



Activity Report 2011

Project-Team ASCLEPIOS

Analysis and Simulation of Biomedical Images

RESEARCH CENTER
Sophia Antipolis - Méditerranée

THEME
**Computational Medicine and Neuro-
sciences**

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Project-Team ASCLEPIOS

Keywords: Biological Images, Medical Images, Virtual Physiology, Image Processing, Simulation

1. Members

Research Scientists

Nicholas Ayache [Team Leader, Senior Researcher, INRIA, HdR]
Olivier Clatz [Junior Researcher, INRIA]
Hervé Delingette [Senior Researcher, INRIA, HdR]
Stanley Durrleman [Junior Researcher détaché Corps Télécom]
Grégoire Malandain [Senior Researcher, INRIA, HdR]
Xavier Pennec [Senior Researcher, INRIA, HdR]
Maxime Sermesant [Junior Researcher, INRIA]

Technical Staff

Benoît Bleuzé
Michael Knopke
Vincent Garcia
Brina Goyette
Federico Spadoni
Stephan Schmitt
John Stark

PhD Students

Barbara André [Funding Cifre Mauna Kea Technologies, 2011]
Marine Breuille [Ministry of Research, 2012]
François Chung [Funding 3D Anatomical Human, 2011]
Ezequiel Geremia [Funding Microsoft, 2012]
Arnaud Le Carvanec [UCL, 2014]
Hervé Lombaert [Ecole Polytechnique de Montréal, 2012]
Marco Lorenzi [Funding Neurolog, 2012]
Kristin McLeod [Funding Care4Me, 2013]
Stéphanie Marchesseau [Funding euHeart, 2012]
Adityo Prakosa [Funding Philips and euHeart, 2012]
Liliane Ramus [Funding Cifre DOSIsoft, 2011]
Jatin Relan [Funding EC euHeart, 2012]
Christof Seiler [University of Bern, 2013]
Erin Stretton [Funding Care4Me, 2013]
Hugo Talbot [Funding INRIA, 2013]
Nicolas Toussaint [Funding KCL INRIA, 2012]
Jan Margeta [Funding Microsoft, 2014]
Vikash Gupta [Funding INRIA, 2014]

Administrative Assistant

Isabelle Strobant [TRS, Research Team Assistant, Inria]

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 French Academy of Medicine etc.).
- **Christof Seiler** received the Young Investigator award at the Miccai 2011 conference held in Toronto for his paper[68] .
- **Kristin McLeod** and **Adityo Prakosa** received the Best Paper awards for their article on the evaluation of algorithms for cardiac motion recovery [64] at the MICCAI 2011 STACOM Workshop.
- **Hervé Lombaert** received a Best Paper Award at the FIMH 2011 conference in New York for his paper on human cardiac fiber atlas[56] .
- **Marco Lorenzi** received an Honorable mention (runner-up) for the Erbsmann Award at the IPMI conference, Irsee, Germany, 2011 for this paper[61] .
- **Olivier Clatz** and Pierre Fillard (EPI Parietal) were awarded at the national contest for the creation of start-up companies in the category "Emergence"

BEST PAPERS AWARDS :

[68] **Proceedings of Medical Image Computing and Computer Assisted Intervention 2011 (MICCAI)**. C. SEILER, X. PENNEC, M. REYES AGUIRRE.

[64] **Proc. MICCAI Workshop on Statistical Atlases and Computational Models of the Heart: Mapping Structure and Function (STACOM11)**. K. MCLEOD, A. PRAKOSA, T. MANSI, M. SERMESANT, X. PENNEC.

[56] **Proceedings of FIMH Conference 2011**. H. LOMBAERT, J.-M. PEYRAT, P. CROISILLE, S. RAPACCHI, L. FANTON, P. CLARYSSE, H. DELINGETTE, N. AYACHE.

[61] **Proceedings of Information Processing in Medical Imaging (IPMI'11)**. M. LORENZI, N. AYACHE, X. PENNEC.

3. Scientific Foundations

3.1. Introduction

Tremendous progress has been made in the automated analysis of biomedical images during the past two decades [100]. 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 [91], [89]. Regarding the target applications, a good review of the state of the art can be found in the book *Computer Integrated Surgery* [87], in N. Ayache's article [95] and in the more recent syntheses [96] [100]. The scientific journals *Medical Image Analysis* [82], *Transactions on Medical Imaging* [88], and *Computer Assisted Surgery* [90] 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) [85], [86] or ISBI'2010 (Int. Symp. on Biomedical Imaging) [84].

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 [101], [117]. 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 [120], or to measure some functional properties of the heart from dynamic sequences of Magnetic Resonance [94], Ultrasound or Nuclear Medicine images [102].

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

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.

(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 [107].

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 [121].

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 [114] and to the Mouse Brain Atlas Project [93]). 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 [119]). Significant efforts have been made since that time to develop a theory for statistical shape analysis (one can refer to [99] for a good synthesis, and to the special issue of Neuroimage [118] 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 [109]: 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.

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

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.

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 [113], [106], [97], [115], [103]). 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. [116], [110]) 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 [98]:

- the first level is mainly geometrical, and addresses the construction of a digital description of the anatomy [92], essentially acquired from medical imagery;
- the second level is physical, involving mainly the biomechanical modeling of various tissues, organs, vessels, muscles or bone structures [104];
- the third level is physiological, involving a modeling of the functions of the major biological systems [105] (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 [83].

These different levels of modeling are closely related to each other, and several physiological systems may interact together (e.g. the cardiopulmonary interaction [108]). 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 [105], [106]). 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], Brina Goyette, Federico Spadoni, 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

- ACM: J.3
- Programming language: C/C++

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 by the Asclepios research project in collaboration with the Athena, Parietal and Visages Inria research projects. 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/7, Linux Fedora Core, MacOSX, and is fully multithreaded.

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

- Version: 2.0
- Keywords: Medical Image Processing
- License: Proprietary Licence
- Type of human computer interaction: QT
- 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. *Spatial Decision Forests for MS Lesion Segmentation in Multi-Channel MR Images*

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

- A new approach for MS lesions segmentation was proposed [33]
- Random forest for automatic segmentation of MS lesions in 3D MR images
- Features: multi-channel MR intensities, priors, long-range spatial context, symmetry
- Quantitative evaluation shows significant improvement over the MICCAI Grand Challenge 2008
- The automatically learned decision sequence mimics the state-of-the-art pipeline
- Independent validation carried out by the MICCAI Challenge website 2008
- Exhaustive analysis of the discriminative power of channels and features
- Analysis of the influence of random forest's meta-parameters on the classification performance

5.1.2. *Left Ventricle Segmentation from Cardiac 4D Cine MRI Sequences*

Participants: Jan Margeta [Correspondant], Ezequiel Geremia, Nicholas Ayache, Antonio Criminisi [MSR].

This work was performed in collaboration with Microsoft Research and was partly supported through its PhD Scholarship Programme.

- We extend the previous work for multiple sclerosis lesion segmentation of Geremia et al. [33] for spatio-temporal cardiac images.
- A fully automatic two layer left ventricle segmentation algorithm from 4D cardiac cine MRI sequences (See Fig. 2) was proposed for MICCAI STACOM LV segmentation challenge [63] using a random forest classification algorithm.
- Spatio-temporal features are used in the random forest framework to learn the segmentation task without explicitly defining the segmentation rules.
- Machine learning based MRI intensity standardization and pose normalization preprocessing pipeline was proposed to deal with diverse cardiac MRI datasets.

5.1.3. *Design and use of anatomical atlases for automatic segmentation: application to radiotherapy of the head and neck region*

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

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

In the context of radiotherapy of the head and neck, we propose different strategies to design anatomical atlases and we compare their performances for automatic segmentation [28]:

- We investigate average atlas construction, atlas stratification and patient-specific strategies based on the selection and fusion of the most appropriate atlases for each patient. We compared global, regional and local selection and fusion of the atlases.
- We show that the proposed patient-specific strategies enable to significantly improve the quality of the automatic segmentation in comparison with average atlas strategies. Visual results are presented on figure 3.
- We evaluated the proposed algorithms in two different contexts: segmentation of the lymph node levels and the organs at risk for radiotherapy planning, and segmentation of the teeth for post-irradiation dental care management. Automatic segmentations of the teeth are shown on figure 4.

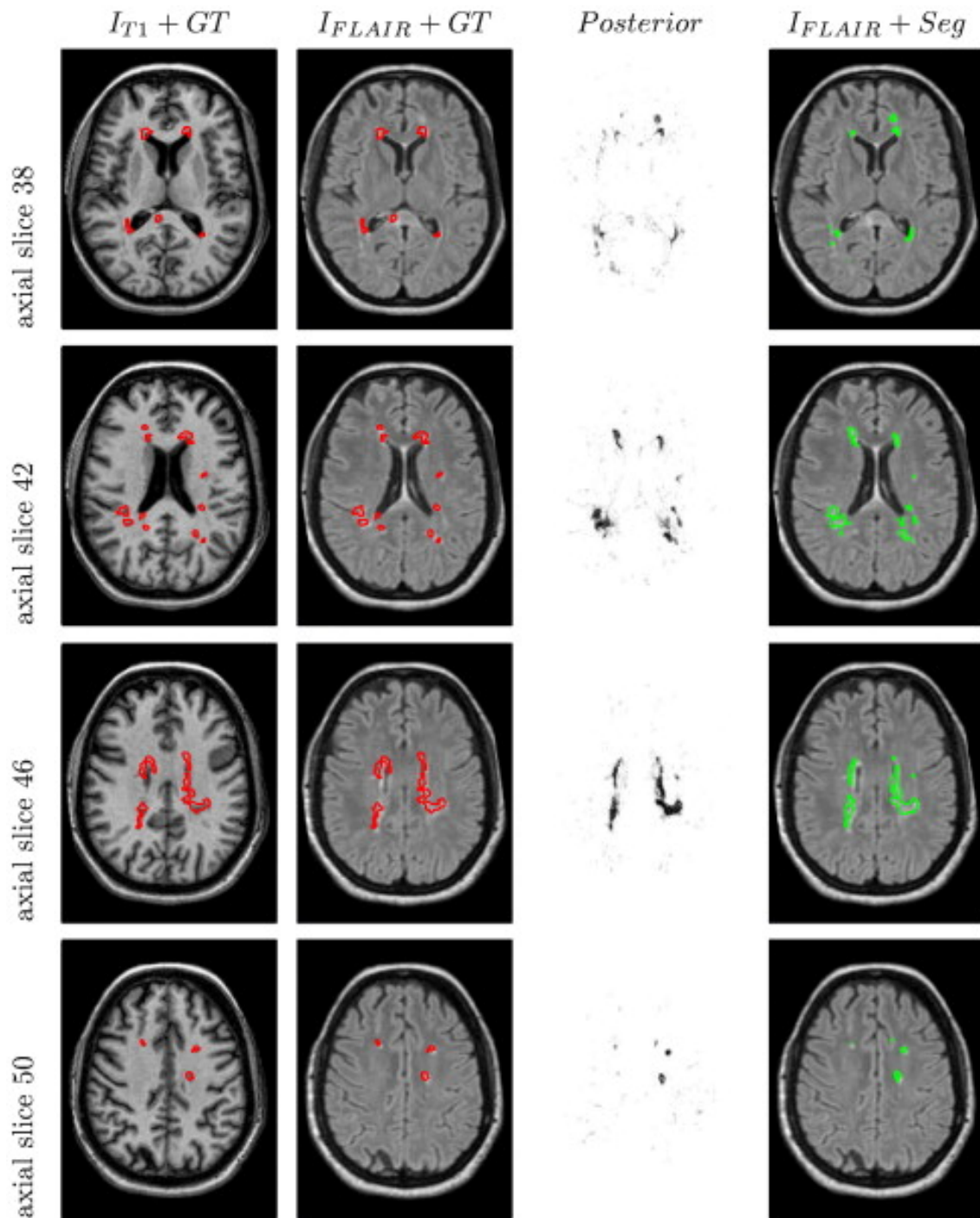


Figure 1. **Segmenting Case CHB05 from the public MSGC dataset.** From left to right: preprocessed T1-weighted (I_{T1}), T2-weighted (I_{T2}) and FLAIR MR images (I_{FLAIR}) overlaid with the associated ground truth GT, the posterior map $Posterior = (P_{lesion}(\mathbf{v}_k))_k$ displayed using an inverted grey scale and the FLAIR sequence overlaid with the segmentation ($Seg = (Posterior \geq \tau_{posterior})$ with $\tau_{posterior} = 0.5$). Segmentation results show that most of lesions are detected. Although some lesions are not detected, e.g. peri-ventricular lesion in slice 38, they appear enhanced in the posterior map. Moreover the segmentations of slices 38 and 42 show peri-ventricular regions, visually very similar to MS lesions, but not delineated in the ground truth.

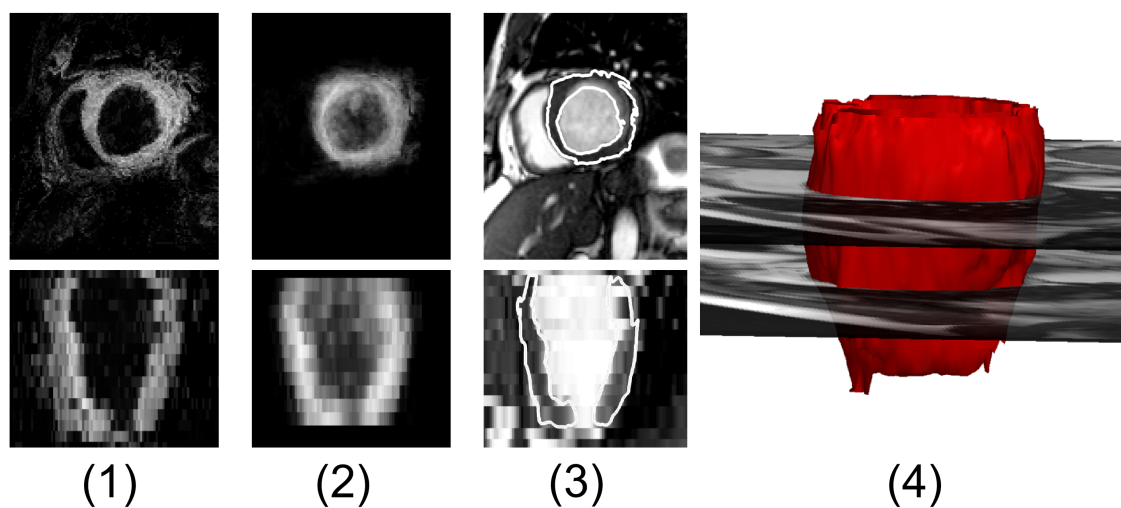


Figure 2. Two classification layers are used for left ventricle segmentation with random forests. (1) first layer posterior probability is used as a weight map for context aware MRI intensity standardization and cardiac pose normalization, (2) second layer is then used for a more confident left ventricle segmentation, (3) second level posterior probability isocontour overlay, (4) volumetric visualisation of the obtained segmentation.

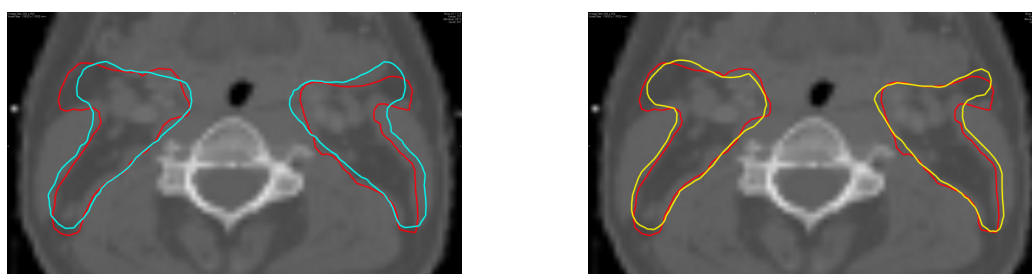


Figure 3. Atlas-based segmentation of the lymph node level II using the average atlas (blue contours on left figure) and using the atlas that is locally adapted to the patient's anatomy (yellow contours on right figure), compared with the manual contours (red contours on both figures).

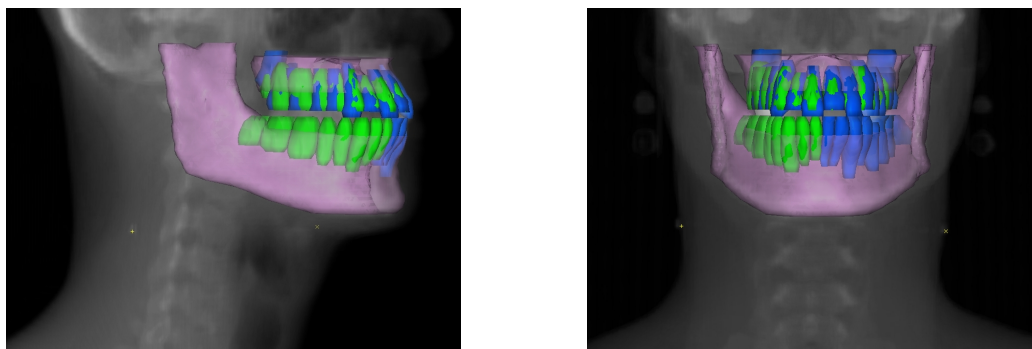


Figure 4. Automatic segmentation of the teeth using a multi-atlas framework (in green) in comparison with the manual segmentation (in blue). Both segmentations are represented on the upper jaw.

5.2. Biological Image Analysis

5.2.1. Pre-clinical molecular imaging: reconstruction of tumors in rodents with SPECT imaging

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

This work is jointly conducted with the Transporter in Imagery and Oncologic Radiotherapy team (TIRO, CEA-CAL-UNSA) located in Nice.

The coupled CT and SPECT device allows to image both the anatomy (with the CT) and physiology information targeted by a dedicated radio-pharmaceutical tracer (here the tumors, with the SPECT). However, tumor quantification is impaired by the respiratory motion that induces an artificial enlargement of the moving structures. We propose then to select all the motion-less phases from a 4D SPECT images to reconstruct a motion-free 3D image. In addition, we also propose to correct for the heterogeneity of the respiratory cycles by re-tagging the SPECT raw data.

The resulting 3D motionless gated image shows improvement of volume accuracy compared to the non gated SPECT image; and noise reduction compared to the 4D SPECT image (see Figure 5)

5.3. Computational Anatomy

5.3.1. The Kernel Bundle framework: Sparse Multiscale Diffeomorphic Deformations

Participants: Stefan Sommer [DIKU], Mads Nielsen [DIKU], François Lauze [DIKU], Xavier Pennec [Correspondant].

This work is performed in collaboration between DIKU (University of Copenhagen) and Asclepios (Inria). It was initiated during a 5 month visit of Stefan Sommer in 2011.

In the analysis and modeling of anatomical deformations, we expect deformations to have both large and small scale components. However, we expect these large and small scale deformation to occur at different places. Thus, one would like to represent anatomical deformations with a small number of deformation atoms are different scales that are sparsely distributed across space and scale.

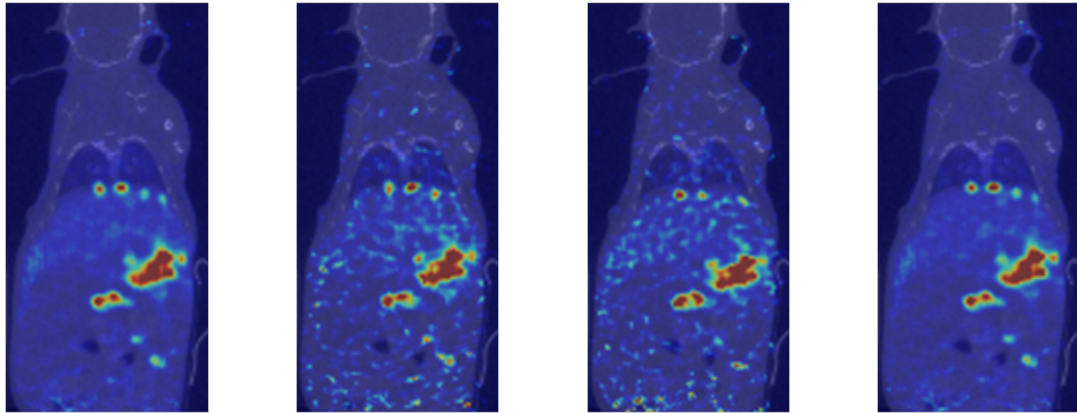


Figure 5. Coronal slices of fused SPECT and CT images from a NOD-SCID mouse (data acquired with GE eXplore speCZT CT 120): central hot spots reveal intraperitoneal metastasis from adenocarcinoma of the colon (PROb-mNIS). Left to right: non gated, phase at end of expiration, phase at end of inhalation, and motionless gated.

- In [71], we propose a multi-scale kernel bundle framework (LDDKBM) that extends the LDDMM framework by incorporating multiple kernels at multiple scales in the registration. Experiments show that the method automatically adapts to the right scales, and it therefore removes the need for classical scale selection methods.
- In [72], we derive the Kernel Bundle EPDiff evolution equations, which provide optimal warps in this new framework.

5.3.2. Longitudinal modeling of the structural changes of the brain in Alzheimer’s disease.

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

This work is done in collaboration with LENITEM, IRCCS San Giovanni di Dio Fatebenefratelli, Brescia, Italy.

This work addresses the analysis and the quantification of the longitudinal structural changes of the brain affected by Alzheimer’s disease (AD). We propose a framework based on the non-rigid registration of brain MRIs using stationary velocity fields. In 2011, the main scientific developments were:

- Unbiased detection of the structural changes in the brain [60]. The method robustifies the Demons diffeomorphic registration by estimating and removing the multiplicative and additive intensity biases affecting the images.
- Definition of a population-based atlas for the longitudinal brain structural changes. In this work we proposed the Schild’s Ladder as a general method for parallel transporting the subject-specific longitudinal deformation trajectories in a reference space [61]. The work was awarded with the runner-up prize at the “Information Processing in Medical Imaging (IPMI)” conference in Irsee, Germany. Other transport methods from the Lie group theory have been successively proposed and investigated [62].
- Group-wise statistical analysis of the brain longitudinal changes in multiple time points [60]. The framework has been applied for the analysis of the longitudinal brain changes in healthy subjects at risk of AD, and the results showed an accelerated progression of atrophy for the subjects positive to

the marker of Alzheimer $A\beta_{42}$ (see Figure 6).

Finally, the above framework has been promoted to the neuroscience community as diagnostic tool and support for clinical trials [75].

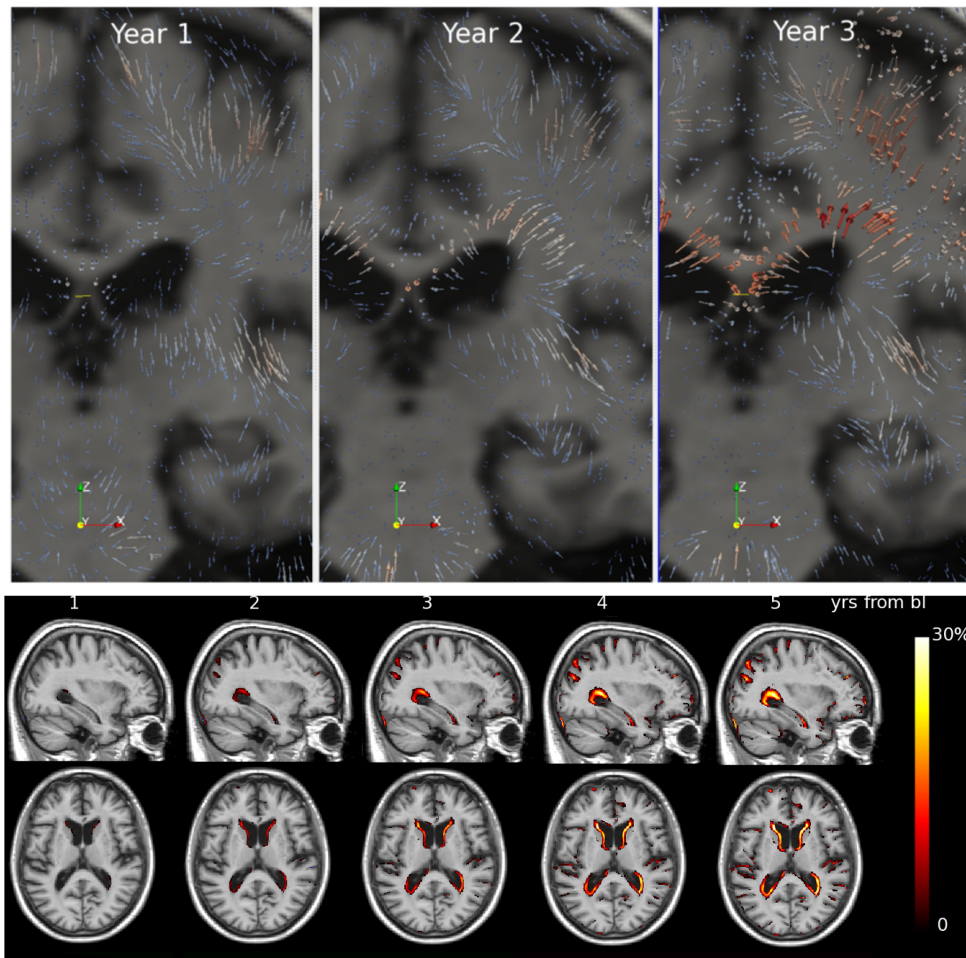


Figure 6. Top. Average longitudinal brain atrophy for the healthy subjects at risk for Alzheimer's disease ($A\beta_{42}$ positive). Bottom. Annual percentage differential evolution modelled for the $A\beta_{42}$ positive group with respect to the healthy aging. The analysis shows an increased ventricular expansion and the matter loss in the cortex and in the temporal areas.

5.3.3. Statistical Analysis of White Matter Fiber Bundles

Participants: Stanley Durrleman [Correspondant], Pierre Fillard [Parietal, INRIA Saclay], Xavier Pennec, Alain Trouvé [CMLA, ENS Cachan], Nicholas Ayache.

This work is an application of the generic morphometric method developed in 2009 to the statistical analysis of the shape and texture of white matter fiber bundles extracted from Diffusion Tensor Images (DTI).

- Registration, Atlas Estimation and Variability Analysis of White Matter Fiber Bundles Modeled as Currents [32].

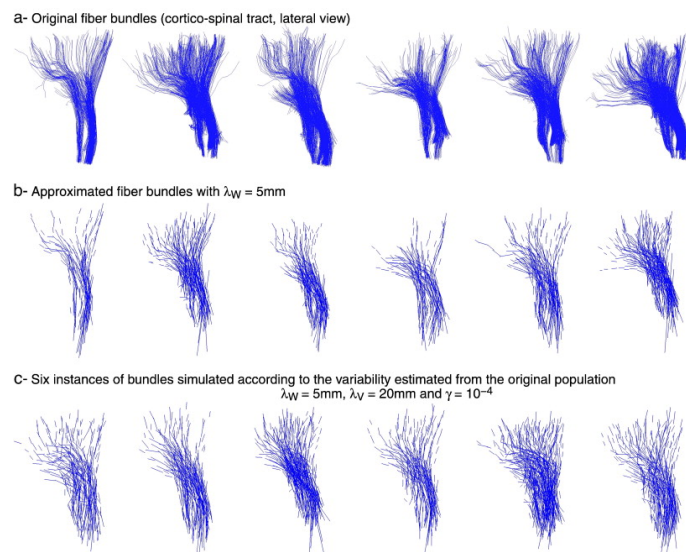


Figure 7. The proposed method estimates a variability model from the white matter fiber bundles extracted from six subjects (a-original data, b- same data approximated at the current resolution). The model allows us to synthesize artificial bundles that reproduce the variability in shape and in fiber density estimated from the original data (c).
 Image taken from [32]

5.3.4. Comparison of endocranial ontogenies in chimpanzees and bonobos

Participants: Stanley Durrleman [Correspondant], Xavier Pennec, Alain Trouvé [CMLA, ENS Cachan], Nicholas Ayache, José Braga [AMIS, Univ. Toulouse 3].

This work has been performed in the context of the INRIA collaborative project ARC 3D-Morphine (PI: Sylvain Prima, IRISA) and a follow-up collaboration with José Braga at Université Paul Sabatier, Toulouse.

This work quantifies ontogenetic differences between bonobo and chimpanzee endocrania, using dental development as a timeline. Synthetic endocranial trajectories are estimated from time series cross-sectional data. Then, differences in morphology and in rate of shape changes is quantified using the spatiotemporal registration introduced in 2009.

- Comparison of the endocranial ontogenies between chimpanzees and bonobos via temporal regression and spatiotemporal registration.

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

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

Parts of this work were performed within the framework of the EU project Care4me ITEA2, and the INRIA ARC Sirap, in collaboration with St Thomas Hospital, King's College London, the REO team from INRIA Rocquencourt and Necker Paediatric Hospital in Paris.

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

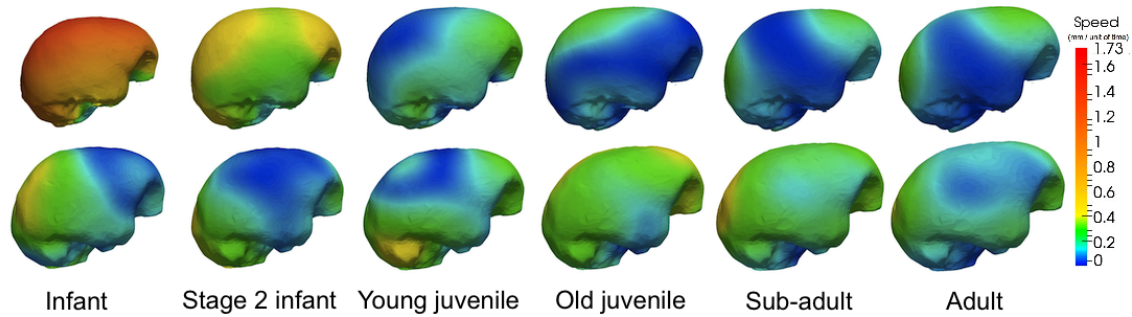


Figure 8. Typical endocranial trajectory of bonobos (top) and chimpanzees (bottom) estimated from time series cross-sectional surface data (59 chimpanzees and 60 bonobos)

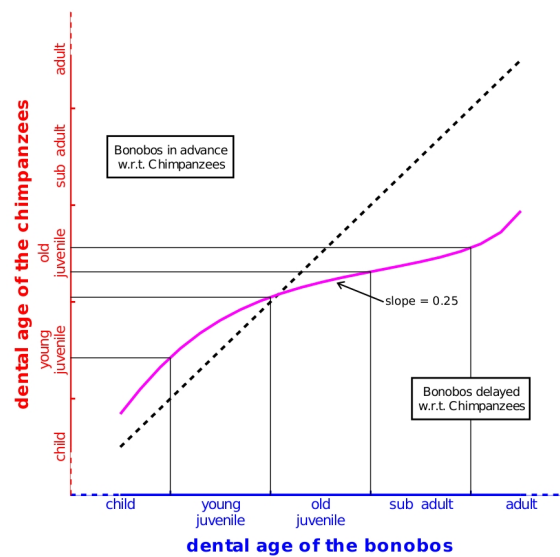


Figure 9. Graph of time-wrap (magenta curve) putting into correspondence the developmental stages of the bonobos to that of the chimpanzees. The function measures the differences in rate of shape changes over time between the endocranial trajectories estimated in Fig. 8. This shows that the bonobos endocranial ontogeny is retarded by a factor 0.25 compared to that of the chimpanzees.

- The iLogDemons motion tracking algorithm of Mansi et. al [37] was applied to a data-set of 15 subjects and 1 phantom each with a cine-MR, tagged-MR and echocardiography sequence as a part of the STACOM workshop challenge at MICCAI 2011 [64]. The paper received the Best Paper Award for the Motion Challenge.
- The work of Mansi et. al for a statistical model of cardiac growth in the right ventricle [38] was extended to the left ventricle to obtain a bi-ventricular cardiac growth model for patients with repaired tetralogy of Fallot (see Fig.10).
- The preliminary analysis of a statistical model for reduced blood flow simulations in the pulmonary artery proposed in 2010 is currently being extended to a journal version to further analyse the method on a larger data-set.

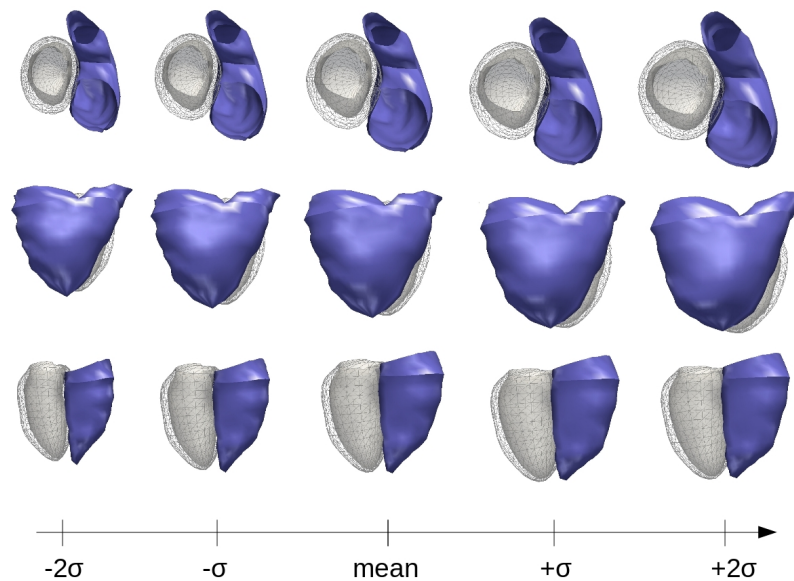


Figure 10. Mean growth model computed from a population of 13 repaired tetralogy of Fallot patients. Both ventricles grow as body surface area (used as an index of growth) increases.

5.3.6. Statistical Modeling of Shapes Using Trees of Locally Affine Transformations

Participants: Christof Seiler [Correspondant], Xavier Pennec, Mauricio Reyes [Institute for Surgical Technology and Biomechanics, University of Bern, Switzerland].

This work is performed in the context of the joint PhD of Christof Seiler at the Institute for Surgical Technology and Biomechanics, University of Bern, Switzerland and Asclepios INRIA.

The goal of this work is to analyze anatomical shapes through deformations defined with few but important and intelligible parameters. Advances towards this goal were the following in 2011.

- Fusion of the Log-demons registration and the Log-Euclidean polyaffine framework. The results of the new registration method applied to femur CT's was presented at SPIE [69].
- Decomposition of diffeomorphic deformations into a tree of locally affine transformations applied to mandible CT's. This work won the young scientist award at MICCAI 2011 in Toronto [68].

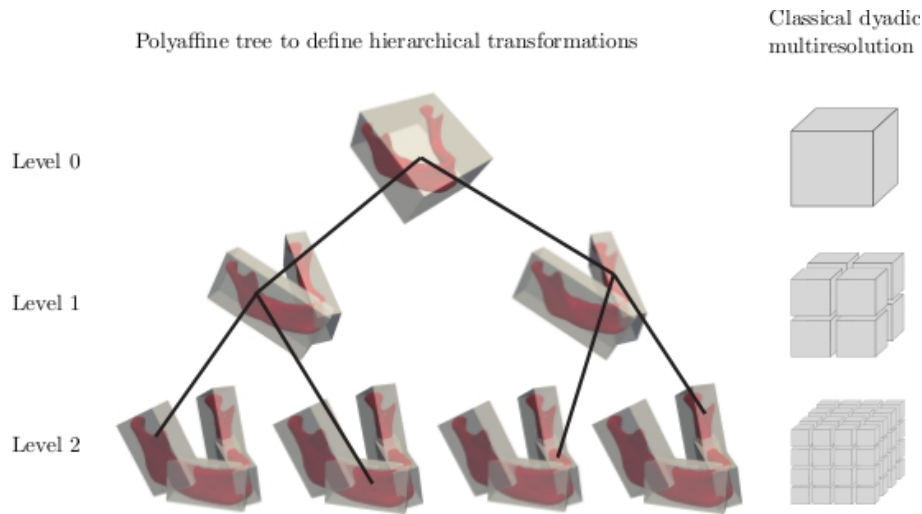


Figure 11. First three levels of space decomposition. Left: Our new method decomposes the image domain using a tree of oriented bounding boxes. Right: For comparison, a traditional approach using a dyadic multiresolution scheme.

5.3.7. Atlas of Cardiac Fiber Architecture from DT-MRI

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

This work is a collaboration between Creatis, Lyon and INRIA Sophia Antipolis, including members of Ecole Polytechnique of Montreal. Financial support is partly from the National Science and Engineering Research Council of Canada, and the Michael Smith Foreign Study Program.

The variability of the cardiac fiber architecture has been investigated in a human population. An automatic method has been developed to construct an atlas of DTMRI images. A statistical analysis has been carried on using the Log-Euclidean metric.

- An automatic method has been developed to construct an atlas of DTMRI images. The first human atlas of DTMRI has been build [56]. This work received the Best Paper Award at the FIMH 2011 conference in New York City.
- Results have also been published in [59] where the variability of the cardiac architecture is measured using the Log-Euclidean metric.
- The variability of the cardiac laminar sheets in human DTMRI has been studied [58].
- Differences in a population of normal and abnormal hearts have been investigated [57].

5.4. Computational Physiology

5.4.1. Tumor Growth Modeling

Participants: Erin Stretton [Correspondant], Nicholas Ayache, Hervé Delingette, Bjoern Menze, Ender Konukoglu, Ezequiel Geremia, Emmanuel Mandonnet.

This work was funded by Care4me.

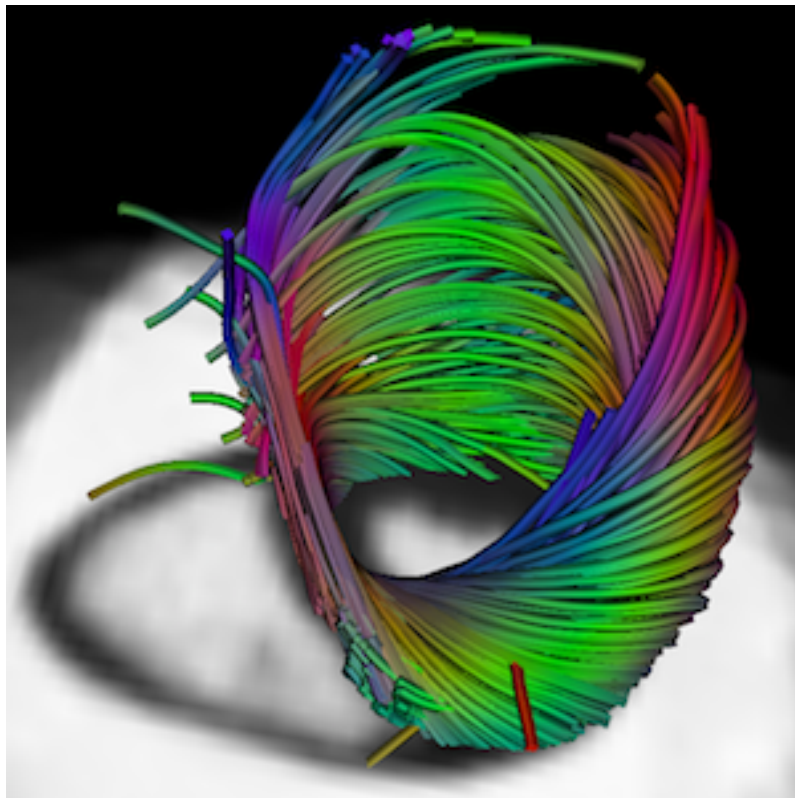


Figure 12. Tracked fibers from the human atlas of DTMRI of the myocardium.

- Performing a sensitivity analysis of long time series of multi-modal data.
- Improving our current models and their inputs, including creating a white matter and brain mask template with the help of a neurosurgeon and integrating the Powell bound constrained optimization into the minimization routine.
- Performed comparison of using a patient DTI, an atlas DTI or no DTI at all showing the difference in accuracies in the simulation results since the patient DTI is not always available in a clinical setting or is of poor quality. We found that using an atlas DTI produced only slightly less accurate results than using a patient DTI, where as using no DTI at all did not produce accurate results.

5.4.2. Synthetic Echocardiographic Image Sequences for Cardiac Inverse Electro-Kinematic Learning

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.

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

- A database of 120 synthetic 3D echocardiography (US) sequences is created based on a cardiac electromechanical model (see Figure 13).
- Kinematic descriptors are extracted from the displacement field estimated from the synthetic 3D US sequence using the iLogDemons non-rigid registration method [37].
- Cardiac inverse electro-kinematic learning is done by using the database of synthetic 3D US sequences in order to estimate the cardiac depolarization times for the given kinematic descriptors [67]. First evaluation on two clinical sequences from patients with Left Bundle Branch Block shows encouraging results.

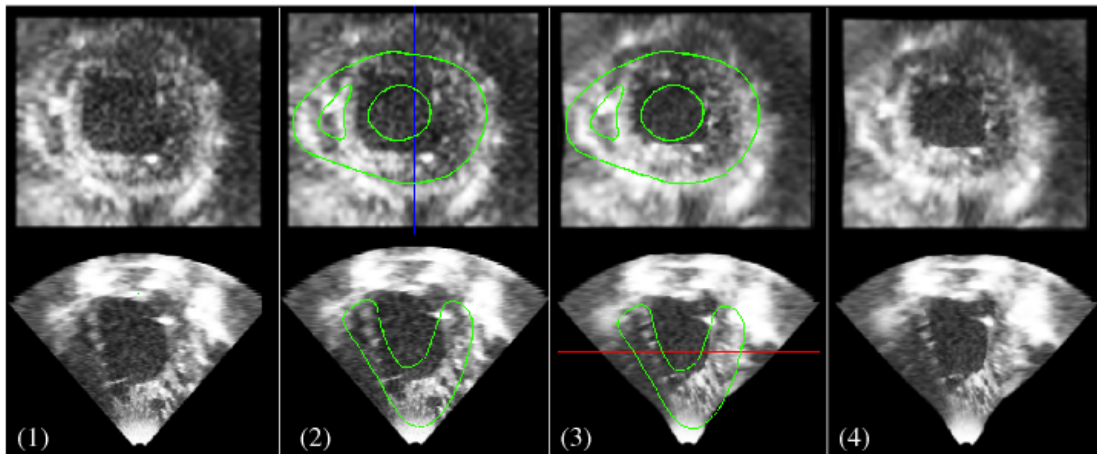


Figure 13. *Synthetic 3D US. (1) original real image with (2) contour of the mesh at the corresponding time from the model simulation overlaid, (3) synthetic image generated with the model simulation with model contour overlay, (4) synthetic image.*

5.4.3. Prediction of patient-specific Ventricular Tachycardia for radio-frequency ablation therapy planning

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

This work is funded by the FP7 European Project euHeart.

In this work, we build a patient-specific cardiac electrophysiology (EP) model derived from hybrid XMR imaging and non-contact electro-anatomical mapping procedure on a patient with heart failure. The model is then used to predict patient-specific arrhythmias, such as induced ischemic Ventricular Tachycardia (VT) (Fig. 14) and leads in generation and evaluation of patient-specific VT circuits, with critical exit points for Radio Frequency (RF) ablation. These predictions are now validated with some clinical cases, with electrophysiology mapping of induced VT in patients undergoing the clinical VT-Stim procedures (Fig. 14).

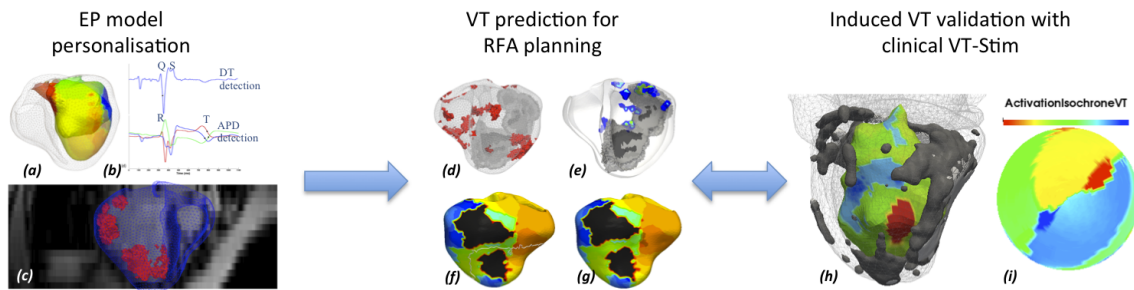


Figure 14. (a & b) Analysis of electroanatomical mapping data, to personalise the depolarisation and repolarisation wavefront dynamics. (c) Anatomical data personalisation along with ischemic regions (red). (d) A VT inducibility map showing regions with high probability of inducing VT with a VT-Stim procedure. (e) Critical exit point map showing the most eligible regions for RF ablation success. (f & g) An example of one of the various induced VT circuits, with VT-Stim model prediction. (h & i) Induced VT circuit in a clinical case (red = exit point).

5.4.4. Real-time simulation of catheter ablation in the context of cardiac arrhythmia

Participants: Hugo Talbot [Correspondant], Federico Spadoni, Maxime Sermesant, Hervé Delingette, Stephane Cotin.

This work is performed in the context of the euHeart project and the PhD of Hugo Talbot in collaboration with the Shacra (INRIA, Lille Nord Europe) team.

- This work aims at simulating in real-time the endovascular procedure of radiofrequency ablation of the left ventricle for patient suffering from Ventricular Tachycardia.
- Fast simulation of electrophysiology has been reached with a Eikonal model[40].
- Use the SOFA platform for simulating endovascular navigation and cardiac electrophysiology.

5.4.5. Personalized model of the heart for cardiac therapy planning

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

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

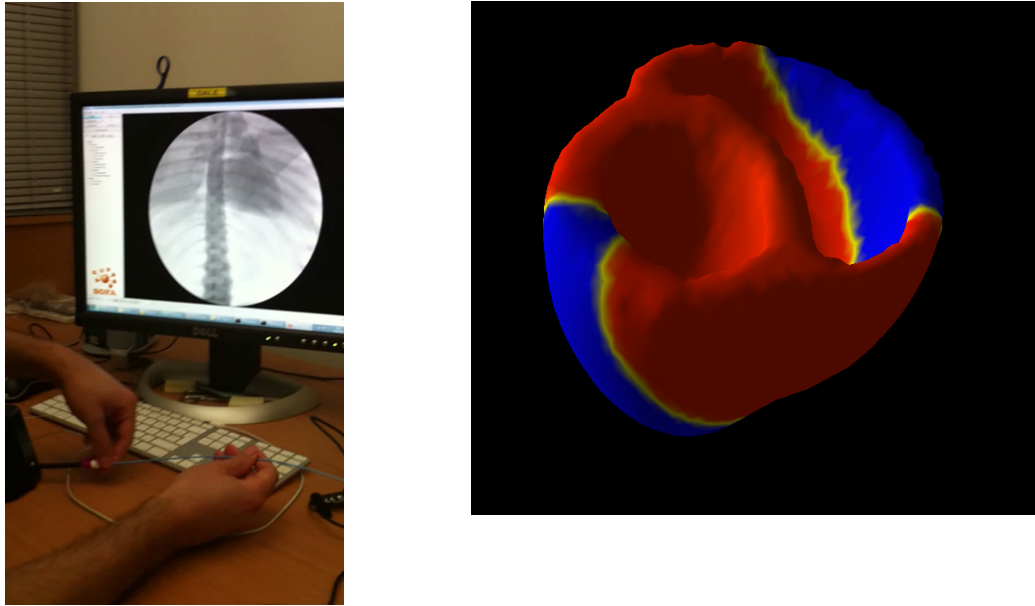


Figure 15. (Left) Simulation of catheterization with a force-feedback device; Simulation of cardiac electrophysiology.

- We improved the existing electromechanical model of the heart (see Fig 16) to include mechanical non linearity, viscosity and strain rate dependent contractility. It was implemented in SOFA with a new four valves model to deal with the cardiac phases and enforce isovolumetric constraint.
- We have obtained first personalization of cardiac mechanics from 3 cine-MRI cases using a variational approach (adjoint method)[54].

6. Contracts and Grants with Industry

6.1. CIFRE PhD Fellowships

6.1.1. Dosisoft

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

6.1.2. 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.

6.2. Other contracts

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

⁶<http://www.maestro-research.org/>

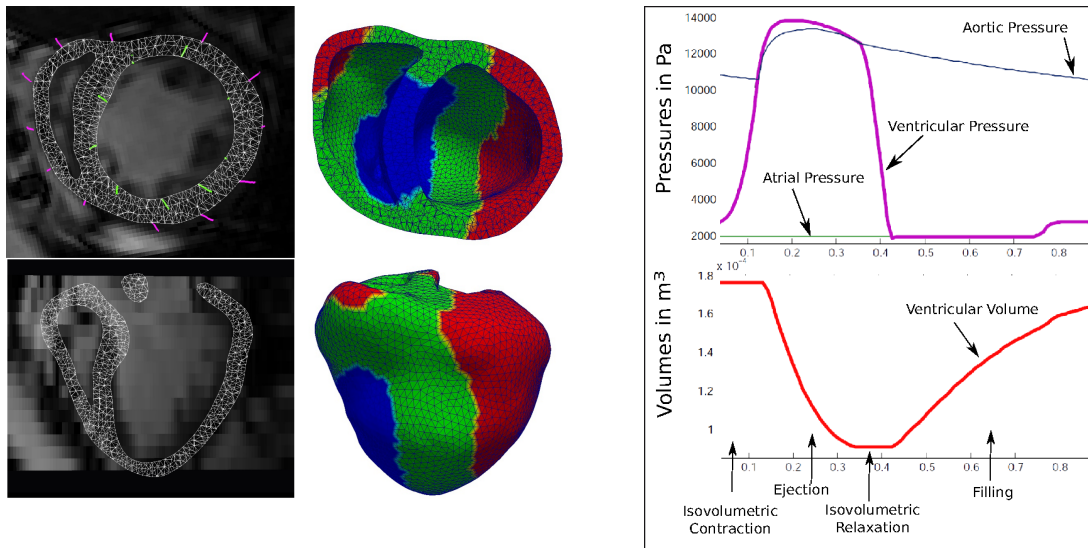


Figure 16. (Left) Electromechanical model of the heart that is coupled with medical images; (Right) Pressures and volumes curves of the left ventricle resulting from the simulation of one cardiac cycle.

7. Partnerships and Cooperations

7.1. National initiatives

7.1.1. ANR KaraMetria

Participants: Xavier Pennec [correspondant], Vikash Gupta, 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.

7.1.2. 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.

7.1.3. 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).

7.1.4. Collaboration with national hospitals

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

7.1.4.1. 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 [111], [112].

7.1.4.2. 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.

7.1.4.3. 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.

7.1.4.4. CHU de Bordeaux

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

7.2. European Initiatives

7.2.1. FP7 Projects

7.2.1.1. EUHEART

Participants: Hervé Delingette [Correspondant], Nicholas Ayache, Adityo Prakosa, Ken C.L. Wong, Federico Spadoni, Jatin Relan, Stéphanie Marchesseau, Maxime Sermesant.

Title: euHeart

Type: COOPERATION (ICT)

Defi: Virtual Physiological Man

Instrument: Integrated Project (IP)

Duration: June 2008 - May 2012

Coordinator: Philips Technologie GmbH Forschungslaboratorien (Germany)

Others partners: Philips Technologie GmbH (DE), The University of Oxford (UK), Universitat Pompeu Fabra (SP), The University of Sheffield (UK), INRIA, French National Research Institute in Informatics and Mathematics (FR), King's College London (UK), Academisch Medisch Centrum bij de Universiteit van Amsterdam (NL), Universität Karlsruhe (TH) (DE), Institut National de la Santé et de la Recherche Médicale, INSERM (FR), Philips Medical Systems Nederland BV (NL), Berlin Heart GmbH (DE), HemoLab BV (NL), Universitätsklinikum Heidelberg (DE), Volcano Europe SA / NV (BE), Hospital Clínico San Carlos de Madrid (SP), Philips Ibérica S.A. (SP)

See also: <http://www.euheart.eu/>

Abstract: The euHeart project (Ref 224495), is a 4-year 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. Asclepius 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. The research performed in this project is partially described in section 5.4.4 and 5.4.5

7.2.1.2. PASSPORT

Participant: Hervé Delingette [Correspondant].

Title: PASSPORT

Type: COOPERATION (ICT)

Defi: Virtual Physiological Man

Instrument: Specific Targeted Research Project (STREP)

Duration: June 2008 - November 2011

Coordinator: IRCAD, (France)

Others partners: IRCAD (FR), ETHZ (CH), TUM (DE), UCL (UK), ICL (UK), IZBI (DE), INSERM (FR), Storz (DE), U, Strasbourg (FR)

See also: <http://www.passport-liver.eu>

Abstract: The PASSPORT project (Ref 223894) is a 3-year 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. INRIA is involved in this project through the teams Alcove, Shacra and Asclepios and around the software platform SOFA which serves as the integration platform for the project.

7.2.1.3. VPH NOE

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

Type: COOPERATION (ICT)

Defi: Virtual Physiological Man

Instrument: Network of Excellence (NoE)

Duration: June 2008 - November 2012

Coordinator: University College London, UK

Others partners: Core members include UCL (UK), Oxford (UK), CNRS (FR), ULB (BE), U. of Nottingham (UK), UPF (ES), U. Auckland (NZ), EMBL (DE), U. Sheffield (UK), Karolinka (SE), ERCIM (FR), IOR (IT).

See also: <http://www.vph-noe.eu/>

Abstract: 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. More precisely, a registration toolbox has been delivered which aims at including registration algorithms from the team and elsewhere into the new version of MedINRIA (2.x).

7.2.2. Collaborations in European Programs, except FP7

7.2.2.1. Care4Me

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

Program: ITEA2

Project acronym: Care4Me

Project title: Cooperative Advanced REsearch for Medical Efficiency

Duration: Sept. 2009 - Sept. 2013

Coordinator: Philips, NL.

Other partners: Alma (ES), Bull (FR), CEA (FR), CIMNE (ES), Compasiss (ES), CVSS (ES), Duodecim (FI), Erasmus MC (NL), ESI (NL), HSP (ES), Helsinki Hosp. (FI), ISI (GGR), LUMC (NL), MediConsult (FI), MEDIS (NL), Nokia (FI), Philips (NL), Pie Medical Imag. (NL), Pohjola (FI), Prowellness (FI), Robotiker (ES), UMC (NL), VTT (FI)

Abstract: This project aims at increasing 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.

7.3. International Initiatives

7.3.1. INRIA Associate Teams

7.3.1.1. CAPNEONATES

Title: Analysis of structural MR and DTI in neonates

INRIA principal investigator: Pierre Fillard [Parietal]

Asclepios investigator: Xavier Pennec

International Partner:

Institution: University of Southern California (United States)

Laboratory: Image Lab at Children Hospital at Los Angeles

Researcher: Natasha Leporé

International Partner:

Institution: University of Pennsylvania (United States)

Laboratory: Penn Image Computing and Science Laboratory

Researcher: Caroline Brun

Duration: 2011 - 2013

See also: <http://www.capneonates.org/>

While survival is possible at increasingly lower gestational ages at birth, premature babies are at higher risk of developing mental disorders or learning disabilities than babies born at term. A precise identification of the developmental differences between premature and control neonates is consequently of utmost importance. Nowadays, the continuously improving quality and availability of MR systems make it possible to precisely determine, characterize and compare brain structures such as cortical regions, or white matter fiber bundles. The objective of this project is to understand the developmental differences of premature versus normal neonates, using structural and diffusion MRI. This work will consist of identifying, characterizing and meticulously studying the brain structures that are different between the two groups. To do so, we propose to join forces between the Parietal team at INRIA and the University of Southern California. Parietal has a recognized expertise in medical image registration and in statistical analyses of groups of individuals. USC has a broad knowledge in MR image processing. In particular, the Children's Hospital at Los Angeles (CHLA), which is part of USC, is in the process of collecting a unique database of several hundreds of premature and normal neonates MR scans. This joint collaboration is consequently a unique chance of addressing key questions pertaining to neonatal and premature development. It will make it possible to elaborate new tools to analyze neonate MR images while tremendously increasing our knowledge of neuroanatomy at such an early stage in life.

7.3.1.2. COMPUTUMOR

Title: Computational Brain Tumor

INRIA principal investigator: Olivier Clatz

International Partner:

Institution: Massachusetts Institute of Technology (United States)

Laboratory: Computer Science and Artificial Intelligence Laboratory (CSAIL)

International Partner:

Institution: German Cancer Research Center (United States)

Laboratory: DKFZ Heidelberg diffusion group

Duration: 2007 - 2012

See also: <http://www-sop.inria.fr/asclepios/projects/boston/>

The CompuTumor associated team has been funded early 2007 and renewed in 2009. The CompuTumor project is dedicated to the study of brain tumor models and their coupling with medical images to better assist diagnosis and therapy. The project 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. More specifically, the project aims at (a) proposing new medical image processing method that could be used to better analyze tumor images, (b) developing new brain tumor models in order to personalise these models with patient data. Microsoft Research has been also recently involved in the collaboration on lesion segmentation. Our most recent activity is described in sections 5.1.1 and 5.4.1 and also on the website of the associated team : <http://www-sop.inria.fr/asclepios/projects/boston/>.

7.3.2. INRIA International Partners

7.3.2.1. Collaboration with international hospitals

7.3.2.1.1. 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.

7.3.2.1.2. 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.

7.3.2.1.3. Other International Hospitals

Collaborations with several other European hospitals have been established through the European projects Passport and euHeart.

7.3.3. Visits of International Scientists

Christof Seiler was a visiting Phd student from University of Bern for a period of 9 months starting in February 2011.

Stefan Sommer was a visiting student from the Dept. of Computer Science, Univ. Copenhagen, for 6 months during the period 2010-2011.

Stephen Marsland (associate professor at Massey University in Palmerston North, New Zealand) was a visiting scientist for 1 month in Oct-Nov 2011.

8. Dissemination

8.1. Animation 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 program committee of International Conference on Medical Image Computing and Computer Assisted Intervention (MICCAI'11), the International Symposium on Biomedical Imaging (ISBI'11), area chair for the International Conference on Information Processing in Computer-Assisted Interventions (IPCAI'11), a program committee member of the MICCAI 2010 Workshop on Statistical Atlases and Computational Models of the heart (STACOM'11), the Iberian Conference on Pattern Recognition and Image Analysis (IbPRIA 2011), the conference on Virtual Reality Interactions and Physical Simulation (VRIPHYS'10). He was a co-organisator of the MICCAI 2011 Workshop on Mesh Processing in Medical Image Analysis and served as a reviewer for the Siggraph'2011 conference,
- G. Malandain was a member of the review committee of the International Conference on Discrete Geometry for Computer Imagery (DGCI'11), the Scientific Meeting of European Society for Magnetic Resonance in Medicine and Biology (ESMRMB'11), and the International Conference on Medical Image Computing and Computer Assisted Intervention (MICCAI'11).
- X. Pennec organized the third MICCAI Workshop on the Mathematical Foundations of Computational Anatomy (MFCA'2011), Toronto, CA, Sept. 22, 2011 <http://www-sop.inria.fr/asclepios/events/MFCA11/>. Proceedings are available as open archive <http://hal.inria.fr/MFCA11/> [77]. He was a member of the program committees of: Int. Conference on Medical Image Computing and Computer Assisted Intervention (MICCAI'2011); workshop on computational diffusion MRI (CDMRI'11); Information processing in medical Images 2011 (IPMI'11); Joint Workshop on High Performance and Distributed Computing for Medical Imaging (HP-MICCAI/MICCAI-DCI 2011); Fourth Workshop on Non-Rigid Shape Analysis and Deformable Image Alignment (NORDIA'11); IEEE Workshop on Mathematical Methods in Biomedical Image Analysis 2012 (MMBIA'212).
- M. Sermesant was a co-organisator of the MICCAI 2011 Workshop on Statistical Atlases and Computational Models of the Heart and the VPH Network of Excellence workshop on medical imaging software.

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 Aviesan national alliance on biosciences. 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 in Nagoya, Japan to evaluate a national program on "Computational Anatomy" funded by the MEXT.

G. Malandain is deputy scientific director of INRIA in charge of the Computational Sciences for Biology, Medicine and the Environment domain. He is member of the Orientation Committee of the GIP Genopole (Evry), and of the Scientific Committee of the MIA department of INRA.

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

Xavier Pennec is a member of the Doctoral follow-up Committee (CSD) at INRIA Sophia Antipolis since 2010, and was a member of the recruitment committee for mathematical professors (commission de spécialistes PR26) at Toulouse University, 2011.

In 2011, he acted as an evaluator for the French National Center for Scientific Research CNRS (PEPII projects), Digiteo (French Cluster of research in Information Science and Technology), the Science Foundation Ireland (SFI), the Fonds de la Recherche Scientifique - FNRS (Belgium), and the Council of Physical Science of the Netherlands Organization for Scientific Research (NWO).

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 Research Foundation Flanders (FWO), for the STIC AmSud Program, for the Estonian Science Foundation, for several project proposals submitted to the French research agency ANR.

M. Sermesant is a 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). He also participates in scientific animation in high schools, presenting research and medical imaging (3 times in 2011).

8.2. Teaching

Master 2 MVA and École Centrale de Paris. H. Delingette and X. Pennec are co-responsible of 2 modules on medical imaging (formation and analysis of medical images) (45 hours of lectures) at the Master MVA of ENS Cachan "Mathématiques, Vision et Apprentissage". The second module is common to the 3rd year of Ecole Centrale Paris.

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)

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

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.

Master PENSUNS (Master Informatique Univ. Nice-Sophia-Antipolis, parcours ENS Lyon) X. Pennec was responsible of a 21h module on Mathematics for Medical Image processing.

Classe Préparatoire, Lycée Stanislas, Cannes. Olivier Clatz was an oral examiner in engineering sciences for 2 hours a week.

8.3. PhD Theses and Internships

8.3.1. PhD defended in 2011

1. Liliane Ramus, *Digital anatomical atlases for radiotherapy planning*, Nice-Sophia Antipolis University, July 2011.
2. François Chung, *Regional shape and appearance modelling for deformable model-based image segmentation*, École des Mines de Paris, January 2011.
3. Barbara André, *Smart Atlas for Endomicroscopy Diagnosis Support*, École des Mines de Paris, October 2011.

8.3.2. Current PhDs

1. Vikash Gupta, *Diffusion tensor imaging of the brain: towards quantitative clinical tools*, Nice Sophia-Antipolis University.
2. Jan Margeta, , Nice Sophia-Antipolis University.
3. Marine Breuille, *Tracking and quantification of tumour processes in rodents with SPECT imaging* , Nice Sophia-Antipolis University.
4. Ezequiel Geremia, *Multi-scale computational models of brain tumors for medical image analysis*, Nice Sophia-Antipolis University.
5. Marco Lorenzi, *Imaging Biomarkers in Alzheimer's Disease* , Nice Sophia-Antipolis University, In collaboration with G. Frisoni, IRCCS Fatebenefratelli, Brescia, Italy.
6. Kristin McLeod, *Modeling of Cardiac Growth and Deformation from Medical Images*, Nice-Sophia Antipolis University. .
7. Adityo Prakosa, *Analysis and Simulation of the heart function from multimodal cardiac images*, Nice-Sophia Antipolis University.
8. Jatin Relan, *Planning of radiofrequency ablation of the heart using electromechanical models personalized from cardiac images and electrophysiological signals*, Ecole des Mines de Paris.
9. Christof Seiler. *Prediction of the Bone Shape from Clinically Relevant Variables*. Joint PhD between University of Nice-Sophia Antipolis and University of Bern, Switzerland.
10. 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.
11. Hugo Talbot, *Simulation of radiofrequency ablation of cardiac cells*, University of Lille.
12. Nicolas Toussaint, *In vivo cardiac DTI* , King's College London, London

8.3.3. Master Student

1. Loic Le Folgoc, *Tumor Growth Parameter Estimation and Source Localization From a Unique Time Point*, Master MVA ENS Cachan and Ecole Centrale Paris.
2. Vikash Gupta, *Statistical atlases of diffusion tensor images*, Master Computational Biology and Biomedicine, University Nice-Sophia Antipolis.
3. Viateur Tuyisenge, , Master Computational Biology and Biomedicine University Nice-Sophia Antipolis.
4. Manivannan Siyamalan, *Interactive Medical Image Segmentation using Fast Graph Partitioning*, Master Computational Biology and Biomedicine University Nice-Sophia Antipolis.
5. Rocio Cabrera Iozoya, *Automatic Analysis and Indexation of Time-Series 4D Cardiac Magnetic Resonance Images*, Master Computational Biology and Biomedicine University Nice-Sophia Antipolis.

8.3.4. Participation to thesis committees

N. Ayache participated as co-supervisor to the PhD thesis of Barbara André (Nice-Sophia Antipolis University), as chair to the PhD thesis of L. Ramus (Nice-Sophia Antipolis University) and Damiano Lombardi (University of Bordeaux) and as referee to the PhD thesis of François Chung (Ecole des Mines de Paris). He also chaired the jury of the Habilitation of Baudouin Denis de Senneville (University of Bordeaux).

Hervé Delingette participated as co-supervisor to the PhD thesis of François Chung (École des Mines de Paris), as referee to the PhD thesis committee of H. Courtecuisse (Lille University), E. Olivi (Nice-Sophia Antipolis University) as reviewer to the PhD thesis committee of J-B. Lagaert (Bordeaux University), J. Schmid (Genève University).

Grégoire Malandain participated as supervisor to the PhD thesis committee of Liliane Ramus (Nice-Sophia Antipolis University), as reviewer to the PhD thesis committee of Z.-Y. Sun (Paris-Sud university) and S. Sharma (Strasbourg University), as reviewer to the Habilitation committee of N. Passat (Strasbourg University) and R. Trebosen (Nice-Sophia Antipolis University).

Xavier Pennec participated as reviewer to the PhD thesis committee of Le Yang (Dept of Mathematics, University of Poitier) and Rémi Cuingnet (University Paris XI Orsay), as member of the PhD thesis committee of Aristeidis Sotiras (Ecole centrale Paris) and as external examiner at the PhD *viva voce* of Marc Modat, University College London, UK.

8.3.5. Invited Lectures

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:
 - at the *French Academy of Medecine*, Paris Dec 2011
 - at the *Maison de la Chimie*, Paris Nov 2011
 - at the *Content-Based Medical Image Retrieval Workshop* associated with the MICCAI'11 conference, Toronto, Canada, in Sept 2011.
 - at the *4th Cardiac Physiome Workshop*, Cambridge University, UK, July 2011
 - at the *ICCU Conference*, Nice, FR, April 2011
 - at the *Tata Institute*, Mumbai, India, Feb 2011
- **Hervé Delingette** gave invited lectures
 - at the CITRIS center of the Berkeley University (USA) on the digital heart on February 23rd,
 - at the EPSRC network meeting on Personalized Models in Swansea (UK) on April 11th,
 - at the mini-symposium on volumetric imaging and parameter identification of the national conference on computational meechanics (CSMA'11) in Giens (France) on May 11th,
 - at the 4th Cardiac Physiome Workshop in Cambridge (UK) on July 10th,
 - at the meeting organized by the european commission on the new research framework program on July 19th,
 - at the Newton Institute Seminar on inverse problems in Cambridge (UK) on August 26th,
 - at the MICCAI 2011 Workshop on Statistical Atlases and Computational Models of the heart (STACOM'11) on Sept. 22nd.
- **Grégoire Malandain** gave an invited keynote talk at the Journées Scientifiques de la Société Française de Physique Médicale (June, 8-10).
- **Xavier Pennec** gave invited lectures:

- at the special session on Information Geometry Sciences of the 23rd GRETSI Symposium on Signal and Image Processing, Bordeaux, September 5-8 2011,
- at the workshop Geometry for Anatomy, Banff International Research Station for Mathematical Innovation and Discovery (BIRS), Banff, Alberta, Canada, Aug. 28 - Sep. 2, 2011,
- at the Fields-MITACS Conference on Mathematics of Medical Imaging, Fields Institute, Toronto, Canada, June 20-24, 2011,
- at the workshop on Manifold Learning, Hausdorff Research Institute for Mathematics, Bonn, Germany, May 30 - June 3, 2011,
- at the Indo-French workshop on "Matrix Information Geometry (MIG)", Thales & Ecole Polytechnique, Palaiseau, February 23-25, 2011,
- at the Oberwolfach week on Trends in Mathematical Imaging and Surface Processing, Mathematisches Forschungsinstitut Oberwolfach, Germany, January 30th - February 5th, 2011,
- at the Colloquium "Le modèle et l'algorithme", INRIA Rocquencourt, March 3 2011.
- at the UCL Center for Medical Imaging (CMIC), London, January 26, 2011,
- at the Department of Computing, Imperial College, London, January 25, 2011.
- **Maxime Sermesant** gave invited lectures:
 - at the SCMR (Society of Cardiovascular Magnetic Resonance) conference,
 - at the ESC (European Society of Cardiology) clinical conference,
 - at the Cardiac Physiome workshop in Oxford.

He also gave an introduction lecture in Antibes and Nice high schools.

8.3.6. Nominations and Prizes

- **Nicholas Ayache** was awarded an ERC grant in Oct 2011, to start in April 2012 with the collaboration of H. Delingette, X. Pennec and M. Sermesant.
- **Nicholas Ayache** was elected CSO (Chief Scientific Officer) of the newly created IHU of Strasbourg (Institut Hospitalo Universitaire) in Nov 2011.
- **Xavier Pennec** was elected a member of the MICCAI Society boards of Directors (2012-2016) and was nominated member of the working group on Incentive Actions (GTAI) of the Scientific and Technological Orientation Council (COST) of INRIA (2011-2013).

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