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Project-Team asclepios

*Analysis and Simulation of Biomedical
Images*

Sophia Antipolis - Méditerranée

Theme : Computational Medicine and Neurosciences

Activity
R *eport*

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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

- Our research results were presented during several prestigious invited lectures (including the Royal Society etc.).
- The team members received several honors and distinctions, including the second Gilles Kahn prize for the PhD of Stanley Durrleman, the best paper awards of Marco Lorenzi and Erik Pernod.

3. Scientific Foundations

3.1. Introduction

Tremendous progress has been made in the automated analysis of biomedical images during the past two decades [115]. 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 [103], [101]. Regarding the target applications, a good review of the state of the art can be found in the book *Computer Integrated Surgery* [99], in N. Ayache's article [107] and in the more recent syntheses [108] [115]. The scientific journals *Medical Image Analysis* [94], *Transactions on Medical Imaging* [100], 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'2010 (Medical Image Computing and Computer Assisted Intervention) [97], [98] or ISBI'2010 (Int. Symp. on Biomedical Imaging) [96].

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 cerebrospinal fluid [138], or to measure some functional properties of the heart from dynamic sequences of Magnetic Resonance [106], 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 images² 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 resolution³ for the observation of small animals (typically rodents). In addition, Optical Imaging (OI) techniques and biophotonics are developing very fast. This includes traditional or Confocal Microscopy (CM), multi-photon confocal microscopy, Optical Coherent Tomography (OCT), 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].

¹Multisequence (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.

²Multimodal 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.

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

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 levels. With optical techniques, molecular imaging makes an extensive use of the fluorescent properties of certain molecules (in particular proteins, e.g. GFP⁴) 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 to the recent tutorial [129] and to the Mouse Brain Atlas Project [105]). 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 anomalies⁵.

Studying the variability of biological shapes is an old problem (cf. the remarkable book "On Shape and Growth" by D'Arcy Thompson [137]). 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 [136] 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.

⁴Green Fluorescent Protein.

⁵The NIH has launched 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.

Quite advanced models have already been proposed to study at the molecular, cellular and organic level a number of physiological systems (see for instance [128], [121], [109], [131], [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. [132], [125]) and the development of new data assimilation methods coping with massive numbers of measurements and unknowns.

There is a hierarchy of modeling levels for CP models of the human body [112]:

- the first level is mainly geometrical, and addresses the construction of a digital description of the anatomy [104], essentially acquired from medical imagery;
- the second level is physical, involving mainly the biomechanical modeling of various tissues, organs, vessels, muscles or bone structures [119];
- the third level is physiological, involving a modeling of the functions of the major biological systems [120] (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 [95].

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. SOFA

Participants: Hervé Delingette [correspondant], Erik Pernod, Stéphanie Marchesseau, Hugo Talbot.

SOFA is an Open Source framework primarily targeted at real-time simulation, with an emphasis on medical simulation. It is mostly intended for the research community to help develop newer algorithms, but can also be used as an efficient prototyping tool. based on an advanced software architecture, it allows to:- create complex and evolving simulations by combining new algorithms with algorithms already included in SOFA- modify most parameters of the simulation (deformable behavior, surface representation, solver, constraints, collision algorithm, etc.) by simply editing an XML file- build complex models from simpler ones using a scene-graph description- efficiently simulate the dynamics of interacting objects using abstract equation solvers- reuse and easily compare a variety of available methods. It is mainly developed by the INRIA team project Shaman, Evasion and Asclepios.

See also the web page <http://www.sofa-framework.org/>.

- ACM: J.2 Physics, J.3 LIFE AND MEDICAL SCIENCES
- Software benefit:- Simulation of the human body
- License: GPL
- License: LGPL
- Type of human computer interaction: console, opengl, qt
- OS/Middleware: linux, windows, mac
- Required library or software: Qt - GPL - GLEW - BSD/MIT - Tinyxml - zlib
- Programming language: C/C++
- Documentation: - each function of the core API and each class in the SOFA modules - doxygen

4.2. MedINRIA

Participants: Benoît Bleuzé, Olivier Clatz [correspondant], Vincent Garcia, Michael Knopke, Stephan Schmitt, Maxime Sermesant, John Stark, Nicolas Toussaint.

MedINRIA is a free collection of softwares developed within the Asclepios research project. It aims at providing to clinicians state-of-the-art algorithms dedicated to medical image processing and visualization. Efforts have been made to simplify the user interface, while keeping high-level algorithms. MedINRIA is available for Microsoft windows XP/Vista, Linux Fedora Core, MacOSX, and is fully multithreaded.

See also the web page <http://www-sop.inria.fr/asclepios/software/MedINRIA/>.

- Version: 1.9
- Keywords: Medical Image Processing
- Patent: PCT/FR2006/000774
- License: Proprietary Licence
- Type of human computer interaction: WxWidget
- OS/Middleware: Windows - Linux - MacOSX
- Required library or software: DTI Track (Proprietary), vtkINRIA3D (CeCillB), Baladin (Proprietary), DT-REFInD (Proprietary)
- Programming language: C++

5. New Results

5.1. Medical Image Analysis

5.1.1. Estimation of 3D Myocardium Strain from Clinical Cine MRI Using Incompressible Log Demons

Participants: Tommaso Mansi [Correspondant], Xavier Pennec, Jean-Marc Peyrat, Hervé Delingette, Maxime Sermesant, Nicholas Ayache.

This work has been performed in the context of the Health-eChild European project in close collaboration with J. Blanc, MD, and Y. Boudjemline, MD, (AP-HP Necker-Enfants Malades, Paris, France).

We investigated mathematically-grounded and efficient approaches to constrain the log-domain demons algorithm to provide incompressible elastic-like deformation for cardiac tissue tracking and strain estimation [30], [55] :

- We first provided a scale-space justification to the demons Gaussian regularisation which enabled us : i) to replace the Gaussian regularisation by an efficient elastic-like separable vector filter ii) to estimated incompressible deformations by parameterising them with divergence-free stationary velocity field.
- It was applied on cine MRI of patients with heart failures and tetralogy of Fallot (see Figure 1), the estimated deformation successfully compared with tagged MRI and ultrasound 2D-strain.

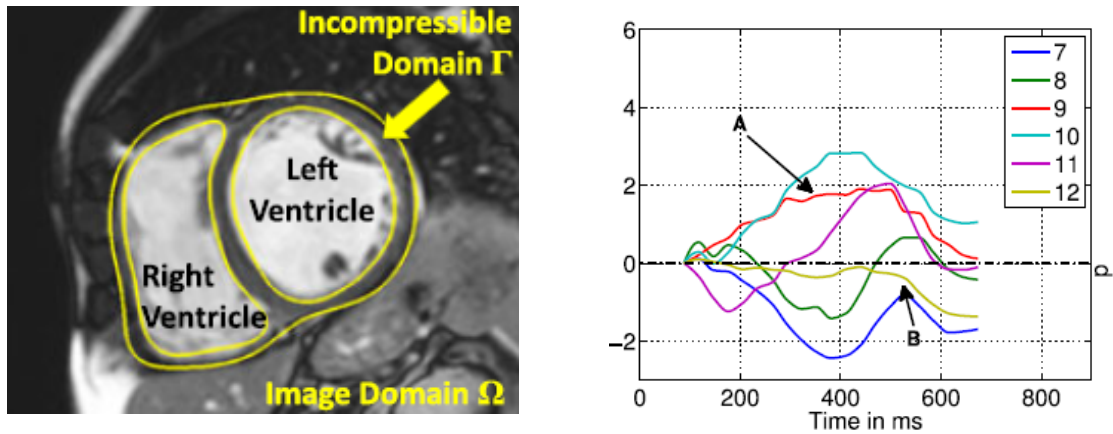


Figure 1. (Left) Short-axis cine-MRI; Incompressibility is ensured only within the myocardium (outlined in yellow). (Right) Circumferential displacements of mid-ventricular AHA regions estimated with incompressible Log Demons algorithm from cine MRI.

5.1.2. Regional appearance modeling for deformable model-based image segmentation

Keywords: classification, clustering, external forces, model, segmentation.

Participants: François Chung [Correspondant], Hervé Delingette.

This work is funded by the FP7 Research Training Network 3D Anatomical Human.

- To improve model-based image segmentation of regions of interest (e.g. lower limb structures, liver, ...) we propose to describe their appearance as Multimodal Prior Appearance Models (MPAM) [111].
- Unlike Principal Component Analysis (PCA) of intensity profiles, MPAM relies on the clustering of intensity profiles (see Figure 2) without an accurate pointwise mesh registration.
- MPAM is described on a reference mesh where each vertex has a probability to belong to several intensity profile classes. Objective of MPAM is to determine optimal external forces that will guide the deformable model in segmentation approaches.

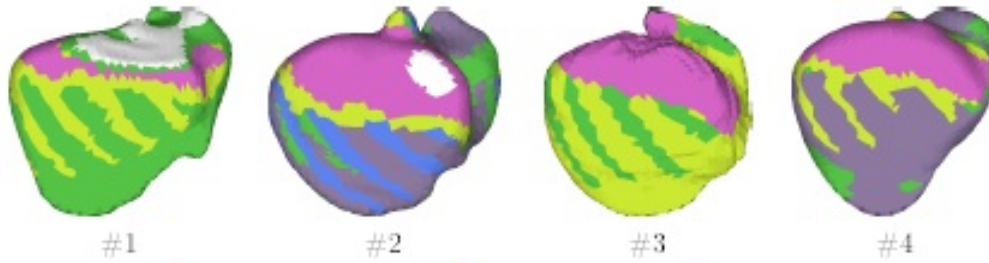


Figure 2. Clustering of intensity profiles on liver meshes. Each color represent a region with homogeneous intensity profiles (from [111]).

5.1.3. Spatial Decision Forests for MS Lesion Segmentation in Multi-Channel MR Images

Keywords: MICCAI Grand Challenge 2008, MS lesions, random forests, segmentation.

Participants: Ezequiel Geremia [Correspondant], Nicholas Ayache, Olivier Clatz, Antonio Criminisi [MSR], Ender Konukoglu [MSR], Bjoern Menze.

- Automatic segmentation of MS lesions in 3D MR images [50] extending the work of [134], [114] based on random forests using as features : multi-channel MR intensities, priors, long-range spatial context, symmetry
- Quantitative evaluation shows significant improvement over the MICCAI Grand Challenge 2008 winner [134]
- A ranking of the most discriminative features and channels is proposed
- The automatically learned decision sequence mimics a previous state-of-the-art pipeline

5.1.4. Design of patient-adapted atlases for radiotherapy planning of the head and neck region

Keywords: Atlas-based segmentation, atlas fusion, atlas selection, head and neck region, patient-adapted atlas, radiotherapy planning.

Participants: Liliane Ramus [Correspondant], Grégoire Malandain, Olivier Commowick [EPI Visages], Vincent Grégoire [UCL].

This work is done in collaboration with DOSIsoft S.A. and Université Catholique de Louvain, and also partly with INRIA Rennes (Visages Team).

In the context of segmentation for radiotherapy planning of the head and neck, we propose different strategies to design anatomical atlases that are adapted to the patient's anatomy. All strategies are based on the selection and the co-registration of a subset of manually delineated images among a database. First, we present in [63] an unbiased method to compare different selection criteria. Second, we propose to apply the selection :

- globally on the entire image with a selection criterion based on clinical information [90],
- or regionally on pre-defined anatomical areas [62],
- or locally for each voxel independently [73].

We show that the regional and local approaches enable improving the segmentation accuracy with respect to a non-specific average atlas (see Figure 4).

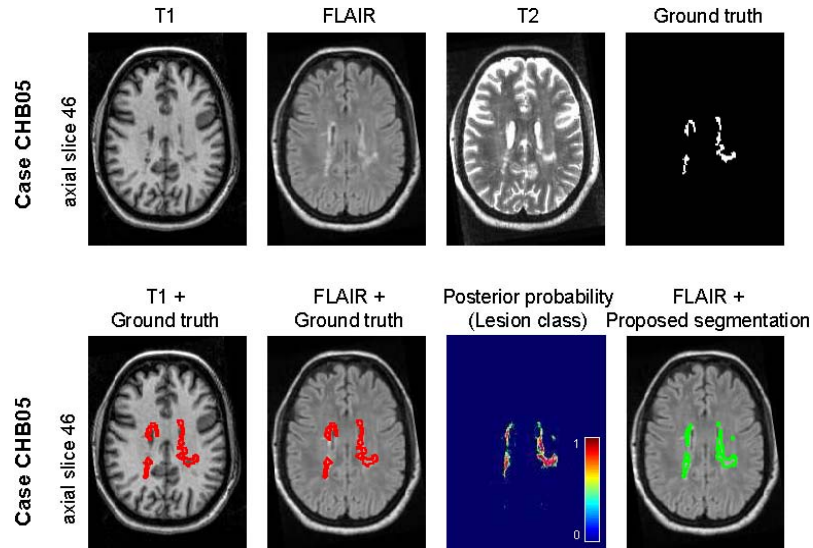


Figure 3. Probability map and segmentation outputed by the random forest compared to the T1 and FLAIR MR images overlaid with the ground truth.

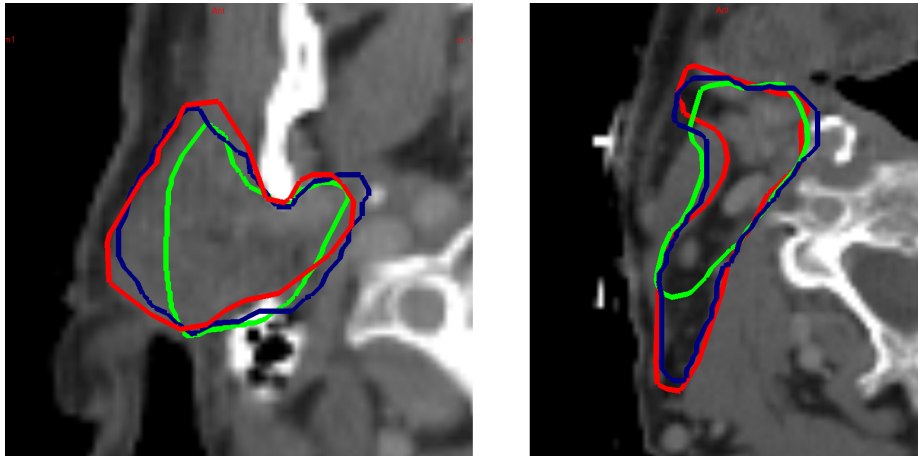


Figure 4. Atlas-based segmentation results using the atlas that is locally adapted to the patient's anatomy (dark blue contours) and using the non-specific average atlas (green contours), compared with the manual contours (red contours). Examples are given for the segmentation of the parotid gland (left figure) and the lymph node level II (right figure).

5.1.5. Dental atlas for automatic segmentation of the teeth to improve post-irradiation dental care management

Keywords: Atlas-based segmentation, dental atlas, head and neck region, post-irradiation dental complications, radiotherapy planning.

Participants: Liliane Ramus [Correspondant], Grégoire Malandain, Juliette Thariat [CAL].

This work is done in collaboration with DOSIsoft S.A., Centre Antoine Lacassagne (CAL) and Université Catholique de Louvain.

- Post-irradiation dental surgery often results in complications such as post-extraction osteoradionecrosis or implant failure. The risk of these complications must be assessed before performing any surgery, and this requires to know the approximate dose received by the teeth involved.
- We propose to construct and use a dental atlas to automatically delineate each tooth, and then to use the automatic contours to estimate *a posteriori* the dose received by each tooth [93], [92].
- Our framework enables estimating the dose with a 2 Gray accuracy, which is clinically sufficient.

5.1.6. Atlas of Human Cardiac Fiber Architecture from DT-MRI

Keywords: cardiac fiber, diffusion tensor imaging, registration.

Participants: Hervé Lombaert [Correspondant], Hervé Delingette, Nicholas Ayache, Jean-Marc Peyrat, Pierre Croisille [CREATIS].

This is a joint work with the research team CREATIS (CNRS, INSERM, University of Lyon, INSA Lyon) in Lyon, France.

- A statistical atlas of diffusion tensor MR images of human hearts has been developed extending the work of Peyrat [130] on canine hearts.
- This atlas leads to the estimation of the mean orientation of cardiac fibers and cardiac sheets in the left ventricle as well as their variability across a small population of human hearts.

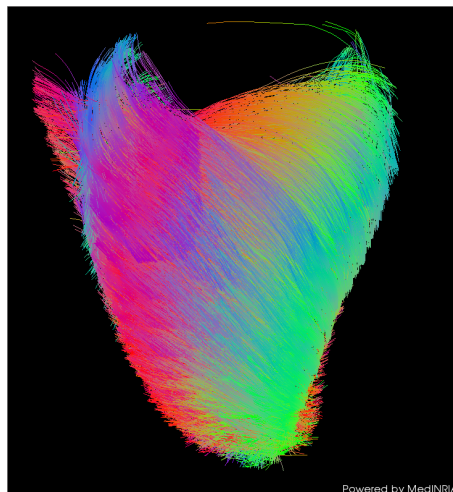


Figure 5. Fiber tracking performed on an average left ventricle template where several diffusion tensor MR images have been registered.

5.1.7. 3D/2D Registration of the Coronary Arteries in Interventional Cardiology

Keywords: 3D/2D, ICP, Interventional Cardiology, Rigid Registration.

Participants: Yonni Lévy [Correspondant], Régis Vaillant [GE Healthcare], Grégoire Malandain, Nicholas Ayache.

This work is done in collaboration with GE Healthcare.

Registering a coronary arteries model (issued from pre-operative CT data) of a patient on an intra-operative fluoroscopy will provide the clinician complementary information on the coronary pathology during the intervention. Also, evaluating the 3D position of the model enables to predict its position when the angulation of the C-arm changes.

Since an artery can be described mainly by its centerline, a geometrical approach for the registration has been chosen: we segment the centerlines of the vascular tree in both images and register them with a robust ICP approach. Preliminary results with a rigid registration approach are presented in figure 6.

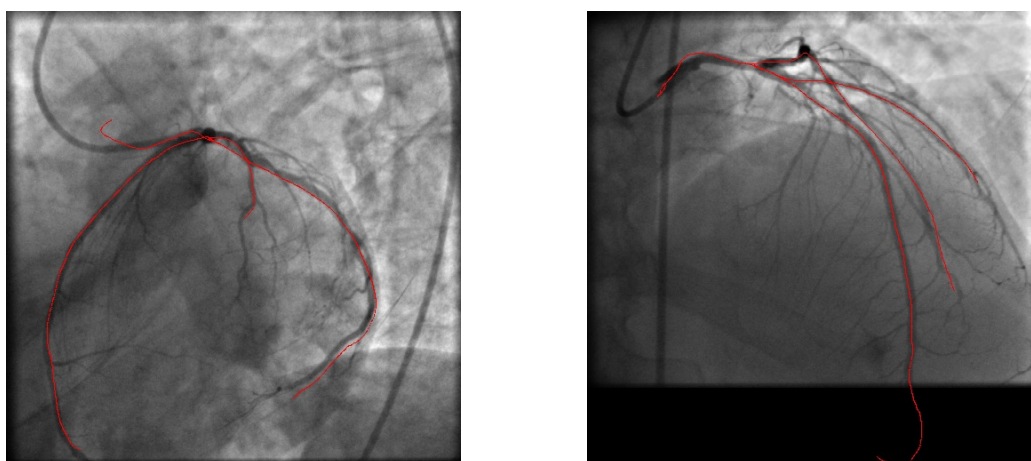


Figure 6. Registration of the left coronary centerline extracted from the same CT (in red) on fluoroscopies taken at 2 different angulations.

5.2. Biological Image Analysis

5.2.1. Content-Based Video Retrieval for Endomicroscopy Diagnosis and Training Support

Keywords: Bag-of-Visual-Words, Content-Based Video Retrieval, Endomicroscopy, Learning Curve, Video-Mosaicing.

Participants: Barbara André [Correspondant], Tom Vercauteren [Mauna Kea Technologies], Nicholas Ayache.

This is a joint work with the company Mauna Kea Technologies (<http://www.maunakeatech.com>) located in Paris.

- To support endomicroscopy diagnosis, a content-based video retrieval method has been developed [45] providing, given a query video, relevant similar videos from an expert-annotated database, as illustrated in Fig. 7.
- From the retrieval results, we learn a diagnosis difficulty predictor in [44] to try to shorten the physician learning curve.

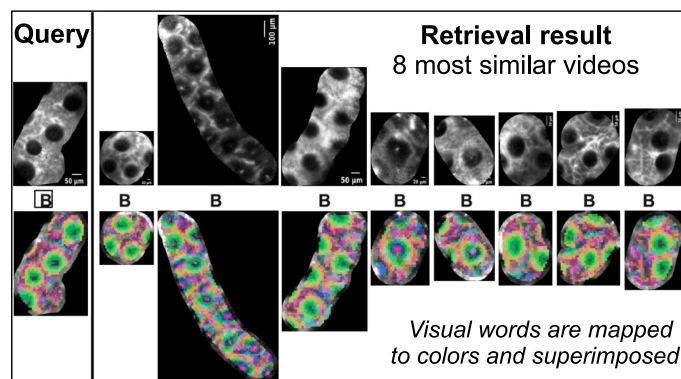


Figure 7. Typical video retrieval result on Colon database. Videos are represented by mosaics. **B** indicates Benign and **N** Neoplastic (not present in this example).

5.2.2. Pre-clinical molecular imaging: Tracking and quantification of tumor processes in rodents with SPECT imaging

Keywords: SPECT/CT, quantification, respiratory motion, small animal, tumor.

Participants: Marine Breuilly [Correspondant], Grégoire Malandain, Nicholas Ayache, Jacques Darcourt [CAL], Philippe Franken [CAL], Thierry Pourcher [CEA].

This is a joint work with the Transporter in Imagery and Oncologic Radiotherapy team (TIRO, CEA-CAL-UNSA).

- Assessment of tumor growth with coupled functional and anatomical images (SPECT and CT). Since the metastasis under study can be located either in the lungs or in the abdominal cavity, the respiratory motion may impair image reconstruction and then the follow-up.
- Study of the respiratory signal to characterize motionless phases, which enables motionless gated reconstruction of SPECT images in alive mice [84]. Non-linear registration of time series of SPECT/CT images (see Figure 8) enables the longitudinal study of the tumor growth.

5.2.3. Microscopy image reconstruction and automatic lineage tracking of the growing meristem cells

Participants: Romain Fernandez [Correspondant], Grégoire Malandain, Christophe Godin [EPI Virtuals Plants], Jean-Luc Verdeil [Cirad], Jan Traas [INRA/ENS Lyon], Pradeep Das [ENS Lyon].

- We studied the tracking of meristem cells using time-lapse confocal microscopy acquisition on early stages flowers of Arabidopsis shoot apical meristems.
- We designed a reconstruction method (MARS) and a tracking algorithm (ALT) in order to map the segmentations of the same meristem at different times, based on a network flow representation in order to solve the cell assignment problem
- The validation by biologists showed the efficiency of the segmentation algorithm on the reconstructed images (nearly 96% of well-identified cells) and of the lineaging algorithm (100% of well-identified lineages in the easiest case and 90% in the hardest).
- This work has been published in the Nature Methods journal [32].

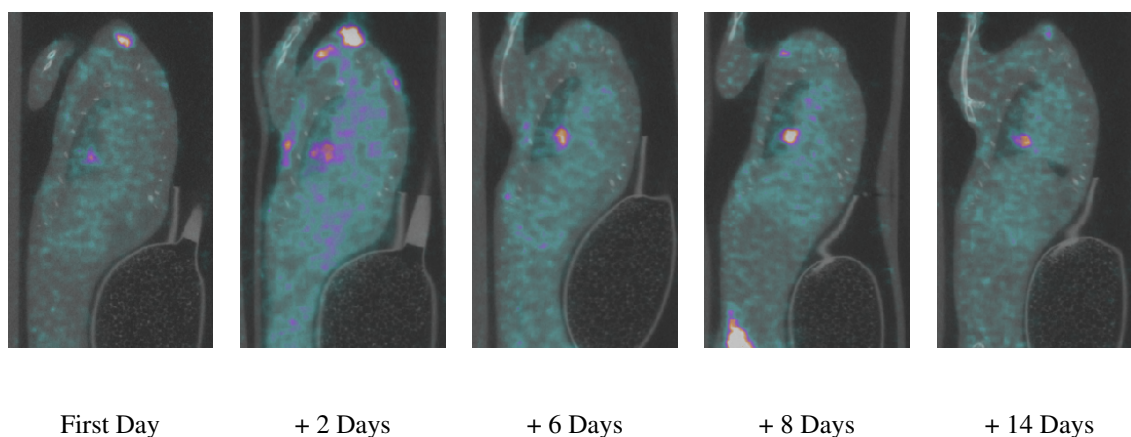


Figure 8. Coronal slices of a time series of registered SPECT images from a NOD-SCID mouse (data acquired with GE eXplore speCZT CT 120): central hot spots reveal pulmonary metastasis from adenocarcinoma of the colon. The first acquisition is performed 5 weeks after injection

5.3. Computational Anatomy

5.3.1. Image markers of the brain's changes in longitudinal images of Alzheimer's disease

Keywords: Alzheimer's Disease, Image Biomarker, Non-rigid registration.

Participants: Marco Lorenzi [Correspondant], Xavier Pennec, Giovanni Frisoni [IRCCS Fatebenefratelli Brescia, Italy], Nicholas ayache.

- Definition of a new measure of the within-subject longitudinal structural changes based on the flux of the deformation field obtained with the Log-Demons registration algorithm. Our framework justifies the use of the log of the Jacobian that was sometimes used for morphometric studies and allows to consistently measure morphometric changes at the local (voxel), regional (Region Of Interest) and global (Brain) level. The algorithm was further enhanced to enforce consistency across multiple time points [54], [88]. This work won a best paper award at the "Spatio Temporal Image Analysis" workshop at MICCAI 2010, Beijing (<http://www.sci.utah.edu/~gerig/MICCAI2010-SpatioTemporal/>).
- Investigation of the power of structural measures of brain changes as surrogate markers for clinical trials (oral presentation at the Clinical Trials on Alzheimer's Disease (CTAD) conference).
- Finalization of the study of the functional markers of the Alzheimer's disease (resting state fMRI) during specific clinical trials for disease modifying drugs.

5.3.2. Statistical analysis of DTI deformations

Participants: Andrew Sweet [Correspondant], Xavier Pennec.

- Fusion of the log-demons framework of [139] and the diffusion tensor image registration scheme of [141]. This new log-demons DTI registration algorithm was presented at the Workshop on Biomedical Image Registration [68].
- Thanks to the simple parameterization of diffeomorphic deformations using the static velocity fields, we defined simple and well defined deformation statistics. An analysis of the statistics produced by registration of a group of 37 HIV/AIDS patients illustrates principal modes of deformation that are anatomically meaningful [67].

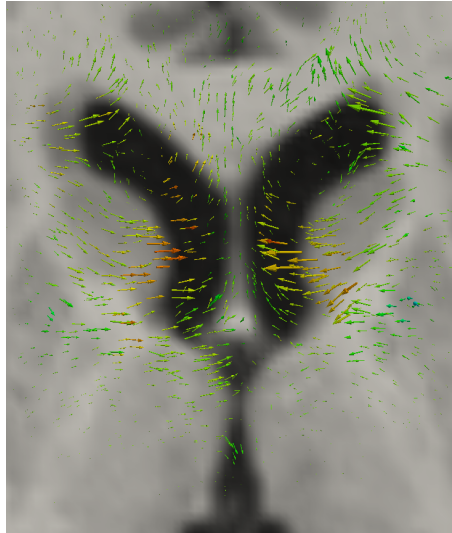


Figure 9. Displacement field of a Log Demons non rigid registration performed for within-subject longitudinal study. It allows to compute the amount of change in specific regions by evaluating the flux of vector fields across surfaces.

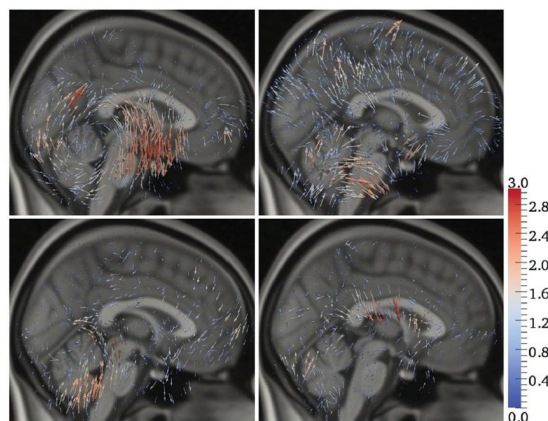


Figure 10. Displacement fields corresponding to the four first modes of deformation computed from all the pairwise registrations of DTI images of 37 subjects.

5.3.3. Statistical Modelling of Cardiac Growth and Deformation from Medical Images

Keywords: Demons Algorithm, Heart, LDDMM Algorithm, Registration, Statistical Modelling.

Participants: Kristin McLeod [Correspondant], Tommaso Mansi, Maxime Sermesant, Xavier Pennec.

Parts of this work were performed within the framework of the EU project Health-e-Child, the EU project Care4me, and the INRIA ARC Sirap, in collaboration with St Thomas Hospital, King's College London (<http://www.kcl.ac.uk/index.aspx>), the REO team from INRIA Rocquencourt (<http://www-roc.inria.fr/REO/>) and Necker Paediatric Hospital in Paris (<http://www.hopital-necker.aphp.fr/>).

This work builds on the statistical analysis framework for surfaces developed by Durrleman and Mansi in 2009.

- Development of a statistical framework based on partial least squares regression and canonical correlation analysis to estimate a generative model of right ventricle growth in a population of 32 patients with repaired tetralogy of Fallot. The growth model was found relevant by cardiologist and correlation of shape with right ventricular regurgitation enabled us to identify pathological remodeling patterns like the apparition of an aneurysm at the right ventricular outflow tract [30], [43].
- The resulting shape analysis pipeline was made available as a freely available modeling tool in the VPH toolkit as a legacy of the Health-eChild EU project to the VPH community <http://www-sop.inria.fr/asclepios/projects/Health-e-Child/ShapeAnalysis> [89], [80].

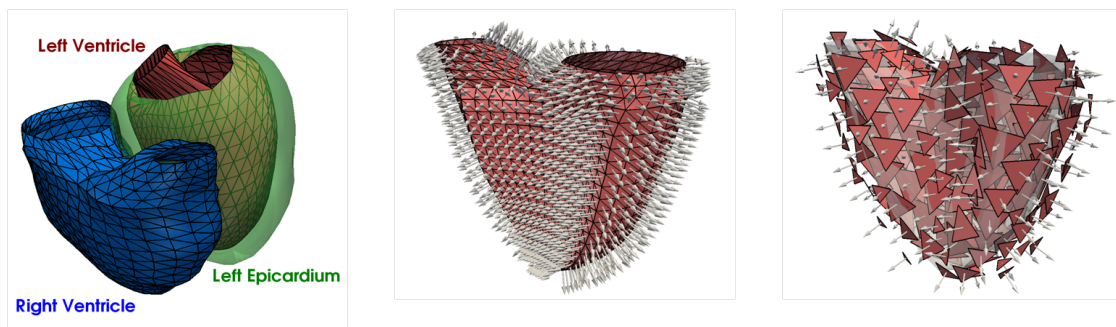


Figure 11. Generative model of heart growth using currents. Right: segmentation of the left and right ventricles. Middle: original shape model of the right ventricle with 1476 delta currents. Left: compressed Shape with 281 delta currents.

- To perform patient-specific blood flow simulations in the pulmonary artery, we designed a generic reduced basis of the functional space for the velocity and pressure fields thanks to a proper orthogonal decomposition in the template space. This reduced patient specific basis is then transported using inter-subject registration, which allows for a faster subject specific flow simulation [57]

5.3.4. Statistical Modelling of shapes using currents

Keywords: Currents, Registration, Shapes, Statistical Modelling.

Participants: Stanley Durrleman [Correspondant], Alain Trouvé [ENS Cachan], Nicholas Ayache, Xavier Pennec.

- Finalized description of a complete, consistent and efficient algorithmic formalism to manipulate currents for statistics on geometric shapes [27].
- Registration and statistical modeling (mean atlas and variability) of white matter fibre bundles extracted from DTI;
- Registration of lung CT images combining intensity, curves and surfaces [51];
- Comparison of the endocast growth of chimpanzees and bonobos via temporal regression and spatiotemporal registration [47], with a noticed oral presentation at the congress of the American Association of Physical Anthropologists in Albuquerque in April 2010 with José Braga [72].

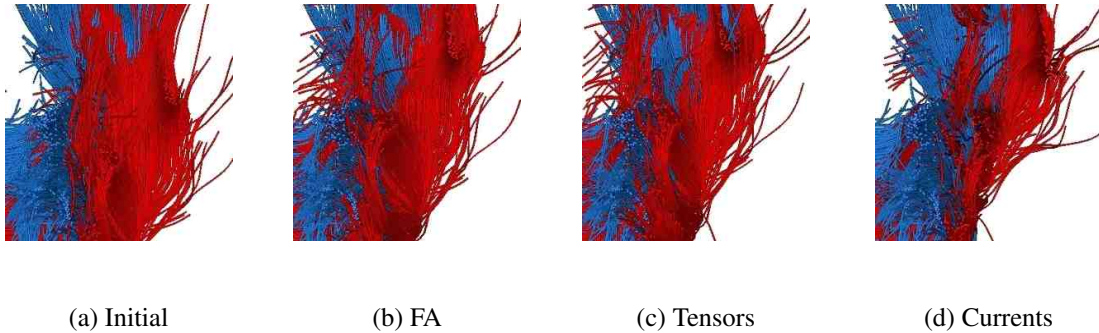


Figure 12. Diffeomorphic registration of two corpus callosum fibers. Initial tracts (a) and registered tracts using FA (b), tensors (c) or fiber bundles (d) as constraints. Overlap of blue and red fiber bundles is greater using currents, especially in the left and right parts of the genu of the corpus callosum.

5.3.5. Modeling bone shapes deformations from 2D observations

Keywords: Diffeomorphic Deformations, Log-Euclidean Framework, Non-Parametric Regression, Parametric Regression, Shapes, Statistical Modelling.

Participants: Christof Seiler [Correspondant], Xavier Pennec, Mauricio Reyes [University of Bern, ISTB, Bern, Switzerland].

This work is performed in the context of the joint PhD of Chr. Seiler at University of Bern, ISTB, Bern, Switzerland and Asclepios INRIA.

The goal is to predict the 3D shape information of the femur (encoded through the static velocity field registering the template CT imager to the virtual patient specific 3D CT image) from low-radiation and cost-effective 2D X-ray images. We studied the approximation using parametric models of an univariate non-parametric regression on individual predictor variables (shaft length and caput collum diaphysis angle) on a database of 182 CT images of femurs. The variance of each predictor can be described using a simple up to second order parametric model. These findings opens the way to the extension to the multivariate case [66].

5.3.6. Computational anatomy of the brain

Keywords: Diffeomorphic Registration, Shapes, Statistical Modelling.

Participants: Caroline Brun [Correspondant, LONI, UCLA], Natasha Leporé [LONI, UCLA], Paul Thompson [LONI, UCLA], Xavier Pennec.

This work is performed in collaboration with the LONI team at UCLA (California, USA), as a follow-up of the Associated team program BrainAtlas.

Following the work initiated over the previous years on fluid registration and statistics on deformations, we proposed:

- a non-conservative Lagrangian mechanics approach to formulate a new statistical algorithm for fluid registration of 3D brain images. Covariance matrices for both the deformation tensors and the displacement fields can be incorporated (separately or jointly) in the non-conservative terms, creating four versions of SAFIRA (acronym for Statistically-Assisted Fluid Image Registration Algorithm) [46].
- The evaluation and comparison of algorithms performance on 92 3D brain scans from healthy monozygotic and dizygotic twins. Using displacement-based empirical statistics consistently leads to more accurate than their counterparts. This suggests the advantages of this approach for largescale neuroimaging studies [31], [71]

5.4. Computational Physiology

5.4.1. Coupled Personalisation of Cardiac Electrophysiology Models for Prediction of Ischemic Ventricular Tachycardia

Keywords: *Arrhythmia simulation, Cardiac Electrophysiology Modelling, Parameter estimation, Reaction-Diffusion Models.*

Participants: Jatin Relan [Correspondant], Maxime Sermesant, Hervé Delingette, Nicholas Ayache.

This work is funded by the FP7 European Project euHeart.

- Construction of a patient-specific cardiac electrophysiology model from hybrid XMR imaging and non-contact electro-anatomical mapping procedure on a patient with heart failure [64](Fig. 13).
- The model is then used to simulate and predict patient-specific arrhythmias, such as induced ischemic Ventricular Tachycardia [64] and allows the generation and evaluation of patient-specific VT-risk maps.

5.4.2. Data assimilation for the estimation of the mechanical parameters of the heart model.

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

This work is funded by the CardioSense3D National Action.

- We build a patient-specific model by coupling an electromechanical model [24] and cine-MRI data.
- Kinematics personalization is performed through a proactive deformable model [110]
- Personalization of mechanical parameters (contractility) is performed through a variational data assimilation [26] method based on the adjoint operator.

5.4.3. Non-Invasive Activation Times Estimation using 3D Echocardiography

Keywords: *3D echocardiography, Kernel Ridge Regression, electrical activation times.*

Participants: Adityo Prakosa [Correspondant], Maxime Sermesant, Hervé Delingette, Eric Saloux [CHU Caen], Pascal Allain [Philips HealthCare], Pascal Cathier [Philips HealthCare], Patrick Etyngier [Philips HealthCare], Nicolas Villain [Philips HealthCare], Nicholas Ayache.

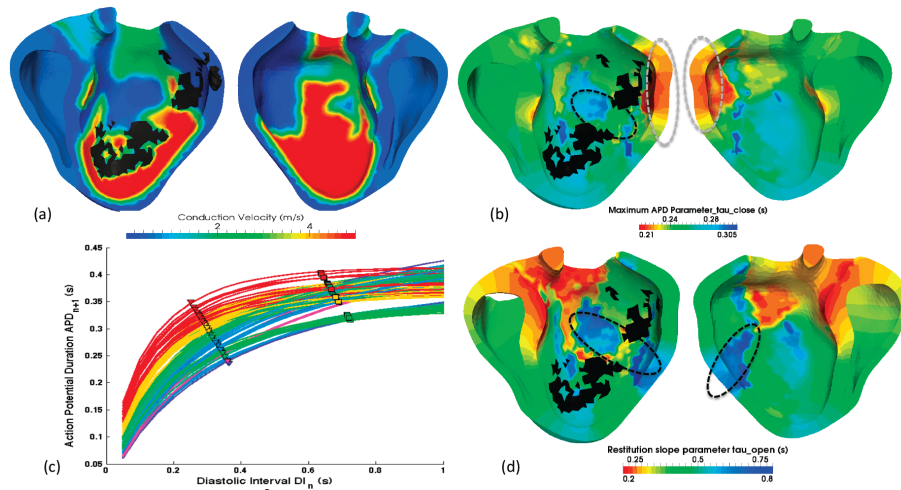


Figure 13. Estimated parameters: (a) conduction velocity estimated from AC maps, (b) APD parameter τ_{close} , lower τ_{close} values correspond to lower measured APD (white ellipse), (c) & (d) APD RC parameter τ_{open} and heterogeneity of the restitution curves for the scar and isthmus (black ellipse), low τ_{open} values (red) correspond to steep RC slopes & high values (blue) correspond to gentle RC slopes.

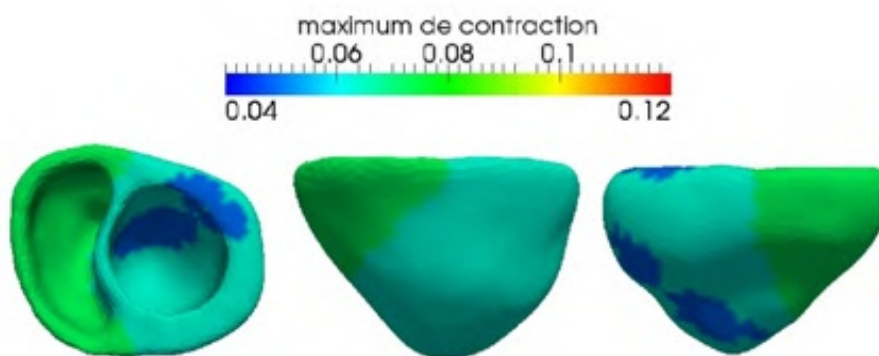


Figure 14. Estimation of maximum contractility parameters on three zones (right and left ventricles and scar region) from a time serie of cine-MR images.

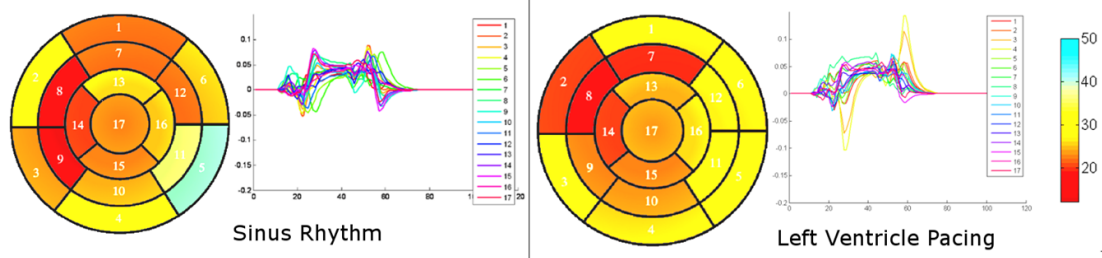


Figure 15. For each AHA segment, estimated Electrical Activation Times (in Bull's eyes) and contraction forces (in graph) learned from kinematics descriptors extracted in echocardiography; (Left) Patient in sinus rythm; (Right) Patient with left ventricular pacing;

This work is done in collaboration with Medisys, Philips Healthcare Suresnes, France, and Cardiology Department of CHU Caen, France.

- 3D echocardiography image registration and motion estimation using incompressible diffeomorphic demons [55]
- Learn kinematic-electrical coupling from a cardiac electromechanical model,
- Patient electrical activation times estimation [61] from extracted kinematic descriptors (see Figure 15).

5.4.4. Multi-scale computational models of brain tumors for medical image analysis

Keywords: brain tumors, gliomas, multi-modal data, sensitivity analyses.

Participants: Erin Stretton [Correspondant], Nicholas Ayache, Olivier Clatz, Hervé Delingette, Ezequiel Geremia.

In the context of Erin Stretton PhD thesis, our objective is to build upon the PhD work of E. Konukoglu [77], [35], [36] on brain tumor growth modeling by :

- Performing a sensitivity analyses of long time series of multi-modal data to look for improvements in our modeling strategies.
- Modeling the effect of various therapies
- Developing a multi-scale modeling approach from microscopic to macroscopic scales.

5.4.5. Tumor Growth Parameters Estimation and Source Localization From a Unique Time Point

Keywords: brain tumors, gliomas, inverse problem.

Participants: Islem Rekik, Stéphanie Allasonnière [Polytechnique], Nicholas Ayache [Correspondant], Olivier Clatz, Hervé Delingette, Ezequiel Geremia.

- We address the problem of tumor parameters estimation based on a unique medical image acquired at a single time point.
- This minimal information can already provide insights into the tumor growth ratio in white and grey matter as well as its original location (see Figure 16).

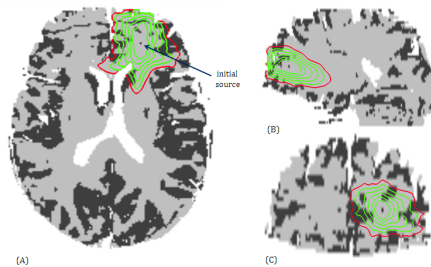


Figure 16. Simulation from a source point of the iso-time contours representing the tumor invasion process with a diffusion ratio dw/dg equal to 25. The synthetic tumor whose boundary is displayed (red) is created by thresholding the generated time distance map. (A) represents the axial slice, (B) coronal slice and (C) sagittal slice.

5.4.6. Multiplicative Jacobian Energy Decomposition method for hepatic and cardiac modeling

Keywords: Cardiac therapy simulation, Liver surgery simulation.

Participants: Stéphanie Marchesseau [Correspondant], Hervé Delingette.

This work has been performed in the context of the Passport European project

- New method for hyperelastic materials that leads to faster FEM calculation
- New model for liver surgery simulation that includes viscosity, porosity and hyperelasticity (see Figure 17). Two papers have been published on this subject [37], [56].
- This method is being applied on cardiac modelling and simulation, improving existing electromechanical models with mechanical non linearity and pressure based changes of cardiac phases.

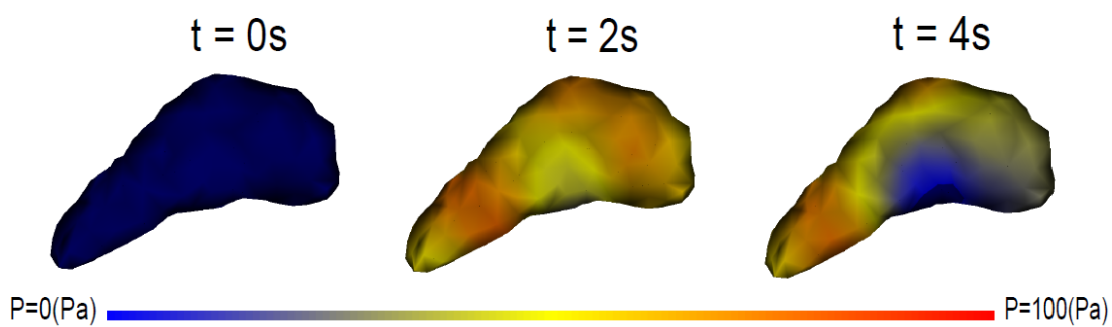


Figure 17. Pressure field of the porous component on a liver under gravity.

5.4.7. Cardiac Motion Estimation using a ProActive Deformable Model: Evaluation and Sensitivity Analysis

Keywords: Cardiac motion estimation, proactive deformable model, sensitivity analysis.

Participants: Ken C.L. Wong [Correspondant], Maxime Sermesant, Hervé Delingette, Nicholas Ayache.

This work has been performed in the context of the euHeart european project.

- The cardiac motion estimation framework based on a proactive deformable model [24] is promising for extracting patient-specific cardiac motion from medical images (see Figure 18).
- This research provides a sensitivity analysis of this framework to study the impacts of different model parameters under the influences of image information [70].

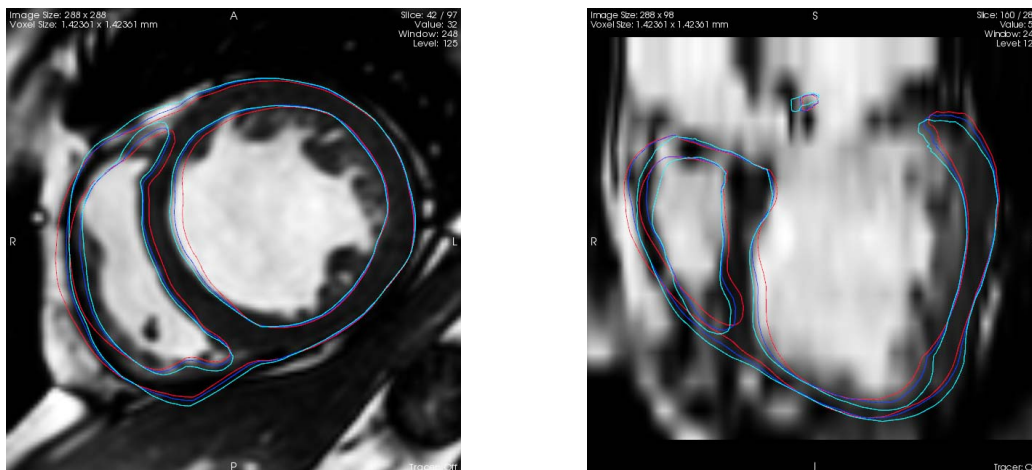


Figure 18. Short and long axis view of a cine MRI image with the traces of proactive deformable models of the heart associated with different image force scaling (from [70]).

5.4.8. Interactive Electrophysiology Simulation based on the SOFA Platform

Keywords: Cardiac Electrophysiology, Gesture training, SOFA, radio-frequency ablation.

Participants: Erik Pernod [Correspondant], Maxime Sermesant, Hugo Talbot, Jatin Relan, Hervé Delingette.

- Development of an interactive simulator of radiofrequency ablation of cardiac tissue in case of ventricular tachycardia [60] (see Figure 19). This work received the best paper award at the conference VCBM'2010.
- The simulation, implemented on the software platform SOFA, involves the simulation of electrophysiology based on fast multi-front anisotropic eikonal models [133].
- Endovascular catheterization simulator have been recently acquired to have a realistic gesture training.

6. Contracts and Grants with Industry

6.1. European Marie Curie RTN project 3D Anatomical Human

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

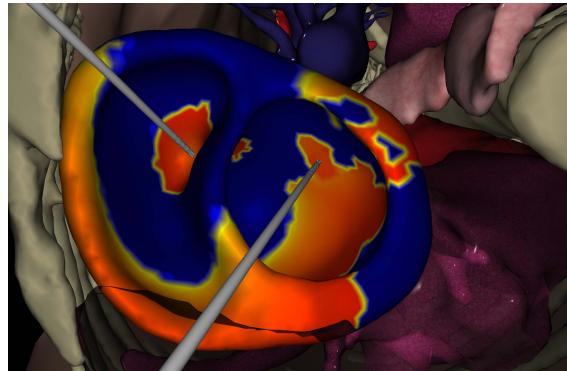


Figure 19. Simulation of Ventricular Tachycardia (VT) ablation. The left catheter is at the apex of the right ventricle to pace the heart at different frequencies. The right catheter is within the left ventricular cavity in order to ablate the isthmus between two scars responsible for re-entries. Colored surfaces represent the electrophysiological wave propagation simulated with a multi-front eikonal model (from [60]).

The Research Training Network 3D Anatomical Human (MRTN-CT-2006-035763 , <http://3dah.miralab.unige.ch/>) 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. François Chung has been hired as ESR (Early Staged Researcher) and Tobias Heimann as ER (Experienced Researcher). In this context, INRIA has collaborated with UCL (UK) and University of Geneva for the acquisition and segmentation of the MR images of the lower limbs and with Istituti Ortopedici Rizzoli (Italy) and EPFL (Switzerland) for the biomechanical modeling of the knee. Other research groups include the Vrije Universiteit Brussel (Belgium), Aalborg University (Denmark) and CRS4 (Italy).

The project has ended in september 2010 after a plenary meeting was organized in Chania, Creta on May 23-24 2010. Also in 2010, Asclepios has hosted several students for a few weeks from research groups involved in this Marie-Curie project : I. Ciuciu from Vrije Universiteit Brussel, J. Iglesias from CRS4 and J. Schmid from University of Geneva.

6.2. Virtual Physiological Human Network of Excellence

Participants: Benoît Bleuzé [correspondant], Olivier Clatz, Maxime Sermesant, Nicholas Ayache.

The Virtual Physiological Human Network of Excellence (VPH NoE) is a EU seventh Framework funded project, working to connect and support researchers in the VPH field within Europe and beyond. INRIA is one of the core members, and is more dedicated, through Asclepios, to the data fusion part of the VPH toolkit.

- The registration toolbox is a deliverable realised for the VPH. The goal is to incorporate registration algorithms from the team and elsewhere into the new version of MedINRIA (2.x). the core of this task is the writing of a framework to easily include these algorithms within the user-friendly graphical interface of MedINRIA[83].
- Also the team is part of a VPH effort to create guidelines helping researchers to characterise and publish data on the VPH portal.

6.3. PASSPORT

Participants: Stéphanie Marchesseau, Erik Pernod, Hervé Delingette [Correspondant].

The PASSPORT project (Ref 223894, <http://www.passport-liver.eu/>) is a 3-year (2008-2011) STREPS European project which aims at developing patient-specific models of the liver. Those models should integrate anatomical, functional, mechanical, appearance, and biological descriptions of the liver. More precisely, it is expected to simulate the liver deformation due to breathing as well as the liver regeneration after hepatectomy.

INRIA is involved in this project through the teams Alcove, Shaman and Asclepios and around the software platform SOFA which will serve as the integration platform for the project. IRCAD (Strasbourg) is the project leader which also gathers TUM (Munich, Germany), UCL (London, UK), ETH (Zurich, Switzerland), ICL (London, UK), INSERM (Paris), ULP (Strasbourg), IZBI (Leipzig, Germany).

One plenary meeting has been organized in 2010 in Strasbourg. We have collaborated with the Fluid Mechanics department of the University of Strasbourg in order to build a realistic biomechanical model [37] of the liver and integrate it in the SOFA platform.

6.4. euHeart

Participants: Nicholas Ayache, Florence Billet, Hervé Delingette [Correspondant], Tommaso Mansi, Adityo Prakosa, Ken C.L. Wong, Jatin Relan, Stéphanie Marchesseau, Maxime Sermesant.

The euHeart project (Ref 224495, <http://www.euheart.eu/>) is a 4-year (2008-2012) integrated European project which aims at developing personalized, and clinically validated multi-physics, multi-level models of the heart and great vessels. Those models need to be tightly integrated with signal and image processing tools in order to assist clinical decision making and to help reducing morbidity and mortality rates associated with cardiovascular diseases.

Asclepios is leading a workpackage on radiofrequency ablation for which electromechanical models of the heart are used to improve the planning of radiofrequency ablation lines for patient suffering from atrial fibrillation and ventricular tachycardia. This project is lead by Philips Research and also involves two other Inria teams (Macs and Reo) as well as Univ. of Oxford (UK), Univ. of Auckland (New Zealand), Univ. of Pompeu Fabra (Barcelona, Spain), Univ. of Karlsruhe (Germany), King's College London (UK), Univ. of Sheffield (UK), Amsterdam Medical Center (The Netherlands). Two plenary and two topical meetings in WP6 have been organized in 2010. The research performed in this project is partially described in sections 5.4.7, 5.4.2 and 5.4.6.

6.5. Health-e-Child

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

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 pediatric 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 pediatric 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 pediatricians make the right decisions. In this project, the role of the Asclepios team is to model the congenital heart pathologies of the right ventricle and the grown of brain tumors. A description of the work done is available at <http://www-sop.inria.fr/asclepios/projects/hec/>.

6.6. Cooperative Advanced REsearch for Medical Efficiency (Care4Me)

Participants: Grégoire Malandain [Correspondant], Nicholas Ayache, Hervé Delingette, Xavier Pennec, Kristin McLeod, Erin Stretton, Maxime Sermesant.

The ITEA2 European project Cooperative Advanced REsearch for Medical Efficiency (Care4Me) aims to increase quality and productivity in the healthcare care cycle by using more advanced medical imaging and decision support methods while combining them with different knowledge sources, from early diagnosis to treatment and monitoring. The final outcome of this project are clinical prototypes of novel medical image analysis and decision support systems for three specific disease areas (cancer, cardio-vascular and neurodegenerative diseases), that connect to the hospital information systems using a new system architecture.

In this project, the role of the Asclepios team is to develop atlas of the ageing brain and the beating heart, and to model tumor growth.

6.7. Microsoft Research Award

Participants: Nicholas Ayache [Correspondant], Grégoire Malandain, Olivier Clatz, Hervé Delingette, Xavier Pennec, Maxime Sermesant.

This European prize funded by Microsoft Research and awarded jointly by the Royal Society (UK) and the Académie des Sciences (FR) allows us to co-fund some basic research efforts on the development of personalized models of brain tumors, cardiac function, and brain anatomy; The grant was awarded for a period of 18 months, starting in Nov. 2008.

6.8. CIFRE PhD Fellowships

6.8.1. Dosisoft

The work of Liliane Ramus, *Digital anatomical atlases for radiotherapy planning*, is supported by a PhD fellowship from the Dosisoft company.

6.8.2. Mauna Kea Technologies

The work of Barbara André, *Smart Atlas for the Early Diagnosis of Gastrointestinal Cancers from Optical Biopsy Images*, is supported by a PhD fellowship from the Mauna Kea Technologies company.

6.9. Other contracts

The contracts Cancéropôle PACA CPER Telius, Maestro⁶, Miniara, Philips, and Siemens are described in our previous activity reports.

7. Other Grants and Activities

7.1. National initiatives

7.1.1. INRIA Large Collaborative Effort CARDIOSENSE3D

Participants: Hervé Delingette [coordinator], Nicholas Ayache, Maxime Sermesant, Florence Billet, Tommaso Mansi, Adityo Prakosa, Nicolas Toussaint, Jatin Relan.

The CARDIOSENSE3D action is a large initiative action (2005-2010) on the topic of cardiac simulation. This action gathers the expertise of four INRIA research teams (Asclepios, Macs, Reo and Sisyphe) 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.

⁶<http://www.maestro-research.org/>

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

7.1.2. ANR KaraMetria

Participants: Xavier Pennec [correspondant], Andrew Sweet, Marco Lorenzi.

KaraMetria is the concatenation of Kara ("head", "brain" in ancient Greek), and Metria ("measure"). This ANR-funded project (2010-2012, <http://sites.google.com/site/karametria/>) aims at: developing an extensible image registration framework able to map anatomical descriptors (such as sulcal lines or white matter fibers) of the brain shape from one subject to another : providing all necessary statistical tools to compare a subject with a group or compare groups of subjects based on the aforementioned registration framework ; and identifying biomarkers of certain brain pathologies and psychiatric disorders. In particular, we target the study of a population of depressive teenagers. This project is led in collaboration with the LNAO at CEA, the MAP5 laboratory from the University Paris Descartes, and the INSERM U797 unit.

7.1.3. ANR TechLog NeuroLOG

Participants: Xavier Pennec [correspondant], Andrew Sweet, Pascal Girard, Marco Lorenzi, Grégoire Ma-landain.

The ARN TLOG NeuroLOG (2007-2010, <http://neurolog.polytech.unice.fr>): project addresses 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; extraction and quantification of relevant parameters for different pathologies such as: Multiple sclerosis, Brain Vascular Stroke, Brain tumors, and Alzheimer's disease.

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). The Asclepios team was particularly involved in the design of the image analysis pipelines for the detection of longitudinal changes in AD and in morphometric changes in populations from DTI images.

7.1.4. INRIA Cooperative Research Initiative 3DMorphine

Participants: Xavier Pennec [correspondant], Stanley Durrleman.

The aim of this two-year Collaborative Research Initiative is to devise, implement, validate and apply new mathematical and computational methods for the automated morphometric analysis of extant and extinct hominid cranial virtual endocasts. The particular interest of the Asclepios team is on the morphometric analysis of endocasts on different populations of subjects, including: modern humans, fossil pre-humans and humans (such as South African australopithecines, European Cro-Magnons and Neandertals), and the closest extant relatives of modern humans (i.e. chimps and bonobos).

The action is led by S. Prima from the Visages team at INRIA, Rennes, France. Other participants include the ICAR team at CNRS, Montpellier, France, the lab of paleoanthropology and anatomical imaging at the Université Paul Sabatier, Toulouse, France and the lab of general histology, neuroanatomy and neuropathology at the Université Libre de Bruxelles, Belgium.

7.1.5. INRIA Cooperative Research Initiative SIRAP

Participants: Maxime Sermesant [correspondant], Xavier Pennec, Tommaso Mansi, Kristin McLeod.

The aim of this Collaborative Research Initiative is to develop physiological and statistical models of the right ventricular outflow tract of repaired Tetralogy of Fallot patients in order to help the design and implant of valves. This action is led by Jean-Frederic Gerbeau from the REO team, INRIA Rocquencourt. It is in collaboration with the pediatric cardiologist Younes Boudjemline, Necker Hospital, Paris.

7.1.6. Consulting for Industry

- Nicholas Ayache is scientific consultant for the company Mauna Kea Technologies (Paris).
- 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).

7.1.7. Collaboration with national hospitals

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

7.1.7.1. 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 [126], [127].

7.1.7.2. 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.

7.1.7.3. CHU de Nice, Hôpital L'Archet

We continue our collaboration with Pr. Dellamonica and Dr. Vassallo of the infectiology department on the study of cognitive impairment in HIV patients.

7.1.7.4. CHU de Bordeaux

We have initiated a collaboration with Pr Michel Haïssaguere and Pr Pierre Jais on the modeling of cardiac electrophysiology and arrhythmias.

7.1.8. Collaboration with international hospitals

7.1.8.1. 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 lead by Pr Reza Razavi. The XMR facility within this hospital is a unique possibility to validate and exploit the cardiovascular modelling work.

7.1.8.2. Children Hospital, Boston

A collaboration with Dr Simon Warfield, director of the Computational Radiology Laboratory has been active for several years, especially on the issue of atlas-based image segmentation and registration.

7.1.8.3. Other International Hospitals

Collaborations with several other European hospitals have been established through the European projects Heath-eChild and euHeart (see sections 6.5 and 6.4).

7.2. Foreign Associated Team: CompuTumor

Participants: Nicholas Ayache, Olivier Clatz [Correspondant], Antonio Criminisi [Microsoft Research], Pierre Fillard, Ezequiel Geremia, Polina Golland [CSAIL, MIT], Ender Konukoglu [Microsoft Research], Bjoern Menze [CSAIL, MIT], Xavier Pennec, Hervé Delingette, Erin Stretton, Simon Warfield [CRL, Harvard Medical School], William Wells [CSAIL, MIT], Boon Thye Thomas Yeo [CSAIL, MIT].

The CompuTumor associated team has been funded early 2007 and renewed in 2009. This project is dedicated to the study of brain tumor models and their integration with medical images to better assist diagnosis and therapy. The project strongly relies on the current collaborations between INRIA and world leading teams with complementary technical and clinical expertise in Boston and Nice. Microsoft Research has been also recently involved in the collaboration on lesion segmentation [50]. Our most recent activity [58], [40], [75], [52], [36], [77], [35] is described in sections 5.4.5, 5.1.3 and 5.4.4 and also on the website of the associated team : <http://www-sop.inria.fr/asclepios/projects/boston/>.

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**⁷. This scientific journal was created in 1996 and is published by Elsevier.
- H. Delingette is a member of the editorial board of the journal *Medical Image Analysis* (Elsevier).
- I. Stobant is editorial coordinator for Medical Image Analysis, Elsevier (since october 2001).
- I. Stobant is editorial assistant for Transactions on Medical Image Analysis, IEEE (since october 2001)
- N. Ayache is associated editor of **IEEE Transactions on Medical Imaging**⁸.
- N. Ayache is a member of the editorial board of the following journals: new SIAM Journal on Imaging Sciences, *Medical Image Technology* (Japanese journal) 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).
- X. Pennec is a member of the editorial board of the journal *Medical Image Analysis* (Elsevier), of the *International Journal on Computer Vision* (Kluwer) and of the SIAM Journal on Imaging Sciences (SIIMS).

8.1.2. Participation in the organization of conferences

- H. Delingette was a member of the scientific review committee of International Conference on Medical Image Computing and Computer Assisted Intervention (MICCAI'10), the International Symposium on Biomedical Imaging (ISBI'10), area chair for the International Conference on Information Processing in Computer-Assisted Interventions (IPCAI'10), a program committee member of the second Eurographics Workshop on Visual Computing for Biology and Medicine Visualization (VCBM'10), the MICCAI 2010 Workshop on Statistical Atlases and Computational Models of the heart (STACOM'10), the Iberian Conference on Pattern Recognition and Image Analysis (IbPRIA 2011), the International Conference on Computer Graphics Theory and Applications (GRAPP'10), the conference on Virtual Reality Interactions and Physical Simulation (VRIPHYS'10).
- G. Malandain was a member of the program committee of the International Conference on Medical Image Computing and Computer Assisted Intervention (MICCAI'10), and a member of the review committee of the International Symposium on Biomedical Imaging (ISBI'10).
- X. Pennec organized the Workshop on Spatio-Temporal Image Analysis for Longitudinal and Time-Series Image Data (STIA 2010), Beijing, China, Sept. 20, 2010. with T. Fletcher and G. Gerig. <http://www.sci.utah.edu/~gerig/MICCAI2010-SpatioTemporal/>, and the Virtual Physiological Human track of the Final Health-e-Child conference, Sestri-Levante, Italy, April 23-24, 2010. He was a member of the program committees of Mathematical method in Biomedical Images (MMBIA 2010), Workshop on Biomedical Image Registration (WBIR 2010), Computational Diffusion MRI workshop (CDMRI 2010), Statistical Atlases and Computational Models of the Heart (STACOM 2010), Medical Computer Vision (SCV 2010), and a member of the review committee of MICCAI 2010 and Volume Graphics (VG 2010).
- M. Sermesant was a co-organisator of the MICCAI 2010 Workshop on Statistical Atlases and Computational Models of the heart.

⁷http://www.elsevier.com/wps/find/journaleditorialboard.cws_home/620983/editorialboard

⁸<http://www.ieee-tmi.org/>

8.1.3. Scientific animation

Nicholas Ayache is member of the scientific council of the Institute for Technologies of INSERM. He is also a member of the "Comité de la Recherche Biomédicale en Santé Publique (CRBSP)" of the Nice hospitals since 2008. He was invited to Tokyo in Japan (4-11 Feb) to evaluate a national program on "Computational Anatomy" funded by the MEXT. He was also invited to Beijing in China to evaluate the LIAMA (Nov 6-13) as a member of its visiting committee.

G. Malandain is deputy scientific director of INRIA in charge of the Computational Sciences for Biology, Medicine and the Environment domain. He has chaired the local experimentation and software development committee (CDT) until Nov 1st 2010. He was member of the AERES evaluation committee for the institute IS2BM of the CEA.

O. Clatz is a member of the scientific committee and evaluator for the research cluster ISLE of Rhône-Alpes.

X. Pennec was an evaluator for several project proposals submitted to the French research agency ANR, for the Fonds de la Recherche Scientifique - FNRS (Belgique), for the Science Foundation of Ireland, for the US-Israel Binational Science Foundation (BSF) and for the Natural Sciences and Engineering Research Council of Canada (NSERC). He is also a member of the local committee for PhD follow-up (Comité de suivi doctoral).

H. Delingette was a member of the local committee in charge of the scientific selection of visiting scientists applications (Comité Nice). He was an evaluator for the integrated European project ARTREAT, for the Netherlands Organisation for Scientific Research (NWO), for the University of Reims Champagne-Ardenne, for the European Space Agency, for several project proposals submitted to the French research agency ANR.

M. Sermesant is an evaluator for the Biotechnology and Biological Sciences Research Council (BBSRC), and the National Institute for Health Research (NIHR), EPSRC United Kingdom, and New Zealand and Netherlands Research councils. He is member of the CUMIR (local committee representing the users of computer services) and of the CCC (local committee in charge of the selection of funding for courses and conferences organisation).

8.2. University teaching

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

Master IFI - Computational Biology, Univ. Nice-Sophia-Antipolis. X. Pennec is responsible of a 21h module on Computational Anatomy and Physiology, with the participation of H. Delingette (9h)

Master IMA, Université Pierre et Marie Curie. G. Malandain gave a 3 h course.

Diplôme Inter Universitaire - Radiothérapie externe Haute Technicité. G. Malandain gave a 3 h course.

Enseignement post-universitaire: imagerie en radiothérapie externe. G. Malandain gave a 3 h course.

Classe Préparatoire, Lycée Stanislas. During the academic year, Olivier Clatz is an oral examiner in engineering sciences for 2 hours a week.

8.3. PhD Theses and Internships

8.3.1. PhD defended in 2010

1. Florence Billet, *Assimilation de données images pour la personnalisation d'un modèle électromécanique du coeur*, Nice Sophia-Antipolis University, July 2010.
2. Stanley Durrleman, *Statistical models of currents for measuring the variability of anatomical curves, surfaces and their evolution*, PhD Thesis, Nice Sophia Antipolis University, March 2010.

3. Romain Fernandez, *Reconstruction tridimensionnelle et suivi de lignées cellulaires à partir d'images de microscopie laser : application à des tissus végétaux*, Thèse de sciences, Université Montpellier 2, November 2010. Committee : C. Fiore (president), L. Blanc-Feraud (reviewer), N. Peyrieras (reviewer), C. Godin, P. Das. J.-L. Verdeil, G. Malandain.
4. 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, July 2010.
5. Tommaso Mansi, *Image-Based Physiological and Statistical Models of the Heart, Application to Tetralogy of Fallot*, PhD Thesis, Ecole Nationale Supérieure des Mines de Paris, September 2010.

8.3.2. Current PhDs

1. Barbara André, *Smart Atlas for the Early Diagnosis of Gastrointestinal Cancers from Optical Biopsy Images*, École des Mines de Paris. Cifre collaboration with Mauna Kea Technologies.
2. Marine Breuille, *Tracking and quantification of tumour processes in rodents with SPECT imaging*, Nice Sophia-Antipolis University.
3. François Chung, *Regional shape and appearance modelling for deformable model-based image segmentation*, École des Mines de Paris.
4. Ezequiel Geremia, *Multi-scale computational models of brain tumors for medical image analysis*, Nice Sophia-Antipolis University.
5. Yonni Levy, *Advanced Guidance in interventional cardiology*, École des Mines de Paris.
6. Marco Lorenzi, *Imaging Biomarkers in Alzheimer's Disease*, Nice Sophia-Antipolis University, In collaboration with G. Frisoni, IRCCS Fatebenefratelli, Brescia, Italy.
7. Kristin McLeod, *Modeling of Cardiac Growth and Deformation from Medical Images*, Nice-Sophia Antipolis University.
8. Adityo Prakosa, *Analysis and Simulation of the heart function from multimodal cardiac images*, Nice-Sophia Antipolis University.
9. Liliane Ramus, *Digital anatomical atlases for radiotherapy planning*, Nice-Sophia Antipolis University. Cifre collaboration with Dosisoft.
10. Jatin Relan, *Planning of radiofrequency ablation of the heart using electromechanical models personalized from cardiac images and electrophysiological signals*, Ecole des Mines de Paris.
11. Christof Seiler, *Prediction of the Bone Shape from Clinically Relevant Variables*. Joint PhD between University of Nice-Sophia Antipolis and University of Bern, Switzerland.
12. Erin Stretton, *Modelling and simulation of brain tumor growth from time-series of 3-D MR images to improve diagnosis and therapy*, Ecole des Mines de Paris.
13. Hugo Talbot, *Simulation of radiofrequency ablation of cardiac cells*, University of Lille.
14. Nicolas Toussaint, *In vivo cardiac DTI*, King's College London, London

8.3.3. Master Student

1. Islem Rekik, *Tumor Growth Parameter Estimation and Source Localization From a Unique Time Point*, Master MVA ENS Cachan.

8.3.4. Participation to thesis committees

- N. Ayache participated as co-supervisor to the PhD thesis of Florence Billet (Nice University), Tommaso Mansi (Ecole des Mines de Paris) and Stanley Durrleman (Nice-Sophia Antipolis University), as reviewer to the Habilitation jury of Emmanuel Mandonnet (Neurosurgeon, Pitié Salpêtrière) in May 2010

Hervé Delingette participated as co-supervisor to the PhD thesis of Florence Billet (Nice University), Tommaso Mansi (Ecole des Mines de Paris), as chair to the PhD thesis committee of T. Jund (Strasbourg University), as reviewer to the PhD thesis committee E. Essafi (Ecole Centrale Paris).

Grégoire Malandain participated as referee to the PhD thesis committees of A. Besbes (Ecole Centrale Paris) and R. Fernandez (Montpellier II university), as reviewer to the PhD thesis committee of H. Boisgontier (Strasbourg University), B. Combès (Rennes 1 university), D. Garcia (Rennes 1 university), J. Lebenberg (Paris-Sud 11 university), Z. Ouksili (Toulouse university) and A. Cifor (Nottingham university), and as chair to the PhD thesis committees of J. Vandemeulebroucke (INSA Lyon) and J. Wojak (Télécom ParisTech).

Xavier Pennec participated as co-supervisor to the PhD thesis committees of Heike Hufnagel (University of Hamburg / Lubeck. July 2010), Tommaso Mansi (Ecole des Mines de Paris, September 2010), Stanley Durrleman (Nice-Sophia Antipolis University, March 2010), and as member of the jury of the PhD of Mickaël Savinaud (Ecole centrale Paris, October 2010).

Maxime Sermesant participated as co-supervisor to the PhD thesis committee of Florence Billet (Nice Sophia-Antipolis University) and Tommaso Mansi (Ecole des Mines de Paris).

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 the following invited lectures:
 - invited lectures in February 2010 in Japan at Tokyo University for the opening lecture of the Computational Anatomy Symposium, and at the Nagoya, Gifu and Osaka Universities.
 - a Keynote introduction lecture of the " INRIA-Industry " meeting in Bordeaux
 - an invited lecture for the 60 year birthday of Olivier Faugeras in Sophia Antipolis in June
 - an invited lecture for the 65 year birthday of Mike Brady in Oxford in Sept
 - an invited lecture at the TUM (Munich) in Oct.
 - a Keynote Lecture at the Royal Society in London on Nov 4. during the symposium on "Computational Frontiers in Scientific Discovery".
 - a keynote lecture at Ecole Centrale Paris in Nov 2010
 - an invited lecture at Jiao Tong University of Shanghai (11 november).
 - an invited lecture at GRD Stic-Santé on mathematical models of tumor growth in Paris in Dec 2010.
- **Hervé Delingette** gave invited lectures at the MICCAI 2010 Workshop on Statistical Atlases and Computational Models of the heart (STACOM'10) on Sept. 20th, at the GSIH conference in Spitzingsee (Germany) organized by TUM, at the second EuroNOTES/CTAC/CARS Workshop on NOTES in Geneva on June 25th, at the Philips HealthCare Headquarters in Best (The Netherlands) on June 10th, at the Center of Applied Mathematics at Ecole Polytechniques on October 14th, at the meeting of the "Club des Dirigeants" in Sophia-Antipolis on March 18th.
- **Xavier Pennec** gave invited keynote talks at the 10th Symposium of Mathematical Aspects of Image Processing and Computer Vision (MAIPCV 2010, Sapporo, Hokkaido Univ. November 25-27) and the Workshop on Biomedical Image registration (WBIR'2010, Lübeck, July 12-13) ; and invited lectures at the International seminar of the Computational anatomy project (Tokyo, November 24, 2010), the Traumatic Brain Injuries (TBI) Roadmap Workshop, Chicago on June 7-8, 2010. and the Leon Brillouin transdisciplinary seminar, GdR Science de Géométrie de l'Information (Paris, Mai 28, 2010).
- **Maxime Sermesant** gave invited lectures at Cardiosim 2010 in Nice and the European Society of Cardiology clinical conferences in Stockholm. He also gave an introduction lecture in Antibes, Valbonne and Nice high schools.
- **Stéphanie Marchesseau** gave a introduction lecture at the "la Providence" high school in Nice.

8.5. Nominations and prizes

- **Nicholas Ayache** was appointed on the visiting committee of the LIAMA institute in Beijing that he evaluated on Nov 8-9
- **Stanley Durrleman** received the second Gilles Kahn prize for his PhD [27] co-supervised by N. Ayache, X. Pennec and A. Trouvé.
- **Erik Pernod** received the best paper award of the second Eurographics Workshop on Visual Computing for Biology and Medicine Visualization (VCBM'10) for his paper [60] on interactive simulation of radiofrequency ablation of cardiac tissues.
- **Marco Lorenzi** received the best paper award at the MICCAI workshop STIA 2010 (Spatio-Temporal Image Analysis for Longitudinal and Time-Series Image Data) for his paper [54] on registration of brain images.
- **Ezequiel Geremia** has been nominated for the " young scientist MICCAI Award " for his paper [50] on tumor segmentation at the MICCAI 2010 conference held in Beijing, China.
- **Liliane Ramus** " received the third prize [73] of the " Head & Neck Auto-segmentation Challenge 2010: Segmentation of the Parotid Glands " organized during the MICCAI workshop " Grand Challenges in Medical Image Analysis ".
- **Xavier Pennec** is a co-author of the book chapter Grid Analysis of Radiological Data which received the IGI-Global Medical Information Science Discoveries-Research Book Chapter 2009 Award.

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