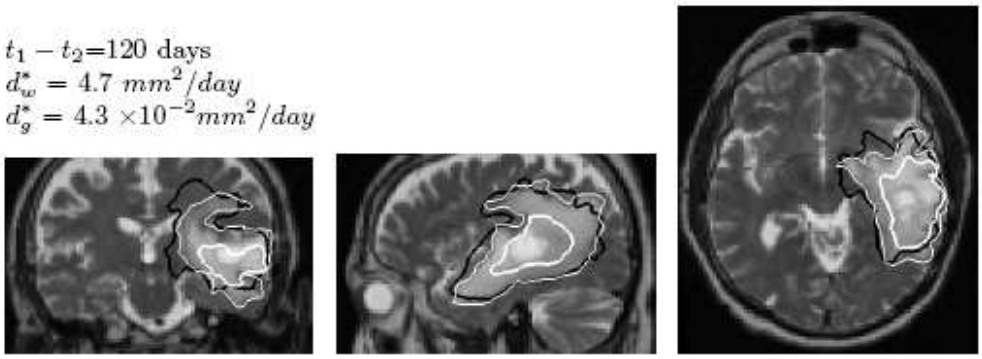


Figure 27. ***Experimental case****.. On the images, we show the tumor delineation obtained from T2 weighted images in the first time point (thick white line) and the second time point (thin white line) which is 120 days later. The black curve demonstrates the result of the simulation obtained by the reduced model using the optimum parameters which are given as* d_w^* *the speed of tumor diffusion in the white matter and* d_g^* *speed of tumor diffusion in the grey matter.*

We are conducting further studies to apply our parameter identification scheme to more general problems such as estimating the initial point of the tumor, estimating different parameters separately and temporal information about the tumor.

5.6. Clinical and Biological Validation

5.6.1. Grid-enabled workflows for medical image analysis applications

Keywords: *accuracy evaluation*, *grid computing*, *rigid registration*.

Participants: Tristan Glatard, Johan Montagnat [I3S], Xavier Pennec.

This project is part of a partnership between the Asclepios team, the I3S laboratory and is funded by the AGIR project of the French ACI "Masses de Données".

Based on the grid workflow already developed for the evaluation of the accuracy of registration algorithms, we investigated the impact of lossy compression on the performance of 4 rigid registration algorithms in an experiment involving 3024 registrations. Thanks to the grid, we could perform registrations required by the study in about 4 hours on dedicated resources whereas 7.5 days would have been needed on a single PC. The bronze standard evaluation framework was shown to be powerful enough to address such a problem in absence of ground truth. In particular, it is highly scalable and makes outliers easily detectable whereas a visual check of a large amount of transformations could not be done in a reasonable amount of time. Results show that the impact of 3D-SPIHT compression on robustness, repeatability and accuracy is quite negligible until a significant compression ratio (48), in particular if the registration algorithm has a good multi-scale handling. Beyond this threshold, the tested methods based on crest-lines are highly penalized: half of the patients can be considered as outliers and their accuracy is lowered by 50%. Surprinsingly, compression even improves the registration accuracy (up to 30% for `Baladin` on our setup) probably because the registration algorithm focuses on informative subsets of the image.

In some scenarii, the workflow description of medical image analysis application may greatly benefit from a partial automation. In particular, being able to automatically add/remove registration algorithms from a complete evaluation workflow would leverage the development cost and foster the use of the bronze standard application. We studied the applicability of a semi-automatic workflow merging algorithm developed in the Rainbow team of the I3S to the bronze standard application [79]. Even if some results have been achieved with this algorithm, some limitations of the studied merging method were highlighted, thus triggering new directions in this domain.

The expressiveness of the workflow description language used for our applications has been studied in order to determine to what extend it would be able to support a broader range of applications. This Scufl language has been shown to be Turing complete, thus ensuring that every computable function could be implemented with it. Yet, perspectives of this study are still open to determine the effort needed to implement particular workflow patterns in Scufl.

The software development of MOTEUR (our grid enabled workflow manager) has been shown to be mature enough to start supporting external applications such as bionformatics ones at the University of Genoa. In particular, the generic application service wrapper that comes with MOTEUR highly simplifies the deployment of legacy codes on the EGEE grid [43]. In order to better support the probabilistic optimization strategies developed last year, we also continued the analysis of the variability of the grid latency on the EGEE production grid. In particular, this latency was shown to be accurately fitted by a mixed log-normal/Pareto model, noticeable by its heavy-tailed nature [70]. The influence of several grid parameters on this model was studied. It appears that EGEE computing sites can be classified into 3 classes, corresponding to slightly different performances in terms of average latency and variability [69].

All these works were also detailed in the PhD manuscript of T. Glatard [29], defended in November 2007.

5.6.2. DTI and Fiber Tracking: indications for Spinal Cord Lesions?

Keywords: *MRI*, *diffusion*, *fiber tracking*, *spine*, *tensor*, *tractography*.

Participants: Pierre Fillard, Denis Ducreux.

Magnetic resonance (MR) imaging plays a major role in the diagnosis and follow-up of spinal cord lesions. The main objectives of spinal cord imaging are to detect and characterize lesions, to assess the feasibility of surgical resection, and to diagnose recurrences and complications of therapy. Conventional MR imaging using T1- and T2-weighted sequences lacks sensitivity in detecting and characterizing cord lesions, such as multiple sclerosis or acute spinal cord infarction. In addition, in patients who have cord tumors, conventional sequences may not be able to clearly identify the transition between the tumor and the surrounding edema. The purpose of this work is to assess whether diffusion tensor MRI and fiber tracking could help to better characterize spinal cord lesions than classical MRI. In this work, we reviewed the different spine-related pathologies and discussed the benefits of using DT-MRI and fiber tracking (FT). To do so, we used the software MedINRIA [88] for DT-MRI processing and fiber reconstruction. Results showed that:

1. In spinal cord tumors, fractional Anisotropy (FA) maps and fiber tracking could be used to better separate the œdema from the tumor. In particular, FT displays fibers that are warped or frankly destroyed.
2. In spinal cord compression, FT helps identifying the site of cord compression by depicting mass effect and discontinuity of white matter fibers.
3. In arteriovenous malformations, FT shows no fiber running through the nidus (center of the malformation), an observation that may become important if surgical resection is contemplated.
4. In syringomyelia (a disorder in which a tubular cavity, called the syrinx, forms within the spinal cord), FT is useful in identifying the spinothalamic tracts in patients (Fig. 28). If tracts are present but displaced by the lesion, patients will have a better outcome than when FT shows thinning or destruction of those.
5. In spinal cord injuries, we showed that FT may be used to ensure anatomic presence of intact fibers, a factor needed for successful grafting. Fibers destroyed by the initial injury do not respond to grafting.

This work was published in Neuroimaging Clinics of North America [40].

6. Contracts and Grants with Industry

6.1. Miniara

Participants: Liliane Ramus, Grégoire Malandain [Correspondant].

MINIARA, whose prime is DOSISOFT, aims at developing a medical imaging workstation together with a modular and versatile software that will be able to propose the latest fusion and registration modules dedicated to different anatomical locations, as well as specialized tools for the image exploitation. Therefore, the phases of diagnosis, simulation, scientific computation and follow-up of the patient could be done on the same workstation. In this project, the Asclepios team will be in charge of the construction of an atlas of the modal areas of the torso, and of the development of registration tools of lungs images.

6.2. CPER TELIUS

Participants: Grégoire Malandain [correspondant], Olivier Clatz, Hervé Delingette.

Within the CPER Telius, Asclepios is involved in several funded research facilities including: a high resolution CT-scan for the diagnosis and treatment of tumors with the Cyberknife (in collaboration with the Centre Antoine Lacassagne), a joint CT/SPECT imaging device dedicated to small animals (in collaboration with the TIRO team of Nice Sophia-Antipolis university), surgery simulators (in collaboration with the neurosurgery department of the Pasteur hospital, Nice), and a cellular imaging microscope (in collaboration with IPMC).

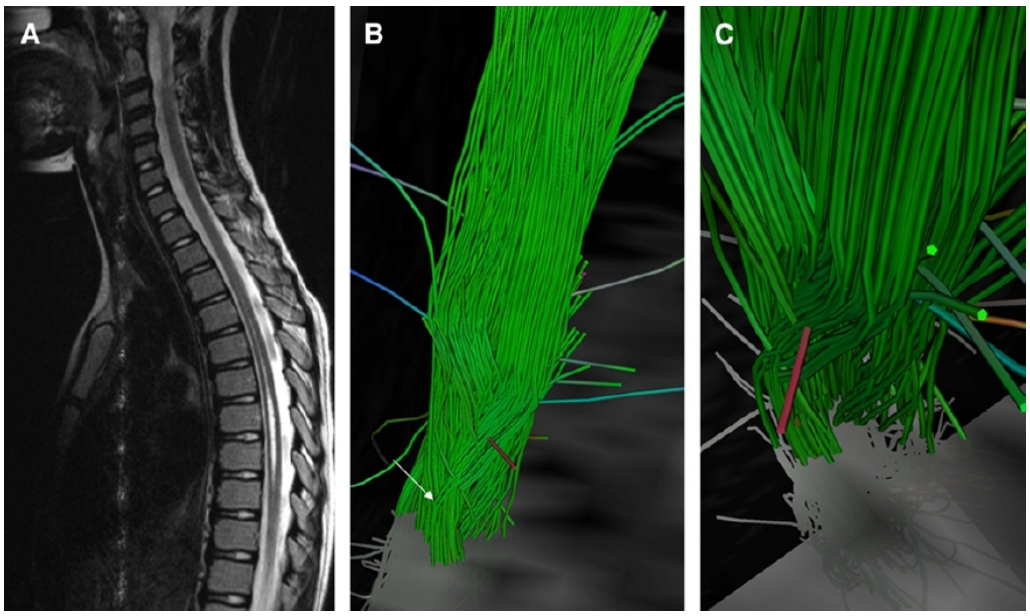


Figure 28. Fluid-filled cavity in the thoracic spinal cord. (A) Midsagittal T2-weighted image shows syrinx in the lower thoracic cord. (B) FT map shows that the syrinx alters the shape of white matter fibers especially the spinothalamic tracts (arrow), which may explain symptoms in some patients. (C) Magnified FT map demonstrates the decussating tracts that are warped by the cavitation (arrow). Objective warping or tracts may lead to decompression even in patients who have small syrinxes.

6.3. Cancéropôle PACA

Participants: Grégoire Malandain [correspondant], Pierre-Yves Bondiau.

Within the Cancéropôle PACA project, funded for the 2007-2010 period, Asclepios will be in charge of the construction of an atlas of the modal areas of the torso, in collaboration with the Centre Antoine Lacassagne, Nice, the Institut Paoli Calmette, Marseille, and the Timone Hospital, Marseille.

6.4. Maestro

Participants: Jimena Costa, Hervé Delingette, Grégoire Malandain [Correspondant].

MAESTRO[7] is an integrated project funded by the EC. It features a program on research and development on major clinical and technological aspects for the innovative radiotherapy treatments which are crucial for patient safety. The integrated project incorporates basic translational research on hi-tech equipment for clinics in close collaboration with industrials, research centres and European health services.

Within this project, Asclepios is involved, in collaboration with Dosisoft, in the automatic delineation of structures for radiotherapy planning.

6.5. Philips

Participants: Hervé Delingette [Correspondant], Damien Lepiller, Maxime Sermesant.

Philips Medical System Research in Paris has contracted the Asclepios team to investigate the analysis of 2D and 3D echocardiographic images in order to better understand, diagnose and plan the phenomenon of cardiac asynchrony, one common type of heart failure.

Following the work of C. Marboeuf, the objective of this work is to fuse cardiac motion information from multiple image modalities (Tissue Doppler Imaging, MR, 2D and 3D echocardiography) and to assess quantitatively the amount of motion asynchrony that can be observed in different regions of the heart.

6.6. European Marie Curie project "3D Anatomical Human"

Participants: François Chung, Olivier Clatz, Hervé Delingette [correspondant].

The Research Training Network "3D Anatomical Human" is a European project aiming at developing realistic functional three-dimensional models for the human musculoskeletal system, the methodology being demonstrated on the lower limb. The research groups involved are the University of Geneva (Switzerland), the Istituti Ortopedici Rizzoli (Italy), the University College London (UK), the Vrije Universiteit Brussel (Belgium), Aalborg University (Denmark), EPFL (Switzerland), CRS4 (Italy).

This 4 year project has started in October 2006 with a plenary meeting team in Sophia-Antipolis. In 2007, two additional plenary meetings have been organized, the first in Geneva in May and the second in London in September. One early stage researcher (Phd student) has been recruited from June 2007: François Chung. In the scope of the project, Asclepios should develop segmentation algorithms for the segmentation and motion tracking of anatomical structures (bone, cartilage, muscle) from static and dynamic MR images of the lower limb (cf section 5.2.1).

6.7. Odysseus

Participants: Hervé Delingette [Correspondant], Nicholas Ayache.

This EUREKA project involves three industrial partners (Karl Storz, SimSurgery and France Telecom), a cancer research institute (IRCAD) and three groups from INRIA (Alcove, Asclepios and Evasion). Its objective is to build computer-aided diagnosis, surgery planning and surgery simulation software to increase the efficiency of therapies against cancer of the lower abdomen. In this project, Asclepios is involved in the development of soft tissue models in a surgery simulation platform.

[7] http://www.maestro-research.org/

This project has ended in March 2007, with a plenary meeting organized in Strasburg on March 7th and 8th 2007. A follow-up of this project, the PASSPORT project, has been submited for funding as a STREPS project within the 7th Framework Program of the European Union.

6.8. Health-e-Child

Participants: Xavier Pennec [Correspondant], Nicholas Ayache, Maxime Sermesant, Hervé Delingette, Stanley Durrleman, Ender Konukoglu, Thomas Mansi.

The European project Health-e-Child (IST 027749, http://www.health-e-child.org/), coordinated by Siemens, Germany, aims to create an IT platform to share paediatric knowledge and clinical data based on grid technologies. The project currently brings together eight European countries and intends to integrate heterogeneous biomedical data from three clinical specialities (cardiology, neurology and rheumatology) coming from three paediatric hospitals in Europe (Hôpital Necker in Paris, France, Giannina Gaslini institute in Genoa, Italy, and Great Ormond Street Hospital in London, Great-Britain). This integration should lead to a better understanding of the pathologies studied, and, in the long term, provide real tools to help paediatricians make the right decisions. In this project, the role of the Asclepios team is to model the pathologies that Health-e-child is focussing on, based on our expertise on anatomical statistics, on the modelling of the heart and brain tumours.

For cardiac diseases, the electro-mechanical model of the heart was calibrated to simulate a healthy child heart. Simulations with modified parameters in accordance with clinical observations were also performed for cardiomyopathies and right-ventricular overloads giving the first disease-specific (but still patient generic) models. The clinical parameters (ejection fraction, volume variation, etc) are comparable with standard values and the results, which are publicly available in the deliverable D11.2 [92] http://www-sop.inria.fr/asclepios/projects/hec/content/cardiac/index.html, were qualitatively validated by the clinicians. To obtain a better heart geometry, we have experimented a 4-chamber segmentation prototype on a few high quality 3D MRI. These segmentations were used as the geometric basis of generic disease adapted electro-mechanical simulation of the heart. However, such high quality 3D MRI images are normally not available in the standard clinical workflow. To go one step further towards patients-specific models, we have designed and developed a new parametric shape model of the normal and disease heart based on standard clinical measurements that are acquired routinely. The goal is to obtain a personalized 3D geometrical shape model of the heart even with standard 2D images and measurements (see Section 5.5.4).

In order to improve the intrepretation of brain images, we have designed a registration module which was made publicly available in the June 25 release of MedINRIA http://www-sop.inria.fr/asclepios/software/MedINRIA/ (see also Section 4.1). Discussions with clinicians revealed that this tool might be very useful for the oncologist in the clinical workflow to compare longitudinal exams without coming back to the radiologist. The Health-e-Child demonstration at the conference EGEE'07, which was featuring in particular a live demo of this "Registration Tool", was one of the 3 runners-up for the best demo prize.

In order to go one step further towards atlas to patient registration, some deep technical work was performed in computational anatomy in order to better understand how to model efficiently the variability of curves and surfaces (see Sections 5.4.7). The developed methods were tested on a database of segmented brain structures of normal / autistic / developmentally delayed childs with 1 and 2 time points that we can access thanks to a collaboration with Guido Gerig (Univ. Utah) / Martin Styner (UNC Chapel-Hill).

For brain tumors, an important step was reached for planning patient-adapted irradiation margins for radiotherapy on a single 3D MRI thanks to the tumor growth model: experiments with simulated tumors showed that this better targets tumor cells and avoids healthy tissue than the usual constant margin. New fast numerical schemes to estimate the tumor cells density that take into account correct boundary conditions have also been designed and implemented (see Section 5.5.5). A summary of the current work on tumor modelling was provided in deliverable D11.2 [92] which is available online at http://www-sop.inria.fr/asclepios/projects/hec/. Following the June meeting with clinician, two new axes were initiated on predicting the location of recurrence of brain tumors after surgery and on the detection of tumor growth for slowly growing tumors (most of the cases in HeC).

6.9. Siemens

Participants: Jean-Marc Peyrat, Hervé Delingette, Xavier Pennec [correspondant], Nicholas Ayache.

A contract has been established in 2005 between Asclepios and Siemens Corporate Research, Princeton, for establishing a methodology to predict and evaluate the accuracy and robustness of registration methods in image guided surgery, with application to concrete clinical problems. After the departure of Antoine Azar, the subject has been shifted toward the modeling of the cardiac anatomy. This study involves in particular Jean-Marc Peyrat through his PhD in the Asclepios team (see also Section 5.4.2).

6.10. CIFRE PhD Fellowships

6.10.1. Dosisoft

The work of Olivier Commowick on the design and evaluation of digital anatomical atlases and dedicated to non-rigid registration tools for radiotherapy planning was supported by a PhD fellowship from the Dosisoft company.

It is pursued by another PhD fellowship, granted to Liliane Ramus, from the Dosisoft company, that aims to study thoroughly the proposed approach and to extend it to other anatomical locations.

6.10.2. Mauna Kea Technologies

The work of Tom Vercauteren on the mosaicing and analysis of temporal sequences of *in vivo* confocal microscopic images (see Sectiona 5.3.2 and 5.2.5) is supported by a PhD fellowship from the Mauna Kea Technologies company.

7. Other Grants and Activities

7.1. Regional initiatives

7.1.1. Regional PhD fellowships

Ender Konukoglu is partially supported by a "Région Provence-Alpes Côte d'Azur" PhD fellowship.

7.2. National initiatives

7.2.1. INRIA Large Collaborative Effort CARDIOSENSE3D

Participants: Hervé Delingette [coordinator], Nicholas Ayache, Maxime Sermesant, Florence Billet, Nicolas Toussaint.

The national action CARDIOSENSE3D has been launched in May 2005 on the topic of cardiac simulation. This 4-year action gathers the expertise of four INRIA research teams (Asclepios, Macs, Reo and Sosso2) on this multi-disciplinary research topic.

CardioSense3D has three main objectives:

1. To build a cardiac simulator that couples four different physiological phenomena
2. To estimate patient specific parameters and state variables from observations (images, electrophysiology mappings) of the cardiac activity,
3. To build several applications to solve clinical problems related to the diagnosis or therapy of cardiac pathologies.

H. Delingette is in charge of the coordination of this action. More information can be found at the following web site http://www.inria.fr/CardioSense3D/

7.2.2. ACI Masse de Donnée AGIR

Participants: Xavier Pennec [correspondant], Tristan Glatard, Johan Montagnat [I3S].

Grid Analysis of Radiological Images Data http://www.aci-agir.org/ (in French: Analyse Globalisée des données d'Imagerie Radiologique - AGIR) is a multi-disciplinary research project with focus on leveraging medical imaging algorithms through grid systems, funded by the French Research Ministry through the ACI (Action Concertée Incitative) Masses de Données.

AGIR gathers researchers in computer science, physics and medecine from CNRS, INRIA, Universities, INSERM, and hospitals. Its goals are to to define and validate new grid services that address some of the requirements of complex medical image processing and data manipulation application ; and new medical image processing algorithms that take advantage of the underlying grid infrastructure for computing and data intensive needs. The project started in september 2004, and supports the PhD of T. Glatard, jointly supervised by X. Pennec at ASCLEPIOS and J. Montagnat at RAINBOW (I3S, Nice University). We refer the reader to Section 5.6.1 for the scientific results of the project.

7.2.3. RNTL NeuroLOG

Participants: Xavier Pennec [correspondant], Tristan Glatard, Grégoire Malandain, Jean-Christophe Souplet.

The project NeuroLOG http://neurolog.polytech.unice.fr/ is funded by the French National Research Agency (ANR-06-TLOG-024) and is adressing software technologies for the integration of processes, data and knowledge in neurological medical imaging:

- Management and access of partly structured data, heterogeneous and distributed in an open environment.
- Access control and protection of private medical data. Control of workflows implied in complex computing process on grid infrastructures.
- Control of workflows implied in complex computing process on grid infrastructures.
- Extraction and quantification of relevant parameters for three different pathologies: Multiple sclerosis, Brain Vascular Stroke and Brain tumors.

This is a multi-disciplinary project which associates partners in software technologies (I3S at Sophia-Antipolis, LRI in Orsay), databases (Business Objects, LaRIA, Visages at IRISA-Rennes) and medical imaging (Visages at IRISA-Rennes, Visioscopie, U594, IFR49, Asclepios at INRIA-Sophia).

7.2.4. ATP CIRAD Meristem Grant

Participants: Romain Fernandez [CIRAD], Christophe Godin [Virtual Plants], Jean-Luc Verdeil [CIRAD], Grégoire Malandain [Correspondant], Olivier Devillers [Geometrica].

Contractor for Virtual Plants: CIRAD. From December 2005 until December 2008

3D imagery and geometrical modeling of meristems. The aim of this Action Thématique Programmée of CIRAD is twofold. We first intend to design 3D visualization techniques of the meristem architecture at cellular and molecular levels. Second, we aim at developing a generic geometric model of the meristem able to support various treatments and modelling processes at cell scale (characterization of meristem geometry, cell growth, mechanical forces, circulation of hormone fluxes, ...). Data will be collected from bi-photon microscopy at CIRAD (in the context of the RIO imaging platform) on rice, a model plant for agronomy, and on other perennial species to characterize the state of the meristem at different phenological states or for different environmental constraints. The project includes several teams from CIRAD, INRA and IRD, and 3 INRIA projects: Asclepios, Geometrica and Virtual Plants.

7.2.5. QUALICORE

Participants: Grégoire Malandain [correspondant], Jean-Christophe Souplet, Christine Lebrun [Neurology, Pasteur Hospital, Nice], Stéphane Chanalet [Radiology, Pasteur Hospital, Nice].

QUALICORE is a phase IV pharmaceutical study which is funded by SERONO and that aimed at evaluated the quality of life of Multiple Sclerosis patients under treatment. Five national hospitals participate to it, namely Clermont-Ferrand, Dijon, Marseille, Montpellier and Nice. Asclepios is in charge of the MR image processing package.

7.2.6. INRIA Cooperative Research Initiative BrainVar

Participants: Xavier Pennec [coordinator], Stanley Durrleman, Pierre Fillard.

Understanding and modelling the individual anatomy of the brain and its variability across a population is made difficult by the absence of meaningful physical models for comparing different subjects, the complexity of shapes, and the high number of degrees of freedom implied. This also raises the need for statistics on objects like curves, surfaces and deformations that do not belong to standard Euclidean spaces. Applications are very important both in neuroscience, to minimise the influence of the anatomical variability in functional group analyses, and in medical imaging, to better drive the adaptation of generic models of the anatomy (atlas) into patient-specific data.

Each research team is currently investigating independently particular aspects of the general problem and is proposing different but often complementary approaches. The goal of this INRIA cooperative research initiative is to federate the efforts of several groups in France (Asclepios, INRIA Sophia Antipolis; LNAO Neurospin, CEA - DSV - DRM- SHFJ; Neurospin, INRIA Futurs; MMiXT, CNRS UPR640 LENA, Pitié-Salpétrière; VisAGeS, IRISA Rennes; LSIS, UMR 6168, LXAO team, Marseille; CMLA, ENS Cachan) to identify the challenges for a future potential neuro-anatomic plateform. The general research themes are related to anatomical and functional neuroimaging on one hand and on computational anatomy on the other hand.

In 2007, we organized 5 days of scientific meeting:

- February 9, visio-conference: Kickoff meeting.
- April 3 at Neurospin, Saclay: Registration and variability of sulcal lines and surfaces.
- June 1st, at INRIA Sophia-Antipolis (joint meeting with the DMRI Cooperative Research Initiative): Diffusion imaging.
- Sept. 17 at Neurospin, Saclay: growth and evolution of the brain.
- Sept. 18 at ENS Cachan: mathematical foundations of computational anatomy.

These scientific meeting sessions were very productive: a total of 30 presentations for about 20 people at each meeting. Program, participants and results are detailed on the BrainVar web page http://www-sop.inria.fr/asclepios/projects/ARCBrainVar/.

7.2.7. Consulting for Industry

- Nicholas Ayache is member of the Scientific Council of Dosisoft (Paris), a subsidiary from the Gustave Roussy Institute and the Curie Institute (Paris). He is scientific consultant for the company Mauna Kea Technologies (Paris).
- Hervé Delingette is a scientific consultant for the company Median and a member of the scientific council of the company QuantifiCare.
- Grégoire Malandain is a member of the technical council of the company Dosisoft (Paris), a subsidiary from the Gustave Roussy Institute and the Curie Institute (Paris) and a scientific consultant for the company Median.
- Xavier Pennec is a scientific consultant for the company Median and a member of the scientific council of the company QuantifiCare.

7.2.8. Collaboration with national hospitals

Here we provide a list of research centers in national hospitals with whom we collaborate in common research projects.

7.2.8.1. IRCAD, hôpitaux de Strasbourg

Pr. Marescaux and L. Soler : hepatic surgery simulation segmentation of abdominal structures from CT scan images and augmented reality for guidance in hepatic surgery [127], [128].

7.2.8.2. Hôpital de la Pitié-Salpétrière, Paris

Dr. J. Yelnik (INSERM U.289), Pr. D. Dormont, and E. Bardinet (CNRS) are our partners in a collaboration with Medtronic [110].

7.2.8.3. Centre anti-cancer Antoine Lacassagne, Hôpital Pasteur, Nice

Dr. Bondiau participates in our research on atlas registration for radiotherapy planning and on tumour growth simulation.

7.2.8.4. CHU de Nice, Hôpital Pasteur

We continue our collaboration with Dr. C. Lebrun-Frenay of the neurology department, and with Dr. Chanalet of the radiology department, within the framework of a study on the temporal evolution of MS lesion load.

7.2.9. Collaboration with international hospitals

7.2.9.1. St Thomas' Hospital, King's College London, United Kingdom

Maxime Sermesant is a part-time lecturer in the Interdisciplinary Medical Imaging Group, Division of Imaging Sciences, St Thomas' Hospital, King's College London. The XMR facility within this hospital is a unique possibility to validate and exploit the cardiovascular modelling work.

7.3. Foreign Associated Team: Brain Atlas

Participants: Xavier Pennec [Correspondant], Stanley Durrleman, Pierre Fillard, Nicholas Ayache, Caroline Brun [LONI, UCLA], Natasha Lepore [LONI, UCLA], Paul Thompson [LONI, UCLA].

Since its creation in September 2001, the associated team program between the Asclepios laboratory at INRIA and the laboratory of NeuroImaging at the UCLA School of Medicine has enabled an active collaboration between both structures, with the objective of comparing and analyzing the performances and behaviors of image processing algorithms devoted to the building of brain atlases.

In 2007, we continued the research axis on the estimation of the anatomical variability of the brain from sulcal lines in the framwork of the PhD of P. Fillard. In the previous works, we modeled the variability of each individual cortical position by a 3x3 covariance matrix. However, anatomical correlation between different brain regions are overlooked in this type of model where structures are considered independently. We developped this year a new methodology to study the joint variability of any pair of cortical positions (Green's function), based on the 6x6 total covariance matrix. As this object is once again a tensor, we can reuse a large part of the previously developped artillery for extrapolation from sparse measures on sulci (our data) to the whole brain. The resulting 6x6 tensor field is then analyzed in canonical correlation (see Section 5.4.5). As expected, one finds a significant local correlation around any test point. More interestingly, the symmetric position in the opposite hemisphere most often exhibit a high correlation as well. This study also reveal new findings with unexpected correlation between different lobes the brain. For instance we observed a correlation between the back of the inferior temporal sulcus and the left and right intra-parietal sulci. The methodology developped and the first results were presented in [68].

In each variability estimation method, the number of degrees of freedom is so huge that part of the measured variability is likely to be biased consistently and to reflect the underlying assumptions of the method rather than the true variability. One idea (which is also developped with other teams in the ARC BrainVar started in 2007) is to analyze the variability of the same data with a different method in order to put into evidence the consensus and the biases induced by each method. In the framework of the PhD of S. Durrleman, we used the same sulcal lines as above (provided by P. Thompson through this associated team program), and a diffeomorphic registration algorithm based on courants (a generalisation of distributions that allows to model consistently lines and surfaces). Then, we analyze here the part of the variability that can be easily explained by a diffeomorphism. Although the statistics are not completely comparable with Fillard's methods (where the noise on lines was included), they globally agree at the level of lobes, and demonstrate interesting differences that we were partly able to explain at lower levels [66].

Thanks to the NSF-INRIA REUSSI internship program, we were able to host the visit of C. Brun (PhD student at UCLA) and L. Lepore (post-doc at UCLA) one week in January and 2 weeks in July in the Asclepios lab. The work that we initiated last year focus on the evaluation of the brain variability using statistics on dense deformations obtained using non-rigid rigid registration of an atlas to the 3D images of many subjects (Tensor based morphometry). A first paper demonstrating that the use of the Riemannian elasticity in fluid registration could lead to more significant statistics for discriminating shapes in normal vs HIV brain images was presented at the MICCAI 2007 Workshop on Statistical Registration [59]. A second research axis was focused on the influence of the shape of the reference image (the mean template) in tensor-based morphometry. We were able to design a method to optimally recenter the template to minimize its influence on the resulting statistics on the Green's deformation tensor [78].

P. Thompson, X. Pennec and S. Durrleman participated to the SAMSI Summer 2007 Program on the Geometry and Statistics of Shape Spaces (Raleigh, NC, USA, July 7-13), with two invited presentations and a poster including results obtained through the Brain-Atlas associated team. X. Pennec, N. Ayache, P. Fillard, S. Durrleman, C. Brun et N. Lepore participated to the conference MICCAI 2007 in octobre 2007 in Brisbane, Australia, with one oral presentation [66] and one poster [78] on the above results, and well as to the associated workshop on statistical registration with one invited presentation from X. Pennec and one regular oral presentation [59]. The results of the collaboration were also presented by X. Pennec at invited seminars (Grenoble Univ., April 26, Montpellier, May 21), and a PhD course at the University of Saragoza, Spain (Sept 12-14).

7.4. Foreign Associated Team: CompuTumor

Participants: Nicholas Ayache [Correspondant], Olivier Clatz [Correspondant], Pierre Fillard, Polina Golland [CSAIL, MIT], Ender Konukoglu, Xavier Pennec, Tom Vercauteren, Simon Warfield [CRL, Harvard Medical School], William Wells [CSAIL, MIT], Boon Thye Thomas Yeo [CSAIL, MIT].

7.4.1. Presentation of the Associated Team

The CompuTumor associated team has been funded early 2007. This project is dedicated to the study of brain tumor models and their confrontation with medical images to better assist diagnosis and therapy. The project will strongly enhance the current collaborations between INRIA and a group of world leading teams with complementary technical and clinical expertise on these topics in Boston and Nice. The proposal is divided into 4 main themes of research, each theme involving at least 2 foreign partners. The first theme is dedicated to the brain tumor models, their evaluation and use in clinical applications. The second theme is dedicated to the development of new algorithms for real time image guided neurosurgery using 3D ultrasound imaging. The third theme is dedicated to the study of the variability of the white matter architecture and its influence on brain tumor growth. The objective of the last theme of this proposal is the development of a neurosurgery simulator to train young surgeons to practice tumor resections. We believe that these four research themes nicely complement each other to bring significant advances in the future understanding, diagnosis and treatment of brain tumors.

7.4.2. Seminar and presentations

1. On September 26th, William Wells gave a talk at INRIA entitled "A Marginalized MAP Approach and EM Optimization for Pair-Wise Registration"
2. On August 30th, Kilian Pohl gave a talk at INRIA entitled "Solving the Mean Field Approximation in the Level Set Framework via the Logarithm of Odds"
3. Nicholas Ayache gave several talk in Boston during his scientific visit: August 23: Harvard: Biorobotics Lab, September 7: CSAIL at MIT, September 28: Electrical Engineering Seminars at Harvard, October 01: Monthly Radiology Seminar at Brigham and Women's hospital, October 10: Martinos Center for Biomedical Imaging at Mass General Hospital
4. On June 29th, Olivier Clatz gave a talk at the REUSSI welcome seminar at INRIA Rocquencourt entitled "Modeling Brain Tumors for Patient-Specific Therapy"

5. On June 20th, Boon Thye Thomas Yeo presented his previous work and work planning to the Asclepios team.

7.4.3. Scientific Publications

Thanks to the NSF-INRIA REUSSI internship program, Boon Thye Thomas Yeo came to the Asclepios Project Team for 3 months starting 1st of June. He developped an algorithm for the diffeomorphic non-linear registration of DTI (see section 5.2.6). Scientific cummunications are expected in ISBI 2008 and IEEE TMI.

During his visit in Boston, Olivier Clatz worked on the validation of non-rigid registration algorithms using DTI. Assessment of the accuracy of nonrigid registration algorithms is a essential and complex issue due to its intricate framework and its application-dependent behavior. We demonstrate that the diffusion MRI provides an independent means of assessing the quality of alignment achieved on the structural MRI. Indeed, diffusion tensor MRI enables the comparison of the local position and orientation of regions that appear homogeneous in conventional MRI. More details can be found in [60]. He also extended the initial work developped in collaboration with the Brigham and Women's Hospital [112] on non-rigid registration of intraoperative images. The algorithm was evaluated during surgery for intraoperative deformation correction [32] and for preoperative image distortion compensation [31].

8. Dissemination

8.1. Promotion of the Scientific Community

8.1.1. Journal editorial boards

N. Ayache is the co-founder and the co-editor in Chief with J. Duncan (Professor at Yale) of**Medical Image Analysis**[8]. This scientific journal was created in 1996 and is published by Elsevier. Its impact factor in 2003 was 4.4, it was 3.2 in 2004, 3.14 in 2005 and 3.26 in 2006.

H. Delingette is a member of the editorial board of the journal *Medical Image Analysis* (Elsevier).

I. Strobant is editorial coordinator for Medical Image Analysis, Elsevier (since october 2001).

N. Ayache is associated editor of **IEEE Transactions on Medical Imaging**[9].

I. Strobant is editorial assistant for Transactions on Medical Image Analysis, IEEE (since october 2001)

N. Ayache is a member of the editorial board of the following journals *Mathematical Modeling and Numerical Analysis (M2N)*, *Medical Image Technology* (Japanese journal) and *Journal of Computer Assisted Surgery* (Wiley). and *Journal of Computer Assisted Surgery* (Wiley).

G. Malandain is a member of the editorial board of the journal *International Journal on Computer Vision* (Kluwer).

8.1.2. Participation in the organization of conferences

N. Ayache was the program chair of MICCAI'07 help in Brisbane Australia between 29 October and 2 November (MICCAI is the flagship international conference in Medical Image Computing and Computer Aided Intervention). He is also a member of the executive board of the MICCAI society. He also was on the program committee of the FIMH Conference held in Salt-Lake City in June 2007 (Functional Imaging and Modeling of the Heart).

H. Delingette was a member of the program committees of the conferences Information Processing in Medical Images (IPMI) 2007, International Conference on Computer Vision (ICCV'07), Computer Vision and Pattern recognition 2007 (CVPR'07), conference on the Functional Imaging and Modeling of the Heart (FIMH'07), VRIPhys 2007, CIARP 2007, 3DIM2007. He was member of the review committee of ISBI'07 and MICCAI'07.

[8] http://www.elsevier.com/wps/find/journaleditorialboard.cws_home/620983/editorialboard
[9] http://www.ieee-tmi.org/

G. Malandain was member of the scientific board of TAIMA'07, ISBI'07, and MICCAI'07.

X. Pennec was a member of the program committees of the conferences MICCAI'07, Information Processing in Medical Images (IPMI) 2007, Int. Symp. on Volume Graphics VG'07, IEEE Work. on Mathematical Methods in Biomedical Image Analysis (MMBIA'07) and a member of the scientific board of ISBI'07.

8.1.3. Scientific animation

N. Ayache was chairman of the "comité des projets de l'INRIA Sophia-Antipolis" (equivalent of VP for science) and a member of the scientific direction of INRIA-Sophia-Antipolis and of the Evaluation Committee of INRIA until August 2007.

I. Strobant was assistant of the "comité des projets de l'INRIA Sophia-Antipolis" from July 2005 to July 2007

Nicholas Ayache is a member of the steering committee of the "Programme National de Recherche" in Biomedical Imaging of INSERM. He is also a member of the "comité sectoriel du département Biologie-Santé of the "Agence Nationale pour la Recherche (ANR)".

G. Malandain is chairing the local experimentation and software development committee (CDL).

X. Pennec was an evaluator for the US-Israel Binational Science Fondation (BSF), the Banff International Research Station for Mathematical Innovation and Discovery (BIRS, Alberta, Canada), and the Natural Sciences and Engineering Research Council (NSERC) of Canada.

H. Delingette was a member of the local computer infrastructure user committee (CUMIR) and the local committee in charge of the scientific selection of visiting scientists applications (Comité Nice).

M. Sermesant is a member of the INRIA-INSERM reflexion group on "modelling living systems". He is an evaluator for the Biotechnology and Biological Sciences Research Council (BBSRC), United Kingdom.

O. Clatz was an evaluator for the Agency for Science, Research & Technology (A*STAR), Singapore.

8.2. University teaching

École Centrale de Paris. N. Ayache, H. Delingette and G. Malandain are co-responsible of 2 modules on medical imaging (formation and analysis of medical images) (45 hours of lectures) with the participation of X. Pennec (9 hours). These 2 modules are common to the Master MVA of ENS Cachan "Mathematiques, Vision et Apprentissage", and to the Master IDB of École Centrale de Paris.

Ecole des Ponts et Chaussées H. Delingette has presented an overview of medical image analysis during a 3h course.

Ecole Supérieure de Chimie, Physique et Electronique (ESPCE). P. Fillard gave 12 hours of lecture on medical imaging, more specially MRI and DT-MRI, an introduction to programming in VTK, as well as an introduction to medical imaging techniques.

Master IGMMV, université de Nice Sophia-Antipolis. G. Malandain is responsible of one module of 15 hours (medical image analysis). H. Delingette is responsible of one module of 15 hours on image segmentation and soft tissue simulation.

Master Génie biomédical, université de Nice Sophia-Antipolis. G. Malandain is responsible of one module of 48 hours (24 hours of lectures + 24 hours of practical work) with the participation of Jean-Christophe Souplet.

Zaragoza University and Polytechnique University of Catalonia (Spain) X. Pennec gave a PhD course (20h) on Statistics on Riemannian Manifolds for Computational Anatomy in September 2007 in the Biomedical Engineering inter-university PhD program.

8.3. PhD Theses and Internships

8.3.1. PhD defended in 2007

1. Olivier Commowick, *Digital anatomical atlases for radiotherapy planning*. University of Nice Sophia-Antipolis, February 14, 2007. Committee: P. Clarysse and L. Collins (reviewers), G. Malandain (supervisor), N. Ayache (president), P.Y. Bondiau, G. Gerig, and V. Grégoire (referees), and H. Kafrouni (invited).
2. Tristan Glatard: *Description, deployment and optimization of medical image analysis workflows on production grids*, University of Nice Sophia-Antipolis, November 20, 2007. Committee: P. Kacsuk (Reviewer), I. Magnin (Reviewer), Ch. Barillot, D. Caromel, Fr. Desprez, C. Germain-Renaud, J. Montagnat (Supervisor), X. Pennec (Supervisor), M. Riveill.

8.3.2. Current PhDs

1. Florence Billet, *Analyse de la fonction cardiaque à l'aide d'un modèle électromécanique du cœur*, Nice-Sophia-Antipolis University. Cardiosense3D.
2. Jonathan Boisvert, *Articulated models for augmented reality: application to minimally invasive spine surgery*. Cotutelle (joint supervision) University of Nice-Sophia-Antipolis / Polytechnique School of Montreal, Canada.
3. François Chung, *Reconstruction et Simulation des muscles et du squelette des membres inf ieures* Nice-Sophia Antipolis University.
4. Jimena Costa, *Segmentation of anatomical structures of the abdomen with deformable models*. École des Mines de Paris.
5. Stanley Durrleman, *Joint modeling of the brain growth and of the population variability. Application to pediatric brain imaging.* Nice-Sophia Antipolis University. In collaboration with A. Trouvé, CMLA, ENS.
6. Romain Fernandez, *3D segmentation and reconstruction of rice's root meristem from multiphoton microscopic images*, Montpellier university. In collaboration with J.C. Godin, Virtual Plants.
7. Pierre Fillard, *Statistical modeling of the anatomical variability of the cortex*, Nice-Sophia Antipolis University.
8. Heike Hufnagel, *Statistical shape analysis of normal and pathological organs within the abdomen*, University of Hamburg. PhD in collaboration with Prof. Dr. Heinz Handels, Institut für Medizinische Informatik, University of Hamburg.
9. Ender Konukoglu, *Modeling and control of tumor growth with medical imaging*. Nice-Sophia Antipolis University.
10. Damien Lepiller, *De l'analyse du mouvement cardiaque à l'évaluation du fonctionnement électrophysiologique du coeur* , Nice-Sophia Antipolis University. Cifre collaboration with Philips.
11. Thomas Mansi *Modelling of paediatric cardiac pathologies*. École des Mines de Paris
12. Jean-Marc Peyrat, *Electro-mechanical models of the heart activity personalized from medical images*, Nice-Sophia Antipolis University.
13. Liliane Ramus, *Digital anatomical atlases for radiotherapy planning*, Nice-Sophia Antipolis University. Cifre collaboration with Dosisoft.
14. Jean-Christophe Souplet, *Analysis of Multiple Sclerosis MRI images*. Nice-Sophia-Antipolis University.
15. Tom Vercauteren, *Mosaicing and analysis of temporal sequences of* in vivo *confocal microscopic images*. École des Mines de Paris.

8.3.3. Participation to thesis committees

Nicholas Ayache participated as president to the PhD thesis committee of O. Commowick (Nice Sophia-Antipolis university) and was a member of the PhD thesis committee of Charles Florin (Ecole Nationale des Ponts et Chaussées).

Hervé Delingette participated as reviewer to the Phd thesis committee of Benjamin Gilles (Genève Univ.), Dobrina Boltcheva (Louis Pasteur Univ., Strasbourg), as referee to the PhD thesis committee of Maxime Taron (Ecole des Ponts et Chaussées), as referee to the Habilitation à Diriger les Recherches committee of Johan Montagnat (Nice Sophia-Antipolis Univ.) and Michael Beuve (Lyon Univ.).

Grégoire Malandain participated as president to the PhD thesis committee of M. Berar (INPG, Grenoble), L. Risser (Toulouse university), and S. Rit (Lyon university), as reviewer to the PhD thesis committee of S. Aouadi (Clermont-Ferrand university), B. Delhay (Lyon university), J. Cousty (Marne-la-Vallée university), F. Lauwers (Toulouse university), A. Moreno (ENST, Paris), and W. Rekik (Paris 6 university), as referee to the PhD thesis committee of A. Charnoz (Strasbourg university), and as supervisor to the PhD thesis committee of O. Commowick (Nice Sophia-Antipolis university).

Xavier Pennec participated as referee to the PhD thesis committee of Ch. Samir (Telecom-Lille and Science and Technology Univ. of Lille), and as supervisor to the PhD thesis committe of T. Glatard (Nice Sophia-Antipolis university).

8.3.4. Training activities

1. Sébastien Novellas, *Segmentation semi-automatique des lymphomes médiastinaux en tomodensitométrie*, University of Nice-Sophia Antipolis, 2007.

8.4. Participation to workshops, conferences, seminars, invitations

We only give here the invited participations. Please refer to general references for the regular participation to conferences with a submission process.

- **Nicholas Ayache** gave an invited lecture to the Colloquium organized to honor the memory of Gilles Kahn in Paris on 12 January, 2007 and gave five invited lectures dedicated to the memory of Gilles Kahn in the USA at the Mayo Clinic (15 June, Rochester), MIT (7 Sept, Cambridge), Harvard (28 Sept, Cambridge), Brigham and Women's Hospital (1 Oct, Boston) and Martinos Research Center (10 Oct, Boston).
- **Olivier Clatz** gave invited lectures on Computational Models of Human Organs and Real Time Surgery Simulation at the *3rd Summer European University on Sugical Robotics* (Montpellier, September 2007) [10]. He also gave invited talks at the *US France Young Engineering Scientists Symposium* (Washington, October 2007) and at Children's Hospital Washington.
- **Hervé Delingette** gave invited talks at the *ISBI 2007 conference* (Washington DC, April 2007), at the *INRIA-NIH workshop* (Washington DC, April 2007), at the workshop *Journ s Nationales de la Recherche en Robotique* (Obernai, Oct. 2007), at the conference VIPImage'07 (Porto, Oct. 2007), at the Honk Kong Univ. of Science and Technology (Hong-Kong, Nov. 2007).
- **Grégoire Malandain** gave invited lectures at the *Workshop on Multimodality Imaging for radiotherapy* (Villejuif, january 2007), the *Conférence internationale de l'ACOMEN (Action COncertée en MÉdecine Nucléaire)* (Nice, may 2007), the *Journées internationales de la Société Française de Neurologie* (Paris, june 2007), and the *Journées de Recherche en Imagerie Médicale* (Dijon, september 2007). He also gave an invited talk at the CIRAD, (Montpellier, january 2007).
- **Xavier Pennec** gave invited talks on Statistical Computing on Riemannian Manifolds for Computational Anatomy at the INRIA-Laboratoire Dieudonne "Mathematics and Life-Science" meeting (Nice, November 16 2007), at the SAMSI Summer 2007 Program on the Geometry and Statistics of Shape Spaces (Raleigh, NC, USA, July 7-13) and at the *Statistical Registration: Pair-wise and Group-wise Alignment and Atlas Formation* workshop (Brisbane, Australia, November 2 2007). He

[10] http://www.lirmm.fr/UEE07/

also gave invited seminars at the GIPSA-lab (ex LIS), Grenoble Univ., April 26, and at the Mathematics and Modeling Institute of Montpellier (IMMM) on Mai 21, 2007.

- **P. Fillard** was invited to give two talks at the *2nd Summer School in Biomedical Engineering, Aug 10-16, Naumburg & Schoenburg, Germany* about one hour each to present some work on tensor processing with Log-Euclidean metrics and a tutorial on the software MedINRIA. He also gave a 30 minute tutorial at *Advances in Diffusion MRI Analysis, Tutorial at MICCAI'07* entitled: "Diffusion Tensor Processing with Log-Euclidean Metrics", and an invited seminar at the University of Eindhoven, Netherlands, in December.

8.5. Nominations and prizes

- **Nicholas Ayache** received the *trophée du chercheur de l'année PACA 2007* awared by the *Nouvel Economiste*. He was elected a member of the College of Fellows of the American Institute for Medical and Biological Engineering (AIMBE).
- **Olivier Clatz** received the 2007 *Prix Le Monde* for best PhD in Science.
- **Tom Vercauteren** was nominated for the MICCAI'07 young scientist award for his article [91].
- **H. Hufnagel** received the *Best scientific work prize* at Bildverarbeitung für die Medizin 2007 for *Point-Based Statistical Shape Models with Probabilistic Correspondences and Affine EM-ICP* coauthored by X. Pennec, J. Ehrhardt, H Handels and N. Ayache.
- **The action CardioSense3D** was among the winners of the ARTS (Apple Research & Technology Support) awards, and received 30,000 Euros worth of Apple hardware, software and assistance.

9. Bibliography

Major publications by the team in recent years

[1] N. AYACHE (editor). *Computational Models for the Human Body*, Handbook of Numerical Analysis (Ph. Ciarlet series editor), Elsevier, 2004.

[2] N. AYACHE, H. DELINGETTE (editors). *Proceedings of the International Symposium on Surgery Simulation and Soft Tissue Modeling*, Lecture Notes in Computer Science, vol. LNCS 2673, Springer-Verlag, Juan-les-Pins, France, June 2003.

[3] V. ARSIGNY, P. FILLARD, X. PENNEC, N. AYACHE. *Log-Euclidean Metrics for Fast and Simple Calculus on Diffusion Tensors*, in "Magnetic Resonance in Medicine", PMID: 16788917, vol. 56, n^{o} 2, August 2006, p. 411-421, ftp://ftp-sop.inria.fr/epidaure/Publications/Arsigny/arsigny_mrm_2006.pdf.

[4] N. AYACHE. *Epidaure: a Research Project in Medical Image Analysis, Simulation and Robotics at INRIA*, in "IEEE Trans. on Medical Imaging", vol. 22, n^{o} 10, October 2003, p. 1185–1201, ftp://ftp-sop.inria.fr/epidaure/Publications/Ayache/Ayache-editorial-ieee-tmi.pdf.

[5] N. AYACHE. *L'analyse automatique des images medicales, etat de l'art et perspectives*, in "Annales de l'Institut Pasteur", Numero special sur les progres recents de l'imagerie medicale, vol. 9, n^{o} 1, avril-juin 1998, p. 13-21.

[6] N. AYACHE, O. CLATZ, H. DELINGETTE, G. MALANDAIN, X. PENNEC, M. SERMESANT. *Asclepios: a Research Project at INRIA for the Analysis and Simulation of Biomedical Images*, in "Proceedings of the Colloquium in Memory of Gilles Kahn", LNCS, In press (20 pages)., Springer, 2007, ftp://ftp-sop.inria.fr/asclepios/Publications/Nicholas.Ayache/Colloquium-Gilles-Kahn-NA-2007.v2.pdf.

[7] C. BLONDEL, R. VAILLANT, G. MALANDAIN, N. AYACHE. *3-D tomographic reconstruction of coronary arteries using a precomputed 4-D motion field*, in "Physics in Medicine and Biology", vol. 49, n^{o} 11, 2004, p. 2197–2208, ftp://ftp-sop.inria.fr/epidaure/Publications/Malandain/blondel-pmb-2004.pdf.

[8] P. CACHIER, E. BARDINET, D. DORMONT, X. PENNEC, N. AYACHE. *Iconic Feature Based Nonrigid Registration: The PASHA Algorithm*, in "CVIU — Special Issue on Nonrigid Registration", vol. 89, n^{o} 2-3, Feb.-march 2003, p. 272–298, ftp://ftp-sop.inria.fr/epidaure/Publications/Cachier/Cachier_CVIU_2003.pdf.

[9] O. CLATZ, M. SERMESANT, P.-Y. BONDIAU, H. DELINGETTE, S. K. WARFIELD, G. MALANDAIN, N. AYACHE. *Realistic Simulation of the 3D Growth of Brain Tumors in MR Images Coupling Diffusion with Mass Effect*, in "IEEE Transactions on Medical Imaging", vol. 24, n^{o} 10, October 2005, p. 1334-1346, ftp://ftp-sop.inria.fr/epidaure/Publications/Clatz/TMI_GBM_clatz.pdf.

[10] H. DELINGETTE, N. AYACHE. *Soft Tissue Modeling for Surgery Simulation*, in "Computational Models for the Human Body", N. AYACHE (editor), Handbook of Numerical Analysis (Ed : Ph. Ciarlet), Elsevier, 2004, ftp://ftp-sop.inria.fr/epidaure/Publications/Delingette/hna-delingette.pdf.

[11] H. DELINGETTE. *General Object Reconstruction based on Simplex Meshes*, in "International Journal of Computer Vision", vol. 32, n^{o} 2, 1999, p. 111-146.

[12] J. DUNCAN, N. AYACHE. *Medical Image Analysis: Progress over two decades and the challenges ahead*, in "IEEE Transactions on Pattern Analysis and Machine Intelligence", vol. 22, n^{o} 1, 2000, p. 85-106.

[13] M. A. GONZÁLEZ BALLESTER, X. PENNEC, M. G. LINGURARU, N. AYACHE. *Generalized Image Models and Their Application as Statistical Models of Images*, in "Medical Image Analysis", MICCAI 2003 Special Issue, vol. 8, n^{o} 3, September 2004, p. 361–369, ftp://ftp-sop.inria.fr/epidaure/Publications/Gonzalez/Gonzalez:MedIA:2004.pdf.

[14] K. KRISSIAN, G. MALANDAIN, N. AYACHE, R. VAILLANT, Y. TROUSSET. *Model-Based Detection of Tubular Structures in 3D Images*, in "Computer Vision and Image Understanding", vol. 80, n^{o} 2, 2000, p. 130–171, ftp://ftp-sop.inria.fr/epidaure/Publications/Malandain/krissian-cviu-2000.pdf.

[15] G. MALANDAIN, É. BARDINET, K. NELISSEN, W. VANDUFFEL. *Fusion of autoradiographs with an MR volume using 2-D and 3-D linear transformations*, in "NeuroImage", vol. 23, n^{o} 1, September 2004, p. 111–127, ftp://ftp-sop.inria.fr/epidaure/Publications/Malandain/malandain-neuroimage-2004.pdf.

[16] J. MONTAGNAT, H. DELINGETTE. *4D Deformable Models with temporal constraints : application to 4D cardiac image segmentation*, in "Medical Image Analysis", vol. 9, n^{o} 1, February 2005, p. 87–100, ftp://ftp-sop.inria.fr/epidaure/Publications/Delingette/montagnat-Media04.pdf.

[17] X. PENNEC, N. AYACHE, J.-P. THIRION. *Landmark-based registration using features identified through differential geometry*, in "Handbook of Medical Imaging", I. BANKMAN (editor), chap. 31, Academic Press, September 2000, p. 499-513, ftp://ftp-sop/epidaure/Publications/Pennec/Pennec.HMIP.pdf.

[18] X. PENNEC, P. CACHIER, N. AYACHE. *Tracking Brain Deformations in Time-Sequences of 3D US Images*, in "Pattern Recognition Letters - Special Issue on Ultrasonic Image Processing and Analysis", vol. 24, n^{o} 4-5, February 2003, p. 801–813, ftp://ftp-sop.inria.fr/epidaure/Publications/Pennec/Pennec.Cachier.Ayache.PattRecLetters02.pdf.

[19] G. PICINBONO, H. DELINGETTE, N. AYACHE. *Non-Linear Anisotropic Elasticity for Real-Time Surgery Simulation*, in "Graphical Models", vol. 65, n° 5, September 2003, p. 305–321, ftp://ftp-sop.inria.fr/epidaure/Publications/Delingette/Picinbono-GM03.pdf.

[20] S. PRIMA, S. OURSELIN, N. AYACHE. *Computation of the Mid-Sagittal Plane in 3D Brain Images*, in "IEEE Transaction on Medical Imaging", vol. 21, n° 2, February 2002, p. 122–138, ftp://ftp-sop.inria.fr/epidaure/Publications/Prima/tmi.final.pdf.

[21] D. REY, G. SUBSOL, H. DELINGETTE, N. AYACHE. *Automatic Detection and Segmentation of Evolving Processes in 3D Medical Images: Application to Multiple Sclerosis*, in "Medical Image Analysis", vol. 6, n° 2, June 2002, p. 163-179, ftp://ftp-sop.inria.fr/epidaure/Publications/Rey/rey-media-2002.pdf.

[22] A. ROCHE, G. MALANDAIN, N. AYACHE. *Unifying Maximum Likelihood Approaches in Medical Image Registration*, in "International Journal of Imaging Systems and Technology: Special Issue on 3D Imaging", vol. 11, n° 1, 2000, p. 71–80, ftp://ftp-sop.inria.fr/epidaure/Publications/Roche/ijist00.pdf.

[23] A. ROCHE, X. PENNEC, G. MALANDAIN, N. AYACHE. *Rigid Registration of 3D Ultrasound with MR Images: a New Approach Combining Intensity and Gradient Information*, in "IEEE Transactions on Medical Imaging", vol. 20, n° 10, October 2001, p. 1038–1049, ftp://ftp-sop.inria.fr/epidaure/Publications/Roche/Roche_MR_US_TMI_2001.pdf.

[24] M. SERMESANT, H. DELINGETTE, N. AYACHE. *An Electromechanical Model of the Heart for Image Analysis and Simulation*, in "IEEE Transactions in Medical Imaging", vol. 25, n° 5, 2007, p. 612–625, ftp://ftp-sop.inria.fr/asclepios/Publications/Maxime.Sermesant/TMI2006Sermesant.pdf.

[25] M. SERMESANT, C. FOREST, X. PENNEC, H. DELINGETTE, N. AYACHE. *Deformable biomechanical models: Application to 4D cardiac image analysis*, in "Medical Image Analysis", vol. 7, n° 4, December 2003, p. 475–488, http://authors.elsevier.com/sd/article/S1361841503000689.

Year Publications

Books and Monographs

[26] N. AYACHE, S. OURSELIN, A. MAEDER (editors). *Medical Image Computing and Computer-Assisted Intervention - MICCAI 2007 - Part I*, LNCS, vol. 4791, Springer, Brisbane, Australia, October 2007.

[27] N. AYACHE, S. OURSELIN, A. MAEDER (editors). *Medical Image Computing and Computer-Assisted Intervention - MICCAI 2007 - Part II*, LNCS, vol. 4792, Springer, Brisbane, Australia, October 2007.

Doctoral dissertations and Habilitation theses

[28] O. COMMOWICK. *Création et Utilisation d'Atlas Anatomiques Numériques pour la Radiothérapie (Design and Use of Anatomical Atlases for Radiotherapy)*, Thèse de sciences (PhD Thesis), Université de Nice – Sophia-Antipolis, February 2007, ftp://ftp-sop.inria.fr/asclepios/Publications/Olivier.Commowick/These.pdf.

[29] T. GLATARD. *Description, deployment and optimization of medical image analysis workflows on production grids*, Thèse de sciences (PhD Thesis), Université de Nice – Sophia-Antipolis, November 2007.

Articles in refereed journals and book chapters

[30] E. ANGELINI, O. CLATZ, E. MANDONNET, E. KONUKOGLU, L. CAPELLE, H. DUFFAU. *Glioma Dynamics and Computational Models: A Review of Segmentation, Registration, and In Silico Growth Algorithms and their Clinical Applications*, in "Current Medical Imaging Reviews,", vol. 3, 2007, p. 262-176, ftp://ftp-sop.inria.fr/asclepios/Publications/Olivier.Clatz/Angelini_Clatz_CMIR_2007.pdf.

[31] N. ARCHIP, O. CLATZ, S. WHALEN, P. BLACK, A. GOLBY, F. JOLESZ, S. WARFIELD. *Correction of geometric distortion effects on intra-operative MRI for enhanced visualization in image guided neurosurgery*, in "Neurosurgery", In press, 2008.

[32] N. ARCHIP, O. CLATZ, S. WHALEN, D. KACHER, A. FEDOROV, A. KOT, N. CHRISOCHOIDES, F. JOLESZ, A. GOLBY, P. BLACK, S. WARFIELD. *Non-rigid alignment of preoperative MRI, fMRI, and DT-MRI with intra-operative MRI for enhanced visualization and navigation in image-guided neurosurgery*, in "Neuroimage", vol. 35, n^{o} 2, April 2007, p. 609-24, ftp://ftp-sop.inria.fr/asclepios/Publications/Olivier.Clatz/Archip-Clatz-Neuroimage.pdf.

[33] M. A. AUDETTE, H. DELINGETTE, A. FUCHS, O. BURGERT, K. CHINZEI. *A topologically faithful, tissue-guided, spatially varying meshing strategy for computing patient-specific head models for endoscopic pituitary surgery simulation*, in "Journal of Computer Aided Surgery", vol. 12, n^{o} 1, January 2007, p. 43–52, http://www.informaworld.com/10.1080/10929080601167413.

[34] V. BECKER, T. VERCAUTEREN, C. H. VON WEYERN, C. PRINZ, R. M. SCHMID, A. MEINING. *High Resolution Miniprobe-based Confocal Microscopy in Combination with Video-mosaicing*, in "Gastrointestinal Endoscopy", vol. 66, n^{o} 5, November 2007, p. 1001–1007.

[35] J. BOISVERT, F. CHERIET, X. PENNEC, H. LABELLE, N. AYACHE. *Principal Deformations Modes of Articulated Models for the Analysis of 3D Spine Deformities*, in "Electronic Letters on Computer Vision and Image Analysis", Submitted, 2007.

[36] J. BOISVERT, F. CHERIET, X. PENNEC, H. LABELLE, N. AYACHE. *Geometric Variability of the Scoliotic Spine Using Statistics on Articulated Shape Models*, in "IEEE Trans. Medical Imaging", In press, 2008, ftp://ftp-sop.inria.fr/asclepios/Publications/Xavier.Pennec/Boisvert.TMI08.pdf.

[37] O. CLATZ, S. LITRICO, H. DELINGETTE, P. PAQUIS, N. AYACHE. *Dynamic Model of Communicating Hydrocephalus for Surgery Simulation*, in "IEEE Transactions on Biomedical Engineering", vol. 54, n^{o} 4, April 2007, p. 755-758, ftp://ftp-sop.inria.fr/epidaure/Publications/Clatz/hydrocephalus_clatz.pdf.

[38] J. DAUGUET, T. DELZESCAUX, F. CONDÉ, J.-F. MANGIN, N. AYACHE, P. HANTRAYE, V. FROUIN. *Three-dimensional reconstruction of stained histological slices and 3D non-linear registration with in-vivo MRI for whole baboon brain*, in "Journal of Neuroscience Methods", vol. 164, 2007, p. 191-204, ftp://ftp-sop.inria.fr/asclepios/Publications/Julien.Dauguet/dauguet07.pdf.

[39] H. DELINGETTE. *Triangular Springs for Modeling Nonlinear Membranes*, in "IEEE Transactions on Visualisation and Computer Graphics", To appear, vol. 14, n^{o} 2, March/April 2008, ftp://ftp-sop.inria.fr/asclepios/Publications/Herve.Delingette/tvcg-membrane.pdf.

[40] D. DUCREUX, P. FILLARD, D. FACON, A. OZANNE, J.-F. LEPEINTRE, J. RENOUX, M. TADIÉ, P. LASJAUNIAS. *Diffusion Tensor Magnetic Resonance Imaging and Fiber Tracking in Spinal Cord Lesions: Current and Future Indications*, in "Neuroimaging Clinics of North America", vol. 17, n^{o} 1, February 2007, p. 137-147.

[41] P. FILLARD, V. ARSIGNY, X. PENNEC, N. AYACHE. *Clinical DT-MRI Estimation, Smoothing and Fiber Tracking with Log-Euclidean Metrics*, in "IEEE Transactions on Medical Imaging", In Press, 2007, ftp://ftp-sop.inria.fr/asclepios/Publications/Pierre.Fillard/Fillard.TMI.2007.pdf.

[42] P. FILLARD, V. ARSIGNY, X. PENNEC, K. M. HAYASHI, P. M. THOMPSON, N. AYACHE. *Measuring Brain Variability by Extrapolating Sparse Tensor Fields Measured on Sulcal Lines*, in "Neuroimage", Also as INRIA Research Report 5887, April 2006. PMID: 17113311, vol. 34, n^{o} 2, January 2007, p. 639–650, ftp://ftp-sop.inria.fr/asclepios/Publications/Pierre.Fillard/Fillard.Neuroimage.2006.pdf.

[43] T. GLATARD, J. MONTAGNAT, D. EMSELLEM, D. LINGRAND. *A Service-Oriented Architecture enabling dynamic services grouping for optimizing distributed workflows execution*, in "Future Generation Computer Systems", To appear, 2008.

[44] T. GLATARD, J. MONTAGNAT, D. LINGRAND, X. PENNEC. *Flexible and efficient workflow deployment of data-intensive applications on GRIDS with MOTEUR*, in "International Journal of High Performance Computing Applications", To appear in the special issue on Workflow Systems in Grid Environments, 2007, http://www.i3s.unice.fr/~glatard/docs/ijhpca.pdf.

[45] M. G. LINGURARU, M. A. GONZÁLEZ BALLESTER, N. AYACHE. *Deformable Atlases for the Segmentation of Internal Brain Nuclei in Magnetic Resonance Imaging*, in "Acta Universitatis Cibiniensis, Technical Series", vol. 2, n^{o} 1, 2007, p. 26-36, ftp://ftp-sop.inria.fr/epidaure/Publications/Gonzalez/Linguraru:Acta:2004.pdf.

[46] G. MALANDAIN. *Applications de la géométrie discrète en imagerie médicale*, in "Géométrie discrète et images numériques", Traités IC2, Hermès, 2007, p. 371–379.

[47] X. PENNEC, P. FILLARD. *Les autoroutes de l'information neuronale*, in "Voir l'invisible", Omniscience, 2007.

[48] X. PENNEC, P. FILLARD. *Avons-nous tous le meme cerveau.*, in "Voir l'invisible", Omniscience, 2007.

[49] J.-M. PEYRAT, M. SERMESANT, X. PENNEC, H. DELINGETTE, C. XU, E. R. MCVEIGH, N. AYACHE. *A Computational Framework for the Statistical Analysis of Cardiac Diffusion Tensors: Application to a Small Database of Canine Hearts*, in "IEEE Transactions on Medical Imaging", vol. 26, n^{o} 11, November 2007, p. 1500-1514, ftp://ftp-sop.inria.fr/asclepios/Publications/Jean-Marc.Peyrat/Peyrat_2007_TMI.pdf.

[50] A. PITIOT, H. DELINGETTE, P. THOMPSON. *Learning Shape Correspondence for n-D curves*, in "International Journal of Computer Vision", vol. 71, n^{o} 1, January 2007, p. 71-88.

[51] M. REYES, G. MALANDAIN, P. M. KOULIBALY, M. A. GONZALEZ-BALLESTER, J. DARCOURT. *Model-based respiratory motion compensation for emission tomography image reconstruction*, in "Phys Med Biol", vol. 52, n^{o} 12, June 2007, p. 3579-600, ftp://ftp-sop.inria.fr/asclepios/Publications/Gregoire.Malandain/reyes-pmb-2007.pdf.

[52] L. THIBERVILLE, S. MORENO-SWIRC, T. VERCAUTEREN, E. PELTIER, C. CAVÉ, G. BOURG HECKLY. *In Vivo Imaging of the Bronchial Wall Microstructure Using Fibered Confocal Fluorescence Microscopy*, in "Am. J. Respir. Crit. Care Med.", Chosen for the cover of the AJRCCM paper issue. PMID: 17023733, vol. 175, n^{o} 1, January 2007, p. 22–31, http://ajrccm.atsjournals.org/cgi/content/abstract/175/1/22.

[53] T. VERCAUTEREN, X. PENNEC, A. PERCHANT, N. AYACHE. *Diffeomorphic Demons Using ITK's Finite Difference Solver Hierarchy*, in "Insight Journal – ISC/NA-MIC Workshop on Open Science at MICCAI 2007", Source code available online, October 2007, http://insight-journal.org/midas/handle.php?handle=1926/510.

[54] T. VERCAUTEREN, A. PERCHANT, N. AYACHE. *In Vivo Microscopy for Real-Time Structural and Functional Cellular Imaging*, in "ERCIM News", vol. 69, April 2007, p. 34–35, ftp://ftp-sop.inria.fr/asclepios/Publications/Tom.Vercauteren/InVivoMicroscopy-ERCIMNews07-Vercauteren.pdf.

[55] J. YELNIK, E. BARDINET, D. DORMONT, G. MALANDAIN, S. OURSELIN, D. TANDE, C. KARACHI, N. AYACHE, P. CORNU, Y. AGID. *A three-dimensional, histological and deformable atlas of the human basal ganglia. I. Atlas construction based on immunohistochemical and MRI data*, in "Neuroimage", vol. 34, n^{o} 2, January 2007, p. 618-38.

Publications in Conferences and Workshops

[56] J. ALLARD, S. COTIN, F. FAURE, P.-J. BENSOUSSAN, F. POYER, C. DURIEZ, H. DELINGETTE, L. GRISONI. *SOFA : an Open Source Framework for Medical Simulation*, in "Studies in health technology and informatics, Medicine Meets Virtual Reality (MMVR)", 2007, p. 13–18, http://www.sofa-framework.org/docs/SOFA_MMVR07.pdf.

[57] N. AYACHE, O. CLATZ, H. DELINGETTE, G. MALANDAIN, X. PENNEC, M. SERMESANT. *Asclepios: a Research Project at INRIA for the Analysis and Simulation of Biomedical Images*, in "Proceedings of the Colloquium in Memory of Gilles Kahn", LNCS, In press (20 pages)., Springer, 2007, ftp://ftp-sop.inria.fr/asclepios/Publications/Nicholas.Ayache/Colloquium-Gilles-Kahn-NA-2007.v2.pdf.

[58] V. BECKER, T. VERCAUTEREN, C. H. VON WEYERN, C. PRINZ, R. M. SCHMID, A. MEINING. *Ultrahochauflösende, Sondenbasierte, Konfokale Lasermikroskopie in Kombination mit Videomosaicing*, in "62. Jahrestagung der Deutschen Gesellschaft für Verdauungs- und Stoffwechselkrankheiten, Bochum, Germany", Zeitschrift für Gastroenterologie, Abstract only, vol. 45(8), August 2007, http://www.thieme-connect.com/ejournals/abstract/zfg/doi/10.1055/s-2007-988304.

[59] C. BRUN, N. LEPORE, X. PENNEC, Y.-Y. CHOU, O. L. LOPEZ, H. J. AIZENSTEIN, A. W. BECKER, P. M. THOMPSON. *Comparison of Standard and Riemannian Fluid Registration for Tensor-Based Morphometry in HIV/AIDS*, in "Proc. of MICCAI'07 Workshop on Statistical Registration: Pair-wise and Group-wise Alignment and Atlas Formation, Brisbane, Australia", 2007, ftp://ftp-sop.inria.fr/asclepios/Publications/Xavier.Pennec/Brun.MICCAI07.RegistrationWorkshop.pdf.

[60] F. J. S. CASTRO, O. CLATZ, J. DAUGUET, N. ARCHIP, J.-P. THIRAN, S. WARFIELD. *Evaluation Of Brain Image Nonrigid Registration Algorithms Based on Log-Euclidean MR-DTI Consistency Measures*, in "Proceedings of IEEE International Symposium on Biomedical Imaging: From Nano to Macro (ISBI'07), Metro Washington DC, USA", 2007, p. 45-48, ftp://ftp-sop.inria.fr/epidaure/Publications/Clatz/ISBI_sanchez.pdf.

[61] P. CHINCHAPATNAM, K. RHODE, A. KING, G. GAO, Y. MA, T. SCHAEFFTER, D. HAWKES, R. RAZAVI, D. HILL, S. ARRIDGE, M. SERMESANT. *Anisotropic Wave Propagation and Apparent Conductivity Estimation in a Fast Electrophysiological Model: Application to XMR Interventional Imaging*, in "Proc. Medical Image Computing and Computer Assisted Intervention (MICCAI'07), Brisbane, Australia", N. AYACHE, S. OURSELIN, A. MAEDER (editors), LNCS, vol. 4791, Springer, October 2007, p. 575-583, ftp://ftp-sop.inria.fr/asclepios/Publications/Maxime.Sermesant/ChinchapatnamMICCAI07.pdf.

[62] O. COMMOWICK, G. MALANDAIN. *Efficient Selection of the Most Similar Image in a Database for Critical Structures Segmentation*, in "Proc. Medical Image Computing and Computer Assisted Intervention (MICCAI'07), Part II, Brisbane, Australia", N. AYACHE, S. OURSELIN, A. MAEDER (editors), LNCS, n^{O} 4792, October 2007, p. 203–210, ftp://ftp-sop.inria.fr/asclepios/Publications/Olivier.Commowick/CommowickMiccai2007.pdf.

[63] M. COSTA, H. DELINGETTE, N. AYACHE. *Automatic Segmentation of the Bladder Using Deformable Models*, in "Proceedings of IEEE International Symposium on Biomedical Imaging: From Nano to Macro (ISBI'07), Metro Washington DC, USA", 2007, p. 904-907, ftp://ftp-sop.inria.fr/epidaure/Publications/Costa/Costa.ISBI.2007.pdf.

[64] J. COSTA, H. DELINGETTE, S. NOVELLAS, N. AYACHE. *Automatic Segmentation of Bladder and Prostate Using Coupled 3D Deformable Models.*, in "Proc. Medical Image Computing and Computer Assisted Intervention (MICCAI'07), Brisbane, Australia", N. AYACHE, S. OURSELIN, A. MAEDER (editors), LNCS, vol. 4791, Springer, October 2007, p. 252-260, ftp://ftp-sop.inria.fr/epidaure/Publications/Costa/Costa.Miccai.2007.pdf.

[65] H. DELINGETTE, M. SERMESANT, J.-M. PEYRAT, N. AYACHE, K. RHODE, R. RAZAVI, E. MCVEIGH, D. CHAPELLE, J. SAINTE-MARIE, P. MOIREAU, M. FERNANDEZ, J.-F. GERBEAU, K. DJABELLA, Q. ZHANG, M. SORINE. *CardiosSense3D: Patient-Specific Cardiac Simulation*, in "Proceedings of IEEE International Conference on Biomedical Imaging: From Nano to Macro (ISBI'07), Metro Washington DC, USA", 12-15 April 2007, p. 628-631, http://www.ieeexplore.ieee.org/xpls/abs_all.jsp?isnumber=4193197&arnumber=4193364&count=356&index=166.

[66] S. DURRLEMAN, X. PENNEC, A. TROUVÉ, N. AYACHE. *Measuring Brain Variability via Sulcal Lines Registration: a Diffeomorphic Approach*, in "Proc. Medical Image Computing and Computer Assisted Intervention (MICCAI), Brisbane, Australia", N. AYACHE, S. OURSELIN, A. MAEDER (editors), LNCS, vol. 4791, Springer, October 2007, p. 675-682, ftp://ftp-sop.inria.fr/asclepios/Publications/Stanley.Durrleman/306_Durrleman.pdf.

[67] F. FAURE, J. ALLARD, S. COTIN, P. NEUMANN, P.-J. BENSOUSSAN, C. DURIEZ, H. DELINGETTE, L. GRISONI. *SOFA: A Modular Yet Efficient Simulation Framework*, in "Surgetica", 2007, http://www-evasion.imag.fr/Publications/2007/FACNBDDG07.

[68] P. FILLARD, X. PENNEC, P. THOMPSON, N. AYACHE. *Evaluating Brain Anatomical Correlations via Canonical Correlation Analysis of Sulcal Lines*, in "Proc. of MICCAI'07 Workshop on Statistical Registration: Pair-wise and Group-wise Alignment and Atlas Formation, Brisbane, Australia", 2007, ftp://ftp-sop.inria.fr/asclepios/Publications/Pierre.Fillard/Fillard.MICCAI07.RegistrationWorkshop.pdf.

[69] T. GLATARD, D. LINGRAND, J. MONTAGNAT, M. RIVEILL. *Impact of the execution context on Grid job performances*, in "International Workshop on Context-Awareness and Mobility in Grid Computing (WCAMG07), Rio de Janeiro", IEEE, May 2007, p. 713–718, http://www.i3s.unice.fr/~johan/publis/WCAMG07.pdf.

[70] T. GLATARD, J. MONTAGNAT, X. PENNEC. *Optimizing jobs timeouts on clusters and production grids*, in "International Symposium on Cluster Computing and the Grid (CCGrid), Rio de Janeiro", IEEE, May 2007, p. 100-107, http://www.i3s.unice.fr/~glatard/publis/ccgrid07.pdf.

[71] H. HUFNAGEL, X. PENNEC, J. EHRHARDT, N. AYACHE, H. HANDELS. *Comparison of Statistical Shape Models Built on Correspondence Probabilities and One-to-One Correspondences*, in "SPIE Symposium on Medical Imaging '08, San Diego, USA", To appear, February 2008.

[72] H. HUFNAGEL, X. PENNEC, J. EHRHARDT, H. HANDELS, N. AYACHE. *Point-Based Statistical Shape Models with Probabilistic Correspondences and Affine EM-ICP*, in "Bildverarbeitung fuer die Medizin 2007", Informatik aktuell, Third prize in category best scientific work., Springer, March 2007, ftp://ftp-sop.inria.fr/asclepios/Publications/Heike.Hufnagel/huf_bvm07.pdf.

[73] H. HUFNAGEL, X. PENNEC, J. EHRHARDT, H. HANDELS, N. AYACHE. *Shape Analysis Using a Point-Based Statistical Shape Model Built on Correspondence Probabilities*, in "Proc. Medical Image Computing and Computer Assisted Intervention (MICCAI'07), Brisbane, Australia", N. AYACHE, S. OURSELIN, A. MAEDER (editors), LNCS, vol. 4791, Springer, October 2007, p. 959-967, ftp://ftp-sop.inria.fr/asclepios/Publications/Heike.Hufnagel/huf_miccai07.pdf.

[74] A. ISAMBERT, V. GREGOIRE, F. BIDAULT, G. CALAIS, O. COMMOWICK, G. MALANDAIN, J. RUAUD, M. TOMSEJ, C. BRAMOULLE, J. BOURHIS, D. LEFKOPOULOS. *Atlas-based automatic segmentation (ABAS) of head and neck (H&N) structures in conformal radiotherapy (CRT): atlas development and preliminary results in clinical context*, in "Acts of the 26th European Society for Therapeutic Radiology and Oncology (ESTRO 2007)", 2007.

[75] E. KONUKOGLU, O. CLATZ, P.-Y. BONDIAU, M. SERMESANT, H. DELINGETTE, N. AYACHE. *Towards an Identification of Tumor Growth Parameters from Time Series of Images*, in "Proc. Medical Image Computing and Computer Assisted Intervention (MICCAI), Brisbane, Australia", N. AYACHE, S. OURSELIN, A. MAEDER (editors), LNCS, vol. 4791, Springer, October 2007, p. 549-556, ftp://ftp-sop.inria.fr/asclepios/Publications/Ender.Konukoglu/Konukoglu_701.pdf.

[76] E. KONUKOGLU, M. SERMESANT, O. CLATZ, J.-M. PEYRAT, H. DELINGETTE, N. AYACHE. *A Recursive Anisotropic Fast Marching Approach to Reaction Diffusion Equation: Application to Tumor Growth Modeling*, in "Proceedings of the 20th International Conference on Information Processing in Medical Imaging (IPMI'07)", LNCS, vol. 4584, 2-6 July 2007, p. 686-699, ftp://ftp-sop.inria.fr/asclepios/Publications/Ender.Konukoglu/ipmi_2007_konukoglu-color.pdf.

[77] J. L. LANDABASO, T. MANSI, C. MOLINA, K. ZANGELIN, P. ENFEDAQUE, J. CANADAS, L. LIZCANO. *A 3D Videoconferencing System with 2D Backwards Compatibility*, in "3DTV Conference 2007", 2007.

[78] N. LEPORE, C. BRUN, X. PENNEC, Y.-Y. CHOU, O. L. LOPEZ, H. J. AIZENSTEIN, J. T. BECKER, A. W. TOGA, P. M. THOMPSON. *Mean Template for Tensor-Based Morphometry using Deformation Tensors*, in "Proc. Medical Image Computing and Computer Assisted Intervention (MICCAI'07), Brisbane, Australia", N. AYACHE, S. OURSELIN, A. MAEDER (editors), LNCS, vol. 4792, Springer, October 2007, p. 826-833, ftp://ftp-sop.inria.fr/asclepios/Publications/Xavier.Pennec/Lepore_MICCAI07.pdf.

[79] C. NEMO, T. GLATARD, M. BLAY-FORNARINO, J. MONTAGNAT. *Merging overlapping orchestrations: an application to the Bronze Standard medical application*, in "International Conference on Services Computing (SCC 2007), Salt Lake City, Utah, USA", IEEE Computer Engineering, July 2007, http://www.i3s.unice.fr/~johan/publis/SCC07.pdf.

[80] A. PERCHANT, T. VERCAUTEREN, F. OBERRIETTER, N. SAVOIRE, N. AYACHE. *Region Tracking Algorithms on Laser Scanning Devices Applied to Cell Traffic Analysis*, in "Proceedings of IEEE International Sym-

posium on Biomedical Imaging: From Nano to Macro (ISBI'07), Metro Washington DC, USA", April 2007, p. 260–263, ftp://ftp-sop.inria.fr/asclepios/Publications/Tom.Vercauteren/RegionTrackingCellTraffic-ISBI07-Perchant.pdf.

[81] J.-M. PEYRAT, M. SERMESANT, H. DELINGETTE, X. PENNEC, C. XU, E. MCVEIGH, N. AYACHE. *Statistical Comparison of Cardiac Fibre Architectures*, in "Proceedings of Functional Imaging and Modeling of the Heart 2007 (FIMH'07)", LNCS, vol. 4466, 7-9 June 2007, p. 413-423, ftp://ftp-sop.inria.fr/asclepios/Publications/Jean-Marc.Peyrat/Peyrat_2007_FIMH.pdf.

[82] M. POP, M. SERMESANT, D. CHUNG, G. LIU, E. MCVEIGH, E. CRYSTAL, G. WRIGHT. *An experimental framework to validate 3D models of cardiac electrophysiology via optical imaging and MRI*, in "Proceedings of Functional Imaging and Modeling of the Heart 2007 (FIMH'07)", LNCS, vol. 4466, 7-9 June 2007, p. 100-109, ftp://ftp-sop.inria.fr/asclepios/Publications/Maxime.Sermesant/FIMH2007Pop.pdf.

[83] M. REYES AGUIRRE, M. LINGURARU, K. MARIAS, N. AYACHE, L.-P. NOLTE, M. A. GONZÁLEZ BALLESTER. *Statistical Shape Analysis via Principal Factor Analysis*, in "Proceedings of IEEE International Symposium on Biomedical Imaging, Metro Washington DC, USA", 2007, p. 1216-1219, ftp://ftp-sop.inria.fr/asclepios/Publications/Mauricio.Reyes/reyes_ISBI07.pdf.

[84] M. SERMESANT, E. KONUKOGLU, H. DELINGETTE, Y. COUDIERE, P. CHINCHAPATNAM, K. RHODE, R. R. ZAVI, N. AYACHE. *An anisotropic multi-front fast marching method for real-time simulation of cardiac electrophysiology*, in "Proceedings of Functional Imaging and Modeling of the Heart 2007 (FIMH'07)", LNCS, vol. 4466, 7-9 June 2007, p. 160-169, ftp://ftp-sop.inria.fr/asclepios/Publications/Maxime.Sermesant/FIMH2007Sermesant.pdf.

[85] J.-C. SOUPLET, C. LEBRUN, P. CLAVELOU, W. CAMU, S. CHANALET, N. AYACHE, G. MALANDAIN. *A comparative study of skull stripping methods in relapsing-remitting multiple sclerosis: Emergence of a new automatic segmentation algorithm*, in "Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS), Prague, Czech Republic", October 2007, ftp://ftp-sop.inria.fr/asclepios/Publications/Jean-Christophe.Souplet/Souplet_2007_ECTRIMS_Skullstripping.pdf.

[86] J.-C. SOUPLET, C. LEBRUN, P. FILLARD, N. AYACHE, P. CLAVELOU, G. MALANDAIN. *SepINRIA : un outil d'évaluation de la charge lésionnelle chez des patients atteints de sclérose en plaques*, in "Journées Internationales de la SFN : Sclérose en Plaques (Multiple Sclerosis), Paris, France", Abstract in Revue Neurologique (Paris) 2007; 163: 6-7, 725, June 2007, ftp://ftp-sop.inria.fr/asclepios/Publications/Jean-Christophe.Souplet/Souplet_2007_SFN_SepINRIA.pdf.

[87] N. TOUSSAINT, M. SERMESANT, P. FILLARD. *vtkINRIA3D: A VTK Extension for Spatiotemporal Data Synchronization, Visualization and Management*, in "Proc. of Workshop on Open Source and Open Data for MICCAI, Brisbane, Australia", October 2007, ftp://ftp-sop.inria.fr/asclepios/Publications/Pierre.Fillard/Fillard.MICCAI07.OpenWorkshop.pdf.

[88] N. TOUSSAINT, J. SOUPLET, P. FILLARD. *MedINRIA: Medical Image Navigation and Research Tool by INRIA*, in "Proc. of MICCAI'07 Workshop on Interaction in medical image analysis and visualization, Brisbane, Australia", 2007, ftp://ftp-sop.inria.fr/asclepios/Publications/Pierre.Fillard/Fillard.MICCAI07.InteractionWorkshop.pdf.

[89] T. VERCAUTEREN, A. OSDOIT, A. PERCHANT, S. LOISEAU. *Mosaicing of Confocal Microscopic Video Sequences: Larger Field of View and still Higher Resolution!*, in "Proc. Digestive Disease Week (DDW'07),

Washington, DC", Gastrointestinal Endoscopy, Abstract only, vol. 65(5), April 2007, AB352, ftp://ftp-sop.inria.fr/asclepios/Publications/Tom.Vercauteren/MosaicingPoster-DDW07-Vercauteren.pdf.

[90] T. VERCAUTEREN, X. PENNEC, E. MALIS, A. PERCHANT, N. AYACHE. *Insight Into Efficient Image Registration Techniques and the Demons Algorithm*, in "Proc. Information Processing in Medical Imaging (IPMI'07), Kerkrade, The Netherlands", Lecture Notes in Computer Science, vol. 4584, Springer-Verlag, July 2007, p. 495–506, ftp://ftp-sop.inria.fr/asclepios/Publications/Tom.Vercauteren/InsightEffRegDemons-IPMI07-Vercauteren.pdf.

[91] T. VERCAUTEREN, X. PENNEC, A. PERCHANT, N. AYACHE. *Non-parametric Diffeomorphic Image Registration with the Demons Algorithm*, in "Proc. Medical Image Computing and Computer Assisted Intervention (MICCAI'07), Brisbane, Australia", N. AYACHE, S. OURSELIN, A. J. MAEDER (editors), Lecture Notes in Computer Science, vol. 4792, Springer-Verlag, October 2007, p. 319–326, ftp://ftp-sop.inria.fr/asclepios/Publications/Tom.Vercauteren/DiffeoDemons-MICCAI07-Vercauteren.pdf.

Internal Reports

[92] C. BASSO, Y. BOUDJEMLINE, S. DURRLEMAN, E. KONUKOGLU, T. MANSI, X. PENNEC, G. PONGIGLIONE, M. SANTORO, M. SERMESANT, B. STOS, N. TOUSSAINT, G. TROCCHIO. *First generation disease models: Image analysis tools, pediatric heart diseases, inflammatory diseases and brain tumors*, Deliverables D11.2, European project Health-e-Child (IST-2004-027749), June 2007, http://www-sop.inria.fr/asclepios/projects/hec/.

[93] P. FILLARD, X. PENNEC, P. M. THOMPSON, N. AYACHE. *Evaluating Brain Anatomical Correlations via Canonical Correlation Analysis of Sulcal Lines*, Research Report, n^{o} 6241, INRIA, 07 2007, https://hal.inria.fr/inria-00159699.

Miscellaneous

[94] C. LEBRUN, S. CHANALET, J.-C. SOUPLET, N. AYACHE, G. MALANDAIN. *Imaging pre-treatment tools and automatic segmentation of lesion burden*, June 2007, Presented in Journées Internationales de la Société Française de Neurologie.

[95] X. PENNEC. *From Riemannian Geometry to Computational Anatomy of the Brain*, ErcimNews 69, special issue Digital patient, January 2007, http://ercim-news.ercim.org/images/stories/EN69/EN69.pdf.

[96] T. VERCAUTEREN, A. PERCHANT, N. AYACHE, X. PENNEC, G. MALANDAIN. *Robust Mosaicing Method with Correction of Motion Distorsions and Tissue Deformations for In Vivo Fibered Microscopy*, August 2007, US patent filing (02/08/2007).

References in notes

[97] J. S. DUNCAN, G. GERIG (editors). *Medical Image Computing and Computer-Assisted Intervention (MICCAI'05), Part I*, LNCS, vol. 3749, Springer, Palm Springs, CA, USA, october 2005.

[98] J. S. DUNCAN, G. GERIG (editors). *Medical Image Computing and Computer-Assisted Intervention (MICCAI'05), Part II*, LNCS, vol. 3750, Springer, Palm Springs, CA, USA, october 2005.

[99] IEEE (editor). *International Symposium on Biomedical Imaging: From Nano to Macro*, IEEE, Arlington, VA, USA, april 2004.

[100] R. H. TAYLOR, S. LAVALLÉE, G. S. BURDEA, R. MÖSGES (editors). *Computer-Integrated Surgery: Technology and Clinical Applications*, MIT Press, 1995.

[101] S. WEBB (editor). *The Physics of Medical Imaging*, Institute of Physics Publishing, 1988.

[102] *The international journal of Medical Robotics + Computer Assisted Surgery*, Wiley.

[103] N. AYACHE, J. DUNCAN (editors). *Medical Image Analysis*, Elsevier.

[104] W. VANNIER, M. VIERGEVER (editors). *Transactions on Medical Imaging*, IEEE.

[105] R. ACHARYA, R. WASSERMAN, J. STEVENS, C. HINOJOSA. *Biomedical Imaging modalities: a tutorial*, in "Computerized Medical Imaging and Graphics", vol. 19, n^{o} 1, 1995, p. 3–25.

[106] P. ALLEN. *Brain Atlas Project*, 2003, http://brain-map.org/welcome.do;jsessionid=1DB51DDFDE6BEC143CE5005682B62003.

[107] L. AXEL, A. MONTILLO, D. KIM. *Tagged magnetic resonance imaging of the heart: a survey*, in "Medical Image Analysis", vol. 9, n^{o} 4, 2005, p. 376–393.

[108] N. AYACHE. *L'analyse automatique des images médicales, état de l'art et perspectives*, in "Annales de l'Institut Pasteur", numéro spécial sur les progrès récents de l'imagerie médicale, vol. 9, n^{o} 1, avril–juin 1998, p. 13–21.

[109] P. BARBIER DE REUILLE, I. BOHN-COURSEAU, K. LJUNG, H. MORIN, N. CARRARO, C. GODIN, J. TRAAS. *Computer simulations reveal novel properties of the cell-cell signaling network at the shoot apex in Arabidopsis*, in "PNAS", vol. 103, n^{o} 5, 2006, p. 1627–1632.

[110] E. BARDINET, D. DORMONT, G. MALANDAIN, M. BHATTACHARJEE, B. PIDOUX, C. SALEH, P. CORNU, N. AYACHE, Y. AGID, J. YELNIK. *Retrospective cross-evaluation of an histological and deformable 3D atlas of the basal ganglia on series of Parkinsonian patients treated by deep brain stimulation (DBS)*, in "Proceedings of MICCAI'05, Palm Springs, California", J. DUNCAN, G. GERIG (editors), LNCS, vol. 3750, Springer Verlag, 2005, p. 385–393, ftp://ftp-sop.inria.fr/epidaure/Publications/Malandain/bardinet-miccai-2005.pdf.

[111] M. BELIK, T. USYK, A. MCCULLOCH. *Computational Methods for Cardiac Electrophysiology*, in "Computational Models for the Human Body", N. AYACHE (editor), Elsevier, 2004, p. 129–187.

[112] O. CLATZ, H. DELINGETTE, I.-F. TALOS, A. J. GOLBY, R. KIKINIS, F. JOLESZ, N. AYACHE, S. WARFIELD. *Robust Non-Rigid Registration to Capture Brain Shift from Intra-Operative MRI*, in "IEEE Transactions on Medical Imaging", vol. 24, n^{o} 11, Nov. 2005, p. 1417-1427, ftp://ftp-sop.inria.fr/epidaure/Publications/Clatz/TMI_intraoperative_clatz.pdf.

[113] I. L. DRYDEN, K. V. MARDIA. *Statistical Shape Analysis*, John Wiley and Sons, 1998.

[114] J. DUNCAN, N. AYACHE. *Medical Image Analysis: Progress over two decades and the challenges ahead*, in "IEEE Transactions on Pattern Analysis and Machine Intelligence", vol. 22, n^{o} 1, 2000, p. 85–106.

[115] P. FILLARD, V. ARSIGNY, X. PENNEC, KIRALEE M. HAYASHI, PAUL M. THOMPSON, N. AYACHE. *Measuring Brain Variability by Extrapolating Sparse Tensor Fields Measured on Sulcal Lines*, in "Neuroimage", Also as INRIA Research Report 5887, April 2006. PMID: 17113311, vol. 34, n^{o} 2, January 2007, p. 639–650, ftp://ftp-sop.inria.fr/asclepios/Publications/Pierre.Fillard/Fillard.Neuroimage.2006.pdf.

[116] N. C. FOX, J. M. SCHOTT. *Imaging cerebral atrophy: normal ageing to Alzheimer's disease*, in "Lancet", vol. 363, n^{o} 9406, 2004.

[117] A. F. FRANGI, W. J. NIESSEN, M. A. VIERGEVER. *Three-dimensional modeling for functional analysis of cardiac images: a review*, in "IEEE Trans Med Imaging", vol. 20, n^{o} 1, January 2001, p. 2-25.

[118] P. C. FRANZONE, L. GUERRI, M. PENNACHIO, B. TACCARDI. *Spread of excitation in 3-D models of the anisotropic cardiac tissue*, in "Mathematical Biosciences", vol. 151, 1988, p. 51–98.

[119] S. GRANGER, X. PENNEC. *Multi-scale EM-ICP: A Fast and Robust Approach for Surface Registration*, in "European Conference on Computer Vision (ECCV 2002), Copenhagen, Denmark", A. HEYDEN, G. SPARR, M. NIELSEN, P. JOHANSEN (editors), LNCS, vol. 2353, Springer, 2002, p. 418–432, ftp://ftp-sop.inria.fr/epidaure/Publications/Granger/eccv-2002.pdf.

[120] P. HUNTER, T. BORG. *Integration from proteins to organs: the Physiome project*, in "Nature Reviews - Molecular Cell Biology", vol. 4, 2003, p. 237–243.

[121] P. HUNTER. *Computational Physiology and the Physiome Project*, 2004, http://nbcr.sdsc.edu/mcmregistration/pdf/Peter_Hunter.pdf.

[122] C. MACAULAY, P. LANE, R. RICHARDS-KORTUM. *In vivo pathology: microendoscopy as a new endoscopic imaging modality*, in "Gastrointestinal Endoscopy Clinics of North America", vol. 14, 2004, p. 595–620.

[123] D. METAXAS, J. KAYES, F. PRIMANIO. *A 3-D virtual environment for modeling mechanical cardiopulmonary interactions*, in "Medical Image Analysis", vol. 3, n^{o} 1, 1997, p. 1–26.

[124] M. I. MILLER. *Computational anatomy: shape, growth, and atrophy comparison via diffeomorphisms*, in "NeuroImage", Special Issue : Mathematics in Brain Imaging, vol. 23, n^{o} Supplement 1, 2004, p. S19–S33.

[125] V. MOREAU-VILLÉGER, H. DELINGETTE, M. SERMESANT, O. FARIS, E. MCVEIGH, N. AYACHE. *Global and Local Parameter Estimation of a Model of the Electrical Activity of the Heart*, Research Report, n^{o} 5269, INRIA, July 2004, http://hal.inria.fr/inria-00070729.

[126] NIH. *Alzheimer's Disease Neuroimaging Initiative*, 2004.

[127] S. NICOLAU, A. GARCIA, X. PENNEC, L. SOLER, N. AYACHE. *An augmented reality system to guide radio-frequency tumour ablation*, in "Computer Animation and Virtual World (previously the Journal of Visualization & Computer Animation)", vol. 16, n^{o} 1, 2005, p. 1–10, ftp://ftp-sop.inria.fr/epidaure/Publications/Pennec/Nicolau.CAVW.pdf.

[128] S. NICOLAU, X. PENNEC, L. SOLER, N. AYACHE. *A complete Augmented Reality Guidance System for Liver Punctures: First Clinical Evaluation*, in "Proceedings of the 8th Int. Conf. on Medical Image Computing and Computer-Assisted Intervention - MICCAI 2005, Part I, Palm Springs, CA, USA, October 26-29", J.

DUNCAN, G. GERIG (editors), LNCS, vol. 3749, Springer Verlag, 2005, p. 539–547, http://springerlink.metapress.com/openurl.asp?genre=article&issn=0302-9743&volume=3749&spage=539.

[129] D. NOBLE. *Modeling the Heart, from genes to cells to the whole organ*, in "Science", vol. 295, 2002, p. 1678–1682.

[130] J. OLIVO-MARIN. *Image Formation and Analysis in Microscopy*, 2004.

[131] X. PENNEC, P. FILLARD, N. AYACHE. *A Riemannian Framework for Tensor Computing*, in "International Journal of Computer Vision", A preliminary version appeared as INRIA Research Report 5255, July 2004., vol. 66, n^{o} 1, January 2006, p. 41–66, ftp://ftp-sop.inria.fr/epidaure/Publications/Pennec/Pennec.IJCV05.pdf.

[132] J.-M. PEYRAT, M. SERMESANT, H. DELINGETTE, X. PENNEC, C. XU, E. MCVEIGH, N. AYACHE. *Towards a Statistical Atlas of Cardiac Fiber Structure*, in "Proc. of the 9th International Conference on Medical Image Computing and Computer Assisted Intervention (MICCAI'06), Part I", LNCS, vol. 4190, Springer Verlag, 2-4 October 2006, p. 297–304, ftp://ftp-sop.inria.fr/epidaure/Publications/Peyrat/Peyrat_MICCAI_2006.pdf.

[133] A. QUARTERONI, L. FORMAGGIA. *Mathematical Modeling and Numerical Simulation of the Cardiovascular System*, in "Computational Models for the Human Body", N. AYACHE (editor), Elsevier, 2004, p. 3–128.

[134] M. SERMESANT, O. FARIS, F. EVANS, E. MCVEIGH, Y. COUDIÈRE, H. DELINGETTE, N. AYACHE. *Preliminary validation using in vivo measures of a macroscopic electrical model of the heart*, in "International Symposium on Surgery Simulation and Soft Tissue Modeling (IS4TM'03), Juan-les-Pins, France", N. AYACHE, H. DELINGETTE (editors), Lecture Notes in Computer Science, vol. 2673, Springer-Verlag, INRIA Sophia Antipolis, 2003, p. 230–243, ftp://ftp-sop.inria.fr/epidaure/Publications/Sermesant/IS4TM2003Sermesant.pdf.

[135] P. THOMPSON, K. HAYASHI, E. SOWELL, N. GOGTAY, J. GIEDD, J. RAPOPORT, G. DE ZUBICARAY, A. JANKE, S. ROSE, J. SEMPLE, D. DODDRELL, Y. WANG, T. VAN ERP, T. CANNON, A. TOGA. *Mapping Cortical Change in Alzheimer's Disease, Brain Development, and Schizophrenia*, in "NeuroImage", Special Issue : Mathematics in Brain Imaging, vol. 23, n^{o} supplement 1, 2004, p. S2–S18.

[136] P. THOMPSON, M. MEGA, K. NARR, E. SOWELL, R. BLANTON, A. TOGA. *Brain Image Analysis and Atlas Construction*, in "Handbook of Medical Image Proc. and Analysis", M. FITZPATRICK, M. SONKA (editors), chap. 17, SPIE, 2000.

[137] P. M. THOMPSON, M. I. MILLER, J. T. RATNANATHER, R. A. POLDRACK, T. E. NICHOLS. *Guest Editorial*, in "NeuroImage", Special Issue : Mathematics in Brain Imaging, vol. 23, n^{o} Supplement 1, 2004, p. S1–S1.

[138] D. W. THOMPSON. *On Growth and Form*, Cambridge Univ. Pr., 1917.

[139] K. VAN LEEMPUT, F. MAES, D. VANDERMEULEN, P. SUETENS. *A unifying framework for partial volume segmentation of brain MR images*, in "IEEE Trans Med Imaging", vol. 22, n^{o} 1, January 2003, p. 105-19.

[140] R. WEISSLEDER, U. MAHMOOD. *Molecular Imaging*, in "Radiology", Special Review, vol. 219, 2001, p. 316–333.