Activity Report 2014

Project-Team ASCLEPIOS

Analysis and Simulation of Biomedical Images

RESEARCH CENTER
Sophia Antipolis - Méditerranée

THEME
Computational Neuroscience and Medecine

Table of contents

Project-Team ASCLEPIOS

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

Creation of the Project-Team: 2005 November 01.

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2. Overall Objectives

2.1. Overall Objectives

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 an even more central role everyday, along with the exploitation of the genetic information attached to each patient.

Facing the need for 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 of extracting 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.

3. Research Program

3.1. Introduction

Tremendous progress has been made in the automated analysis of biomedical images during the past two decades [56]. Readers who are neophytes to the field of medical imaging will find an interesting presentation of acquisition techniques of the main medical imaging modalities in [48], [46]. Regarding target applications, a good review of the state of the art can be found in the book *Computer Integrated Surgery* [44], in N. Ayache's article [51] and in the more recent syntheses [52] [56]. The scientific journals *Medical Image Analysis* [39], *Transactions on Medical Imaging* [45], and *Computer Assisted Surgery* [47] 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) [42], [43] or ISBI'2010 (Int. Symp. on Biomedical Imaging) [41].

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 [57], [67]. It is also possible to obtain from a Magnetic Resonance Image (MRI) of the head a reasonable segmentation into skull tissues, white matter, grey matter, and cerebro-spinal fluid [70], or to measure some functional properties of the heart from dynamic sequences of Magnetic Resonance [50], Ultrasound or Nuclear Medicine images [58].

Despite these advances and successes, statistical models of anatomy are still very crude, resulting in poor registration results in deformable regions of the body, or between different subjects. If some algorithms exploit 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 observed images and signals, but also more efficient tools for detecting anomalies, predicting evolutions, simulating and assessing 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 are the images multidimensional (3 spatial coordinates and possibly one temporal dimension), but medical protocols tend to include multi-sequence (or multi-parametric) [1] and multi-modal images [2] for each single patient.

Despite remarkable efforts and advances during the past twenty years, the central problems of segmentation and registration have not been solved in the general case. It is our objective in the short term to work on specific versions of these problems, taking into account as much *a priori* information as possible on the underlying anatomy and pathology at hand. It is also our objective to include more knowledge of the physics of image acquisition and observed tissues, as well as of 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 3.3 and 3.4.

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. Computational Anatomy

The objective of the Computational Anatomy (CA) is the modeling and analysis of biological variability of human anatomy. Typical applications cover the simulation of average anatomies and normal variations, the discovery of structural differences between healthy and diseased populations, and the detection and classification of pathologies from structural anomalies [3].

Studying the variability of biological shapes is an old problem (cf. the remarkable book "On Shape and Growth" by D'Arcy Thompson [69]). Significant efforts have been made since that time to develop a theory for statistical shape analysis (one can refer to [55] for a good synthesis, and to the special issue of Neuroimage [68] for recent developments). Despite all these efforts, there are 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).

[1] Multisequence (or multiparametric) imaging consists in acquiring several images of a given patient with the same imaging modality (e.g. MRI, CT, US, SPECT, etc.) but with varying acquisition parameters. For instance, using Magnetic Resonance Imaging (MRI), patients followed for multiple sclerosis may undergo every six months a 3-D multisequence MR acquisition protocol with different pulse sequences (called T1, T2, PD, Flair etc): by varying some parameters of the pulse sequences (e.g Echo Time and Repetition Time), images of the same regions are produced with quite different contrasts depending on the nature and function of the observed structures. In addition, one of the acquisitions (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 the measurement for instance of the direction of white matter fibers in the brain (the 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 a subtle higher T2* signal which can be detected with sophisticated image processing techniques.

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

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

There is a classical stratification of the problems into the following 3 levels [64]: 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.

3.4. 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 where CP can be used for instance to better understand the basic processes leading to the appearance 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 [65], [62], [53], [66], [59]). 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 comparing the model with the available biomedical images and signals and possibly also 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 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 [54]:

- the first level is mainly geometrical, and addresses the construction of a digital description of the anatomy [49], essentially acquired from medical imagery;
- the second level is physical, involving mainly the biomechanical modeling of various tissues, organs, vessels, muscles or bone structures [60];
- the third level is physiological, involving a modeling of the functions of the major organic systems [61] (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 [40].

These different levels of modeling are closely related to each other, and several physiological systems may interact with each other (e.g. the cardiopulmonary interaction [63]). 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 [61], [62]). 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 medical 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 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, ...

3.5. Clinical 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, validation is necessary for the transformation of new ideas 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 help stimulate of new ideas and concepts.

4. New Software and Platforms

4.1. SOFA

Participants: Hervé Delingette [correspondent], Federico Spadoni, Stéphanie Marchesseau, Hugo Talbot, Sophie Giffard-Roisin, Roch-Philippe Mollero.

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 new algorithms, but can also be used as an efficient prototyping tool. Based on an advanced software architecture, it allows : the creation of complex and evolving simulations by combining new algorithms with algorithms already included in SOFA; the modification of most parameters of the simulation (deformable behavior, surface representation, solver, constraints, collision algorithm, etc.) by simply editing an XML file; the building of complex models from simpler ones using a scene-graph description; the efficient simulation of the dynamics of interacting objects using abstract equation solvers; the reuse and easy comparison of a variety of available methods. It was developed mainly by the Inria team projects Shacra, 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: LGPL
- Type of human computer interaction: console, opengl, qt
- OS/Middelware: 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: Maxime Sermesant [correspondent], Florian Vichot, Hakim Fadil, Loïc Cadour, Michael Buckingham.

MedInria is a medical imaging software platform developed by the Asclepios research project in collaboration with the Athena, Parietal and Visages Inria research projects. It aims at providing clinicians with 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.

The core of medInria is open source with a BSD license; additional plug-ins can have any license.

The latest release of medInria, 2.2.1, was made in September 2014. See also the web page https://med.inria.fr.

- Version: 2.2.1
- License: BSD
- Keywords: Medical Image Processing
- Dependencies: Qt, DTK, VTK, ITK, TTK, MIPS
- Programming language: C++
- Supported OSes: Windows (XP/Vista/7/8), Linux (Fedora/Ubutu), Mac OS X (10.6-10.9)

4.3. MUSIC

Participants: Maxime Sermesant [correspondent], Florian Vichot, Hakim Fadil, Loïc Cadour, Florent Collot, Mathilde Merle [Software Engineer IHU LIRYC].

MUSIC is a software developed by the Asclepios research project in close collaboration with the IHU LIRYC in order to propose functionalities dedicated to cardiac interventional planning and guidance. This includes specific tools (algorithms of segmentation 1, registration, etc.) as well as pipelines. The software is based on the MedInria platform.

For more information, see the web page https://team.inria.fr/asclepios/software/music/. See also: http://videotheque.inria.fr/videotheque/media/28294 for a video on the MUSIC software application.

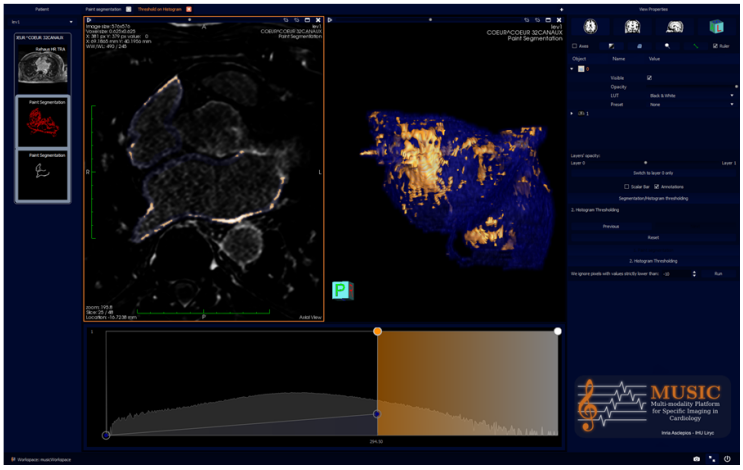

Figure 1. Segmentation of atrial fibrosis using adaptive histogram thresholding based on the MUSIC Software.

- Version: 1.0
- License: Proprietary
- Dependencies: MedInria, Qt, DTK, VTK, ITK, TTK, MIPS
- Programming language: C++
- Supported OSes: Windows (XP/Vista/7/8), Linux (Fedora/Ubuntu), Mac OS X (10.6-10.10)

4.4. VP2HF platform

Participants: Maxime Sermesant [correspondent], Hakim Fadil, Loïc Cadour.

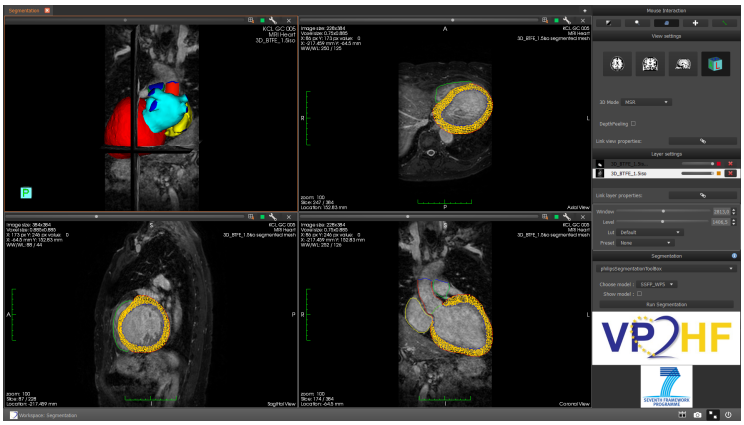

Figure 2. Philips segmentation tool within the VP2HF platform

The VP2HF software is developed by the Asclepios team and brings together all the research produced by the VP2HF's partners. It contains MedInria plugins implemented by teams such as UPF Barcelona, KCL, and specific tools provided by Philips (algorithms of segmentation 2, scar segmentation, ...). It aims at integrating in a single clinical workflow, tools to improve the therapy selection and treatment optimisation for patients suffering from heart failure.

- Version: 1.0
- License: Proprietary
- Keywords: Medical Image Processing
- Dependencies: MedInria, Qt, DTK, VTK, ITK, TTK, MIPS
- Programming language: C++
- Supported OSes: Windows (XP/Vista/7/8), Linux (Fedora/Ubuntu), Mac OS X (10.6-10.10)

5. New Results

5.1. Highlights of the Year

- Nicholas Ayache was elected a member of the Académie des sciences on 18th Nov. 2014.
- Nicholas Ayache received the "Grand Prix Inria – Académie des sciences 2014" for his major contributions to Informatics and Computational Sciences at Inria.
- Nicholas Ayache taught the "Personalized Digital Patient" course at the Collège de France on the annual chair "Informatics and Computational Sciences".
- Hervé Lombaert was awarded and ranked 1st in computer science at the highly selective NSERC Postdoctoral Fellowship (Top funding agency in Canada).
- Nina Miolane and Bishesh Khanal won the first prize in the "Popular Vote Awards" at the MICCAI 2014 Educational Challenge for their video on "Statistics on Lie groups for Computational Anatomy".

BEST PAPER AWARD :

[12] **Parameter Estimation For Personalization of Liver Tumor Radiofrequency Ablation in MICCAI Workshop on Abdominal Imaging – Computational and Clinical Applications**. C. AUDIGIER, T. MANSI, H. DELINGETTE, S. RAPAKA, V. MIHALEF, D. CARNEGIE, E. BOCTOR, M. CHOTI, A. KAMEN, D. COMANICIU, N. AYACHE.

5.2. Medical Image Analysis

5.2.1. 3D/2D Coronary Arteries Registration

Participants: Thomas Benseghir [correspondent], Grégoire Malandain [Morpheme Team], Régis Vaillant [GE-Healthcare], Nicholas Ayache.

This work has been performed in colaboration with GE-Healthcare (Buc) and the Morpheme team at Inria SAM.

3D/2D Registration, Computed Tomography Angiography, X-ray Fluoroscopy, Coronary Arteries, Vascular Tree

Integrating vessel calcifications and occlusion information, extracted from pre-operative 3D CT angiography images into a live fluoroscopic 2D image can greatly improve the guidance of percutaneous coronary interventions. Such task requires a registration step that must provide relevant correspondences between these two complementary modalities. We are developing a framework aiming at preserving the topology of the vascular structures matched between both images.

The introduction of topology in the pairing procedure allows to decrease the mismatches with respect to geometrically-based pairing procedures (e.g. Iterative Closest Point), which, in turn, improves the success rate of the registration method. This is exemplified by Fig. 3 where the proposed pairing method is compared to ICP.

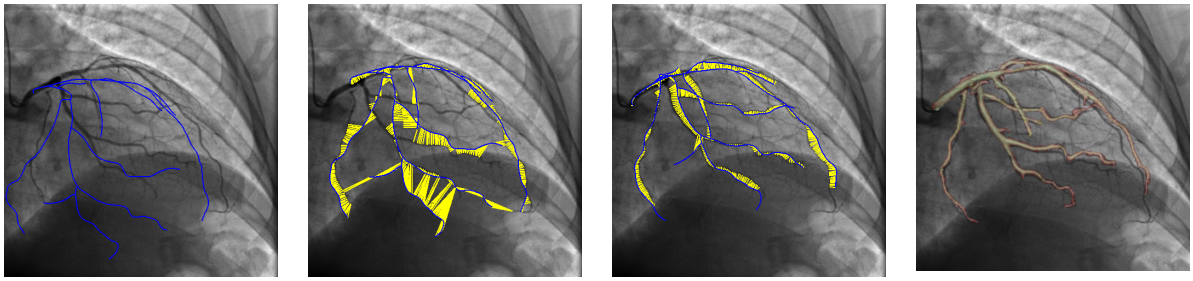

Figure 3. From left to right: 1. initial pose estimate (3D centerlines projection in blue); 2. iterative closest point algorithm registered position (point-pairings in yellow); 3: proposed method registered position; 4: resulting fusion between the two modalities

5.2.2. Video Synchronization: An Approach Towards Endoscopic Re-localization

Participants: Anant Suraj Vemuri [correspondent], Nicholas Ayache.

Endoscopy, Barrett's Esophagus, Re-localization, Electromagnetic Tracking

- Barrett's esophagus is the pre-malignant lesion for the majority of patients with esophageal adenocarcinoma. The evolution of the disease involves endoscopic surveillance for patients every 3-6 months, according to the Seattle protocol.
- The approach is labor-intensive and the primary problem is the inter-operative re-localization of these biopsy sites to guide the treatment.

- In an earlier work we had proposed a general framework for inter-operative biopsy site re-localization framework by introducing an Electro-magnetic tracking system (EMTS) into the loop and providing a way to inter-operatively register video sequences to provide a guided navigation in the esophagus.
- This work has been extended further to fit the operating room workflow. Two external landmarks have been added to the system setup as shown in Fig.4, to obtain a complete reference frame with respect to the patient and to make the registration, patient specific [38]. The patient-localized reference frame allows the recovery of complete $SE(3)$ including the roll angle about the esophageal axis.

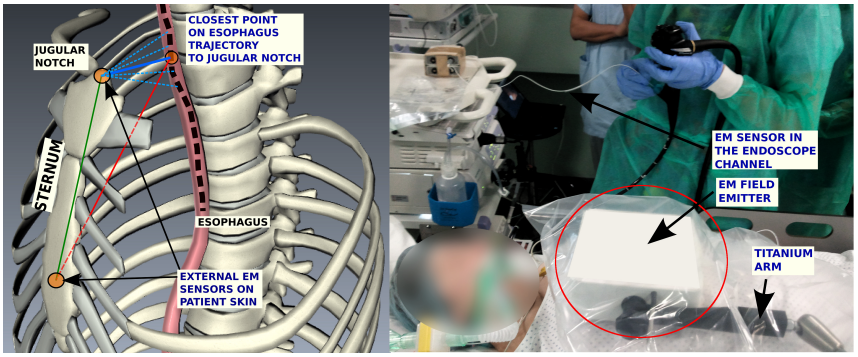

Figure 4. (Left) The orange circular markings indicate the position of the sensors taken as anatomical landmarks to form the reference frame for the patient. (Right) System setup in the operating room.

5.2.3. A sparse Bayesian framework for non-rigid registration

Participants: Loic Le Folgoc [correspondent], Hervé Delingette, Antonio Criminisi, Nicholas Ayache.

This work has been partly supported by Microsoft Research - Inria joint laboratory through its PhD Scholarship Programme and the European Research Council through the ERC Advanced Grant MedYMA (on Biophysical Modeling and Analysis of Dynamic Medical Images).

Registration, Automatic Relevance Determination, Uncertainty Quantification

We propose a sparse Bayesian framework for non-rigid registration. It provides a principled approach to efficiently find an optimal, sparse parameterization of deformations among any preset, widely overcomplete range of basis functions. It addresses open challenges in state-of-the-art registration, such as the automatic joint estimate of model parameters (e.g. noise and regularization levels). We have evaluated the feasibility and performance of our approach on cine MR, tagged MR and 3D US cardiac images, and show state-of-the-art results on benchmark datasets evaluating accuracy of motion and strain (see Fig.5). This work was presented during the MICCAI 2014 conference[20].

5.2.4. Segmentation and anatomic variability of the cochlea and other temporal bone structures from medical images

Participants: Thomas Demarcy [correspondent], Hervé Delingette, Clair Vandersteen, Dan Gnansia [Oticon Medical], Nicholas Ayache.

This work is funded by a CIFRE grant involving Oticon Medical (Vallauris) and performed in collaboration with the IUFC Nice (Pr. Guevara) and CHU Nice (Pr. Raffaelli) .

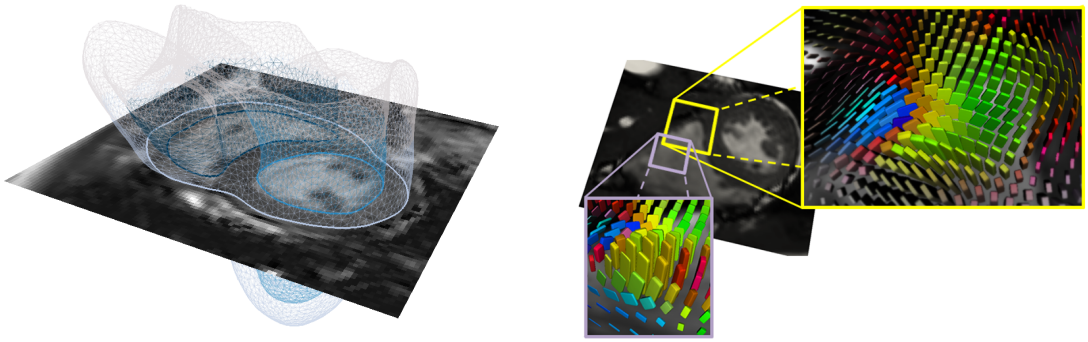

Figure 5. (Left) Mesh contour propagated to end systole via the registration output; (Right) Spatial uncertainty visualized as a tensor map.

image segmentation ; surgery planning ; shape modelling ; anatomic variability ; cochlear implant ; temporal bone

- We applied semi-automatic segmentation methods to extract anatomical structures on the inner ear on both micro-CT and CT scan images.
- μ-CT and CT images acquired on the same subject were fused with their segmentation.
- We designed a teaching tool[37] for advanced visualization of temporal bone structures (see Fig. 6).

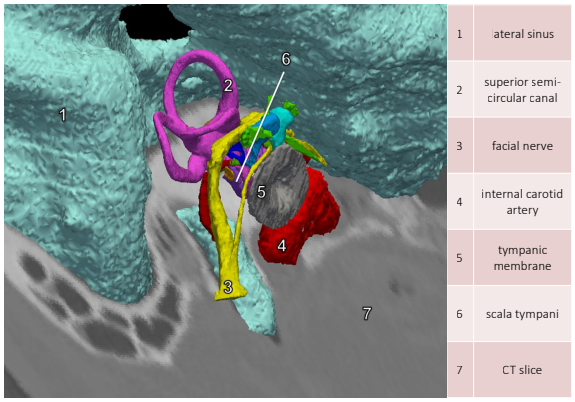

Figure 6. Virtual view of the posterior tympanotomy approach fused with a CT-scan

5.2.5. Understanding cardiac planes of acquisition

Participants: Jan Margeta [correspondent], Nicholas Ayache, Daniel C Lee [Northwestern University], Antonio Criminisi [Microsoft Research Cambridge].

This work has been partly supported by Microsoft Research through its PhD Scholarship Programme, by ERC Advanced Grant MedYMA (on Biophysical Modeling and Analysis of Dynamic Medical Images), and by the VP2HF FP7 research project.

Cardiac imaging, Machine learning, Magnetic resonance, Data wrangling

DICOM image format defines several tags by which the images can be queried and filtered. Many useful tags are however not standardized and must be cleaned prior to any large scale analysis.

- We developed a machine learning method for automatic recognition of cardiac planes of acquisition (See Fig. 7 for sample predictions).
- Our image based method achieved state of the art performance.
- This work was presented[23] at the Medical Image Understanding and Analysis conference in London.

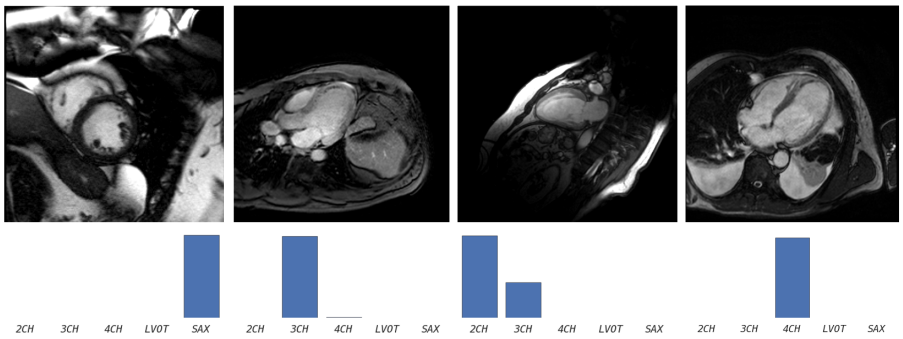

Figure 7. Examples of cardiac acquisition plane predictions and confidences

5.3. Computational Anatomy

5.3.1. Statistical Analysis of Diffusion Tensor Images of the Brain

Participants: Marco Lorenzi [Correspondent], Nicholas Ayache, Xavier Pennec.

Image non-linear registration, Longitudinal modeling, Alzheimer's disease

Alzheimer's disease is characterized by the co-occurrence of different phenomena, starting from the deposition of amyloid plaques and neurofibrillary tangles, to the progressive synaptic, neuronal and axonal damages. The brain atrophy is a sensitive marker of disease progression from pre-clinical to the pathological stages, and computational methods for the analysis of magnetic resonance images of the brain are currently used for group-wise (cross-sectional) and longitudinal studies of pathological morphological changes in clinical populations. The aim of this project is to develop robust and effective computational instruments for the analysis of longitudinal brain changes. In particular novel methods based on non-linear diffeomorphic registration have been investigated in order to reliably detect and statistically analyze pathological morphological changes [5] (see Fig.8). This project is also focused in the comparison of the trajectories of longitudinal morphological changes [31] estimated in different patients. This is a central topic for the development of statistical atlases of the longitudinal evolution of brain atrophy.

5.3.2. Statistical Learning via Synthesis of Medical Images

Participants: Hervé Lombaert [Correspondent], Nicholas Ayache, Antonio Criminisi.

This work has been partly supported by a grant from Microsoft Research-Inria Joint Centre, by ERC Advanced Grant MedYMA (on Biophysical Modeling and Analysis of Dynamic Medical Images)

Statistical learning, Synthesis

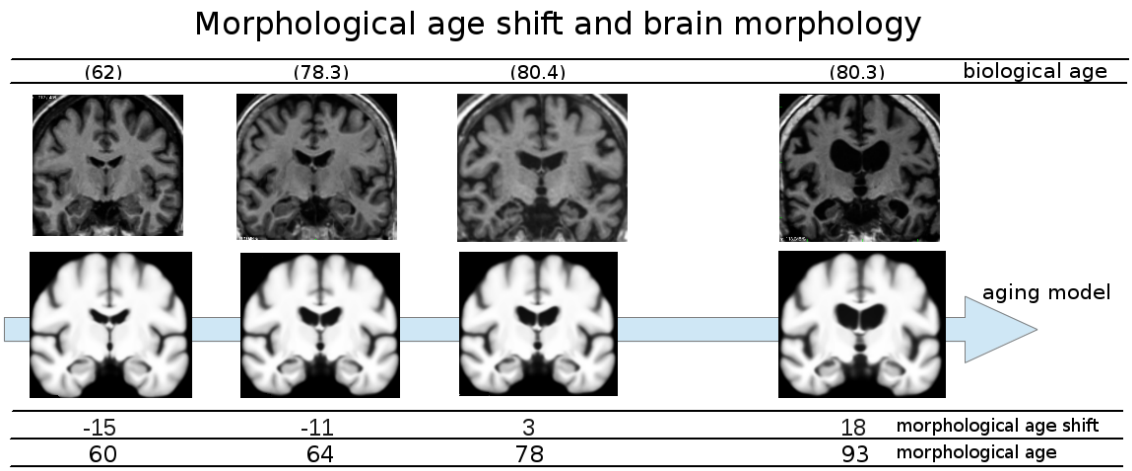

Figure 8. Modeled longitudinal brain changes in normal aging extrapolated from -15 to 18 years, and corresponding observed patient anatomies with estimated morphological age and age shift (biological age in parenthesis). Our modeling framework describes meaningful anatomical changes observed in clinical groups.

Machine learning approaches typically require large training datasets in order to capture as much variability as possible. Application of conventional learning methods on medical images is difficult due to the large variability that exists among patients, pathologies, and image acquisitions. The project aims at exploring how realistic image synthesis could be used, and improve existing machine learning methods.

First year tackled the problem of better exploiting existing training sets, via a smart modeling of the image space (Fig. 9), and applying conventional random forests using guided bagging [21]. Synthesis of complex data, such as cardiac diffusion images (DTI), was also done. Synthesis of complex shapes, using spectral graph decompositions, is currently on-going work.

The modeling of shapes also includes novel representations based on the spectral decomposition of images[4] which are more robust to large deformations when comparing multiple patients.

5.3.3. Statistical analysis of heart shape, deformation and motion

Participants: Marc-Michel Rohé [correspondent], Xavier Pennec, Maxime Sermesant.

This work was partly supported by the FP7 European project MD-Paedigree and by ERC Advanced Grant MedYMA (on Biophysical Modeling and Analysis of Dynamic Medical Images)

Statistical analysis, Registration, Reduced order models, Machine learning

The work aims at developping statistical tools to analyse cardiac shape, deformation, and motion. In particular, we are interested in developping reduced order models so that the variability within a population described by a complex model can be reduced into few parameters or modes that are clinically relevant. We use these modes to represent the variability seen in a population and to relate this variability with clinical parameters, and we build group-wise statistics which relate these modes to a given pathology. We focus on cardiomyopathies and the cardiovascular disease risk in obese children and adolescents.

5.3.4. Geometric statistics for Computational Anatomy

Participants: Nina Miolane [Correspondent], Xavier Pennec.

Lie groups, pseudo-Riemannian, Statistics, Computational Anatomy

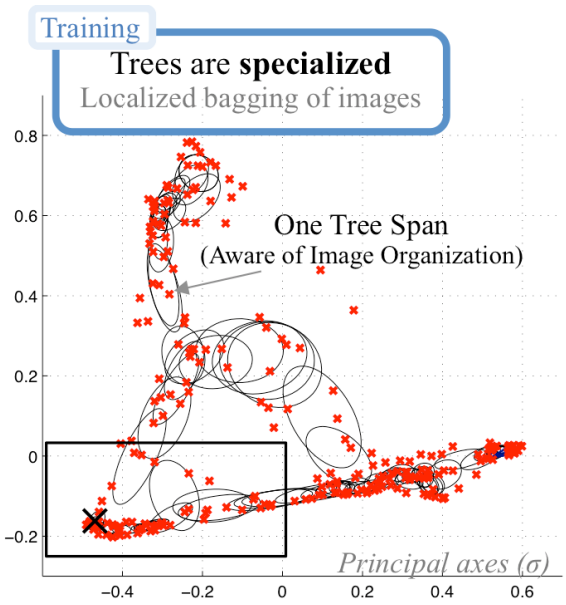

Figure 9. Laplacian Forest, where images are here represented as points, and where decision trees are trained using the spatial organization of these images on a reduced space.

Lie groups are widely used in mathematical models for Medical Imaging. In Computational Anatomy for example, an organ's shape can be modeled as the deformation of a reference shape, in other words : as an element of a Lie group. If one wants to analyze the variability of the human anatomy, e.g. to help diagnose diseases, one has to perform statistics on Lie groups. We investigate the geometric structures on Lie groups that enable to define consistent statistics. A Lie group G is a manifold with an additional group structure. Statistics on *Riemannian* manifolds have be studied throughout the past years. One may wonder if we could use the theory of statistics on Riemannian manifolds for statistics on G. To this aim, we need to define a Riemannian metric on the Lie group that is *compatible with the group structure*: a so-called *bi-invariant* metric. However, it is known that most Lie groups do not admit any bi-invariant metric. One may wonder if we could generalize the theory of statistics on Riemannian manifolds to pseudo-Riemannian manifolds and use it for statistics on G. To this aim, we need to define a bi-invariant pseudo-metric on G. How many Lie groups do admit such a pseudo-metric and can we compute it? These investigations and their results (see Fig. 10) were presented at MaxEnt 2014 [24].

5.3.5. Statistical Analysis of Diffusion Tensor Images of the Brain

Participants: Vikash Gupta [correspondent], Nicholas Ayache, Xavier Pennec.

Population specific multimodal brain atlas for statistical analysis of white matter tracts on clinical DTI.

HIV virus can cross the hematoencephallic barrier and affect the neural connectivity in the human brain causing compromised motor controls, loss in episodic, long term memory and working memory, loss in attention/concentration and visual agnosia. These cognitive losses are characterized by the neuropsychological (NP) test scores and believed to be correlated with destruction of white matter (WM) integrity among the HIV patients. For quantifying the loss in WM integrity, the HIV subjects are compared against controls using a tract based spatial statistics (TBSS) routine. The standard TBSS routines uses univariate statistics using the fractional anisotropy (FA) maps. However, we improved on the existing routines using tensor based registration for normalizing the diffusion tensor images (DTI) followed by a multivariate statistics using the full tensor

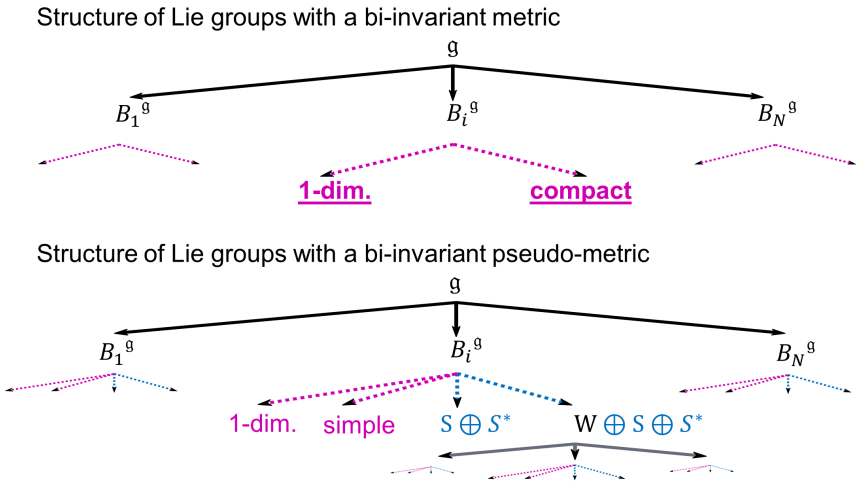

Figure 10. Structure of Lie groups on which one can define a bi-invariant metric or a bi-invariant pseudo-metric. The black levels of the tree represent the adjoint decomposition of the Lie algebra, the dashed lines represent the possible algebraic types of the substructures. Note the recursive construction in the pseudo-Riemannian case.

information. With the improved method it is possible to detect differences in WM regions which was not possible using the existing TBSS routines. For this study a population specific multimodal (T1 and DTI) brain atlas was developed from the population. The joint atlas also contains a probabilistic parcellation of WM regions in the brain which can be used for region of interest (ROI) based statistical studies (see Fig.11).

5.3.6. Longitudinal Analysis and Modeling of Brain Development

Participants: Mehdi Hadj Hamou [correspondent], Xavier Pennec, Nicholas Ayache.

This work is partly funded through the ERC Advanced Grant MedYMA 2011-291080 (on Biophysical Modeling and Analysis of Dynamic Medical Images).

Brain development, adolescence, longitudinal analysis, non-rigid registration algorithm, extrapolation, interpolation

This work is divided into 2 complementary studies about longitudinal trajectories modeling:

- Diffeomorphic registration parametrized by Stationary Velocity Fields (SVF) is a promising tool already applied to model longitudinal changes in Alzheimer's disease. However, the validity of these model assumptions in faithfully describing the observed anatomical evolution needs to be further investigated. In this work, we thus analyzed the effectiveness of linear regression of SVFs in describing anatomical deformations estimated from past and future observations of the MRIs.
- Due to the lack of tools to capture the subtle changes in the brain, little is known about its development during adolescence. The aim of this project is to provide quantification and models of brain development during adolescence based on diffeomorphic registration parametrized by SVFs (see Fig.12). We particularly focused our study on the link between gender and the longitudinal evolution of the brain. This work was done in collaboration with J.L. Martinot et H. Lemaître (Inserm U1000).

5.4. Computational Physiology

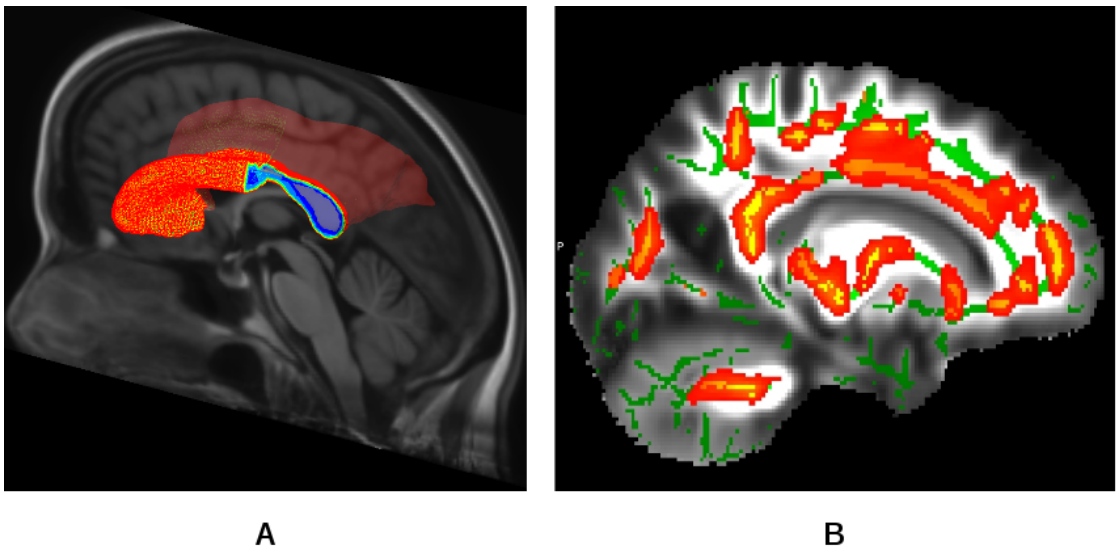

Figure 11. ***A:*** *Probabilistic parcellation of corpus callosum with blue and red being the maximum and minimum probability regions respectively.* ***B:*** *Multivariate statistics on white matter tracts. The red-yellow sections show statistically significant differences*

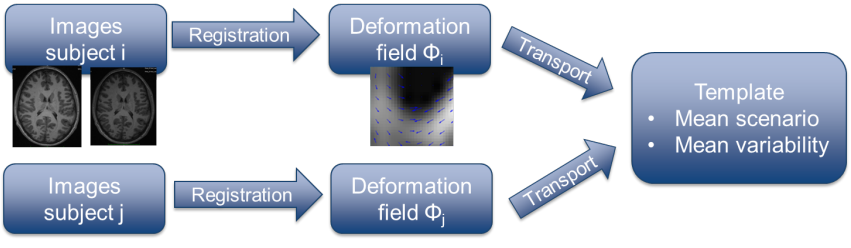

Figure 12. Pipeline for the longitudinal analysis of brain development during adolescence.

5.4.1. Biophysical Modeling and Simulation of Longitudinal Brain MRIs with Atrophy in Alzheimer's Disease

Participants: Bishesh Khanal [correspondent], Nicholas Ayache, Xavier Pennec.

This work has been partly supported by the European Research Council through the ERC Advanced Grant MedYMA (on Biophysical Modeling and Analysis of Dynamic Medical Images).

Alzheimer's Disease (AD), modeling brain deformation, biophysical model, simulation

- We propose a biophysical model of brain deformation due to atrophy in Alzheimer's Disease(AD) [17]. The model allows simulation of longitudinal brain MRIs with a desired level of atrophy in brain parenchyma. Here we enhanced our previous implementation to model brain parenchyma and cerebrospinal fluid (CSF) differently so that there is no need to prescribe atrophy in CSF region (see Fig.13).
- The model could be used to explore different possible hypotheses about evolution of atrophy in the brain and how it affects the brain shape changes.

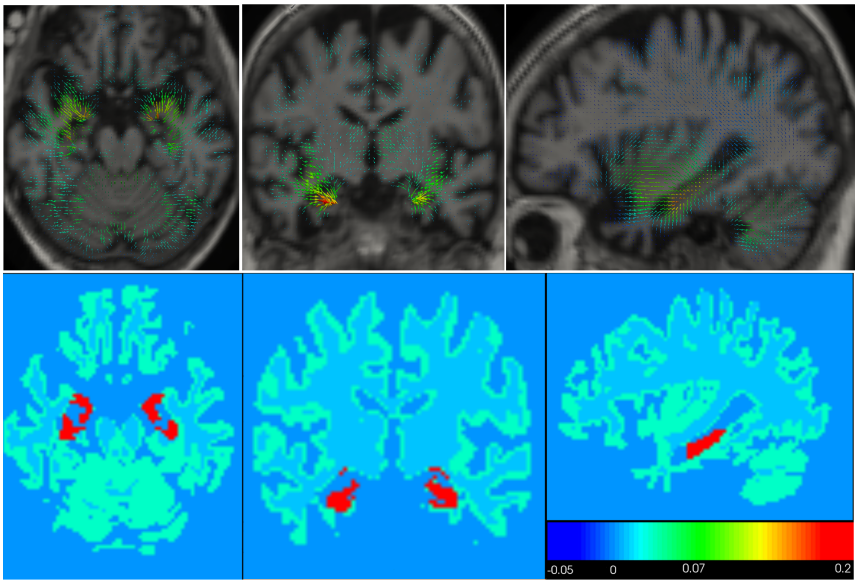

Figure 13. An example of obtained deformation field (top) from the model for the prescribed atrophy (bottom). From left to right: Axial, Coronal and Sagittal views.

5.4.2. Glioblastoma : Study of the vasogenic edema

Participants: Matthieu Lê [correspondent], Hervé Delingette, Jan Unkelbach [Massachussetts General Hospital], Nicholas Ayache.

This work is carried out between Ascelpios research group, Inria Sophia Antipolis, France and the Department of Radiation Oncology of the Massachusetts General Hospital, Boston, USA.

Glioblastoma, Vasogenic Edema, Radiotherapy, Target Delineation

- We studied the impact of anti-angiogenic treatment on the MRI appearance of glioblastoma.
- We studied how MRI extracted features could help distinguish between the vasogenic edema and the tumor infiltration[22].

- We analyzed the impact of excluding the vasogenic edema from the gross tumor volume during radiation therapy (see Fig. 14). Our approach leads to a dose more comformal to the underlying tumor cell density knowing that prescribing less dose might open the way for later re-irradiation.

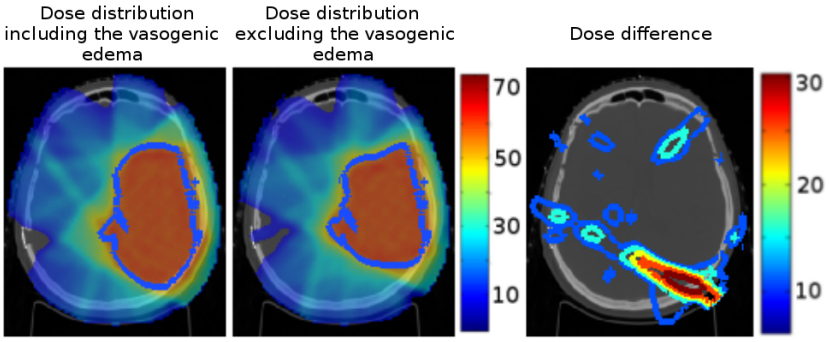

Figure 14. Comparison of the dose distribution including the vasogenic edema (clinical practice) and the excluding the estimated vasogenic edema (proposed method).

5.4.3. Image-based Prediction of Cardiac Ablation Targets

Participants: Rocio Cabrera Lozoya [correspondent], Maxime Sermesant, Nicholas Ayache.

Electrophysiology, ablation planning, machine learning

Ventricular radio-frequency ablation (RFA) can have a critical impact on preventing sudden cardiac arrest but is challenging due to a highly complex arrhythmogenic substrate. We aim at identifying local image characteristics capable of predicting the presence of local abnormal ventricular activities (LAVA). This could lead to pre-operatively and non-invasively improve and accelerate the procedure.

- We present the use of intensity and texture-based local imaging features in the vicinity of myocardial scar and grey zones towards the prediction of RFA target localisation (see Fig.15).
- We detail the uncertainty in the data and explore its impact on the classification results.
- A preliminary output with visual interpretation and potential use in a clinical environment was presented.
- The encouraging obtained results warrant further investigation and open up possibilities for non-invasive cardiac arrhythmia ablation planning. [13]

5.4.4. Personalised Canine Electromechanical Model of the Heart

Participants: Sophie Giffard-Roisin [correspondent], Maxime Sermesant, Hervé Delingette, Stéphanie Marchesseau, Nicholas Ayache.

This work has been supported by the European Project FP7 under grant agreement VP2HF (no 611823) and the ERC Advanced Grant MedYMA (on Biophysical Modeling and Analysis of Dynamic Medical Images).

Cardiac Modelling, Personalised Simulation, Electrical and Mechanical Simulation

- We studied the coupled electro-mechanical modelling of the heart, where the mechanics is handled by the Bestel-Clement-Sorine model while the electrophysiological phenomena is driven by an Eikonal model (see Fig. 16).

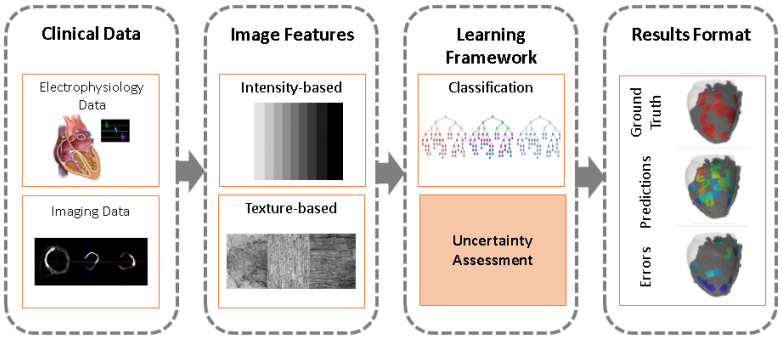

Figure 15. Pipeline showing the processing of our multimodal data. It includes an image feature extraction phase, followed by a classification with uncertainty assessment stage. The rightmost panel shows the preliminary output result format for a clinical environment.

- We participated to the STACOM'2014 LV Mechanics Challenge in Boston[15] where four healthy canine clinical data (left ventricles) were provided. The validation was performed on local displacements. Our model has been calibrated by a quantitative sensitivity study as well as a personalized automatic calibration.

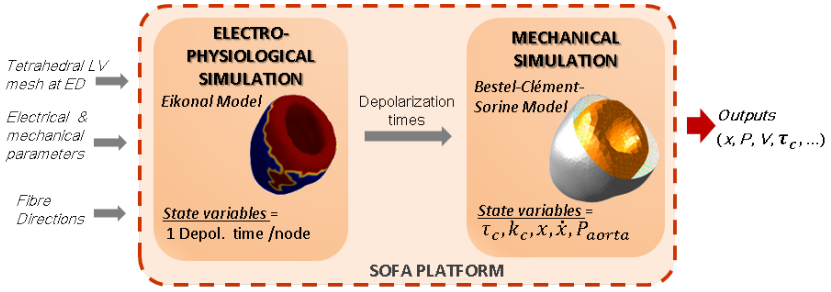

Figure 16. Complete electromechanical pipeline used for the simulations of four healthy canine hearts.

5.4.5. Computational modeling of radiofrequency ablation for the planning and guidance of abdominal tumor treatment

Participants: Chloé Audigier [correspondent], Hervé Delingette, Tommaso Mansi, Nicholas Ayache.

This PhD is carried out between Asclepios research group, Inria Sophia Antipolis and the Image Analytics and Informatics global field, Siemens Corporate Research, Princeton, USA.

Radio Frequency Abation, Patient-Specific Simulation, Lattice Boltzmann Method, Computational Fluid Dynamics, Heat Transfer, Therapy Planning, Liver

Radiofrequency abation (RFA) is a minimally invasive therapy suited for liver tumor ablation. However a patient-specific predicitive tool to plan and guide the treatment is required. We developed a computational framework for patient-specific planning of RFA (see Fig.17) :

- a personalised forward model of RFA:
- A patient-specific detailed anatomical model of the liver is estimated from standard CT image and meshed to generate a tetrahedral volume mesh. The structures of interest include the parenchyma, lesion, hepatic vein and vena cava.
- A Computation Fluic Dynamic and porous media solver using the Lattice Boltzmann Method is used to compute the patient-specific blood flow in the hepatic circulatory system and the blood flow distribution inside the parenchyma.
- Bio-heat equation has been implemented with a Lattice Boltmann Method also to model efficiently the heat propagation in biological tissues accounting for the cooling effect of neighboring vessels. A cell death model have been combined to account for the cellular necrosis.

Then this forward model is used to estimate patient-specific model parameters as presented in the ABDI workshop at MICCAI 2014 [12]. This work presented obtained the best paper award of the workshop.

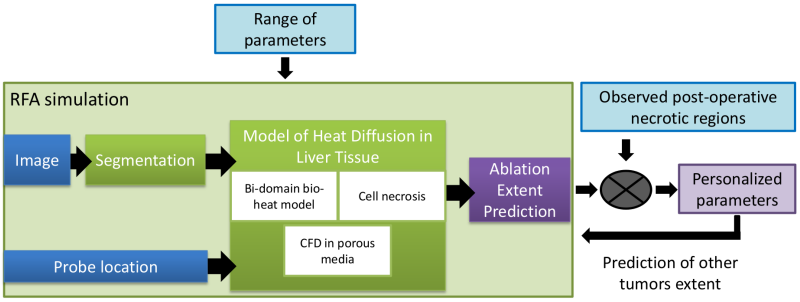

Figure 17. Steps of the proposed method for parameters personnalisation (blue: input, green: processes, purple: output).

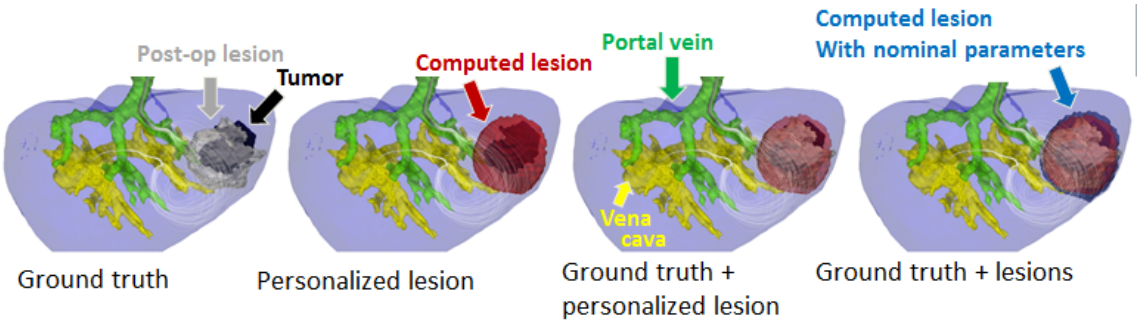

Figure 18. Predicted necrosis compared qualitatively well with ground truth (necrosis zone observed on a post-operative image).

5.4.6. Multi-channel patch-based glioma segmentation

Participants: Nicolas Cordier [correspondent], Hervé Delingette, Nicholas Ayache.

Part of this work was funded by the European Research Council through the ERC Advanced Grant MedYMA (on Biophysical Modeling and Analysis of Dynamic Medical Images).

Brain, MRI, Glioma, Patch-based Segmentation, Tumor Simulation

The segmentation of glioblastoma, the most severe case of brain tumors, is a crucial step for diagnostic assessment and therapy planning. In order to perform the manual delineation of the tumor compartments, the clinicians have to concurrently screen multi-channel 3D MRI, which makes the process both time-consuming and subject to inter-expert delineation variability. We are building upon the patch-based segmentation framework, the state-of-the-art for the segmentation of healthy brain structures, to present automatic glioma segmentation algorithms. Our 2013 submission to the MICCAI Brain Tumor Segmentation Challenge has been improved by:

- replacing the heuristic label fusion strategy with a more robust approach,
- integrating information such as statistics of appearance and position,
- generating configurations of synthetic training patches,
- filtering out the training patches for which the labels are less reliable (see Fig.19).

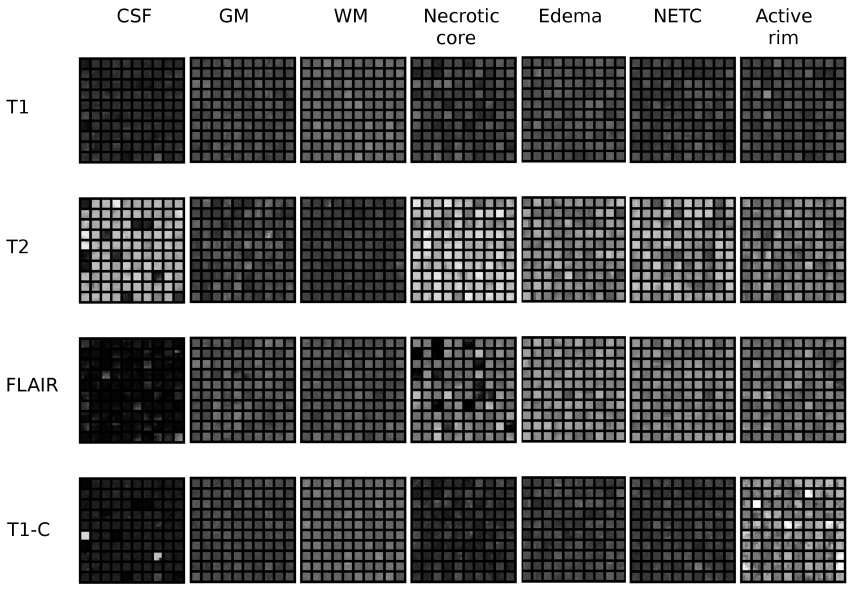

Figure 19. 2D slices of randomly sampled 3D multi-channel patches. From left to right: the different MR channels (T1, T2, T2-FLAIR, contrast enhanced T1). From top to bottom: cerbrospinal fluid (CSF), grey matter (GM), white matter (WM), necrotic tumor core, edema, non-enhancing tumor core (NETC), and active rim.

6. Bilateral Contracts and Grants with Industry

6.1. CIFRE PhD Fellowships

6.1.1. General Electric

The work of Thomas Benseghir, *3D/2D Coronary Registration for Interventional Cardiology Guidance*, is supported by a PhD fellowship from the General Electric company.

6.1.2. Neurelec/Oticon Medical

The work of Thomas Demarcy, *Segmentation and anatomic variability of the cochlea and other temporal bone structures from medical images*, is supported by a PhD fellowship from the Neurelec/Oticon Medical company.

6.2. Inria - Mauna Kea Technologies I-Lab SIWA

Participants: Nicholas Ayache [correspondent], Xavier Pennec, Irina Vidal-Migallón, Marzieh Kohandani Tafreshi, Julien Dauguet, Tom Vercauteren, Barbara André.

This I-lab involves the Mauna Kea Technologies company.

The first focus of this I-lab is to develop efficient and friendly content-based image retrieval (CBIR) tools to help user to make a diagnosis. The resulting smart atlas has been published in 3 clinical [27], [28], [19] and one methodological [18] conferences. The second focus is on image registration to provide near real-time and robust image registration tools built on GPU implementations for image stabilization and super-resolution as it is a critical method for the smart atlas.

For more information, see https://lisa.sophia.inria.fr/siwa-loasis-numerique-dinria-et-de-mauna-kea-706.html.

6.3. Microsoft Research

Microsoft Research is funding through the Inria-Microsoft joint lab the projects "4D Cardiac MR Images" and "Medilearn" aiming at analyzing large databases of cardiac images to help the diagnosis of cardiac diseases and planning of therapy. This project involves A. Crimisi from MSR and partially funds the Phds of Loic Le Folgoc and Jan Margeta as well as the post doctoral stay of Hervé Lombaert.

6.4. Spin-off company Therapixel

Therapixel is a spin-off of the Asclepios (Inria Sophia Antipolis) and Parietal (Inria Saclay) project teams founded in 2013. Therapixel makes surgical information systems. It relies on depth sensing, advanced software processing and innovative user interfaces to provide touchless control of the computer. This technology allows for a direct control of the computer that sterility constraints made impractical in the past. Therapixel obtained in 2014 the CE marking of its product on touchless visualization of medical images.

6.5. Other contracts

The contracts with Philips and Siemens are described in our previous activity reports.

6.6. National Initiatives

6.6.1. Consulting for Industry

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

6.6.2. Collaboration with national hospitals

Asclepios is collaborating with the following 3 IHU (University Hospital Institute) in France : the IHU-Strasbourg (Pr J. Marescaux and L. Soler) on image-guided surgery (N. Ayache serves as Chief Scientific Officer), the IHU-Bordeaux (Pr M. Haïssaguere and Pr P. Jaïs) on cardiac imaging and modeling and the IHU-Pitié Salpétriére (Dr. O. Colliot and S. Durrleman) on neuroimaging.

We also have long term collaborations with the CHU Nice and Centre Antoine Lacassagne in Nice.

Asclepios is part of the EQUIPEX MUSIC with Bordeaux University Hospital in order to build an XMR interventional room equipped with a medInria workstation.

7. Partnerships and Cooperations

7.1. European Initiatives

7.1.1. FP7 & H2020 Projects

7.1.1.1. MD PAEDIGREE

Type: FP7

Defi: ICT for Health, Ageing Well, Inclusion and Governance

Instrument: Integrated Project

Objectif: Virtual Physiological Human

Duration: March 2013 - February 2017

Coordinator: Ospedale Pediatrico Bambino Gesu, Rome, Italy.

Partner: Siemens AG (DE), Siemens SCR (USA), Maat France (FR), MOTEK (NL), EMP (DE), VUmc (NL), Lynkeus (IT). Universities: KU Leuven (BE), Fraunhofer (DE), UMC Utrecht (NL), TU Delft(NL), Sheffield (UK), Athens (GR), Genoa (IT), Transilvania din Brasov (RO); Hospitals: OPBG (Roma, IT), Gaslini (Genoa, IT), GOSH/UCL (London, UK), JHU (Baltimore, USA).

Inria contact: Xavier Pennec

See also: http://www.md-paedigree.eu/

Abstract:MD-Paedigree is a clinically-driven and strongly VPH-rooted project, where 7 world-renowned clinical centres of excellence pursue improved interoperability of paediatric biomedical information, data and knowledge by developing together a set of reusable and adaptable multi-scale models for more predictive, individualised, effective and safer paediatric healthcare, being scientifically and technologically supported by one of the leading industrial actors in medical applications in Europe operating in conjunction with highly qualified SMEs and some of the most experienced research partners in the VPH community. MD-Paedigree validates and brings to maturity patient-specific computer-based predictive models of various paediatric diseases, thus increasing their potential acceptance in the clinical and biomedical research environment by making them readily available not only in the form of sustainable models and simulations, but also as newly-defined workflows for personalised predictive medicine at the point of care. These tools can be accessed and used through an innovative model-driven infostructure powered by an established digital repository solution able to integrate multimodal health data, entirely focused on paediatrics and conceived of as a specific implementation of the VPH-Share project, planned to be fully interoperable with it and cooperating, through it, also with p-Medicine. MD-Paedigree's goals are to integrate and share highly heterogeneous biomedical information, data and knowledge, using best practices from the biomedical semantic Web; develop holistic search strategies to seamlessly navigate through and manage the integrative model-driven infostructure and digital repository; jointly develop reusable, adaptable and composable multi-scale VPH workflow models, support evidence-based translational medicine at the point of care, and ultimately facilitate collaborations within the VPH community.

7.1.1.2. VP2HF

Type: FP7

Defi: ICT for Health, Ageing Well, Inclusion and Governance

Instrument: Specific Targeted Research Project

Objectif: Virtual Physiological Human

Duration: October 2013 - September 2016

Coordinator: King's College London (UK)

Partner: Philips Research Hamburg (DE), Universitat Pompeu Fabra (SP), Inria, French National Research Institute in Informatics and Mathematics (FR), Université Catholique de Louvain (BE), Caen University Hospital (FR), Philips Research Paris (FR), Simula Research Laboratory (NO), Centron Diagnostics (UK).

Inria contact: Maxime Sermesant

See also: http://vp2hf.eu/

Abstract: Heart failure (HF) is one of the major health issues in Europe, affecting 6 million patients and growing substantially because of the ageing population and improving survival following myocardial infarction. The poor short to medium term prognosis of these patients means that treatments such as cardiac re-synchronisation therapy and mitral valve repair can have substantial impact. However, these therapies are ineffective in up to 50% of the treated patients and involve significant morbidity and substantial cost. The primary aim of VP2HF is to bring together image and data processing tools with statistical and integrated biophysical models mainly developed in previous VPH projects, into a single clinical workflow to improve therapy selection and treatment optimisation in HF. The tools will be tested and validated in 200 patients (including 50 historical datasets) across 3 clinical sites, including a prospective clinical study in 50 patients in the last year of the project. The key innovations in VP2HF that make it likely that the project results will be commercially exploited and have major clinical impact are: 1) all tools to process images and signals, and obtain the statistical and biophysical models will be integrated into one clinical software platform that can be easily and intuitively used by clinicians and tried out in the prospective clinical study; and 2) by utilising a decision tree stratification approach, only the appropriate parts of the tool chain, that will add maximum value to the predictions, will be used in individual patients, so that the more resource intensive parts will be used when they will add real value. We expect that the study results of substantial improved efficacy of decision making over current guidelines, and an integrated package that is used as part of clinical workflow will ensure the industrial project partners, in particular Philips, will develop project outputs into dedicated products that will have significant clinical impact.

7.1.1.3. MedYMA

Type: FP7

Instrument: ERC Advanced Grant

Duration: April 2012 - March 2017

Coordinator: Inria (France)

Inria contact: Nicholas Ayache

Abstract: During the past decades, exceptional progress was made with in vivo medical imaging technologies for capturing the anatomical, structural and physiological properties of tissues and organs in a patient, with an ever increasing spatial and temporal resolution. The physician is now faced with a formidable overflow of information, especially when a time dimension is added to the already hard to integrate 3-D spatial, multimodal and multiscale dimensions of modern medical images. This increasingly hampers the early detection and understanding of subtle image changes which can have a vital impact on the patient's health. To change this situation, this proposal introduces a new generation of computational models for the simulation and analysis of dynamic medical images. Thanks to their enerative nature, they will allow the construction of databases of synthetic, realistic medical image sequences simulating various evolving diseases, producing an invaluable new resource for training and benchmarking. Leveraging their principled biophysical and statistical foundations, these new models will bring remarkable added clinical value after they are personalized with innovative methods to fit the medical images of any specific patient. By explicitly revealing the underlying evolving biophysical processes observable in the images, this approach will yield new groundbreaking image processing tools to correctly interpret the patient's condition (computer aided diagnosis), to accurately predict future evolution (computer aided prognosis), and

to precisely simulate and monitor an optimal and personalized therapeutic strategy (computer aided therapy). First applications will concern high impact diseases including brain tumors, Alzheimer's disease, heart failure and cardiac arrhythmia and will open new horizons in computational medical imaging.

7.1.2. Inria International Partners

7.1.2.1. Stanford, Statistics Department

France Stanford collaborative project grant (2013-2014):*Understanding Lower Back Pain through Geometric Statistical Analysis of computed tomography (CT) Images*. Stanford, Statistics Dept & Nice Univ. Hospital. Principal investigators X. Pennec (Inria) and S. Holmes (Stanford). Collaboration on statistics on group-valued trees and geometric subspace learning.

7.1.2.2. Informal International Partners

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

Maxime Sermesant is a visiting lecturer in the Division of Imaging Sciences and Biomedical Engineering, St Thomas' Hospital, King's College London lead by Pr Reza Razavi. The XMR facility within this hospital is a unique opportunity to validate and exploit the cardiovascular modelling work.

7.1.2.2.2. Massachusetts General Hospital, Boston

A collaboration with Dr Jan Unklebach, Assistant Professor of Radiation Oncology and Dr Jayashree Kalpathy-Cramer, radiology instructor was initiated in 2013 around the topics of tumor growth modeling, radiotherapy planning and edema characterization from MRI. Matthieu Lê spent 2013 in the department of Radiation Physics at MGH.

7.1.2.2.3. Other International Hospitals

Collaborations with several other European hospitals have been established through the European projects VP2HF and MD PAEDIGREE.

7.2. International Research Visitors

7.2.1. Visits to International Teams

7.2.1.1. Research stays abroad

- Chloé Audigier spent 3 months at Siemens, Princeton, USA from September 22, 2014 to January 30, 2015.
- Jan Margeta spent 3 months at Microsoft Research, Cambrige, UK from July 1, 2014 to September 23, 2014.

8. Dissemination

8.1. Promoting Scientific Activities

8.1.1. Scientific events organisation

8.1.1.1. general chair, scientific chair

- **N. Ayache** organized a new course on the "Personalized Digital Patient" at Collège de France for the annual chair on "Informatics and Computer Sciences". He gave 9 lectures and invited 26 lecturers including H. Delingette and X. Pennec from the Asclepios team.

8.1.1.2. member of the organizing committee

- **X. Pennec** was co-organizer of the MICCAI workshop STIA'14 (Spatio-Temporal Image Analysis for longitudinal and time series image data), which was held at Cambridge, MA (USA) on September 18;

- **M. Sermesant** was a co-chair of the MICCAI 2014 Workshop Statistical Atlases and Computational Models of the Heart and a co-organiser of the UCL Centre for Cardiovascular Imaging and Inria Asclepios Project collaborative workshop: Translational Applications of Cardiovascular Models.

8.1.2. Scientific events selection

8.1.2.1. member of the conference program committee

- **X. Pennec** was program committee member of the MICCAI 2014 conference (Cambridge, MA, USA), area chair for ICPR 2014 conference (Stockholm, Sweden), and area chair of the International Symposium on Biomedical Imaging (ISBI'15).
- **H. Delingette** was program committee member of the RFIA 2014 conference, the conference on Virtual Reality Interactions and Physical Simulation (VRIPHYS'14), the International Symposium on BioMedical Simulation (ISBMS 2014).

8.1.2.2. reviewer

- **H. Delingette** was reviewer for the International Symposium on Biomedical Imaging (ISBI'12), the conference on Virtual Reality Interactions and Physical Simulation (VRIPHYS'14), the International Symposium on BioMedical Simulation (ISBMS 2014), the conference on Medical Image Computing and Computer Assisted Intervention(MICCAI 2014), the European Conference on Computer Vision (ECCV 2014).
- **M. Sermesant** was a reviewer for the MICCAI 2014 and EMBS conferences.
- **X. Pennec** was reviewer for the sixth Workshop on Non-Rigid Shape Analysis and Deformable Image Alignment (NORDIA'14); the workshop on computational diffusion MRI (CDMRI'14); the MICCAI 2014 Workshop on Medical Computer Vision (MCV'14); the 6th International Workshop on Biomedical Image Registration (WBIR'2014); the 24th biennial international conference on Information Processing in Medical Imaging (IPMI 2015).

8.1.3. Journal

8.1.3.1. member of the editorial board

- **N. Ayache** is the co-founder and the Co-Editor in Chief with J. Duncan (Professor at Yale) of *Medical Image Analysis* [4]. This scientific journal was created in 1996 and is published by Elsevier.
- **N. Ayache** is Associated Editor of *IEEE Transactions on Medical Imaging* [5] and a member of the editorial board of the following journals: *Medical Image Technology* (Japanese journal) and *Journal of Computer Assisted Surgery* (Wiley).
- **H. Delingette** is a member of the editorial board of the journal *Medical Image Analysis* (Elsevier).
- **I. Strobant** is editorial coordinator for *Medical Image Analysis*, Elsevier (since october 2001) and editorial assistant for *IEEE Transactions on Medical Image Analysis*, (since october 2001).
- **X. Pennec** is a member of the editorial board of the journal *Medical Image Analysis* (Elsevier), of the *International Journal of Computer Vision* (Springer), of the SIAM *Journal on Imaging Sciences (SIIMS)*, and of the *Journal of Mathematical Imaging and Vision (JMIV)*.

8.1.3.2. reviewer

- **H. Delingette** was reviewer for the following journals : *Medical Image Analysis* (Elsevier), IEEE Transactions in Medical Imaging, IEEE Transactions in Biomedical Engineering, Computer Vision and Image Understanding, Biomedical Engineering, The Visual Computer, Expert Review of Medical Devices, Journal of Fluids and Structures.

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

- **X. Pennec** was reviewer for the following journals : International Statistical Review (ISR), Medical Image Analysis (MedIA), IEEE Transactions in Medical Imaging (TMI), NeuroImage (NIMG), Symmetry, a chapter of a Springer book, IEEE Transactions on Pattern Analysis (PAMI), Int. journal of Computer Vision (IJCV), Journal of mathematical imaging and vision (IJCV), SIAM journal on Imaging Sciences (SIIMS).
- **M. Sermesant** was reviewer for the following journals: Nature Scientific Reports, Journal of the American College of Cardiology, IEEE Transactions on Medical Imaging, Medical Image Analysis, International Journal for Computer Assisted Radiology and Surgery, Computers in Biology and Medecine.

8.1.4. Invited Lectures

We only list invited talks here. Please refer to general references for regular participation in conferences with a submission process.

- **Nicholas Ayache** gave the following invited lectures:
  - Inaugural lecture at Collège de France on 10 April 2014 entitled "From Medical Images to the Digital Patient"
  - Keynote lecture at the ICIP 2015 conference (Oct. 28 2014)
  - Keynote lecture at Sanofi (Nov. 28 2014)
  - Invited lectures at the "Forum of Laureates" (Dec. 11 2014).
- **Hervé Delingette** gave the following invited lectures:
  - at the *Deformable Object Manipulation international workshop* held in Lyon (Japan).
  - at the Medical Imaging Summer School in Favignana (Italy)
  - at a Seminar in College de France within the chair "Informatique et sciences numériques" of Nicholas Ayache on the personalized digital patient, Paris, May 6th, 2014.
  - the Summer School on Medical Simulation in Lyon (France).
- **Xavier Pennec** gave the following invited lectures:
  - séminaire de théorie du contrôle, Univ. Toulon, Decembre 11, 2014.
  - Int. workshop on Geometry of Information and Optimization (GIO), Bordeaux, December 4-5, 2014.
  - Geometrical Models in Vision workshop, semester on Geometry, Analysis and Dynamics on Sub-Riemannian Manifolds, Institut Henry Poincarré, Paris - October 22nd-24th, 2014.
  - the Medical Imaging Summer School (MISS'14) in Favignana (Italy), July 2014.
  - Symposium on Statistical Shape models & Applications (Shape 2014), Delémont, Swiss, June 11-13 2013. Keynote speaker.
  - Seminar at College de France within the chair "Informatique et sciences numériques" of Nicholas Ayache on the personalized digital patient, Paris, May 13, 2014.
  - MICCAI PC Workshop, Cambridge, MA, USA, May 16, 2014.
  - Séminaires du Laboratoire de Mécanique, Lille Univ., March 20 2014.
- **Maxime Sermesant** gave invited lectures at the Frontiers Conference on Pediatrics and Congenital Heart Diseases, at the European Society of Cardiovascular Magnetic Resonance, and the opening lecture at the Science and Technology Department Day of Bordeaux University.

8.1.5. Other Scientific Animation Activities

- **Nicholas Ayache** a member of the "Comité de la Recherche Biomédicale en Santé Publique (CRBSP)" of the Nice hospitals since 2008. He was invited to Tokyo, Japan in February 2014 to evaluate a national program on "Computational Anatomy" funded by the MEXT.
- **Xavier Pennec** is a member of the MICCAI Society Board of Directors, of the Doctoral follow-up Committee (CSD) at Inria Sophia Antipolis, and in charge of the relationships of Inria-Sophia with the Nice University Hospital (CHU). In 2014, he was a member of the jury of the Vienna Science and Technology Fund (WWTF) for their 2014 call on imaging.
- **H. Delingette** is a member of the local committee in charge of the scientific selection of visiting scientists (Comité NICE) and the local committee on the immersive platform. He was an evaluator for the integrated European project ARTREAT, for the National Commission for Scientific and Technological Research of the Government of Chile (CONICYT). He was involved in the redaction of the application of the Unversité Cote d'Azur to the IDEX bid.
- **M. Sermesant** acted as an evaluator for the the Natural Sciences and Engineering Research Council of Canada (NSERC). He is a member of the Medical Simulation Working Group of Aviesan and of the CCC (local committee in charge of the selection of funding for courses and conferences organisation). He organized two hackfests for the medInria software.

8.2. Teaching - Supervision - Juries

8.2.1. Teaching

Master : H. Delingette and X. Pennec, Introduction to Medical Image Analysis, 34h course, Master 2 MVA, ENS Cachan, France

Master : H. Delingette and X. Pennec, Advanced medical Imaging, 29h course, Master 2 MVA and École Centrale de Paris, France

Master : H. Delingette and X. Pennec, Computational Anatomy and Physiology, 21h course, Master CBB - Computational Biology and Biomedicine, Univ. Nice-Sophia Antipolis.

8.2.2. Supervision

8.2.2.1. PhD defended in 2014

1. Erin Stretton, *Simulation of patient-specific glioma models for therapy planning*. Nice Sophia-Antipolis University, November 2014.
2. Hugo Talbot, *Simulation of Radiofrequency ablation of cardiac cells*. University of Lille, July 2014. [[1]]

8.2.2.2. Current PhDs

1. Chloé Audigier, *Modeling radio-frequency ablation for the planning of abdominal tumors resection*, Nice Sophia-Antipolis University. Started in April 2012.
2. Thomas Benseghir, *3D/2D Coronary Registration for Interventional Cardiology Guidance*, Nice Sophia-Antipolis University. Started in March 2012.
3. Rocio Cabrera Lozoya, *Radio frequency ablation planning for cardiac arrhythmia treatment through biophysical modelling and machine learning approaches*, Nice Sophia-Antipolis University. Started in February 2012.
4. Nicolas Cordier, *Simulation and Analysis and Simulation of Brain Tumors Images*, University of Lille. Started in February 2012.
5. Pietro Gori , *Statistics on the brain connectivity of patients with neurological diseases*, University of Paris. Started in 2012. Thesis in collaboration with the Aramis project-team, co-directed by O. Colliot, S. Durrleman and N. Ayache.

6. Vikash Gupta, *Diffusion tensor imaging of the brain: towards quantitative clinical tools*, Nice Sophia-Antipolis University. Started in November 2011.
7. Mehdi Hadj Hamou, *Biophysical modeling of the anatomical evolution of the brain*, Nice Sophia-Antipolis University. Started in September 2012.
8. Bishesh Khanal, *Modeling the atrophy of the brain in Alzheimer's disease*, Nice Sophia-Antipolis University. Started in November 2012.
9. Loic Le Folgoc, *Biophysical Personalization of Cardiac Models based on Machine Learning*, Nice Sophia-Antipolis University. Started in June 2012.
10. Jan Margeta, *Indexation of time-series 4D cardiac MR images*, Ecole des Mines de Paris. Started in March 2011.
11. Nina Miolane, *Geometric Statistics in Computational Anatomy: Template Estimation and Subspace Learning in Manifolds, Lie groups and Stratified Spaces*, Nice-Sophia Antipolis University. Started in November 2013.
12. Hugo Talbot, *Simulation of Radiofrequency ablation of cardiac cells*, University of Lille. Started in September 2010.
13. Anant Vemuri, *Augmented reality for image-guided surgery*, Nice-Sophia Antipolis University. Started in 2012.
14. Marc-Michel Rohé, *Analyse statistique spatio-temporelle des formes, déformations, flots et propriétés physiologiques du cœur*, Nice-Sophia Antipolis University. Started in 2014.
15. Sophie Giffard-Roisin, *Non-invasive Estimation of Cardiac Electrophysiological Parameters*, Nice-Sophia Antipolis University. Started in 2014.
16. Roch Mollero, *Uncertainty quantification in personalized electromechanical models. Application to cardiomyopathies and obesity*, Nice-Sophia Antipolis University. Started in 2014.
17. Thomas Demarcy, *Segmentation and anatomic variability of the cochlea and other temporal bone structures from medical images*, Nice-Sophia Antipolis University. Started in 2014.

8.2.2.3. Masters Thesis

1. Sophie Giffard-Roisin, *Evaluation of Personalised Canine Electromechanical Cardiac Models*. MVA Master, ENS Cachan. From April 2014 to August 2014.
2. Clair Vandersteen, *New concepts in mini-invasive cochlear implantation surgery applied to a surgical virtual planification*. Surgical Sciences Master, Medicine faculty Créteil Paris XI. From november 2013 to october 2014.

8.2.3. Juries

N. Ayache was co-supervisor of the Phd thesis of E. Stretton (École des Mines de Paris).

Hervé Delingette was co-supervisor of the Phd theses of E. Stretton (École des Mines de Paris) and H. Talbot (Université de Lille I), reviewer in the PhD thesis committee of Blandine Romain (Ecole Centrale de Paris), of Jordan Bano (Université de Strasbourg), of Petru-Stefan Manescu (Université de Lyon), of Mathieu Bailet (Université Joseph Fourier de Grenoble) and examinor in the PhD thesis committee of Elisa Schenone (Université Paris VI), Xavier Faure (Université de Lyon I), and Ahmed Yureidini (Université Lille I).

Maxime Sermesant was examinor in the PhD thesis committee of H. Talbot (Université de Lille I).

8.3. Popularization

Maxime Sermesant gave 2 presentations in 2014 about research and medical imaging in local high schools (Lycée Tocqueville in Grasse and Lycée Saint Exupéry in Saint Raphaël).

9. Bibliography

Publications of the year

Doctoral Dissertations and Habilitation Theses

[1] H. TALBOT. *Interactive Patient-Specific Simulation of Cardiac Electrophysiology*, Université des Sciences et Technologies de Lille, July 2014, https://hal.inria.fr/tel-01097201

Articles in International Peer-Reviewed Journals

[2] A. AMELOT, E. STRETTON, H. DELINGETTE, N. AYACHE, S. FROELICH, E. MANDONNET. *Expert-validated CSF segmentation of MNI atlas enhances accuracy of virtual glioma growth patterns*, in "Journal of Neuro-Oncology", 2014, forthcoming [*DOI :* 10.1007/s11060-014-1645-5], https://hal.inria.fr/hal-01081410

[3] Y. KOMATSU, A. JADIDI, F. SACHER, A. DENIS, M. DALY, N. DERVAL, A. SHAH, H. LEHRMANN, C.-I. PARK, R. WEBER, T. ARENTZ, G. PACHE, M. SERMESANT, N. AYACHE, J. RELAN, M. MONTAUDON, F. LAURENT, M. HOCINI, M. HAISSAGUERRE, P. JAIS, H. COCHET. *Relationship Between MDCT-Imaged Myocardial Fat and Ventricular Tachycardia Substrate in Arrhythmogenic Right Ventricular Cardiomyopathy*, in "Journal of the American Heart Association", 2014, vol. 3, n^{o} 4, 10 p. [*DOI :* 10.1161/JAHA.114.000935], https://hal.inria.fr/hal-01095772

[4] H. LOMBAERT, L. GRADY, X. PENNEC, N. AYACHE, F. CHERIET. *Spectral Log-Demons: Diffeomorphic Image Registration with Very Large Deformations*, in "International Journal of Computer Vision", May 2014, vol. 107, n^{o} 3, pp. 254-271 [*DOI :* 10.1007/s11263-013-0681-5], https://hal.inria.fr/hal-00979616

[5] M. LORENZI, X. PENNEC, G. B. FRISONI, N. AYACHE. *Disentangling Normal Aging from Alzheimer's Disease in Structural MR Images*, in "Neurobiology of Aging", September 2014 [*DOI :* 10.1016/J.NEUROBIOLAGING.2014.07.046], https://hal.inria.fr/hal-01061017

[6] B. MENZE, A. JAKAB, S. BAUER, J. KALPATHY-CRAMER, K. FARAHANI, J. KIRBY, Y. BURREN, N. PORZ, J. SLOTBOOM, R. WIEST, L. LANCZI, E. GERSTNER, M.-A. WEBER, T. ARBEL, B. AVANTS, N. AYACHE, P. BUENDIA, L. COLLINS, N. CORDIER, J. CORSO, A. CRIMINISI, T. DAS, H. DELINGETTE, C. DEMIRALP, C. DURST, M. DOJAT, S. DOYLE, J. FESTA, F. FORBES, E. GEREMIA, B. GLOCKER, P. GOLLAND, X. GUO, A. HAMAMCI, K. IFTEKHARUDDIN, R. JENA, N. JOHN, E. KONUKOGLU, D. LASHKARI, J. ANTONIO MARIZ, R. MEIER, S. PEREIRA, D. PRECUP, S. J. PRICE, T. RIKLIN-RAVIV, S. REZA, M. RYAN, L. SCHWARTZ, H.-C. SHIN, J. SHOTTON, C. SILVA, N. SOUSA, N. SUBBANNA, G. SZEKELY, T. TAYLOR, O. THOMAS, N. TUSTISON, G. UNAL, F. VASSEUR, M. WINTERMARK, D. HYE YE, L. ZHAO, B. ZHAO, D. ZIKIC, M. PRASTAWA, M. REYES, K. VAN LEEMPUT. *The Multimodal Brain Tumor Image Segmentation Benchmark (BRATS)*, in "IEEE Transactions on Medical Imaging", 2014, 33 p. [*DOI :* 10.1109/TMI.2014.2377694], https://hal.inria.fr/hal-00935640

[7] A. PORRAS, M. ALESSANDRINI, M. DE CRAENE, N. DUCHATEAU, M. SITGES, B. BIJNENS, H. DELINGETTE, M. SERMESANT, J. D'HOOGE, A. FRANGI, G. PIELLA. *Improved Myocardial Motion Estimation Combining Tissue Doppler and B-Mode Echocardiographic Images*, in "IEEE Transactions on Medical Imaging", June 2014, vol. 33, n^{o} 11, pp. 2098 - 2106 [*DOI :* 10.1109/TMI.2014.2331392], https://hal.inria.fr/hal-01095151

[8] A. SUINESIAPUTRA, B. COWAN, A. O. AL-AGAMY, M. A. ALATTAR, N. AYACHE, A. S. FAHMY, A. M. KHALIFA, P. MEDRANO-GRACIA, M.-P. JOLLY, A. H. KADISH, D. C. LEE, J. MARGETA, S.

K. WARFIELD, A. YOUNG. *A Collaborative Resource to Build Consensus for Automated Left Ventricular Segmentation of Cardiac MR Images*, in "Medical Image Analysis", 2014, vol. 18, n° 1, pp. 50-62 [*DOI :* 10.1016/J.MEDIA.2013.09.001], https://hal.inria.fr/hal-00857223

[9] Y. TARABALKA, G. CHARPIAT, L. BRUCKER, B. MENZE. *Spatio-Temporal Video Segmentation with Shape Growth or Shrinkage Constraint*, in "IEEE Transactions on Image Processing", September 2014, vol. 23, n° 9, pp. 3829-3840, https://hal.inria.fr/hal-01052543

[10] K. C. WONG, M. SERMESANT, K. RHODE, M. GINKS, C. ALDO RINALDI, R. RAZAVI, H. DELINGETTE, N. AYACHE. *Velocity-based cardiac contractility personalization from images using derivative-free optimization*, in "Journal of the mechanical behavior of biomedical materials", December 2014, 17 p. [*DOI :* 10.1016/J.JMBBM.2014.12.002], https://hal.inria.fr/hal-01095725

International Conferences with Proceedings

[11] M. ALESSANDRINI, B. HEYDE, S. CYGAN, M. SERMESANT, H. DELINGETTE, O. BERNARD, D. CRAENE, J. D'HOOGE. *Elastic registration vs. block matching for quantification of cardiac function with 3D ultrasound: Initial results of a direct comparison in silico based on a new evaluation pipeline*, in "IEEE International Ultrasonics Symposium", Chicago, United States, September 2014, pp. 608 - 611 [*DOI :* 10.1109/ULTSYM.2014.0149], https://hal.inria.fr/hal-01095790

[12] *Best Paper*
C. AUDIGIER, T. MANSI, H. DELINGETTE, S. RAPAKA, V. MIHALEF, D. CARNEGIE, E. BOCTOR, M. CHOTI, A. KAMEN, D. COMANICIU, N. AYACHE. *Parameter Estimation For Personalization of Liver Tumor Radiofrequency Ablation*, in "MICCAI Workshop on Abdominal Imaging – Computational and Clinical Applications", Boston, United States, September 2014, https://hal.inria.fr/hal-01067709.

[13] R. CABRERA LOZOYA, J. MARGETA, L. LE FOLGOC, Y. KOMATSU, B. BENJAMIN, J. RELAN, H. COCHET, M. HAISSAGUERRE, P. JAIS, N. AYACHE, M. SERMESANT. *Confidence-based Training for Clinical Data Uncertainty in Image-based Prediction of Cardiac Ablation Targets*, in "bigMCV Workshop MICCAI 2014", Boston, United States, September 2014, https://hal.inria.fr/hal-01069085

[14] M. DE CRAENE, M. ALESSANDRINI, P. ALLAIN, S. MARCHESSEAU, I. WAECHTER-STEHLE, J. WEESE, E. SALOUX, H. G. MORALES, R. CUINGNET, H. DELINGETTE, M. SERMESANT, O. BERNARD, J. D 'HOOGE. *Generation of ultra-realistic synthetic echocardiographic sequences*, in "IEEE 11th International Symposium on Biomedical Imaging (ISBI)", Beijing, China, IEEE, April 2014, pp. 73 - 76 [*DOI :* 10.1109/ISBI.2014.6867812], https://hal.inria.fr/hal-01095133

[15] S. GIFFARD-ROISIN, S. MARCHESSEAU, L. LE FOLGOC, H. DELINGETTE, M. SERMESANT. *Evaluation of Personalised Canine Electromechanical Models*, in "Proceedings of the 5th international STACOM workshop", Boston, United States, O. CAMARA, T. MANSI, M. POP, K. RHODE, M. SERMESANT, A. YOUNG (editors), Springer, September 2014, n° 8896, https://hal.inria.fr/hal-01087841

[16] P. GORI, O. COLLIOT, L. MARRAKCHI-KACEM, Y. WORBE, F. DE VICO FALLANI, M. CHAVEZ, S. LECOMTE, C. POUPON, A. HARTMANN, N. AYACHE, S. DURRLEMAN. *A Prototype Representation to Approximate White Matter Bundles with Weighted Currents*, in "MICCAI 2014 - 17th International Conference on Medical Image Computing and Computer Assisted Intervention", Boston, United States, September 2014, https://hal.inria.fr/hal-01010702

[17] B. KHANAL, M. LORENZI, N. AYACHE, X. PENNEC. *A Biophysical Model of Shape Changes due to Atrophy in the Brain with Alzheimer's Disease*, in "MICCAI 2014 - 17th International Conference Medical Image Computing and Computer-Assisted Intervention", Boston, United States, P. GOLLAND, N. HATA, C. BARILLOT, J. HORNEGGER, R. HOWE (editors), LNCS - Lecture Notes in Computer Science, Springer, Springer, September 2014, vol. 8674, pp. 41-48 [*DOI :* 10.1007/978-3-319-10470-6_6], https://hal.inria.fr/hal-01006478

[18] M. KOHANDANI TAFRESHI, N. LINARD, B. ANDRÉ, N. AYACHE, T. VERCAUTEREN. *Semi-automated Query Construction for Content-based Endomicroscopy Video Retrieval*, in "Medical Image Computing and Computer Assisted Intervention (MICCAI)", Boston, United States, September 2014, https://hal.inria.fr/hal-01010673

[19] M. KOHANDANI TAFRESHI, B. NAPOLÉON, A.-I. LEMAISTRE, M. GIOVANNINI, V. JOSHI, J. DAUGUET, N. AYACHE, B. ANDRÉ. *Smart Atlas for Supporting the Interpretation of needle-based Confocal Laser Endomicroscopy (nCLE) of Pancreatic Cysts: First Classification Results of a Computer-Aided Diagnosis Software based on Image Recognition*, in "Digestive Disease Week (DDW 2014)", Chicago, United States, May 2014, https://hal.inria.fr/hal-01010701

[20] L. LE FOLGOC, H. DELINGETTE, A. CRIMINISI, N. AYACHE. *Sparse Bayesian Registration*, in "MICCAI - 17th International Conference on Medical Image Computing and Computer Assisted Intervention", Boston, United States, September 2014 [*DOI :* 10.1007/978-3-319-10404-1_30], https://hal.inria.fr/hal-01006605

[21] H. LOMBAERT, D. ZIKIC, A. CRIMINISI, N. AYACHE. *Laplacian Forests: Semantic Image Segmentation by Guided Bagging*, in "MICCAI 2014 - 17th International Conference Medical Image Computing and Computer-Assisted Intervention", Boston, United States, P. GOLLAND, N. HATA, C. BARILLOT, J. HORNEGGER, R. HOWE (editors), LNCS - Lecture Notes in Computer Science, Springer, September 2014, vol. 8674 [*DOI :* 10.1007/978-3-319-10470-6_62], https://hal.inria.fr/hal-01009672

[22] M. LÊ, H. DELINGETTE, J. KALPATHY-CRAMER, E. GERSTNER, H. A. SHIH, T. BATCHELOR, J. UNKELBACH, N. AYACHE. *Multimodal Analysis of Vasogenic Edema in Glioblastoma Patients for Radiotherapy Planning*, in "Workshop Image-Guided Adaptive Radiation Therapy", Boston, United States, September 2014, https://hal.inria.fr/hal-01093397

[23] J. MARGETA, A. CRIMINISI, D. C. LEE, N. AYACHE. *Recognizing cardiac magnetic resonance acquisition planes*, in "MIUA - Medical Image Understanding and Analysis Conference - 2014", London, United Kingdom, Reyes-Aldasoro, Constantino Carlos and Slabaugh, Gregory, July 2014, https://hal.inria.fr/hal-01009952

[24] N. MIOLANE, X. PENNEC. *Statistics on Lie groups : a need to go beyond the pseudo-Riemannian framework*, in "MaxEnt 2014", Amboise, France, September 2014, https://hal.inria.fr/hal-01091515

[25] H. TALBOT, F. SPADONI, C. DURIEZ, M. SERMESANT, S. COTIN, H. DELINGETTE. *Interactive Training System for Interventional Electrocardiology Procedures*, in "6th International Symposium on Biomedical Simulation - ISBMS 2014", Strabsourg, France, October 2014, pp. 11 - 19 [*DOI :* 10.1007/978-3-319-12057-7_2], https://hal.inria.fr/hal-01078209

National Conferences with Proceedings

[26] H. DARMANTÉ, B. BUGNAS, R. B. D. DOMPSURE, L. BARRESI, N. MIOLANE, X. PENNEC, F. DE PARETTI, N. BRONSARD. *Analyse biométrique de l'anneau pelvien en 3 dimensions – à propos de 100*

scanners, in "89e Réunion annuelle de la SOFCOT", Paris, France, Revue de Chirurgie Orthopédique et Traumatologique, November 2014, vol. 100, n^{o} 7 [*DOI :* 10.1016/J.RCOT.2014.09.076], https://hal.inria.fr/hal-01094711

Conferences without Proceedings

[27] M. KOHANDANI TAFRESHI, V. JOSHI, A. MEINING, C. LIGHTDALE, M. GIOVANNINI, J. DAUGUET, N. AYACHE, B. ANDRÉ. *Smart Atlas for Supporting the Interpretation of probe-based Confocal Laser Endomicroscopy (pCLE) of Biliary Strictures: First Classification Results of a Computer-Aided Diagnosis Software based on Image Recognition*, in "Digestive Disease Week (DDW 2014)", Chicago, United States, May 2014, https://hal.inria.fr/hal-01010765

[28] M. KOHANDANI TAFRESHI, Y.-Q. LI, R. PITTAYANON, D. PLESKOW, V. JOSHI, P. CHIU, J. DAUGUET, N. AYACHE, B. ANDRÉ. *Smart Atlas for Supporting the Interpretation of probe-based Confocal Laser Endomicroscopy (pCLE) of Gastric Lesions: First Classification Results of a Computer-Aided Diagnosis Software based on Image Recognition*, in "Digestive Disease Week (DDW 2014)", Chicago, United States, May 2014, https://hal.inria.fr/hal-01010762

Scientific Books (or Scientific Book chapters)

[29] *Spatio-temporal Image Analysis for Longitudinal and Time-Series Image Data*, Lecture notes in computer science, Springer International PublishingCambridge, United States, January 2015, vol. 8682, 89 p. [*DOI :* 10.1007/978-3-319-14905-9], https://hal.inria.fr/hal-01114150

[30] A. FRANGI, D. FRIBOULET, N. AYACHE, H. DELINGETTE, T. GLATARD, C. HOOGENDOORN, L. HUMBERT, K. LEKADIR, I. LARRABIDE, Y. MARTELLI, F. PEYRIN, X. PLANES, M. SERMESANT, M. VILLA-URIOL, T. WHITMARSH, D. ATKINSON. *Image Based Modelling*, in "Computational Biomedicine", P. COVENEY, V. DIAZ, P. HUNTER, M. VICECONTI (editors), Oxford University Press, 2014, pp. 59 - 82, https://hal.archives-ouvertes.fr/hal-01016455

[31] M. LORENZI, X. PENNEC. *Discrete Ladders for Parallel Transport in Transformation Groups with an Affine Connection Structure*, in "Geometric Theory of Information", F. NIELSEN (editor), Signals and Communication Technology, Springer, 2014, pp. 243-271 [*DOI :* 10.1007/978-3-319-05317-2_9], https://hal.inria.fr/hal-00933229

[32] X. PENNEC, P. FILLARD. *Statistical Computing On Non-Linear Spaces For Computational Anatomy*, in "Handbook of Biomedical Imaging: Methodologies and Clinical Research", N. PARAGIOS, J. DUNCAN, N. AYACHE (editors), Springer, 2014, forthcoming, https://hal.inria.fr/inria-00616201

Books or Proceedings Editing

[33] S. DURRLEMAN, T. FLETCHER, G. GERIG, M. NIETHAMMER, X. PENNEC (editors). *Spatio-temporal Image Analysis for Longitudinal and Time-Series Image Data*, Lecture Notes in Computer Science, SpringerUnited States, 2015, vol. 8682, https://hal.inria.fr/hal-01108202

[34] N. PARAGIOS, J. DUNCAN, N. AYACHE (editors). *Handbook of Biomedical Imaging: Methodologies and Clinical Research*, Springer, 2014, 590 p. , https://hal.inria.fr/inria-00616178

Research Reports

[35] M. BAUER, M. BRUVERIS, P. HARMS, B. KHESIN, S. MARSLAND, P. MICHOR, K. MODIN, O. MÜLLER, X. PENNEC, S. SOMMER, F.-X. VIALARD. *Math in the Cabin - Shape Analysis Workshop in Bad Gastein*, Brunel University London ; University of Vienna, July 2014, https://hal.archives-ouvertes.fr/hal-01076953

Other Publications

[36] L. LE FOLGOC, H. DELINGETTE, A. CRIMINISI, N. AYACHE. *Technical Appendix on Sparse Bayesian Regression*, September 2014, MICCAI - 17th International Conference on Medical Image Computing and Computer Assisted Intervention, Technical appendix to a MICCAI 2014 conference paper. Loïc Le Folgoc, Hervé Delingette, Antonio Criminisi, and Nicholas Ayache: Sparse Bayesian Registration, https://hal.inria.fr/hal-01002861

[37] C. VANDERSTEEN, T. DEMARCY, H. DELINGETTE, C. RAFFAELLI, J. LAUDANSKI, T. POURCHER, J. DARCOURT, P. FRANKEN, D. GNANSIA, N. AYACHE, N. GUEVARA. *Teaching tool for advanced visualization of temporal bone structures by fusion of μCT and CT scan images*, October 2014, 8th International Symposium on Objective Measures in Auditory Implants [*DOI :* 10.13140/2.1.1517.6007], https://hal.inria.fr/hal-01108877

[38] A. S. VEMURI, A. SPORTES, S. A. NICOLAU, J. MARESCAUX, N. AYACHE, L. SOLER. *Video Synchronization: An Approach to Biopsy Site Re-localization*, December 2014, 1. Introduction2. Related work3. System setup4. Evaluation, https://hal.inria.fr/hal-01089196

References in notes

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

[40] M. GAZZANIGA (editor). *The Cognitive Neurosciences*, MIT Press, 1995

[41] *International Symposium on Biomedical Imaging: From Nano to Macro*, IEEERotterdam, 2010

[42] T. JIANG, N. NAVAB, J. P. PLUIM, M. A. VIERGEVER (editors). *Medical Image Computing and Computer-Assisted Intervention (MICCAI'10), Part I*, Lecture Notes in Computer Science, SpringerBeijing, China, September 2010, vol. 6361

[43] T. JIANG, N. NAVAB, J. P. PLUIM, M. A. VIERGEVER (editors). *Medical Image Computing and Computer-Assisted Intervention (MICCAI'10), Part II*, Lecture Notes in Computer Science, SpringerBeijing, China, September 2010, vol. 6362

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

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

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

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

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

[49] M. J. ACKERMAN. *The Visible Human Project*, in "Proceedings of the IEEE : Special Issue on Surgery Simulation", March 1998, vol. 86, n° 3, pp. 504–511

[50] L. AXEL, A. MONTILLO, D. KIM. *Tagged magnetic resonance imaging of the heart: a survey*, in "Medical Image Analysis", 2005, vol. 9, n° 4, pp. 376–393

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

[52] N. AYACHE, O. CLATZ, H. DELINGETTE, G. MALANDAIN, X. PENNEC, M. SERMESANT. *Asclepios: a Research Project-Team at Inria for the Analysis and Simulation of Biomedical Images*, in "From semantics to computer science: essays in honor of Gilles Kahn", Y. BERTOT, G. HUET, J.-J. LÉVY, G. PLOTKIN (editors), Cambridge University Press, 2009, http://www.inria.fr/sophia/asclepios/Publications/Nicholas.Ayache/Colloquium-Gilles-Kahn-NA-2007-v5.pdf

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

[54] H. DELINGETTE, X. PENNEC, L. SOLER, J. MARESCAUX, N. AYACHE. *Computational Models for Image Guided, Robot-Assisted and Simulated Medical Interventions*, in "Proceedings of the IEEE", September 2006, vol. 94, n° 9, pp. 1678- 1688, http://www.inria.fr/sophia/asclepios/Publications/Herve.Delingette/IEEE-proceedings-Robotics.pdf

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

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

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

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

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

[60] E. HAUG, H.-Y. CHOI, S. ROBIN, M. BEAUGONIN. *Human Models for crash and impact Simulation*, in "Computational Models for the Human Body", N. AYACHE (editor), Elsevier, 2004, pp. 231–452

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

[62] P. HUNTER. *Computational Physiology and the Physiome Project*, 2004

[63] D. METAXAS, J. KAYES, F. PRIMANIO. *A 3-D virtual environment for modeling mechanical cardiopulmonary interactions*, in "Medical Image Analysis", 1997, vol. 3, n° 1, pp. 1–26

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

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

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

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

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

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

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