INSTITUT NATIONAL DE RECHERCHE EN INFORMATIQUE ET EN AUTOMATIQUE

Project-Team Epidaure

Epidaure, Projet Images, Diagnostic AUtomatique, RobotiquE

Sophia Antipolis

THEME BIO

Table of contents

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2. Overall Objectives

The aim of the project is the development of new tools for medical imaging and robotics.

The images under consideration correspond to anatomical or functional medical images: conventional radiologic imaging, X-ray imaging, magnetic resonance imaging (MRI: anatomical, angiographic, functional...), isotope and nuclear imaging (SPECT: single-photon emission computed tomography, PET: positron emission tomography), ultrasound or echographic imaging, histological imaging, microscopy, monocular or stereoscopic video sequences, etc.

The main target applications are :

1. assistance to diagnosis,
2. surgery simulation (either virtual reality or robotic),
3. image-guided therapy (planning, control, follow-up), which may require augmented reality techniques and robotics.

The tools developed in the project may find additional applications, in particular in the neurosciences (brain functional imaging), in pharmacology (image-based drug trials), in biology (3D confocal microscopy), in geology (3D seismologic images), in archeology and paleontology (CT imaging of fossils), and in industrial control processes (imaging of manufactured objects).

3. Scientific Foundations

3.1. Introduction

A taxonomy of problems to be tackled by medical image analysis techniques can be established as follows : restoration, segmentation, registration, morphometry, statistics, movement, visualisation, simulation and medical robotics. In this section, each of these problems will be described.

Readers who are neophyte to the field of medical imaging will find an interesting presentation of acquisition techniques of the main medical imaging modalities in [103][99]. Regarding the target applications, a good review of the state of the art can be found in the book *Computer Integrated Surgery* [98], in N. Ayache's article [105] and in the more recent synthesis [113]. The scientific journals *Medical Image Analysis* [101], *Transactions on Medical Imaging* [102], and *Computer Assisted Surgery* [100] are also good reference material. A review of the past work of the Epidaure team can be found in a guest editorial of IEEE TMI [104].

3.2. Restoration

Image restoration is a process of image enhancement, in which certain defects related to the physical acquisition process are removed. Two classical examples of image restoration are bias correction and noise reduction.

MRI images are commonly corrupted by a *multiplicative bias*, which needs to be removed in order to obtain equivalent intensity values for the same tissue across the image (e.g. a similar intensity for all points in the brain corresponding to white matter). Bias correction methods have been created, mainly based on a classification process in which each point is classified according to the tissue it contains (cf. 3.3).

Many techniques have been created to reduce the noise arising from the image acquisition process. Linear filtering methods apply low-pass filters which reduce noise, but tend to soften edges, thus resulting in fuzzy

images. On the other hand, *anisotropic diffusion* techniques are very effective to smooth an image while preserving important discontinuities, and their results are remarkable.

3.3. Segmentation

Segmentation is the process of extracting points, lines or regions, which are then used as inputs for complementary tasks such as registration, measurement, movement analysis, visualisation, etc. An introduction to this subject can be found in [106]. Although there is no general solution to the segmentation problem, there exist a set of mathematical tools and algorithms that can be combined to solve specific problems. Related recent work on the segmentation of brain images combining a priori information (from an atlas) and bias correction can be found in [141][140][129].

3.3.1. Thresholding

Thresholding is the simplest segmentation procedure. It consists on extracting regions having intensity values superior to a given threshold. The boundaries of such regions can thus be defined via an implicit function, and they are called iso-surfaces (or iso-intensity surfaces). They can be approximated to a precision finer than that of the original image matrix by a set of polygonal facets, using Lorensen and Cline's "Marching Cubes" algorithm [124].

3.3.2. Deformable models

They are curves or surfaces that evolve in a 2-D or 3-D space to get to delimit an anatomic (or pathologic) structure. The evolution of the model is guided by the simultaneous optimization of two criteria. The first one is a measure of the geometric regularity of the model, using for example local curvature measures. The second one measures a property of the intensity at image points traversed by the deformable model, e.g. the norm of the intensity gradient to favor the attraction of the model towards points having a high contrast. These methods are very effective. The user can initialize the model in an approximative manner around a region of interest. The model then evolves from this initial gross solution to automatically improve the fit to the boundary of the region to be detected. Such an approach is generally much more robust than simple intensity thresholding. These models are also very popular for the analysis of temporal images : in fact, the solution at a given instant is used as initialization for the image taken at the following instant. For an excellent review of the use of deformable models in medical image analysis, the reader is pointed to McInerney and Terzopoulos' article [126].

3.3.3. Multi-scale analysis

It is based on a theory allowing for the application of image analysis at variable resolutions. An excellent tutorial on the subject has been written by B.M. Ter Haar Romeny [132]. Multi-scale analysis is particularly useful for the detection of vessels or other anatomical structures independently of their size. Multi-scale analysis is strongly related to anisotropic diffusion, introduced above. More information can be found in Krissian's thesis [121].

3.3.4. Mathematical morphology and discrete topology

Mathematical morphology theory is based on the definition of local operators that can be used to extract and modify shapes [133]. Discrete topology allows to characterize and modify the topology of manifolds, either locally or globally [120]. Thanks to these operators, it is possible to introduce a priori knowledge about the shape and/or topology of the objects to be segmented (vessels [122], cortex, sulci [115]).

3.3.5. Differential operators

Differential operators can be used in 3-D images to characterize singular points, lines, or surfaces. For example, boundaries can be defined as the locations of points whose intensity gradient norm is locally maximum in the direction of the gradient. Surfaces defined in such a way correspond to location of high intensity contrast, and can be useful for the delimitation of anatomical or pathologic structures.

Complex differential operators can be used to locally compute crest lines on iso-intensity surfaces. Crest lines are the extrema of principal curvature, and they correspond intuitively to the sites where the surface is

very curved. Crest lines can be defined implicitly at the intersection of two iso-surfaces and extracted by the << Marching Lines >> algorithm in a very efficient manner, as proven by Thirion and Gourdon [136].

This analysis can be refined by conserving only the extremal points of the crest lines, which correspond to second differential extremality. Since such lines and points are invariant to rotation and translation, they can be used for rigid registration tasks [107].

3.4. Registration

Registration is a recurrent issue in medical image analysis. It is required for example to compare images of a same patient acquired at different times, or with different imaging modalities. In such cases, it can be rigid or non-rigid registration. Registration is also necessary to compare different patients. Then, it is always a case of non-rigid registration. A good review article can be found in [98][125] and also in Alexis Roche's thesis [131].

Rigid registration consists in searching for a rotation and a translation (6 degrees of freedom) allowing to superimpose one of the images (the model) onto the other one (the scene). The difficulty of this problem is different if we deal with images from a single modality (monomodal registration) or several modalities (multimodal registration). Some monomodal registration methods employ crest lines or extremal points (cf. above) issued from a preliminary segmentation process. In general, these methods are not suited for multimodal registration. In such cases, other techniques based on the minimization of a distance measure or a statistical correlation between images are employed. Recently, several authors have shown that mutual information is a powerful criterion for multimodal image registration without previous segmentation.

Non-rigid registration is a more difficult problem, since the number of parameters to be optimized can be much more elevated than in rigid registration. Thus, one can pass from the 6 parameters of rigid transformation to 12 for affine transformation, and more for high-order polynomial transformations. Some methods are based on the extraction of geometric invariants for the considered family of transformations. Others search for a dense deformation field (a "free-form" transformation) and impose a regularity constraint. Such methods use voxel intensities directly as basic information [109][138][108].

Finally, registration can also be formulated between a volumetric image and a 2-D projection. For example, a pre-operative 3-D angiographic MRI can be registered to an intra-operative 2-D X-ray angiogram. Other applications involve virtual reality or augmented reality [114].

3.5. Atlases, morphometry and statistical analysis

Morphometry is the quantitative study of the geometry of shapes, and in particular it involves the computation of mean shapes and the analysis of variations about such mean.

The definition of statistics about shape requires an appropriate formalization, since in general they are applied on differential manifolds that are not vector spaces (e.g. lines, planes, frames, oriented points, spatial rotations, etc). The reader may refer to the excellent works of Small [134] and Dryden [112], which also present in a unified manner the founding work of Kendall and Bookstein. See also Pennec's thesis [127] for important extensions to 3-D. The applications concerned include the computation of probabilistic anatomical atlases and inter-patient comparison.

In other cases, the focus of interest is not shape, but directly the intensity information. This is the case for the analysis of functional images, in which the intensity of each voxel gives an activation level of the brain when executing a certain task. The statistical analysis procedure consists in this case in determining whether the activation level is significant across a population of subjects following the experiment. A statistical method for the comparison of images is then necessary, which can be done for instance by the software that has become the de facto standard (SPM: Statistical Parametric Mapping [117]). Other recent approaches are detailed in the PhD thesis of B. Thirion [137] and G. Flandin [116].

3.6. Movement

The analysis of movement in dynamic images is a difficult task, since data are 4-dimensional (3 spatial dimensions plus time).

Image analysis can be employed to produce a vector field describing the displacement of each point between two consecutive images. A more global representation of the movement can also be obtained by employing a dynamic model represented by a few quantitative parameters.

To recover the displacement between two successive images, deformable models (cf. the section on segmentation) can be employed. Alternatively, one can also use methods based on differential features, such as boundaries or points of high curvature.

Certain images are obtained with an inherent physical marking of points or lines : such is the case of *tagged MRI*, in which tissues are magnetized differently following a regular geometric pattern (typically a grid pattern). Such grid is visible in the first image, and its deformation can be tracked in the following images. In the case of phase-contrast MRI, a local estimate of displacement and speed is obtained at each point and each time step [110].

In a more general fashion, one can study the apparent movement between two images of a same patient acquired at different times. In order to do this, the images are registered using a rigid registration algorithm, and then a vector field of apparent deformation is recovered by a non-rigid registration method based on intensities, e.g. [139]. It is then possible to use differential operators on this field (e.g. the Jacobian) to detect and quantify temporal evolution [130].

3.7. Visualisation

Historically, the visualisation of volumetric images use to be the most active research subject in the field of 3-D medical image analysis. Gabor Herman published a review on the theme [118], which can be completed with a review of the main algorithms and visualisation systems published by Stytz et al [135]. In general, visualisation requires a preliminary segmentation procedure, although some recent techniques do not require such preprocessing [119].

3.8. Surgery simulation

This research field aims at the definition of geometrical and biomechanical models of organs and soft tissues to simulate in real time their deformation, cutting and stitching. Real time constraints imply that images must be generated at 24 Hz, and force computation for force feedback devices must be updated at about 300 Hz.

A number of works exist that employ mass-spring models, since they allow a relatively simple implementation and reasonable computing times.

Finite elements provide a more refined modeling of the biomechanical properties of soft tissues. They are less commonly employed, since their implementation is more complex and they are computationally expensive.

A review of the state of the art can be found in H. Delingette's article [111] and book chapter [33], and in G. Picinbono's thesis [128].

3.9. Medical robotics

The processes involved in passing from a simulation to the concrete realization of a robot-assisted surgical intervention have received a lot of attention in the last few years. For an introduction to this domain, the reader can refer to [98].

4. Application Domains

4.1. New tools for improved diagnosis

The automatic analysis of medical images can offer a set of new tools to assist the diagnosis process. Among them, one can list the following :

1. The extraction of quantitative parameters about shape and texture : this must be applicable to any anatomical or pathological structure in three dimensions.
2. The detection of changes between two images : it must offer the doctor an automatic detection and quantitative measurement of all changes apparent between two images of the same modality depicting the same patient at different temporal instants. This may be employed to arrive at a diagnosis earlier, and also to evaluate the effect of a therapeutic treatment.
3. Fusion of information provided by different modalities : it must permit the combination of complementary information about a patient. Images of different modalities should be superimposed on a common reference image.
4. Comparison of images of two different patients : tools must be provided in order to compare images of a given modality depicting two different patients. Such tools must allow to compare the nature and severity of similar pathologies, or the extraction of similar images from an image data base.
5. Construction of anatomical and functional << probabilistic >> atlases : the automatic comparison of images of different patients must permit the construction of statistical representations of the shapes and intensities contained in the images. Such atlases may be used to accurately determine the location of structures in any medical image, and to detect and measure quantitatively any abnormal variation.
6. Measuring movement of dynamic organs and articulations from temporal 3D image sequences : in this case, data are four dimensional (3 spatial dimensions and a temporal dimension). The extraction of quantitative measures of movement is a very demanding task, which invariably requires some type of computer processing.
7. Volumetric and dynamic visualisation of images : the qualitative analysis of 3-D and 4-D images by the medical staff must benefit from developments in visualisation techniques. Examples include the realistic presentation of the relative position of several anatomical or pathological structures, or the dynamic 3-D visualisation of moving organs and articulations. Furthermore, it is possible to simulate most endoscopic inspections from 3-D images.

4.2. New tools for improved therapy

Once a diagnosis is established, medical images can play an important role for simulating, controlling and validating the therapy. This applies to a multitude of application domains, such as radiotherapy, traditional surgery, video-surgery, interventional radiology, chimiotherapy, etc.

1. Simulation : it is possible to make use of the geometric and functional information coming from 3-D medical images to build a model of a *virtual patient*. Such a model must allow to simulate a set of therapeutic protocols in order to accurately evaluate their effect.
   The model can be built from images of a normal person and be used for teaching and training of certain therapeutic procedures (e.g. endoscopic surgery). This model may be customized to reflect rare pathologies or complex interventions.
   For current medical practice, such a model can be adapted to the anatomy of a particular patient by the use of medical images. This must allow to experiment and evaluate the progress rendered by new therapies on a particular patient. It can be predicted that medical simulators may become as popular amongst surgeons as flight simulators are for pilots.

2. Control : during a surgical intervention, medical images can help control the operation. In fact, augmented reality techniques provide a direct super-imposition on the patient (or indirectly on a video screen) of anatomical and pathological structures acquired previously (pre-operative) or during (intra-operative) the intervention. This provides an invaluable assistance to the position the instruments, e.g. for cutting or implanting a prosthesis, before the operation is effectively performed. Moreover, it may be possible to superimpose the movement of virtual instruments, prepared during the simulation stage, to be compared in real time to the movements of the surgeon. Finally, certain interventions can be performed by a medical robot, which can make use of intra-operative images for better guidance.
3. Validation : to conclude, the tools developed for assistance to diagnosis can be applied to compare images acquired prior and after a therapy, in order to evaluate quantitatively its effect.

5. Software

5.1. Baladin

Keywords: *Multimodal image registration*.

Participant: Grégoire Malandain [Correspondant].

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

6. New Results

6.1. Introduction

Current research activities are focused on:

- Segmentation of medical images and computation of quantitative parameters of diagnostic value.
- Rigid and deformable registration of monomodal (temporal or spatial evolution, inter-patient comparison) or multimodal (complementarity of different image sources) images.
- Statistical image and shape analysis (morphometry, functional images).
- Motion analysis and medical simulation.

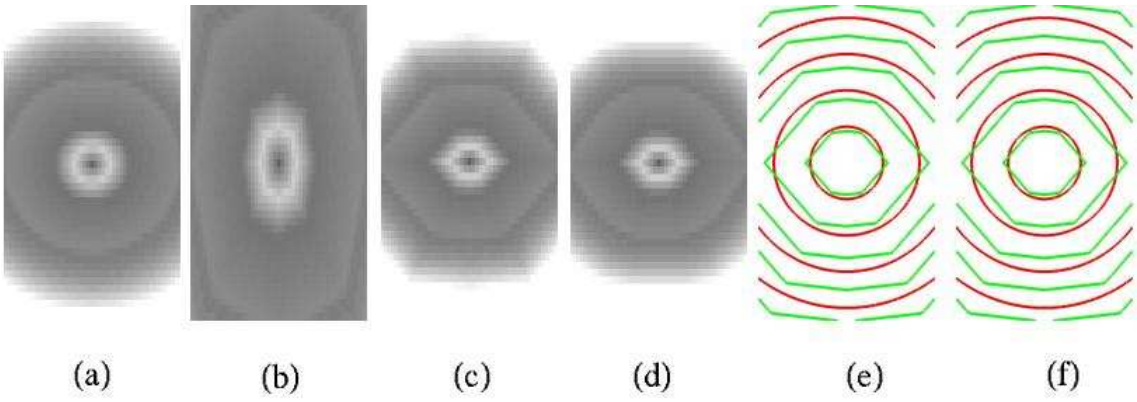


Figure 1. Examples of 2-D distance maps on anisotropic grids: (a) Euclidean distance map ; (b) Chamfer map computed with a 3×3 *mask originally devoted to isotropic images ; (c) Chamfer map computed with a* 3×3 *anisotropic mask whose coefficients where chosen with our method ; (d) Chamfer map computed with a* 5×5 *anisotropic mask whose coefficients where chosen with our method ; (e) Euclidean isolines (red) together with* 3×3 *anisotropic chamfer map (c) isolines (green) ; (f) Euclidean isolines (red) together with* 5×5 *anisotropic chamfer map (d) isolines (blue).*

6.2. Image segmentation

6.2.1. 3-D chamfer distances and norms in anisotropic grids

Keywords: *Farey triangulation*, *anisotropic lattice*, *chamfer distance*.

Participants: Céline Fouard, Grégoire Malandain.

Chamfer distances are widely used in image analysis and many authors have investigated the computation of optimal chamfer mask coefficients. Unfortunately, these methods are not systematized: calculations have to be conducted manually for every mask size or image anisotropy. Since image acquisition (e.g. medical imaging) can lead to discrete anisotropic grids with unpredictable anisotropy value, automated calculation of chamfer mask coefficients becomes mandatory for efficient distance map computations. We propose an automatic construction for chamfer masks of arbitrary sizes. This allows, first, to derive analytically the relative error with respect to the Euclidean distance, in any 3-D anisotropic lattice, and second, to compute optimal chamfer coefficients. In addition, the resulting chamfer map verifies discrete norm conditions [35]. Figure 1 shows examples of chamfer maps computed with chamfer coefficients found with our method.

6.2.2. Brain microvascular network study : extraction of morphometric parameters

Keywords: *Chamfer map*, *Confocal microscopy*, *Medical imagery*, *Segmentation*, *Skeletonization*, *Vascular network*.

Participants: Céline Fouard, Grégoire Malandain.

This research takes place in the Microvisu3D Project which is the result of a collaboration between: U455 unit of the INSERM laboratory (Institut National de la Santé et de la recherche médicale); the IMFT laboratory (Institut de Mécanique des Fluides de Toulouse); the companies INDEED and TGS; and the project EPIDAURE of INRIA through the CIFRE PhD fellowship of C. Fouard.

Our aim is to provide anatomists and neuroanatomists with software tools to quantitatively analyze 3-D images of the cerebral micro-vascular network.

Such analyses require the input images to be both of high resolution and of large size, in order to take into account the smallest capillaries and to cover areas of the brain sufficiently wide to be statistically relevant,

respectively. As such input data cannot be acquired at once, we propose to pave the image area with smaller images acquired with a confocal microscope to obtain an "image mosaic". We developed dedicated building tools for this kind of mosaic to allow large and precise images. But these images are too large to be loaded and processed at once in the memory of a standard computer. We therefore developed dedicated image analysis tools (filtering, thresholding, mathematical morphology, discrete topology tools, ...).

Micro-vascular network analysis requires center lines extraction and diameters estimation. Discrete geometry is an appropriate and powerful framework since we have to compute distance maps for both tasks. To obtain the best trade-off between precision and computational cost, we choosed chamfer distances (see section 6.2.1) that can guide skeletonisaton algorithms. To ensure the homotopy of the skeleton while minimizing the number of disk access (to guaranty an acceptable computational time), we designed a new skeletonization algorithm that allows independant skeletonization of sub-images [65][64].

The developed algorithms have been integrated within the ergonomic software Amira and are currently in use at the INSERM research institute. Moreover, these tools can also be applied to plant roots study [71].

6.2.3. Multi-Image Registration and Mosaicing for Fibered Confocal Microscopy: Application to Quantitative Analysis of Tumor Angiogenesis

Keywords: *Fibered Confocal Microscopy*, *Mosaicing*, *Multi-Image Registration*, *Tumoral Angiogenesis*.

Participants: Tom Vercauteren, Nicholas Ayache.

In collaboration with Mauna Kea Technologies, Paris.

At least 90 % of adults cancers derive from epithelial cells. Some characteristics of cancers are still being discovered today: resistance to programmed cellular death (apoptosis), enhanced spreading capabilities (metastasis), modification of the cellular architecture, ...

In order to better understand tumors development, theoretical and animal models are being studied. The Cell vizio, developed by Mauna Kea Technologies, is a fibered confocal fluorescence microscopy system for in vivo and in situ molecular imaging with cellular resolution.

Within this setting, quantitative measurements are of great interest to understand biological phenomena, distinguish between different types of cellular architectures, ...A trustful statistical analysis is limited by the amount of data and for some specific applications, the field of view provided by the Cell vizio is considered too small to be representative.

Our first goal will be to enhance the quality of the images acquired by the Cell-vizio by bringing specific structures to the fore. We will then extend field of view of the Cell vizio by developing a mosaicing algorithm for video sequences of tissue scans. This mosaicing algorithm will use non-rigid multi-image registration techniques in order to correct for the tissue deformations due to the contact with the imaging probe. A third goal will be to develop some application specific tools to extract information, such as the vascular network, from the reconstructed mosaic. Finally we will be able to compare different acquisitions based on this extracted information.

6.2.4. Partial Volume Effect Quantification and Multiple Sclerosis Lesion Segmentation in Brain MRI

Keywords: *CSF*, *EM*, *Expectation Maximisation*, *MRI*, *atlas*, *brain*, *cerebro-spinal fluid*, *gray matter*, *histogram*, *joint histogram*, *lesion*, *manual segmentation*, *multiple sclerosis*, *partial volume effect*, *segmentation*, *statistical*, *validation*, *white matter*.

Participants: Guillaume Dugas-Phocion, Miguel Ángel González Ballester, Grégoire Malandain, Christine Lebrun, Nicholas Ayache.

This work is performed in close collaboration with Christine Lebrun and Caroline Bensa (Neurology Departement), and Stéphane Chanalet (Radiology Department), at Pasteur Hospital, Nice.

The Expectation Maximization algorithm is a powerful probabilistic tool for brain tissue segmentation. The framework is based on the Gaussian mixture model in MRI, and employs a probabilistic brain atlas as a prior to produce a segmentation of white matter, grey matter and cerebro-spinal fluid (CSF). However, several artifacts

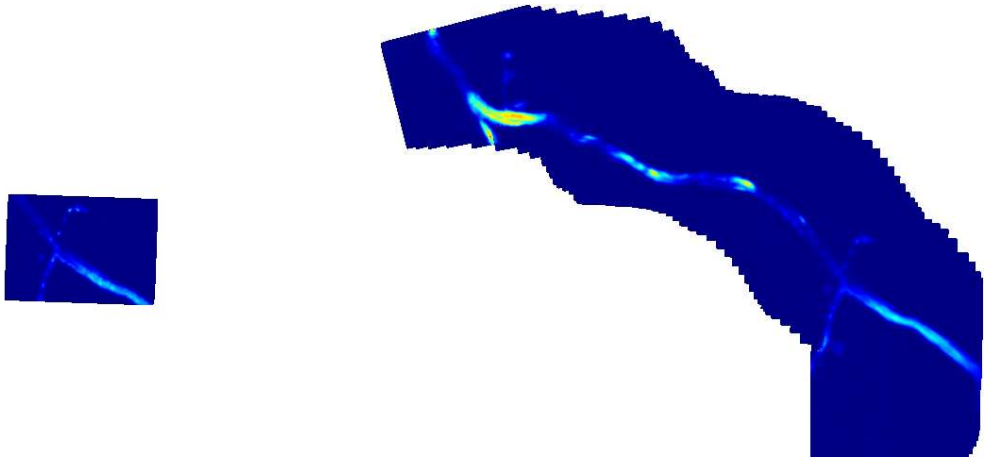


Figure 2. Peripheral axon in live Thy1-YFP adult male mice. Left: A single image (width 400 μm). Right: A preliminary result showing a reconstructed mosaic from a sequence of 65 images (width 1.4 mm). Source images are courtesy of Igor Charvet Dept. Of Pathology, Centre Medical Universitaire, Geneva.

can alter the segmentation process. For example, CSF is not a well defined class because of the large quantity of voxels affected by the partial volume effect which alters segmentation results and volume computation. In this study, we show that ignoring vessel segmentation when handling partial volume effect can also lead to false results, more specifically to an over-estimation of the CSF variance in the intensity space. We also propose a more versatile method to improve tissue classification, without a requirement of any outlier class, so that brain tissues, especially the cerebro-spinal fluid, follows the Gaussian noise model in MRI correctly.

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

Keywords: *3D echography*, *cardiac imaging*, *echocardiography*, *motion analysis*, *radiotherapy*, *segmentation*, *segmentation*, *simplex meshes*, *tracking*.

Participants: Jimena Costa, Hervé Delingette, Gregoire Malandain.

This work is performed in the framework of the MAESTRO european integrated project, in collaboration with the company Dosisoft.

The objective of this work, that started in October 2004, is to devise new supervised segmentation methods for the segmentation of anatomical structures of the lower abdomen (bladder, rectum, prostate,...) in the context of radiotherapy planning. To reach this objective, we plan to use segmentation methods based of deformable simplex meshes since they are well suited for enforcing shape and appearance knowledge about the anatomical structures of interest.

6.2.6. Differentiation of CJD Forms by Intensity Quantification in MRI of the Brain - Definition and Evaluation of new MRI-based Ratios

Keywords: *Creutzfeldt-Jakob Disease*, *MRI of the brain*, *intensity quantification*, *internal nuclei*, *sporadic CJD*, *variant CJD*.

Participants: Marius George Linguraru, Nicholas Ayache, Miguel Angel Gonzalez Ballester, Eric Bardinet [CNRS UPR640-LENA], Didier Dormont [CHU Pitié Salpétrière], Jean-Philippe Brandel [INSERM U360].

This work was within the GIS-Prions Project.

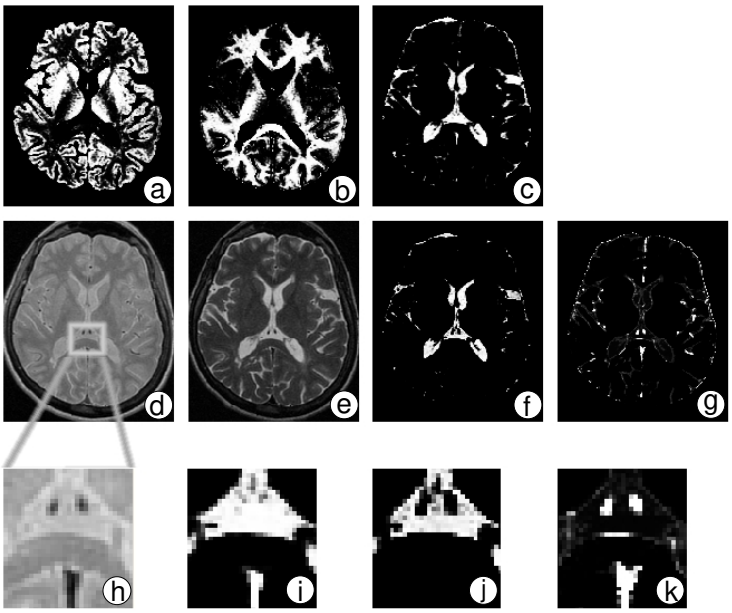


Figure 3. Final segmentation: grey matter (a), white matter (b), CSF without vessel class (c), T2 MRI (d), Proton Density MRI (e), CSF (f), other class including vessels (g). Zoom : Proton Density (h), CSF without vessel class (i), CSF (j), other class including vessels (k).

We present a method for the analysis of basal ganglia (including the thalamus) for the detection and classification of human spongiform encephalopathy in multisequence MRI of the brain. One common feature of most forms of prion protein infections is the appearance of hyperintensities in the deep grey internal nuclei of the brain in FLAIR images. We employ T1, T2 and Flair-T2 MR sequences for the detection of intensity deviations in the internal nuclei.

First, the brain internal nuclei are segmented using brain atlases (one probablistic and one labelled) [40]. The segmentation results in an accurate delineation of the internal nuclei in patient images. Images are processed using spatial registration and intensity normalisation. Subsequently the abnormal MR intensity distributions in the patient internal nuclei are detected using a foveal segmentation (adaptive thresholding) [123]. Figure 4 show typical detection results in a sporadic Creutzfeldt-Jakob Disease (sCJD) a variant CJD (vCJD) patients. The results are robust over the patient data and in accordance to the clinical ground truth.

Our method further allows the quantification of intensity distributions in basal ganglia. The caudate nuclei are highlighted as main areas of diagnosis of sCJD, in agreement with the histological data. The algorithm permitted to classify the intensities of abnormal signals in sCJD patient FLAIR images with a more significant hypersignal in caudate nuclei (10/10) and putamen (6/10) than in thalami. Defining normalised MRI measures of the intensity relations between the internal grey nuclei of patients, we robustly prompt all CJD patients from a database of patients and controls. Furthermore, we differentiate sCJD and vCJD patients, as a first attempt towards an automatic classification tool of human spongiform encephalopathies (Figure 5).

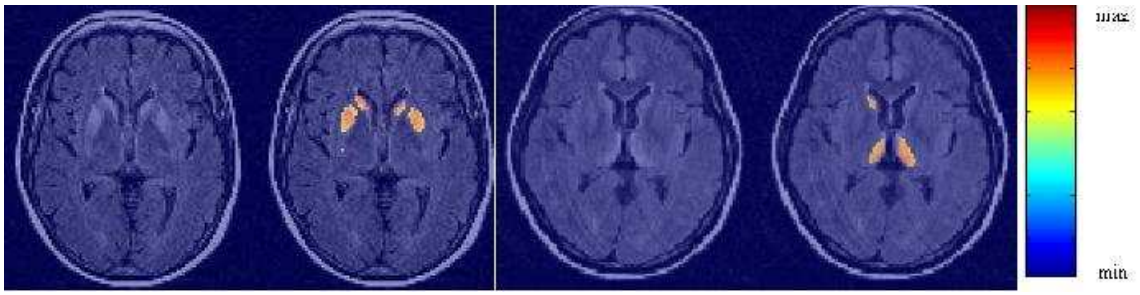


Figure 4. Detection results on patient data. Left (1 and 2) a sCJD case with stronger hyperintensities in the head of caudate and putamen. Right (3 and 4) a vCJD case with stronger hyperintensities in the pulvinar. We present for each case an original cross-section of the FLAIR MR image with abnormal hyperintensities in the internal nuclei and next the same cross-section superimposed with the CJD detection map produced by our algorithm.

6.2.7. Respiratory motion correction in Positron Emission Tomography (PET)

Keywords: *Positron Emission Tomography*, *image reconstruction*, *nuclear medecine*, *oncology*.

Participants: Mauricio Reyes, Grégoire Malandain, Jacques Darcourt.

This work is done in collaboration with the Centre Antoine Lacassagne (Nuclear Medicine Department).

During an emission tomography exam of lungs, respiratory motion causes artifacts in the reconstructed image, which lead to misinterpretations and imprecise diagnosis. Solutions like respiratory gating, correlated dynamic PET techniques, list-mode data based techniques and others have been tested with improvements over the spatial activity distribution in lungs lesions, but with the disadvantages of requiring extra hardware or more expensive scanner systems. The objective of this work was to incorporate respiratory motion corrections directly into the process of image reconstruction, without any additional acquisition protocol consideration. For this, a procedure of correction inside the probability matrix in the classical MLEM algorithm has been implemented which takes into account the spatio-temporal relationship of each voxel in the structure under study. The model accounts for displacement and volume deformation of voxels. To test the methodology,

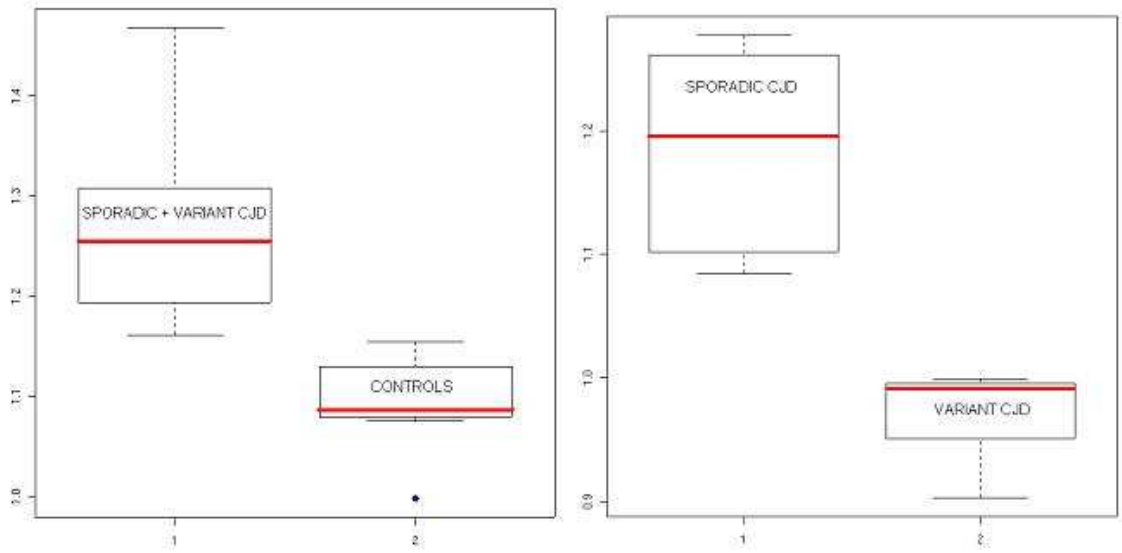


Figure 5. The box plots of the two groups. On the left: 1 - CJD patients, including the sCJD and vCJD cases; 2 -controls. On the right: 1 - sCJD cases, 2 - vCJD cases. The group medians are shown as central bold red lines and the outlier as blue circle.

simulations were carried out using the NCAT thorax phantom in conjunction with the SimSET library. A small lesion was added to the phantom anatomy and real respiratory motion, obtained from two MRI images of a human thorax taken at full-expiration and full-inspiration, was incorporated to the phantom in order to simulate breathing during the data acquisition. Isosurfaces were generated for the image reconstructed reference volume (i.e., full-expiration state) and for the non-corrected and corrected image reconstructed volumes. Preliminary results demonstrate a better reconstruction in terms of shape and localisation (see Fig. 6) [91].

6.3. Registration

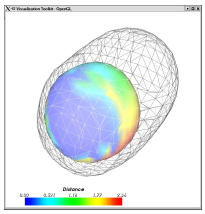
6.3.1. Non-Linear 2D and 3D Registration Using Block-Matching and B-Splines

Keywords: *B-splines*, *block-matching*, *non-linear registration*.

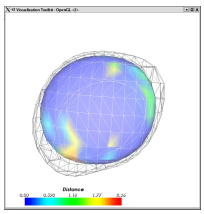
Participants: Heike Hufnagel, Xavier Pennec, Grégoire Malandain.

This work was performed in the framework of the 'Diplomarbeit' that Heike Hufnagel did at Epidaure project for her studies at the university of Luebeck, Germany. Her Diplomarbeit was supervised by Xavier Pennec, Grégoire Malandain, and Nicholas Ayache at INRIA and by Heinz Handels of the university of Luebeck.

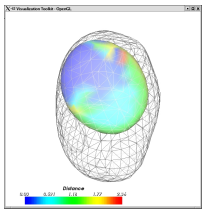
In this work we developed a registration technique to align images that feature anatomical variabilities. The registration algorithm consists of two principal components that are executed alternately. The first component is based on a block-matching technique that identifies a sparse displacement vector field from the iconic features of the two images. Subsequently in the second component, the displacement vectors are used as sampling points to estimate the parametric non-linear transformation T that assigns a corresponding voxel in the target image to each voxel in the source image. We chose the transformation to be represented by B-Splines as they possess mathematical advantages for that task, in particular local support. The algorithm searches the control points that result in the optimal B-Spline approximation. In order to compute the approximation in a robust manner, a weighted Least-Squares approach is employed. The respective minimization is solved by



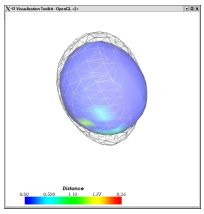
(a) Non-corrected. ZY plane.



(b) Corrected. ZY plane.



(c) Non-corrected. XZ plane.



(d) Corrected. XZ plane.

Figure 6. Qualitative results for a simulated lesion reconstructed in PET (wireframes) without or with motion compensation. The solid shape is the reference lesion (ground truth) with a color code indicating the distance to the reconstructed lesion.

the conjugate gradient algorithm. To minimize the influence of the noise and the lack of sampling points in homogeneous regions, a biharmonic regularization term is integrated in the estimation to smooth undesirable high frequency deformations [96][70].

We applied the registration algorithm on 2D histological slices of the brain and on 3D MR images of the brain and find that this non-linear approach yields qualitatively good registration results with respect to the considered applications (see Fig. 7). Future works will comprise the optimization of the computation time of the program as well as the validation of the algorithm for various typical clinical applications.

6.3.2. Grid-Enabled Non-Rigid Registration of Medical Images

Keywords: *Grid Computing*, *Parallel Computing*, *Registration*.

Participants: Radu Stefanescu, Xavier Pennec, Nicholas Ayache.

The last past of this work was done in collaboration with the Johan Montagnat, Creatis Lab at INSA (Lyon), Derek Hill, Kings College (London, U.K.) and Daniel Rueckert, Imperial College (London, U.K.).

In order for registration methods to be really used in clinical environments, physicians need software tools that are precise and robust. Furthermore, special care must be taken regarding the execution time, which should typically be lower than a few minutes. Previous work resulted in the development of a non-rigid registration algorithm able to reliably recover large deformations with an efficient parallel implementation on a cluster of personal computers [50]. Though accurate, robust and fast, our registration software suffers from several issues regarding its usability: it is command line based, *i.e.* not interactive. We would also like to enable the user to add some medical expertise in order to guide the registration process. Moreover, a cluster of workstations is a parallel computer that usually needs special conditions to operate. Therefore, such a machine cannot lie next to the user and is more likely to find a suitable place as a shared resource in a data center than in an operating or pre-operative planning room.

In order to adress these problems, we implemented the registration as a grid service where a simple graphical user interface (GUI) on the clinical side masters the registration software itself, run on a distant computational

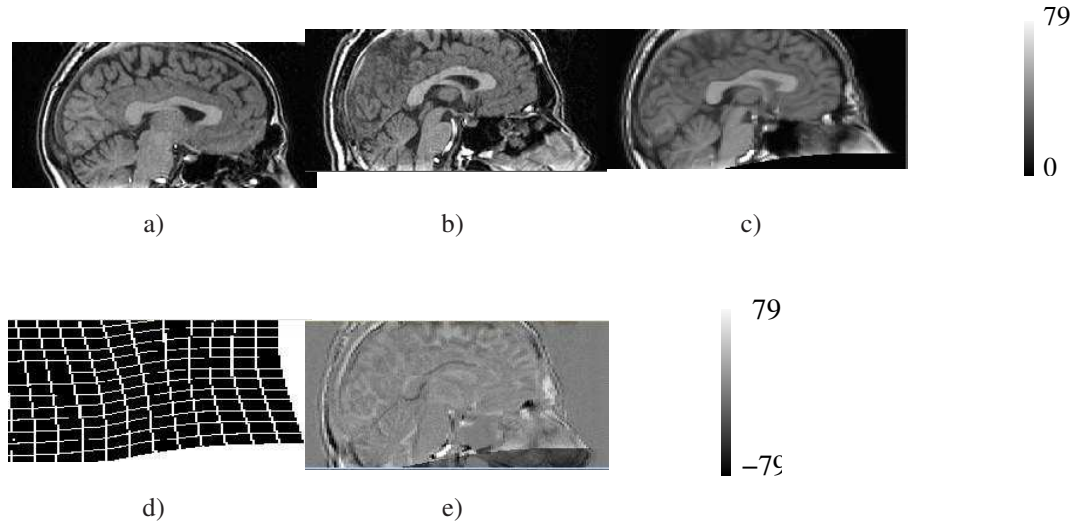


Figure 7. ***Non-Linear Registration of 2D and 3D Images Using Block-Matching and B-Splines.*** *Here, the registration algorithm is applied to two MR volumes of the brain. The figure represents a sagittal slice of the source image a) and a sagittal slice of the target image b). The registration result is the deformed source image c). To make the transformation visible, it is applied to a grid as seen in d). The difference image between the deformed source image and the target image is presented in d).*

center [83][49]. For efficiency reasons, the GUI performs the visualization of the three dimensional images on the user's computer. In the future, it will also incorporate the user feedback into the registration. Our system has been sucessfully tested with a standard internet access, as well as through an ADSL connection.

Our algorithm has also been incorporated into a demonstrator of a grid registration service, implemented using Globus Toolkit 3 [69]. This service was providing access through the Web to four different registration algorithms from different teams and running on different places. In the future, this type of services will enable users from different labs to test and use methods developed elsewhere on their own data or even on data provided by a third party. Furthermore, it opens the way to an objective comparison between the effectiveness of different methods for a given application. This use of such grid services is one of the objectives of the PhD thesis of T. Glatard that began in september 2004 in the framework of the French ACI Masse de données AGIR (see 8.2.1).

6.3.3. Localization of basal ganglia in Parkinsonian patients

Keywords: *Nonrigid registration*, *Parkinson disease*, *atlas registration*, *deep brain stimulation*.

Participants: Radu Stefanescu, Grégoire Malandain, Xavier Pennec, Nicholas Ayache.

This work has been done in collaboration with Eric Bardinet (CNRS) and Jérôme Yelnick (INSERM), both at the La Pitié Salpêtrière hospital, Paris, and was partially funded by Medtronic, Inc.

Deep Brain Stimulation is a procedure that greatly reduces disabling symptoms in patients with Parkinson's disease. The introduction of the electrode inside the brain is performed through surgery. At the La Pitié Salpêtrière hospital in Paris, a stereotactic frame, fixed on the patient's head and visible from different modalities (T1 and T2 weighted MR images) is used as a geometrical referential, and guides the electrodes' insertion. The target is first located on pre-operative images, and then the path of the electrodes is planned through the parenchyma in order to avoid high risk structures. In order to achieve the procedure, one has to first localize the central grey nuclei. This is performed by registering the patient image towards an anatomical

atlas containing a segmentation of the desired structures, followed by a deformation of atlas structures onto the patient's geometry.

The registration occurs in three steps. First, a global affine registration is performed on the two images. Images are then croped to a smaller area containing the structures of interest, and a second affine registration is performed on this area only. Third, a nonrigid registration is performed on the region of interest in the two images, using the algorithm described in [50]. The transformations corresponding to the three registrations (two affine and one nonrigid) are composed, and the segmentations of the structures of interest in the atlas are deformed accordingly (Fig. 8). Since the nonrigid registration was implemented in parallel on a cluster of PC's [51], the whole process takes about 8 minutes using three 3GHz machines.

6.3.4. Augmented Reality for Radio-Frequency Ablation Procedures

Keywords: *3D/2D Registration*, *Augmented Reality*, *Calibration*, *Radio-Frequancies*, *Uncertainty prediction*.

Participants: Stéphane Nicolau, Xavier Pennec, Luc Soler [IRCAD], Nicholas Ayache.

This research theme is done in close collaboration with Pr. L. Soler at IRCAD in Strasbourg.

The purpose of the augmented reality system we developed is to guide the surgeon gesture during radio-frequency ablation procedures in liver surgery. The idea is to superimpose tri-dimensional virtual models extracted from a pre or per-operative CT-scan (reconstruction of the liver, its tumors, the surrounding organs) to a registered view of the electrode manipulated by the surgeon onto 2D video images.

To register the 3D models extracted from the CT-scan onto the 2D video images, we chose a 3D/2D registration method based on radio-opaque markers sticked on the patient skin. Since the available criteria did not fulfill the statistical assumptions of our measurements, we were led to develop a new 3D/2D maximum likelihood registration criterion. Its evaluation previoulsy showed its superiority in terms of accuracy and robustness. To reach real-time processing in the operative room, we developed several algorithms to automatically extract and match radio-opaque markers. A validation study realized on numerous real data showed the efficiency of our methods [43]. Since the system accuracy depends on numerous factors (camera position and angle, marker number, ...), it is not possible to calculate it beforehand. To provide a reliable system, we proposed a technique of covariance propagation that enables to estimate the superimposition error of reconstructed models. A rigorous validation step on synthetic and real data showed that our prediction is correct in our clinical conditions [77].

In parallel, we have enhanced our previous interface [48] that guides the surgeon while introducing the needle toward the target. In collaboration with several medical experts we designed an ergonomic three screen interface (Fig. 9). An experimental evaluation on an abdominal phantom carried out by four surgeons showed that the targeting accuracy was around 2 mm and that the duration of the needle positioning was ten times lower than the usual time needed for that kind of medical gesture [78].

Finally, we performed several clinical experiments on patients (Fig. 10). They showed that our system can be used in the operating room with enough accuracy provided that the breath is monitored and the size of the operative field is controlled [27]. We are currently improving the ergonomy of the system and planning a rigorous validation protocol to prove the efficiency of the system in the operating room.

6.3.4.1. Registration of brain images with an anatomical atlas for radiotherapy planning

Keywords: *Nonrigid registration*, *atlas registration*, *conformal brain radiotherapy*, *irradiation*, *tumors*.

Participants: Olivier Commowick, Radu Stefanescu, Grégoire Malandain, Pierre-Yves Bondiau, Xavier Pennec, Nicholas Ayache.

In collaboration with DOSIsoft SA, Cachan and Centre Antoine Lacassagne, Nice

The treatment of cerebral tumors may involve surgery, radiotherapy, or chemotherapy. Thanks to recent technological advances (on-line definition of the shape of the irradiation beam, irradiation intensity modulation during the treatment), conformal radiotherapy allows a high precision irradiation (homogeneous dose distribution within complex shapes), permitting an improvement of local control and the reduction of the complications. In order to determine the best characteristics of the treatment planning, and to provide the patient

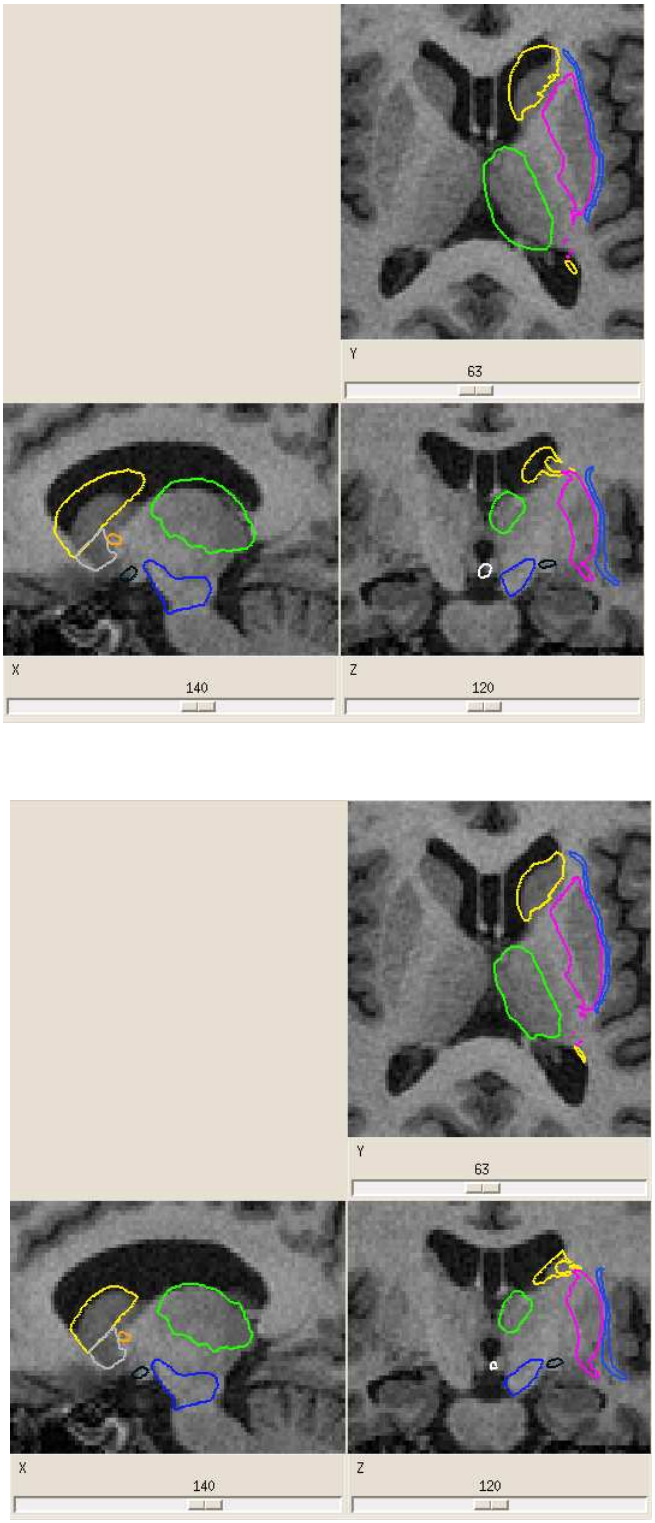


Figure 8. Segmentation of the central grey nuclei using atlas to subject registration: the result of affine registration (top) is compared to the one of affine followed by nonrigid registration (bottom).

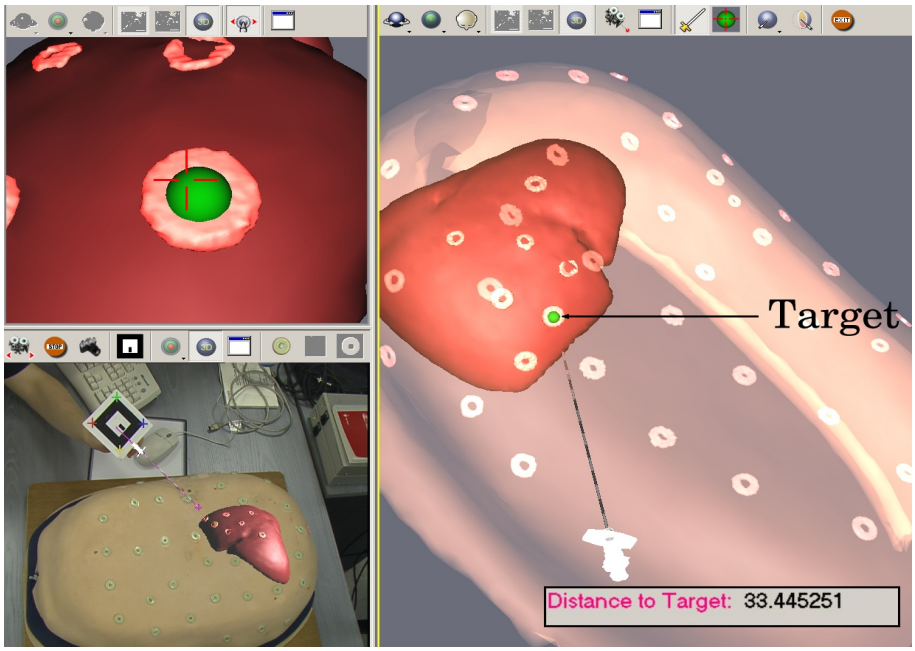


Figure 9. A new display interface for augmented reality in image guided surgery. Bottom left image: the 3D reconstruction of the liver and the virtual needle are superimposed on the external video views of the patient. Top left image: this screen displays the virtual view of a camera set at the needle tip and oriented toward the needle axis (in this image the needle is oriented toward a marker sticked on the liver surface). Right image: one can see on this screen the relative position of the needle with respect to the phantom. We indicate in its corner the virtual distance in mm that separates the needle tip to the target (in this case, a marker center).

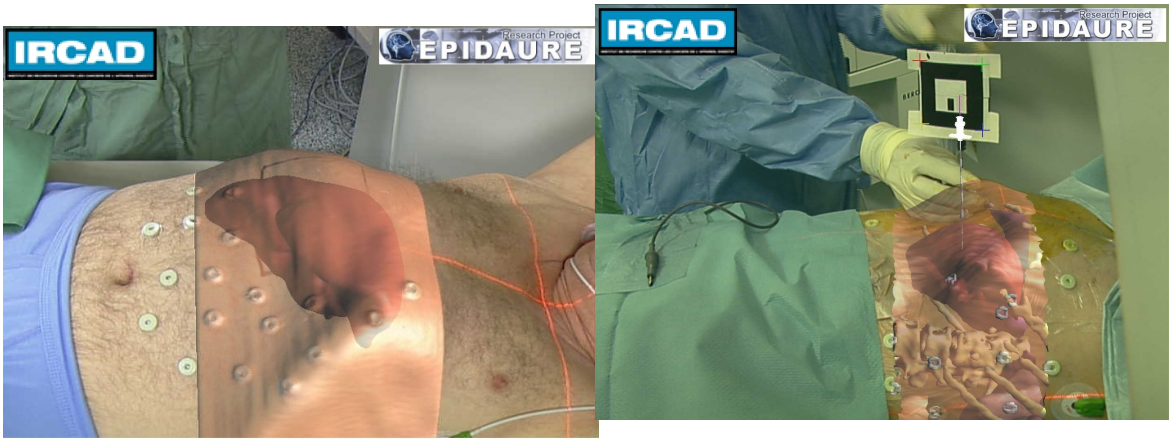


Figure 10. Illustration of the augmented reality view on patient. Left: one can see the liver under the transparent patient skin. Right: the liver, the bones and the virtual needle are superimposed on the video view of the patient at the end of the needle insertion.

follow-up, it is necessary to accurately locate the tumor and all the structures of interest in the brain. An automatic segmentation algorithm of all the critical structures in a patient image is then an invaluable tool for radiotherapy [25].

In order to extract all these structures in a specific patient's image, we chose to build a numerical reference atlas of all the structures we are interested in. This atlas is composed of a couple of images : one simulated T1 MR image and its corresponding labelization.

Registering a brain atlas on the patient's MRI for labeling brain structures is indeed an interesting alternative to manual segmentation. This technique consists in bringing the atlas MRI in global correspondence with the patient's image thanks to an affine transformation. Then the atlas image is warped locally to the patient thanks to an elastic registration [50]. Applying the obtained transformations to the structures available in the label image allow us to segment automatically the patient's anatomy. This algorithm has been integrated as a module in DOSISoft software for radiotherapy planning.

However, pathological structures (surgical resection in the brain, tumor) are outliers with respect to an average anatomy resulting in registration artifacts in these regions. This may spoil the quality of critical structures labeling. We introduced in [82] two methods for delineating a surgical resection and the tumor. We used a priori information on these structures like intensity signatures in MRI or expected tissues given by a statistical atlas. Since our registration method allows to locally control the amount of regularization, we were then able to explicitly introduce those areas in the warping process. Using these individualized atlas allowed us to obtain a better segmentation in the pathological areas (see figure 11).

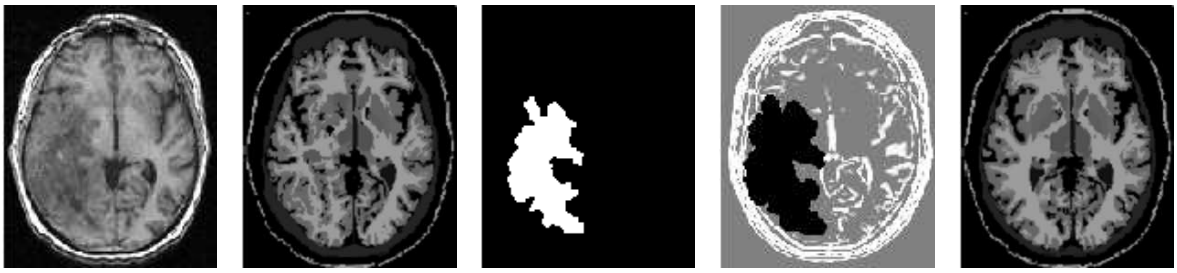


Figure 11. Segmentation of a 3D patient image containing a large tumor (patient's T1 MRI, registration without considering the tumor, tumor mask, confidence map, registration result integrating the tumor).

6.3.4.2. Robust Nonrigid Registration to Capture Brain Shift from Intra-Operative MRI

Keywords: *Non-rigid registration*, *block matching*, *brain shift*, *deformable model*, *finite element model*, *intra-operative magnetic resonance imaging*, *parallel computing*.

Participants: Olivier Clatz, Hervé Delingette, Nicholas Ayache.

This work is performed in close collaboration with the Surgical Planning Laboratory http://splweb.bwh.harvard.edu:8000/, involving in particular Ion-Florin Talos, Alexandra Golby, Ron Kikinis, Ferenc Jolesz, and Simon Warfield.

We present a new algorithm to register 3D pre-operative Magnetic Resonance (MR) images to intra-operative MR images of the brain which have undergone brain shift. This algorithm relies on a robust estimation of the deformation from a sparse noisy set of measured displacements. We propose a new framework to compute the displacements field in an iterative process starting from the approximation and converging toward the interpolation problem. The robustness of the algorithm is achieved through the introduction of an outliers rejection step in this gradual registration process using a weighted least trimmed squares approach. We ensure the validity of the deformation by the use of a model of the brain specific to the patient, discretized with the Finite Element Method (FEM) .

To meet the clinical time constraint, we have parallelized the slowest stage of the algorithm so that we can perform a full brain registration in 35 seconds on a heterogeneous cluster of 15 PCs. The algorithm has been tested on six cases of brain tumor resection, presenting a brain shift up to 14 mm (Figure 12). The results show a remarkable ability to recover internal structure displacements without being disturbed by the tumor resection cavity.

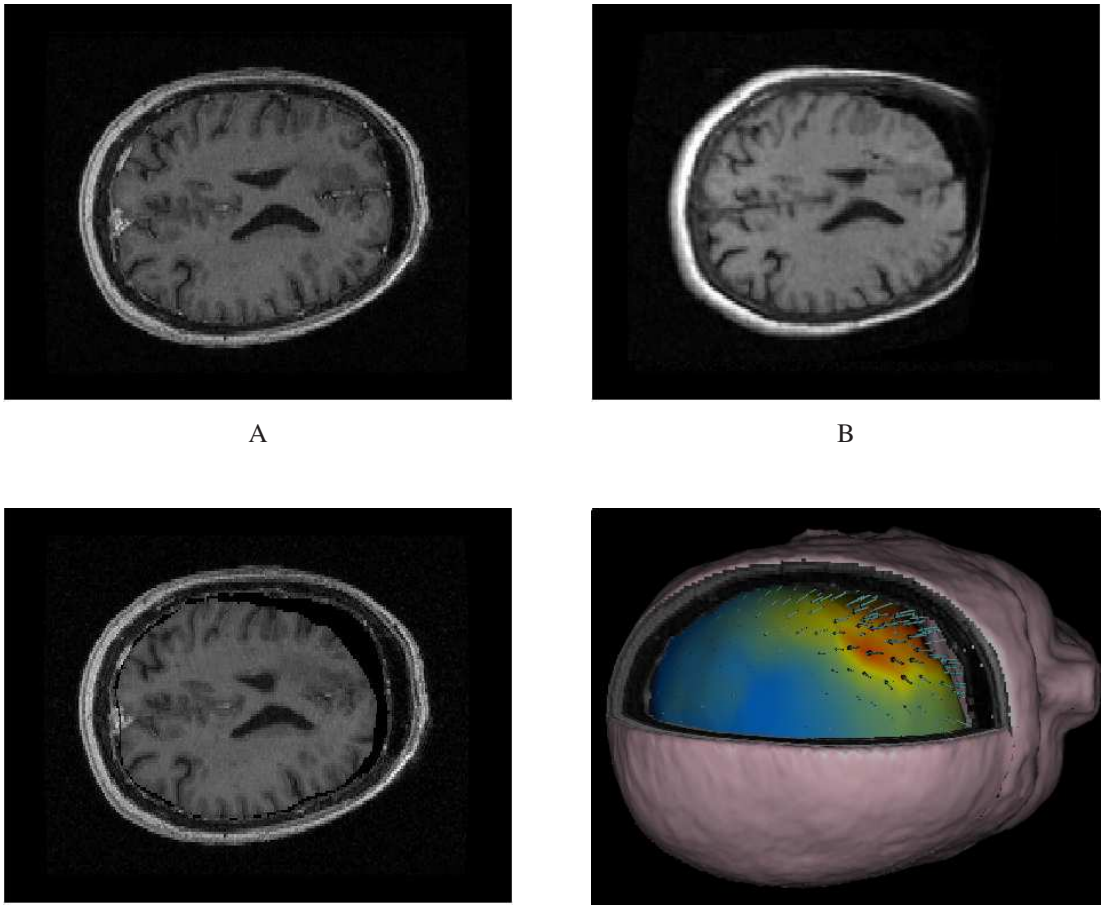


Figure 12. Biomechanics-based intraoperative non-rigid tracking of brain tissues during surgery. (A) Pre-operative T1 weighted MR image of the patient's brain. (B) Intra-operative T1 weighted MR image during a tumor resection procedure. (C) Warping of the pre-operative image on the intra-operative image. (D) 3D visualisation of the displacement field of the brain surface.

This work was presented at the 5th Interventional MRI Symposium [56], and used to evaluate the influence of breathing on the 3D deformation of the liver in [54].

6.4. Atlases, morphometry and statistical analysis

6.4.1. Tensor Computing

Keywords: *DT-MRI*, *Diffusion*, *PDE*, *Regularization*, *Riemannian geometry*, *Tensor Fields*.

Participants: Pierre Fillard, Xavier Pennec, Nicholas Ayache.

Symmetric positive definite matrices, so called tensors, are widely used in medical imaging, either to caracterize the covariance of a stochastic point process or to quantify the local diffusion of water as in DT-MRI. In this work, we developed a consistent Riemannian framework to compute with tensors. We endowed the space of symmetric positive defined matrices with an affine invariant Riemannian metric. We demonstrate that it leads to strong theoretical properties: the cone of positive definite symmetric matrices is replaced by a regular manifold of constant curvature without boundaries (matrices with null eigenvalues are at the infinity), the geodesic between two tensors and the mean of a set of tensors are uniquely defined, etc.

Thanks to this Riemannian metric structure, we generalized to tensor fields many important geometric data processing algorithms such as interpolation, filtering, diffusion and restoration of missing data. For instance, most interpolation schemes and Gaussian filtering can be tackled efficiently through a weighted mean computation. Linear and anisotropic diffusion schemes can be adapted to our Riemannian framework, through partial differential evolution equations (PDEs), provided that the metric of the tensor space is taken into account. For that purpose, we provide intrinsic numerical schemes to compute the gradient and Laplacian operators [89].

We illustrated this framework with various examples from Diffusion Tensor MRI and shape statistics. For instance, we performed an anisotropic regularization of diffusion tensor fields (Fig.13 left) and we developed an extrapolation by Laplacian diffusion of a set of tensors known at given positions to a regular grid (Fig. 13 right). This last application was intensively used in shape statistics to recover the full brain variability from the variability known at specific locations (see section 6.4.2).

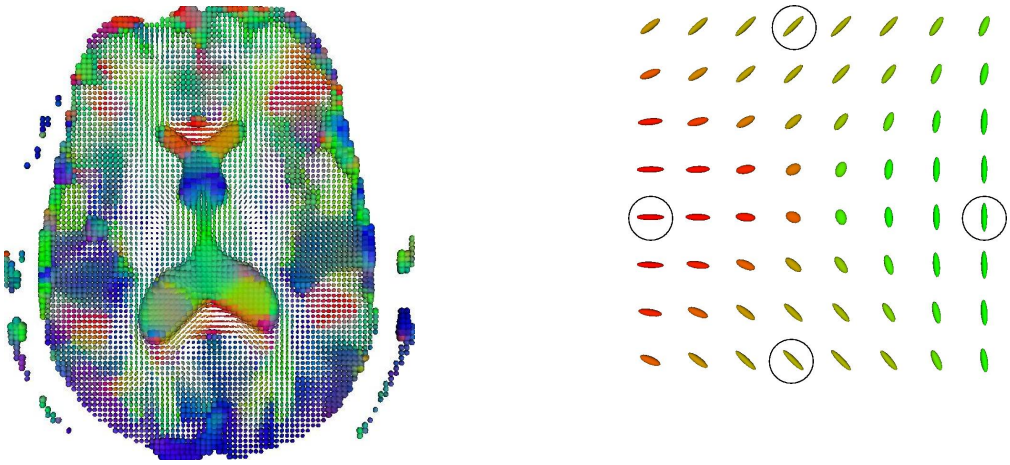


Figure 13. ***Left:*** *Anisotropic filtering of a DTI slice (time step 0.01, $\kappa = 0.046$, 50 iterations): 3D view of the tensors as ellipsoids. The color codes for the direction of the principal eigenvector. Notice that the ventricles boundary and the U-shaped tracts at the boundary of the grey/white matter are very well preserved while both isotropic (ventricles) and anisotropic (splenium) regions are regularized* ***Right:*** *Approximation by the Laplacian diffusion of the 4 circled tensors on a regular grid. One can see that our framework allows to recover very smoothly saddle points of the orientation, which is usually very difficult with classical methods based on the tensor diagonalization.*

6.4.2. Evaluation and Modeling of the Human Brain Variability

Keywords: *Brain Variability*, *PDE*, *Registration*, *Sulcal Lines*.

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

This work is part of the collaboration between the Epidaure team and the associated team LONI (Laboratory of Neuro-Imaging) at UCLA (University of California at Los Angeles). Website: http://www-sop.inria.fr/epidaure/Collaborations/UCLA/. See also Section 8.4.

The LONI has been collecting anatomical MRI from various studies for years. Today, this database contains MRIs from more than 500 subjects. Moreover, each image comes with the segmentation of 36 pairs of sulcal lines manually delineated by experts following a rigorous protocol (http://www.loni.ucla.edu/~khayashi/Public/medial_surface/). In the context of the associated team with the LONI, we are developing methods and tools to analyze this extensive dataset. More precisely, we aim at modeling statistically the anatomical variability of the human brain from statistics on sulcal lines. The size of the database being statistically significant, this research could eventually lead to new findings in neuro-anatomy. One of the goal is also to improve the inter-subject brain registration by providing a variability map as an a prior.

Our strategy is descibed as follow: first, we compute a statistical model for each of the sulcal line. Using the algorithm developed last year by V. Arsigny, we compute for each of the 72 sulci the mean curve and its point to point correspondance with all the instances (Fig. 14 left). In a first approach, we synthetize this information by computing independently the covariance matrix of each point of the mean sulcus (Fig. 14 left). Second, a strategic subset of these matrices are retained, and the total variability is recovered by extrapolating the matrices to the full volume using the framework developed in Sec. 6.4.1. This results in a dense field of 3×3 matrices, whose eigenvectors and eigenvalues give us information about the directions and magnitude of the variability (Fig. 14 right).

First results indicate a qualitatively good agreement with the known variability in different parts of the brain. We are currently designing statistical test to quantitatively verify our results.

To visualize the LONI database and the 3D representation of tensors, we also developed a set of dedicated tools that can: load a set of sulcal lines and display them (the mean sulcal line has a different color to differentiate it); interact with a specific sulcal lines and isolate one instance by selecting its anatomical description in a list; load and display covariance tensors as 3D ellipsoids along the sulcal lines; load a dense field of tensors, to display it slice by slice or with a cropping box delimiting a volume of interest. Figure 15 displays a snapshot of the software running.

6.4.3. On the adequacy of principal factor analysis for the study of shape variability

Keywords: *Principal Component Analysis*, *Principal Factor Analysis*, *registration*, *shape*.

Participants: Miguel Angel Gonzalez Ballester, Marius George Linguraru, Mauricio Reyes Aguirre, Nicholas Ayache.

We propose an alternative to Principal Component Analysis (PCA) for the decomposition of shape variability into more easily interpretable principal modes of variation in morphoanatomic image-based studies. We use, for the first time, Principal Factor Analysis (PFA) for the decomposition of shape variability, and compare its performance with the widely used PCA.

Very few articles have been published proposing alternatives to PCA. Methods based on non-linear decompositions are cumbersome and results are difficult to interpret; Independent Component Analysis (ICA) has been proposed, but it does not perform dimensionality reduction, so a prior pass of PCA is necessary. This is the first time that PFA is proposed for shape analysis, and to our knowledge the only work that results in better interpretability in the modes of variation.

Examples are shown for 2D landmark data sets of corpora callosa (Figure 16) and 3D vector fields from non-rigid registration of ventricles in MRI (Figure 17). PFA provides a decomposition into modes of variation that are more easily interpretable than those of PCA, at a small cost in size (as in theory a larger number of components may be necessary to explain a given percentage of total variability).

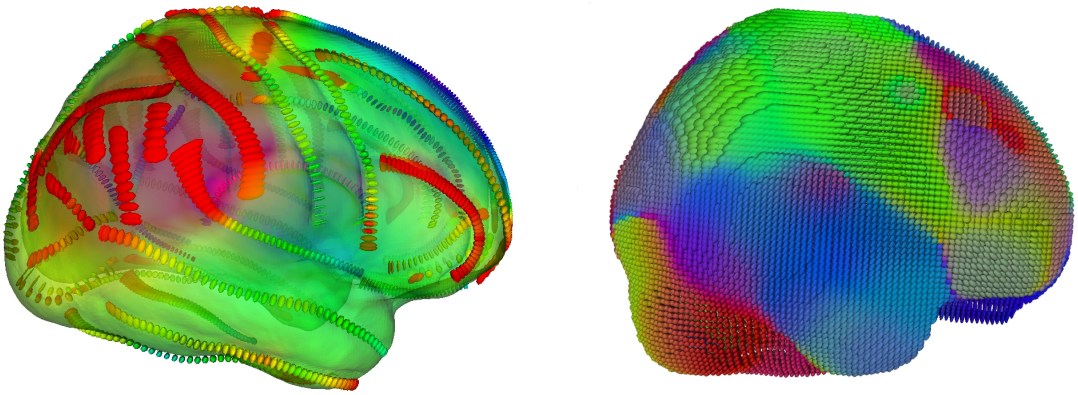


Figure 14. Left: Covariance matrices superimposed with a mean cortex of 82 subjects. Right: Result of the extrapolation of a set of covariance matrices to the full brain. Tensors are displayed on the ICBM 305 brain atlas. The color codes for the principal direction of variability.

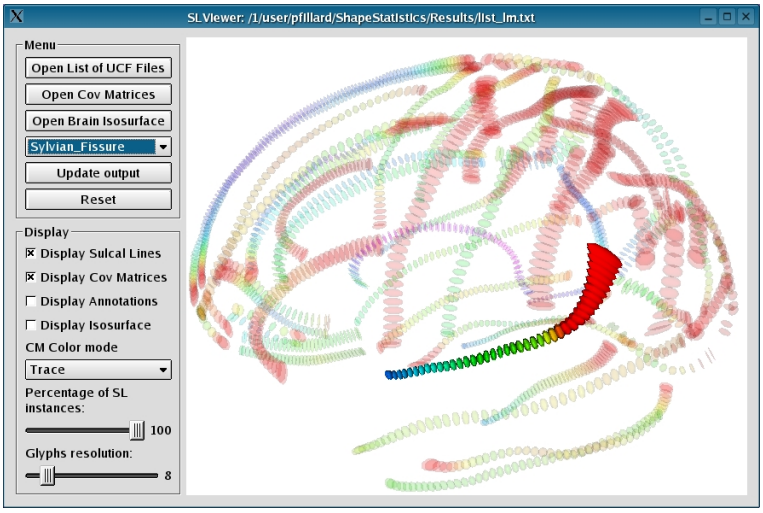


Figure 15. Snapshot of the LONI database viewer (SLViewer). View of the covariance matrices along the Sylvian Fissure.

We argue that it is important to study the potential of factor analysis techniques other than PCA for the application of shape analysis, and defend PFA as a good alternative [67].

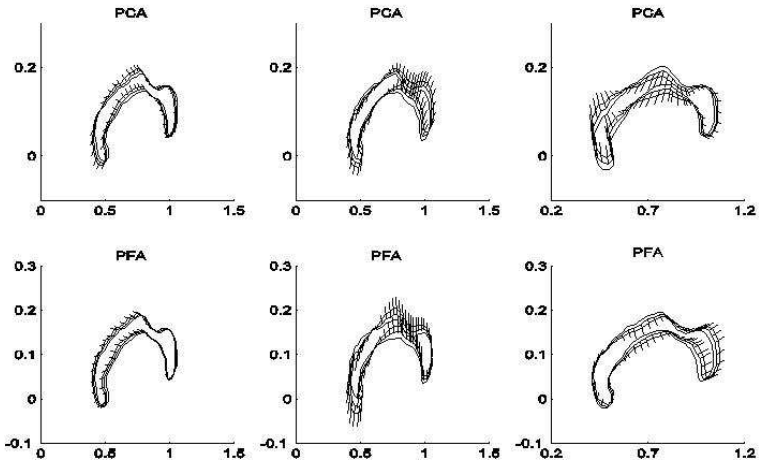


Figure 16. PCA and PFA results on 2D landmark data sets representing corpora callosa. Top: First 3 principal components (ordered from left to right according to the variance explained), and Bottom: first 3 principal factors after Varimax rotation. PFA provides modes of variation that are more easily interpretable and intuitive.

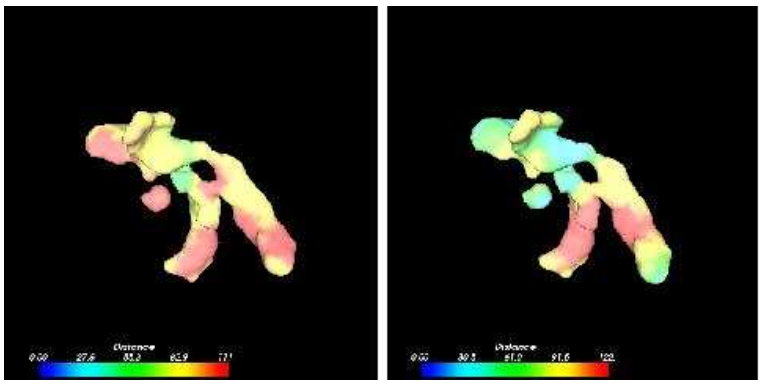


Figure 17. 3D view of the magnitude of the first principal component (left) and principal factor (right) extracted from a training set of 3D displacement vector fields on the surface of brain ventricles. PFA factors have a more localized effect (in the back of the ventricles).

6.5. Motion analysis and medical simulation

6.5.1. Parameters estimation of an electrical model of the heart from in vivo electrical measures.

Keywords: *data assimilation*, *electrical conductivity*, *electrophysiology*, *heart modeling*, *inverse problem*, *parameter estimation*, *reaction-diffusion system*.

Participants: Valérie Moreau-Villéger, Hervé Delingette, Nicholas Ayache, Sylvain Jaume, Maxime Sermesant, Tristan Picart.

This work was partially funded by the scientific direction of INRIA through the Cooperative Research Action ICEMA2 (http://www-rocq.inria.fr/sosso/icema2/icema2.html). The electrical measures on canine hearts are provided by Laboratory of Cardiac Energetics, National Heart Lung and Blood Institute, National Institute of Health (E. McVeigh). The electrical measures on human hearts are provided by the Cardiac MR Research Group, King's College London, Guy's Hospital (D. Hill, D. Hawkes, and R. Razavi).

We study the problem of estimating the electrical conductivity of cardiac tissue from a set of temporal *in vivo* recordings of extracellular potentials. The underlying electrical model is the reaction-diffusion model on the action potential proposed by Aliev and Panfilov. The strategy consists in building an error criterion based upon a comparison of depolarization times between the model and the measures. This error criterion is minimized by a global and then a local adjustment of the model parameters. We have demonstrated the feasibility of this approach on simulated and real *in vivo* measures on the epicardial surface of a canine heart (Figure 18). This work was published in a research report [88]. We are currently working on the extension of this method to estimate the electrical conductivity on the whole myocardium of a human heart.

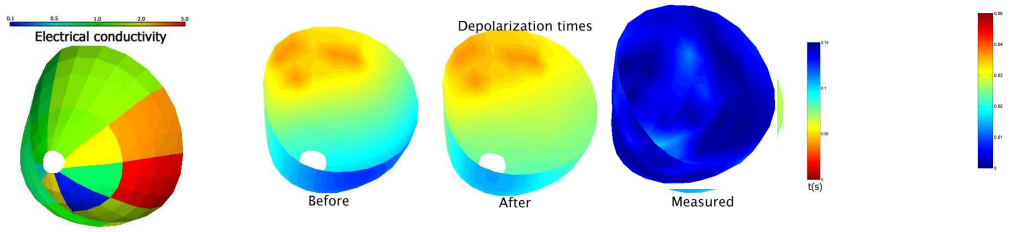


Figure 18. Left: conductivity map obtained from our adjustment method for in vivo measures on a canine heart. Middle: depolarization times obtained after a simulation with an homogeneous conductivity map (left) and with the conductivity map (middle) compared with the measures (right). Right: error (in milliseconds) on the estimated depolarization times between simulation and measures.

6.5.2. Image guided laparoscopic spine surgeries

Keywords: *3D/2D Registration*, *Articulated models*, *Augmented Reality*, *Camera Calibration*.

Participants: Jonathan Boisvert, Xavier Pennec, Nicholas Ayache.

This project is part of a partnership between the Epidaure team, the Montreal's Sainte-Justine hospital and the Polytechnic School of Montreal (Farida Cheriet).

Laparoscopic spine surgery is a relatively new surgical intervention that has been gaining in popularity in the medical community over the years. The advantages of this technique include small incisions, less blood loss, reduced post-operative pain, earlier discharge from the hospital and a faster post-operative rehabilitation. However, the limited visualization offered to the surgeon is a source of difficulties. One of the solutions to this problem is to develop an augmented reality system which will overlay 3D models of anatomical structures (such as vertebrae or the spinal cord) on the laparoscopic images.

Because the spine is a flexible structure, rigid registration of pre-operative images with per-operative images is not suitable. Moreover, the pre-operative images are taken in standing position, thus variation of the spine's curvature between the two sets of images is great. Therefore, we are investigating the use of an articulated model fitted to each image in order to recover the deformation of the spine. Furthermore, we plan to use the articulated model in order to relate the non-rigid motion of fiducial skin markers with the motion of the spine.

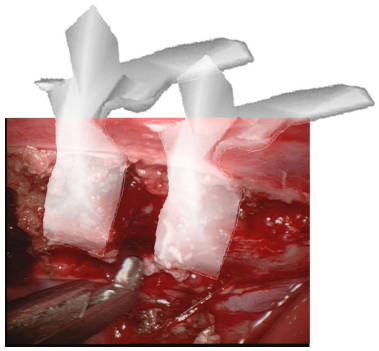


Figure 19. Example of 3D vertebrae models overlayed on a laparoscopic image.

Finally, work has been undertaken to update the laparoscope's calibration during the surgery in order the take into account variations of the laparoscope's internal parameters caused by modifications of the zoom and focus.

6.5.3. Tridimensional Analysis of the heart motion for the study of heart failure

Keywords: *3D echography*, *cardiac imaging*, *echocardiography*, *motion analysis*, *segmentation*, *tracking*.

Participants: Cécile Marboeuf, Hervé Delingette.

This work is performed in close collaboration with the company Philips Medical Systems Research Paris (Olivier Gérard) in the framework of a 3 year research contract.

The objective of this work, that started in September 2004, is to produce a set of software tools that can help clinicians to better understand, diagnose and cure the phenomenon of cardiac asynchrony, one of the type of heart failure. A first step is to use a geometric heart model for the fine analysis of the patient cardiac motion from acquisition of tridimensional echographic images.

6.5.4. Brain Tumor Growth Simulation

Keywords: *Clinical Target Volume*, *Gross Tumor Volume*, *Magnetic Resonance Imaging*, *Tumor*, *biomechanics*, *brain*, *diffusion*, *finite element*, *glioblastoma*, *growth*, *infiltration*, *mass effect*, *model*, *model*, *simulation*.

Participants: Olivier Clatz, Pierre-Yves Bondiau, Hervé Delingette, Maxime Sermesant, Grégoire Malandain, Nicholas Ayache.

This work was performed in close collaboration with the Surgical Planning Laboratory http://splweb.bwh.harvard.edu:8000/ (Simon Warfield).

We propose a new model to simulate the growth of glioblastomas multiforma (GBM), the most aggressive glial tumors. Because the GBM shows a preferential growth in the white fibers and have a distinct invasion speed with respect to the nature of the invaded tissue, we rely on an anatomical atlas to introduce this information into the model. This atlas includes a white fibers diffusion tensor information and the delineation of cerebral structures having a distinct response to the tumor aggression. We use the finite element method (FEM) to simulate both the invasion of the GBM in the brain parenchyma and its mechanical interaction (mass effect) with the invaded structures. The former effect is modeled with either a reaction-diffusion or a Gompertz equation depending on the considered tissue, while the latter is based on a linear elastic brain constitutive equation. In addition, we propose a new coupling equation taking into account the mechanical influence of the tumor cells on the invaded tissues. This tumor growth model is assessed by comparing the in-silico GBM growth (Figure 20) with the real GBM growth observed between two magnetic resonance images (MRIs) of a patient acquired with six months difference. The quality of the results shows the feasibility of

modeling the complex behavior of brain tumors and will justify a further validation of this new conceptual approach.

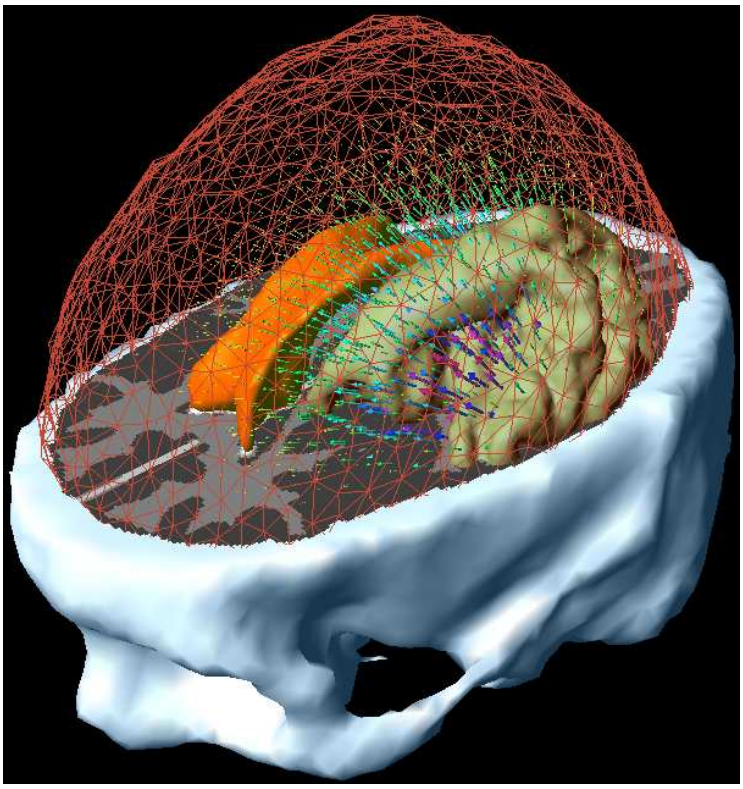


Figure 20. In Silico growth of a brain tumor, combining diffusion and mechanical effects.

This work has been published in an INRIA Research Report [86], and presented at the 7th International Conference on Medical Image Computing and Computer-Assisted Intervention [55].

7. Contracts and Grants with Industry

7.1. Medtronic

Participants: Grégoire Malandain, Radu-Constantin Stefanescu, Xavier Pennec, Nicholas Ayache.

Epidaure participates to a collaboration between CNRS, INRIA, INSERM and Salpétrière Hospital partially funded by Medtronic. Epidaure is involved into the design and evaluation of dedicated non-rigid registration tools for the localization of deep grey nuclei in 3D MR images (cf section 6.3.3).

7.2. Maestro

Participants: Olivier Commowick, Jimena Costa, Hervé Delingette, Grégoire Malandain.

MAESTRO is an integrated project funded by the EC. It features a program on research and development on major clinical and technological aspects for the innovative radiotherapy treatments which are crucial for

patient safety. The integrated project incorporates basic translational research on hi-tech equipment for clinics in close collaboration with industrials, research centres and European health services.

Within this project, Epidaure is involved, in collaboration with Dosisoft, in the automatic delineation of structures for radiotherapy planning (cf section 6.3.4.1 and 6.2.5).

7.3. Philips

Participants: Hervé Delingette, Cécile Marboeuf.

Philips Medical System Research Paris has contracted the Epidaure team to investigate the analysis of 3D echocardiographic images in order to better understand, diagnose and cure the phenomenon of cardiac asynchrony, one common type of heart failure. In the course of this project, Epidaure will provide algorithms for segmenting, tracking and analysing the motion of the mitral valve and myocardial surfaces.

7.4. Odysseus

Participants: Hervé Delingette, François Poyer, Nicholas Ayache.

This EUREKA project involves three industrial partners (Karl Storz, SimSurgery and France Telecom), a cancer research institute (IRCAD) and three groups from INRIA (Alcove, Epidaure and Evasion). Its objective is to build computer-aided diagnosis, surgery planning and surgery simulation software to increase the efficacy of therapies against cancer of the lower abdomen. In this project, Epidaure will be involved in two tasks : the improvement of CT-scan image segmentation based on deformable simplex meshes, and the development of soft tissue models in a surgery simulation platform. A research engineer, François Poyer, funded by the French Ministry of Research, is in charge of technology transfer and software development regarding this second task.

7.5. Siemens

Participants: Antoine Azar, Xavier Pennec, Nicholas Ayache.

In image guided surgery, the accuracy and the reliability of the registration result are critical issues for the surgeon to trust the guiding system. This is all the more true when the image guiding system is aimed at replacing other traditional, but more invasive, landmarks.

A contract has been established between Epidaure and Siemens Corporate research for establishing a methodology to predict and evaluate the accuracy and robustness of registration methods in image guided surgery. This methodology will be applied to a concrete clinical problem, which will be defined during the first year of the contract. This study will involve in particular Antoine Azar, through his DEA and subsequent PhD in the Epidaure team.

7.6. CIFRE PhD Fellowships

7.6.1. Dosisoft

The work of Olivier Commowick on the design and evaluation of digital antomical atlases and dedicated non-rigid registration tools for radiotherapy planning (cf section 6.3.4.1) is supported by a PhD fellowship from the company Dosisoft.

7.6.2. Mauna Kea Technologies

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

7.6.3. TGS

The work of Céline Fouard on segmentation of brain microvascular networks from confocal microscopy images (cf section 6.2.2) was partially supported by a CIFRE PhD fellowship from the company TGS.

8. Other Grants and Activities

8.1. Regional projects

8.1.1. Regional PhD fellowships

Radu-Constantin Stefanescu, Guillaume Dugas-Phocion and Tristan Picart are partially supported by a "Région Provence-Alpes Côte d'Azur" PhD fellowship.

8.2. National projects

8.2.1. ACI Masse de Donnée AGIR

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

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

AGIR gathers researchers in Computer Science, physics and medecine from CNRS, INRIA, University, INSERM, and hospitals. Its goals are to to define and validate new grid services that address some of the requirements of complex medical image processing and data manipulation application ; and new medical image processing algorithms that take advantage of the underlying grid infrastructure for compute and data intensive needs.

Data and computing grids are an opportunity to enlarge the impact of image processing tools and to transfer this experimental research to clinical practice. The availability of algorithms and datasets will ease the development, prototyping, and the validation of algorithms. Advanced users will be able to experiment and compare existing techniques on common data sets. Finally, grid-enabled algorithms will be accessible for clinical use.

Analysing large images at a sufficient speed to support interactive use requires substantial computing power. Combining the medical user expertise and the resource of the Grid in compute and data intensive tasks is a promising way to transfer experimental research first to clinical practice, and then to routine clinical practice.

The project started in september 2004, and supports the PhD of T. Glatard, jointly supervised by X. Pennec at EPIDAURE and J. Montagnat at RAINBOW (I3S, Nice University).

8.2.2. GIS Prions

The GIS-PRIONS (http://www-sop.inria.fr/epidaure/Collaborations/GIS-PRIONS/indexNew.html) project involves a national collaboration between INSERM (Unit 360, Paris), CNRS (Lena, Paris and Unit 6612, Marseille), the Department of Neuroradiology, the Laboratory of Neuropathology and the National Reference Cell of CJD of the La Pitié Salpétrière Hospital in Paris, and the Epidaure Research Group at INRIA, Sophia Antipolis. The study aims to determine the role of adding Magnetic Resonance Spectroscopy and Diffusion Imaging to the conventional imaging modalities towards an earlier Creutzfeldt-Jakob Disease (CJD) diagnosis. Another major goal of this project is the differentiation of different types of CJD.

Our study allows the accurate detection of abnormal MR intensities (prompted by the clinicians) in the deep grey nuclei of the brain of CJD patients and the classification of intensities in sporadic CJD FLAIR images with a more significant hypersignal in the caudate nuclei (10/10 cases) and putamen (6/10) than thalami. The quantification of the higher hyperintensities in the pulvinar of variant CJD patients led to the definition of new MR-based measures to differentiate between CJD cases and healthy controls and between sporadic CJD and variant CJD cases. Similar conclusions resulted through the quantification of metabolite variantions in spectroscopy data between CJD patients and healthy controls [74][66].

8.2.3. Consulting for Industry

- Nicholas Ayache is member of the Scientific Council of Dosisoft (Paris), a subsidiary from the Gustave Roussy Institute and the Curie Institute (Paris). He is also a member of the Strategic Council of QuantifiCare. He is scientific consultant for the company Mauna Kea Technologies (Paris).

- Hervé Delingette is a scientific consultant for the company *Philips Research France* and he is member of the scientific council of the company QuantifiCare.
- Grégoire Malandain is a member of the Technical council of the company Dosisoft (Paris), a subsidiary from the Gustave Roussy Institute and the Curie Institute (Paris).

8.2.4. Collaboration with national hospitals

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

8.2.4.1. IRCAD, hôpitaux de Strasbourg

Pr. Marescaux and L. Soler : hepatic surgery simulation [48], segmentation of abdominal structures from CT scan images and augmented reality for guidance in hepatic surgery (see section 6.3.4 and [27][43][77][78][81]).

8.2.4.2. Hôpital de la Pitié-Salpétrière, Paris

Dr. J. Yelnik (INSERM U.289) and E. Bardinet (CNRS) are our partners in a collaboration with Medtronic. Dr. D. Dormont and Dr. J.-P. Brandel are our collaborators for the GIS *Infections à prions*.

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

Pr. Jacques Darcourt co-supervises the thesis of Mauricio Reyes on breathing motion correction for PET reconstruction (cf section 6.2.7) [91]. Dr. Bondiau has prepared his PhD (defended in october 2004) within our project [25], and participates in our research on atlas registration for radiotherapy planning [53][31] and on tumour growth simulation [55].

8.2.4.4. CHU de Nice, Hôpital Pasteur

We continue our collaboration with Pr. M. Chatel, Dr. C. Lebrun-Frenay and C. Bensa of the neurology department, and with Dr. Chanalet of the radiology, within the framework of a study on the temporal evolution of MS lesion load [58][52][39][59][73][60][61]

8.3. Hosting of foreign researchers

Heike Hufnagel was hosted in the Epidaure project from September 2003 to August 2004 for the training period of her master thesis (Diplomarbeit at the university of Lübeck, supervised by H. Handels (university of Lübeck) and X. Pennec, G. Malandain et N. Ayache (INRIA)). She was also granted a Marie Curie Fellowship for her PhD in the context of the European project IMAVIS from October 2004.

8.4. Foreign associated team

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

Since its creation in September 2001, the associated team program between the Epidaure laboratory at INRIA and the laboratory of NeuroImaging at the UCLA School of Medicine has enabled an active collaboration between both structures, with the objective of comparing and analyzing the performances and behaviors of image processing algorithms devoted to the building of brain atlases. Since summer 2003, we investigate a new axis on the study of the anatomical variability of the brain. Pierre Fillard resumed the work began in 2003 by V. Arsigny on the modeling of the brain variability from manually delineated sulcal lines. First results are very promizing (see Sec. 6.4.2).

In July 2004, Paul Thompson organized a one week summer school on computational anatomy in the IPAM (Institute for Pure and Applied Mathematics, UCLA) framework. N. Ayache, X. Pennec and P. Fillard did participate, along with many LONI reserchers and students. This summer school was a top-level meeting on non-rigid registration and shape statistics for the brain.

Paul Thompson did participate to the tutorial entitled *Detection and Quantification of Evolving Processes in Medical Images*, organized by N. Ayache at MICCAI 2004 in Saint Malo. He also visited the team for two days after the conference.

9. Dissemination

9.1. Promotion of the Scientific Community

9.1.1. Journal editorial boards

Medical Image Analysis N. Ayache is co-founder and co-editor in Chief with J. Duncan (Professor at Yale) of this scientific Journal created in 1996 and published by Elsevier. Its impact factor in 2004 was 4.4.

IEEE Transactions on Medical Imaging N. Ayache is associated editor.

- N. Ayache is a member of the editorial board of the following journals *Medical Image Technology* (Japanese journal), *Videre: a journal of Computer Vision Research* (MIT-Press) and *Journal of Computer Assisted Surgery* (Wiley).
- G. Malandain is a member of the editorial board of the journal *International Journal on Computer Vision* (Kluwer).

9.1.2. Participation in the organization of conferences

N. Ayache is a member of the Executive board of the MICCAI Conference. He organized a tutorial at MICCAI'04. He is executive secretary of the newly created scientific MICCAI society (over 600 members in more than 20 countries). We was also the member of several reviewing boards in 2004. He is member of the program committee of the IEEE Int. Symposium of Biomedical Imaging (ISBI).

G. Malandain was member of the scientific board of DGCI 2005. He was in charge of the tutorials organisation at MICCAI 2004.

H. Delingette was member of the scientific board and area chair for MICCAI 2004, member of the scientific committee of Medical Simulation'04, ICPR'04 and VRIC'04

X. Pennec was member of the program committee of workshops DIDAMIC 2004 (Distributed Databases and processing in Medical Image Computing) and AMI-ARCS 2004 (International Workshop on Augmented environments for Medical Imaging and Computer-aided Surgery), associated to MICCAI 2004. He was also member of the reviewing committe of MICCAI 2004 and ISBI 2004.

9.1.3. Scientific animation

N. Ayache is co-chairing the "comité des projets de l'INRIA Sophia-Antipolis", and a member of the scientific direction of INRIA-Sophia-Antipolis. He is a member of the Evaluation Committee of INRIA.

H. Delingette is a member of the Evaluation Committee of INRIA.

9.2. University teaching

École Centrale de Paris N. Ayache is responsible of 2 modules on medical imaging (formation and analysis of medical images)(45 hours of lectures + 45 hours of small classes) with the participation of N. Ayache, H. Delingette, G. Malandain, R. Vaillant (GEMS) for the lectures) and E. Bardinet, J. Dauguet, B. Grosjean, and S. Jbabdi for the small classes. These 2 modules are common to the DEA MVA of ENS Cachan "Mathematiques, Vision et Apprentissage", and to the Master IDB of École Centrale de Paris.

DEA I3, Université Paris Sud H. Delingette is co-responsible with R. Deriche of a 21 h module about medical imaging and computer vision of which he has taught 12 h.

DEA Image-Vision, université de Nice Sophia-Antipolis G. Malandain is responsible of one module of 15 hours (medical image analysis).

DESS Génie biomédical, université de Nice Sophia-Antipolis G. Malandain is responsible of one module of 48 hours (24 hours of lectures + 24 hours of practical work)

G. Malandain gave a series of lectures at a Summer School in Medical Imaging (Santiago, Chile).

9.3. PhD Theses and Internships

9.3.1. PhD defended in 2004

1. Christophe Blondel, *Modélisation 3D et 3D+t des artères coronaires à partir de séquences rotationnelles de projections rayons X*, Nice-Sophia Antipolis University, March 29, 2004. Jury : M. Barlaud (President), I. Magnin (Referee), P. Grangeat (Referee), N. Ayache (supervisor), E. Coste-Manière, G. Malandain (co-supervisor), and R. Vaillant (co-supervisor).
2. Pierre-Yves Bondiau, *Utilisation et validation du recalage d'image dans l'élaboration du plan de traitement en radiothérapie*, Nice-Sophia Antipolis University, November 22, 2004. Jury: J.-P. Gérard (President), J. Troccaz (Referee), B. Gibaud (Referee), N. Ayache (supervisor), J. Darcourt, J.-L. Habrand, and G. Malandain (co-supervisor).
3. Guillaume Flandin, *Utilisation d'informations géométriques pour l'analyse statistique des données d'IRMf*, Nice-Sophia Antipolis University, April 1, 2004. Jury: M. Cosnard (President), C. Barillot (Referee), L. Garnero (Referee), N. Ayache (Supervisor), J.-B. Poline (Co-supervisor), X. Pennec (Co-supervisor). The Phd was done in close collabrotion with (and partly at) the CEA-SHFJ.
4. Stéphane Nicolau, *Construction d'un système de réalité augmentée pour la chirurgie hépatique*, Nice-Sophia Antipolis University, November 26, 2004. Jury: M. Barlaud (President), N. Navab (Referee), M.-O. Berger (Referee), N. Ayache (Supervisor), E. Coste-Manière, X. Pennec (Co-supervisor), L. Soler (Co-supervisor). The PhD was done in close collaboration and partly at IRCAD, Strasbourg.
5. Rasmus Paulsen, *Statistical Shape modeling of the human ear canal*, Technical University of Denmark, September 15, 2004. Jury : Tim Cootes, H. Delingette, K. Conradsen, R. Larsen

9.3.2. Current PhDs

1. Vincent Arsigny, *Statistical analysis of shapes - Application to anatomical atlases*, École Polytechnique.
2. Jonathan Boisvert, *Articulated models for augmented reality: application to minimally invasive spine surgery*.
3. Olivier Clatz, *Modeling of the biomechanical behavior of the brain: application to the prediction and simulation of neurosurgery*, École des Mines de Paris.
4. Olivier Commowick, *Digital anatomical atlases for radiotherapy planning*.
5. Jimena Costa, *Segmentation of anatomical structures of the abdomen with deformable models*.
6. Julien Dauguet, *Mise en correspondance d'images post-mortem et in-vivo pour le petit animal : application au suivi de modèles animaux chroniques de maladies neuro-dégénératives*, École Centrale Paris. PhD localized at CEA/SHFJ, Orsay, in collaboration with V. Frouin and Ph. Hentraye.
7. Guillaume Dugas-Phocion, *Modeling and segmentation of mutiple sclerosis lesions in multi-sequences MR images*, École des Mines de Paris.
8. Pierre Fillard, *Statistical modeling of the anatomical variability of the cortex*, Nice-Sophia Antipolis University.
9. Céline Fouard, *Extraction de paramètres quantitatifs dans des images médicales 3D de réseaux vasculaires*, Nice-Sophia Antipolis University. CIFRE fellowship from the compagny TGS.
10. Tristan Glatard, *Traitement de masse d'images médicales sur une grille de calcul: application à l'évaluation de protocoles cliniques*, Nice-Sophia Antipolis University. PhD in collaboration with J. Montagnat at the Rainbow team, I3S, Nice-Sophia Antipolis University.
11. Heike Hufnagel, *Statistical shape analysis of normal and pathological organs within the abdomen*, University of Hamburg. PhD in collaboration with Prof. Dr. Heinz Handels, Institut für Medizinische Informatik, University of Hamburg.
12. Cécile Marbœuf, *Analyse fine du mouvement du cœur dans le cadre de l'insuffisance cardiaque*, Ecole des Mines de Paris
13. Valérie Moreau-Villéger, *Analyse du fonctionnement cardiaque à partir de données échocardiographiques et électrophysiologiques*, ENS Cachan.
14. Tristan Picart, *Analyse de la fonction cardiaque à l'aide d'un modèle électromécanique du cœur*, Nice-Sophia-Antipolis University.
15. Mauricio Reyes, *Fusion d'images PET avec des images tomodensitométriques pour la détection précoce des tumeurs pulmonaires*, Nice-Sophia Antipolis University. PhD in collaboration with J. Darcourt, CAL, Nice.
16. Radu-Constantin Stefanescu, *Thérapie guidée par l'imagerie médicale : Parallélisation et validation d'algorithmes de recalage*, Nice-Sophia-Antipolis University.
17. Tom Vercauteren, *Mosaicing and analysis of temporal sequences of in vivo confocal microscopic images*.

9.3.3. Participation to thesis committees

Nicholas Ayache participated as supervisor to several thesis committees: Christophe Blondel, Pierre-Yves Bondiau, Guillaume Flandin, Stéphane Nicolau. He participated to other thesis committes as referee or examinator.

Grégoire Malandain participated to several thesis committees: Marie Chupin (referree, Orsay), Christophe Blondel and Pierre-Yves Bondiau (co-supervisor), and Xavier Tizon (as opponent, Upsala, Sweden). He also participated to the committee of the medicine thesis of Caroline Bensa (Nice).

Hervé Delingette participated to several thesis committees: Rasmus Paulsen (co-supervisor), Julien Lenoir (referree, Lille), Jean Combaz (referee, Grenoble), Christian Duriez (referee, Evry)

Xavier Pennec participated to the PhD thesis committee of Guillaume Flandin and Stéphane Nicolau as co-supervisor.

9.3.4. Training activities

Tristan Picart , *Simulation d'électrocardiogramme couplé à un modèle électro-mécanique du cœur* , Ecole Polytechnique.

Nicolas Savoire , *Measure of blood flow in microvessels from a single confocal image*, [80].

Tom Vercauteren , *Mosaicing of microscopic images for the study of the neoangiogenesis*, Ecole Polytechnique.

9.4. Participation to workshops, conferences, seminars, invitations

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

- **Nicholas Ayache** gave a plenary lecture to the visiting committee of INRIA in March (Paris), at Ecole Polytechnique in May (Paris), at the Maison Française of Oxford in May (UK), at Ecole Polytechnique in May (Paris), at the IPAM symposium on Mathematics in Brain Imaging at UCLA in July (Los-Angeles), at the Medical Imaging and Augmented Reality workshop in August (Beijing), and at the J. Morgenstern Colloquium (Sophia-Antipolis) in October.
- **Hervé Delingette** gave invited lectures at the workshop MJST in Verbier (Switzerland), at an internal Philips colloquium in Eindhoven (The Netherlands), at the technical University of Danemark in Lingby (Danemark), at the summer school in medical imaging organized at Imperial College of London (UK), at the german annual meeting on image guided surgery and medical robotics CURAC'04 in Munich (Germany), at the tutorial on Medical Image Visualization and Simulation during the Eurographics conference held in Grenoble (France).
- **Xavier Pennec** gave a tutorial talk on Grids services for medical image analysis and registration at MICCAI'04 in Saint-Malo, and an invited talk on tensor computing at USC in July 2004.

9.5. Nominations and prizes

- **Nicholas Ayache** joined in 2004 the Advisory Committee of the newly created Shun Hing Institute of Avanced Engineering in Hong-Kong (4 year term); he also joined in 2004 the High Council for the promotion of science and technology between France and Israel. He has been invited to join the steering committee for the Medical Image Computing Platform of the University College London (UCL). He has been a member of the Strategic Council of POP-SUD since 2003.
- **Clément Forest** is among the 15 winners of the "Le Monde de la Recherche" award for his achievement during his Phd Thesis. He also was awarded the "best demonstration award" at the Medical Simulation symposium held in Boston (USA).

10. Bibliography

Major publications by the team in recent years

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