

*Project-Team Epidaure**Epidaure, Projet Images, Diagnostic
AUtomatique, RobotiquE Medical Imaging
& Robotics**Sophia Antipolis*

THEME 3B

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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 [98][142]. Regarding the target applications, a good review of the state of the art can be found in the book *Computer Integrated Surgery* [135], in N. Ayache's article [99] and in the more recent synthesis [107]. The scientific journals *Medical Image Analysis* [145], *Transactions on Medical Imaging* [146], and *Computer Assisted Surgery* [143] are also good reference material. A review of the past work of the Epidauré team can be found in a guest editorial of IEEE TMI [29].

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 [100]. 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][126].

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 [118].

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 [120].

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 [130]. 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 [115].

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 [132]. Discrete topology allows to characterize and modify the topology of manifolds, either locally or globally [113]. 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 [116], cortex, sulci [144]).

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 [101].

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 [135][119] and also in Alexis Roche's thesis [129].

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 [103][138][102].

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 [108].

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 [133] and Dryden [106], which also present in a unified manner the founding work of Kendall and Bookstein. See also Pennec's thesis [124] 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 [110]). Other recent approaches are detailed in the PhD thesis of B. Thirion [137] and G. Flandin [109].

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 [104].

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 [128].

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 [111], which can be completed with a review of the main algorithms and visualisation systems published by Stytz et al [134]. In general, visualisation requires a preliminary segmentation procedure, although some recent techniques do not require such preprocessing [112].

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 [105] and book chapter [34], and in G. Picinbono's thesis [125].

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 [135].

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, chemotherapy, 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. Yav++ Software

Participants: Marc Traina [correspondant], Hervé Delingette, Grégoire Malandain, Xavier Pennec, Éric Bardinet, Nicholas Ayache, Clément Forest, Maxime Sermesant, Olivier Clatz.

Key words: *Visualization, Volumetric Images, meshes, image processing.*

For the past four years, we have developed a generic platform for the visualization and processing of volumetric medical images. This platform combines three characteristics that are required for developing large interactive applications : modularity, portability and scripting ability. The motivation of this platform is twofold. First, it aims at structuring the code being developed inside the Epidaure research group. Second, it is motivated by the belief that for many medical imaging applications, user interaction must be closely linked with medical image processing. The primary targeted application of this platform was the segmentation of medical images based on 3D and 4D deformable models where user interaction is required to guide the surface deformation during the deformation process. We have then extended its scope to solve different problems related to medical image registration and analysis but also to medical simulation.

The different software modules include :

- **Volumetric Image Module** : allow the low-level processing of volumetric images (filtering and mathematical morphology) as well as rigid and non-rigid image registration algorithms.
- **Time series of images module** : allow to handle and visualize time series of volumetric images and simplex meshes.
- **Contour module** : allow the manipulation of 2D and 3D deformable contours.
- **Simplex Mesh Module** : allow to deform a simplex mesh inside a 3D or 4D image.
- **Triangulation and Tetrahedrisation Module** : allow to visualize and deform triangulated surfaces and tetrahedral meshes.
- **Force-Feedback** : allow to interact with force-feedback systems such as the « Phantom » device and the « Laparoscopic Impulse Engine » device.
- **Simulation** : allow to handle a surgery simulator.

5.2. PASHA

Participants: Xavier Pennec [Correspondant], Pascal Cachier, Radu Stefanescu.

Key words: *Non-rigid registration, deformation field, similarity measure, regularization.*

This algorithm computes a dense and non-parametric deformation field between two volumetric images. The similarity metric may be global (Sum of Squared Differences) or local (Local Correlation Coefficient), and is optimized by a gradient descent. The regularization of the deformation field is done using an appropriate kernel (Gaussian, elastic...).

5.3. MIDAS

Participants: Romain Ollivier, Guillaume Flandin, Miguel Ángel González Ballester [Correspondant], Marc Traina.

Key words: *Image database.*

This software responds to the needs for a database for the efficient storage and retrieval of images associated to current and former projects. The implementation combines mySql and PHP and the user interface is web-based.

5.4. GIM Toolbox

Participant: Miguel Ángel González Ballester.

Key words: *Generalized Image Models, statistical shape.*

A matlab toolbox implementing the basic procedures for the construction and use of Generalized Image Models (cf. section 6.4.1) has been developed. The toolbox package also includes a set of examples and a web-based documentation.

5.5. Yasmina

Participants: Grégoire Malandain [Correspondant], Alexis Roche.

Key words: *Multimodal image registration.*

This software allows to register 3-D multimodal medical images with rigid or affine transformations. It is based on the optimization of global similarity measures (correlation coefficient, correlation ratio, mutual information, etc.). As a result, it yields the computed transformation and resampled images.

5.6. Baladin

Participants: Grégoire Malandain [Correspondant], Eric Bardinnet.

Key words: *Multimodal image registration.*

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.

6.2. Image segmentation

6.2.1. Expert knowledge guided segmentation system for brain MRI

This project was conducted in collaboration with Paul M. Thompson, from the LONI laboratory, within the framework of the associated team program.

Key words: *Segmentation, Distance force, Expert system.*

Participants: Alain Pitiot [EPIDAURE and LONI], Hervé Delingette, Nicholas Ayache, Paul M. Thompson [LONI].

Effective segmentation of anatomical structures in possibly complex MRI proves to be especially challenging, given the wide variety of shapes and intensities a structure can present. Yet, image segmentation calls for high precision since the quality of the subsequent studies often depends on how accurately the various structures in

the image can be identified. Automated segmentation systems can thus be powerful tools to help in drawing consistent analyses from a number of images or collect statistical information on anatomical variability.

We addressed in this study the problem of retrieving the boundaries of a selection of target anatomical structures in a 3-D MR image. We approached the issue of boundary finding as a process of fitting a series of deformable templates to the contours of these structures. We chose simplex meshes to model the templates, owing to their fairly simple geometry, which makes it easier to incorporate internal and external constraints. We have focused on devising a segmentation system where maximum use is made of the available medical expertise, either in the form of implicit knowledge (the shape of the structures, their appearance, ...) or of explicit information (the relative distance between structures, the rules for the feedback loops, etc.), implemented as constraints on the meshes.

Figure 1 illustrates the proposed framework. Non-linear registration of a reference MRI serves to initialize a series of simplex meshes (one mesh per target structure) and makes the approach more robust. Each simplex mesh is then iteratively modified to minimize a hybrid local/global energy which incorporates an internal regularization energy, an external term which couples the models to the underlying image features and a global shape-constrained term. Those meshes evolve in parallel, within a rule-controlled framework whose purpose is to maximize the achieved match over each structure while respecting distance, position, etc. constraints (derived from medical expertise).

Details about the segmentation system and discussions about the obtained results can be found in [81].

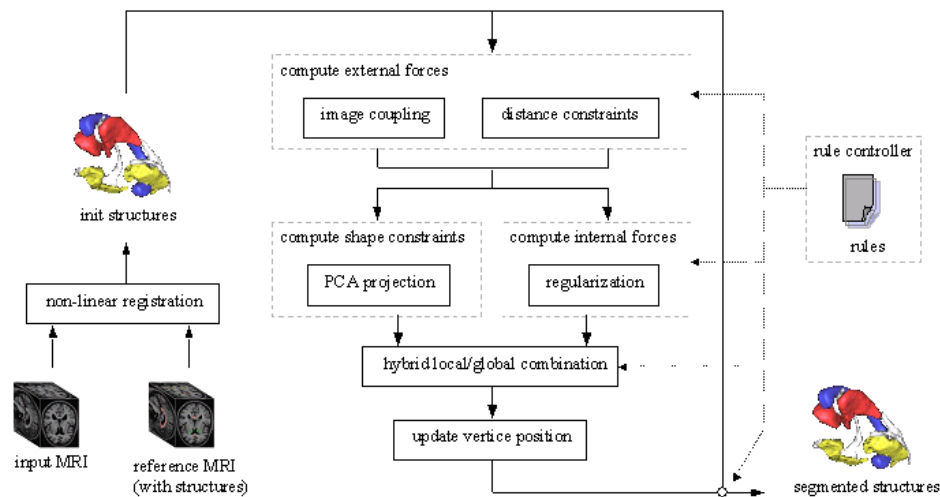


Figure 1. Overview of the expert knowledge guided segmentation system for brain MRI.

6.2.2. A Multiscale Feature Detector for Morphological Analysis of the Brain

Key words: Phase congruency, multiscale analysis, sulci detection.

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

We developed a method for feature extraction for brain morphological studies. Using phase congruency [114], the detection results are not sensitive to image intensity and overcome common difficulties in brain imaging, such as the presence of a bias field. The method outperforms thresholding and gradient-based segmentation approaches and provides a good localization of features. An example of detection is illustrated in Figures 2 and 3.

In addition to feature localization by local energy, phase can be used to classify features relative to their dominant orientation. The orientation of the filter which gives the maximum response across all scales is kept.

At each pixel of a sulcus, the scale that has the largest magnitude coefficients is selected to approximate the structure. Efficiently, this results in a combination of the multiscale information.

A more detailed description of the method can be found in [72].

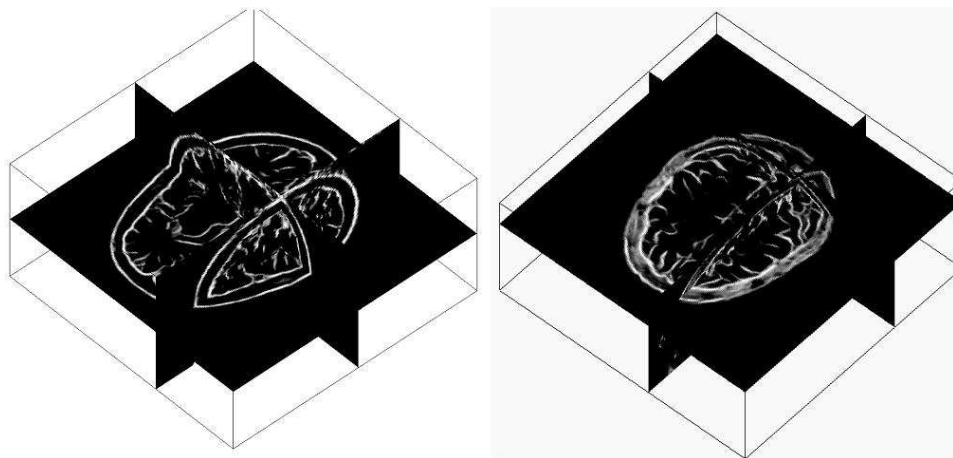


Figure 2. The 3D volumes of detected features on two 256x256x64 T2-weighted MR image data sets.

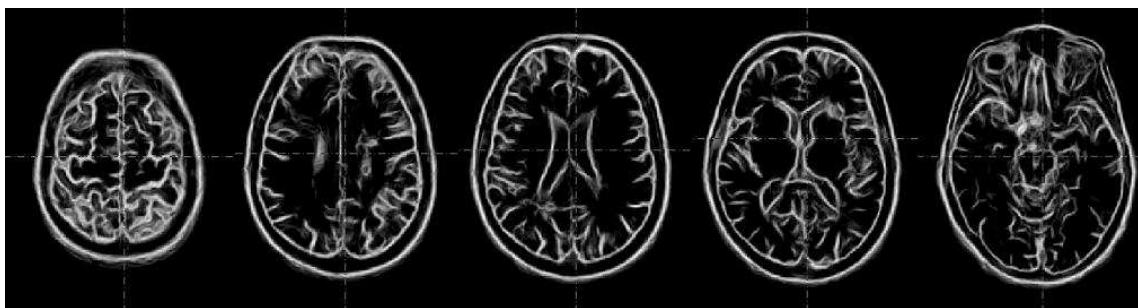


Figure 3. Detection results over five MR image slices.

6.2.3. Detection of Internal Brain Nuclei using A Priori Anatomical Information

Work done as part of the GIS-Prions Project (see Section 8.2.3).

Key words: Brain MRI, Internal nuclei, Segmentation, Non-rigid registration.

Participants: Marius George Linguraru, Miguel Angel Gonzalez Ballester, Xavier Pennec, Nicholas Ayache.

Deep brain grey matter nuclei are relevant to a set of clinical conditions, such as Parkinson's and Creutzfeldt-Jakob diseases. However, their detection in MRI data sets remains a challenging task, due to their small size, anatomical variability, and imaging artifacts. A methodology for the robust detection of deep brain grey matter nuclei in MRI is proposed.

T1- and T2-weighted MR images from each patient are registered to a T1-based statistical brain atlas ("Brainweb" from Montreal Institute of Neurology) applying rigid and affine registration tools developed in our group. A priori anatomical information is provided by a manually segmented image (the "Zubal phantom" from Yale University). This data is also aligned to the Brainweb atlas via an affine transformation and nearest-neighbor interpolation. Direct use of the phantom labels on the aligned patient data gave poor results in the nuclei, thus highlighting the need for non-rigid registration (see Figure 4, right).

The brain and ventricles are extracted using morphological operators on the patient images. Masks containing the ventricles and the non-brain volumes of each patient and the Zubal phantom are registered using our non-rigid registration algorithm [32]. The computed deformation field is then applied to the Zubal phantom and the deformed labels used to segment the grey matter nuclei (Figure 4, left). The use of key anatomical landmarks such as the ventricles and the outline of the brain imposes anatomical constraints in the deformation fields found by the non-rigid registration algorithm. The method is fully automatic and results in an accurate delineation of the internal nuclei in patient images.

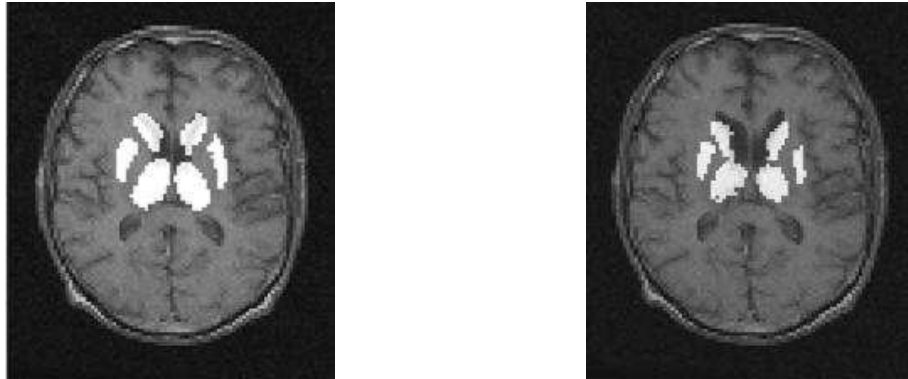


Figure 4. **Detection of Internal Brain Nuclei using A Priori Anatomical Information.** **Right:** The incorrect detection of nuclei using only affine registration. **Left:** After refined registration refinement using the proposed method, the nuclei are accurately depicted.

6.2.4. Robust Detection of CJD Hyper-signals in FLAIR

This work is done in collaboration with the Department of Neurology of the La Pitié Salpêtrière Hospital in Paris, and INSERM, Unit 360, Paris, as part of the GIS-Prions Project (see Section 8.2.3).

Key words: Creutzfeldt-Jakob Disease, Brain MRI, Image normalization, Segmentation.

Participants: Marius George Lingurar, Miguel Angel Gonzalez Ballester, Eric Bardinet, Nicholas Ayache.

A method to detect Creutzfeldt-Jakob Disease (CJD) specific hyper-signals in MRI of the brain is presented. Clinical reports underline the presence of hyper-signals in the grey matter internal nuclei as a clear indication of CJD in FLAIR images. The quality of these images is hampered by the clinical state of patients, which commonly suffer of acute dementia.

The algorithm we propose uses two main stages: pre-processing and detection. In the pre-processing step, images are normalized both spatially and in intensity using affine transformations. Smoothing using anisotropic diffusing is employed to correct image registration errors and reduce noise. The method described in Section 6.2.2 refines the registration results and segments the internal nuclei, namely the head of the caudate, putamen and pulvinar to reduce the number of false positives. Finally, the detection is performed using a simulation of the human visual system (see [117]), an adaptive thresholding technique for improved segmentation results on images with little contrast and significant artifacts. Some detection examples are shown in Figure 5.

6.2.5. Automatic segmentation of multi-spectral brain MRI and application to multiple sclerosis

This work is performed in close collaboration with Christine Lebrun, Pasteur Hospital, Nice, Neurology Unit.

Key words: Multiple sclerosis, MRI, multi-sequence, image fusion.

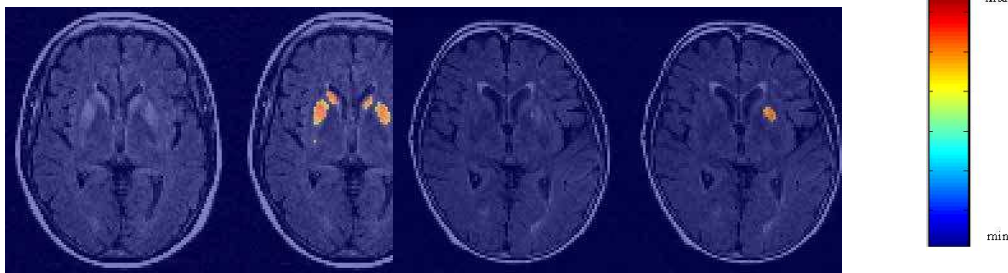


Figure 5. *Detection of CJD hyper-signals in FLAIR sequences of MR images. Left: Detection results in a case of sporadic CJD. Right: Detection results in a case of asymmetric hyper-signals. We show both the original image and the detection map (in color).*

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

Magnetic resonance imaging (MRI) has now become a useful complementary tool to clinical exams for the diagnosis of Multiple Sclerosis (MS). Multiple sequences allow to detect MS lesions and to monitor the global evolution of the disease. However, the intrinsic nature of the lesions and their global variability make image analysis a very difficult task. The goal of this project is to build new techniques to extract lesions in multi-sequence MRI and their inner structure : necrotic core, oedema etc.

Using a multi-sequence acquisition protocol, we first build a mask of brain tissue and generate a fuzzy segmentation of healthy brain tissues - white matter, grey matter, cerebro-spinal fluid - using a probabilistic algorithm derived from the Expectation Maximization technique, including a probabilistic atlas from the Montreal Neurological Institute. An automatic threshold is then extracted from these segmentations, so that we can get a mask of sub-tentorial lesions. We can extract different segmentations and quantifiers from this mask, including T2 and T1 loads. All these results are being validated using manual segmentation on lesions on the different sequences. We are also working on the influence of partial volume effect on segmentation of multiple sclerosis lesions.

6.2.6. Atlas-based segmentation for radiotherapy

Key words: *elastic registration, tumor, radiotherapy.*

Participants: Pierre-Yves Bondiau [Centre A. Lacassagne, Nice], Grégoire Malandain, Olivier Commowick.

Brain tumor radiotherapy requires the volume measurements and the localization of several individual brain structures. Any tool that can assist the physician to perform the delineation would then be of great help. Among segmentation methods, the atlas-based ones are appealing since they are able to segment several structures simultaneously. This study aims to evaluate such a method in a clinical context.

Our brain atlas is made of two 3-D volumes: the first one is an artificial 3-D MR image while the second one consists of the segmented structures in this artificial MR image. The elastic registration of the artificial MR image against a patient MRI yields an elastic transformation that can be applied to the labeled image.

To demonstrate the feasibility of our approach, we applied it on a subset of patients from our image database, and compared the delineation results for the brain-stem against those drawn by a panel of seven experimented physicians. A comprehensive validation of the segmentation method has been conducted on a series of six patients MRI to study the performance of atlas-based segmentation in a clinical context [97].

Tumors and surgical resections can induce large deformations that can not be handle by elastic registration algorithms. We have then investigated the segmentation of such areas in brain images [97].

6.2.7. Estimation of the partial volume effect in MRI

Key words: *Partial volume effect, MRI, sub-voxel accuracy.*

Participants: Miguel Ángel González Ballester, Guillaume Dugas-Phocion, Grégoire Malandain.

A physics-based model of MRI acquisition and its use to obtain sub-voxel accuracy in segmentations was investigated. Current work focused on the use of multi-sequence data.

The use of a simplified model for the partial volume effect based on a set of Gaussian distributions encompassing intensities in PVE voxels was explored. In particular, the segmentation of grey matter and white matter in brain MRI, and its extension to model the interface between white matter and multiple sclerosis lesions was taken into consideration.

A review about the state of the art of partial volume modeling and estimation is in preparation, and will appear in the form of a chapter in the book series *Medical Imaging Systems: Technology & Applications* [35].

6.3. Registration

6.3.1. Piecewise affine registration of biological images

This project was conducted in collaboration with Paul M. Thompson, from the LONI laboratory, within the framework of the associated team program, and with Eric Bardinet from the LENA laboratory in La Pitié Salpêtrière, Paris.

Key words: *Registration, Cluster analysis, Histology.*

Participants: Alain Pitiot [EPIDAURE and LONI], Grégoire Malandain, Eric Bardinet [CNRS-LENA], Paul M. Thompson [LONI].

This research track aims at reconstructing a 3D biological image from a series of 2-D biological images (histological sections or autoradiographs) via pair-by-pair registration. A priori knowledge about the acquisition process for biological images allows us to model the transformation space more accurately. In our case, the cutting process, successive chemical treatments, and the glass mounting step that a slab of tissue undergoes during a histological preparation yield a fairly flexible global transformation that is however locally affine for some identifiable components of the section.

We addressed in this study the problem of automatically registering two images, when the images consist of a number of independent components, subject to linear transformations, and embedded in a global elastic one. We proposed a registration approach closely derived from this model. Given a pair of input images, we first compute a dense similarity field between them with a block matching algorithm. A hierarchical clustering algorithm then automatically partitions this field into a number of classes from which we extract independent pairs of sub-images. Finally, the pairs of sub-images are, independently, affinely registered and a hybrid affine/non-linear interpolation scheme is used to compose the output registered image.

Details about the theory and discussions about its application to a variety of mono- and multi-modal registration cases can be found in [83] and [95]. Figure 6 illustrates the various steps of our approach applied to the registration of two consecutive myelin-stained histological sections of the human brain.

6.3.2. Polyrigid and polyaffine transformations

Key words: *Locally rigid/affine transformations, registration.*

Participants: Vincent Arsigny, Xavier Pennec, Nicholas Ayache.

We have introduced in this work a novel kind of geometrical transformations named polyrigid and polyaffine. These transformations efficiently code for locally rigid or affine deformations with a small number of intuitive parameters. They can describe compactly large rigid or affine movements, unlike most free-form deformation classes. The basic idea is to define, for each component, a rigid or affine transformation and a weight at each point in space that describes the relative influence of this component (typically Gaussian or a mixture of Gaussian). Then, instead of averaging the (weighted) motion due to each component to compute the displacement at any point, we average the speed induced by each component (weighted by the

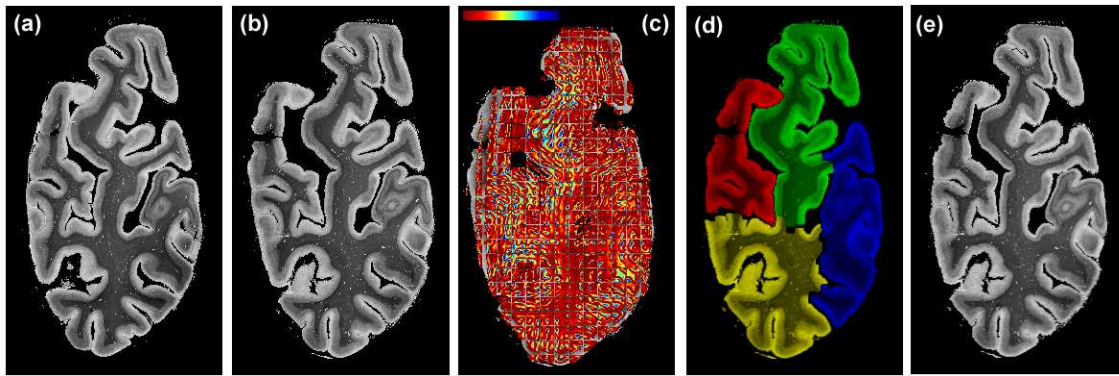


Figure 6. *Piecewise affine registration of histological slices: (a) input reference image; (b) floating image; (c) similarity field (d) registered floating sub-images; (e) final composed locally registered floating image.*

relative influence) and integrate this differential equation to obtain the displacement. That way, the obtained deformation is guaranteed to be diffeomorphic. Very flexible, this tool can be readily adapted to a large variety of situations, simply by tuning the number of rigid or affine components and the number of parameters describing their regions of influence.

The theory of these transformations is described in [48] and in [92], along with their implementation. Their use is exemplified with the registration of successive histological slices of the human brain. These slices usually present rigid or affine artificial deformations which have to be corrected before any 3D reconstruction of the anatomy (Fig. 7). We are currently using these transformations in the field of shape statistics to analyze the deformations around a mean shape.

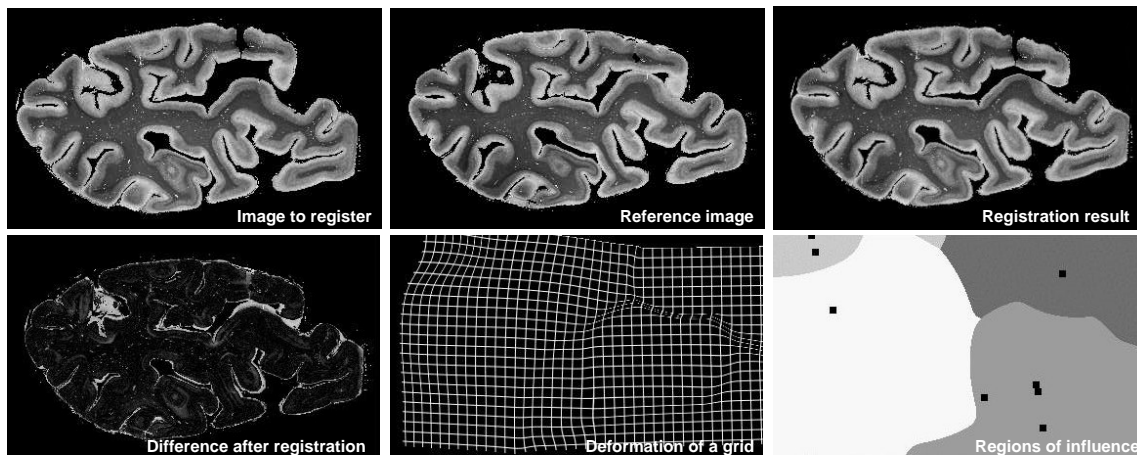


Figure 7. *Registration of histological slices using polyrigid transformations. On top, the two images to register and the registration result. On bottom right, we displayed the closest region of influence of each point. Each of these regions has its own rigid transformation with a smooth transition at their boundaries, as can be seen of the grid deformation (bottom, middle). The difference image after registration (bottom left) shows that the main deformations components have been correctly captured without introducing deformations where there are some real image differences.*

6.3.3. *Parallelization of registration algorithms*

Key words: *Registration, parallel computing, grid.*

Participants: Radu Stefanescu, Xavier Pennec, Nicholas Ayache.

Non-rigid registration is a time-consuming process. In order to make registration useful in a clinical environment, computation time must be reduced from about an hour to several minutes. Rather than simplifying the algorithm and potentially reduce the quality of the results, we chose to parallelize the algorithm. This allows us to drastically reduce the computation time, while preserving the algorithm's performance. The use of a cluster of off-the-shelf personal computers connected through a standard Ethernet network provides sufficient computation power at a low price.

Improvements in our parallelization method for the PASHA algorithm [32] allowed us to increase the parallel acceleration and lower the computation time to a little more than 3 minutes. This opens the possibility of the usage of grid computing for parallel registration. The results presented at HealthGrid 2003 [90] prove the efficiency of inexpensive clusters of workstation for tackling non-rigid registration problems.

6.3.4. *Parallel multi-subject non-rigid registration using a priori information*

Key words: *Multi-subject registration, parallel computing.*

Participants: Radu Stefanescu, Xavier Pennec, Nicholas Ayache.

In multi-subject registration, the spatial variability of the transformation is often very large. In such a case, the linear regularization of the vector field describing the transformation is not sufficient. We propose in this work a better suited method that consists in regularizing by solving a nonlinear heat equation. The conductivity at each point represents the local stiffness of the objects presented in the images. In our preliminary experiments, we dealt with mono-modal images, thus we used the classical sum of squares intensity differences (SSD) as the similarity criterion. We also made a robustness improvement, which allows the similarity criterion to be given more weight in places where the estimation of the matches has more chances to succeed, such as the contours. In order to decrease the registration time to about 5 minutes, a parallel implementation on clusters of workstations has been provided. The parallel algorithm embeds a novel method of parallelization of the AOS diffusion scheme, which is more efficient on clusters of workstations.

The results, presented at MICCAI 2003 [89], showed that multi-subject non-rigid registration of image couples with large differences can be improved by taking into account the local stiffness of the objects presented in the images and by giving more weight in the matching process to voxels that contain more information (see an example in Fig. 8). This algorithm, while more complex than its predecessors, admits a fast parallel implementation on an inexpensive platform, such as a cluster of workstations, thereby opening the way towards using the algorithm in a clinical environment with relatively small hardware investments.

6.3.5. *Non-Rigid Registration Combining Volumetric Biomechanical Model and Block-Matching*

A parallel implementation of the following method has been developed in collaboration with CAIMAN project, INRIA Sophia Antipolis.

Key words: *Registration, Biomechanical model, Finite element, Block matching.*

Participants: Maxime Sermesant, Olivier Clatz, Zhongze li, Stéphane Lanteri, Hervé Delingette, Nicholas Ayache.

Due to the high accuracy of the planning in neurosurgical procedures, tracking intra-operative deformations is a challenging task. Furthermore, the clinical demand for fast non rigid registration will have to be met in a very near future. We propose a new patient-specific registration method which combines a volumetric deformable model and a block-matching approach. This method was presented in [87]. Compared to other registration techniques, this method includes a trade-off between biomechanical regularization and block-matching based correlation directly in a dynamic deformation process. Using a biomechanical model allows to easily introduce anatomically-motivated *a priori* information in order to represent the physical behavior

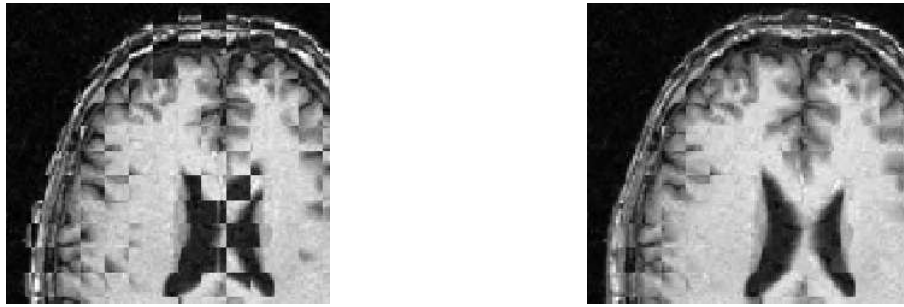


Figure 8. Multi-subject registration using dense a priori information. Mosaics of the two images before (on the left) and after registration (on the right). The algorithm is able to correct for large differences in the shapes of the ventricles. Main sulcal lines, which are present in both subjects, are also well matched. Differences still exist in areas occupied by minor sulcal lines, which are more specific to each individual.

of the registered organ. Compared to other deformable model approaches, this method uses fully volumetric internal *and* external energies. The full registration process takes less than a minute on the INRIA cluster of PCs consisting of 14 Intel Pentium IV/2 Ghz. Results of the registration can be seen on Figure 9.

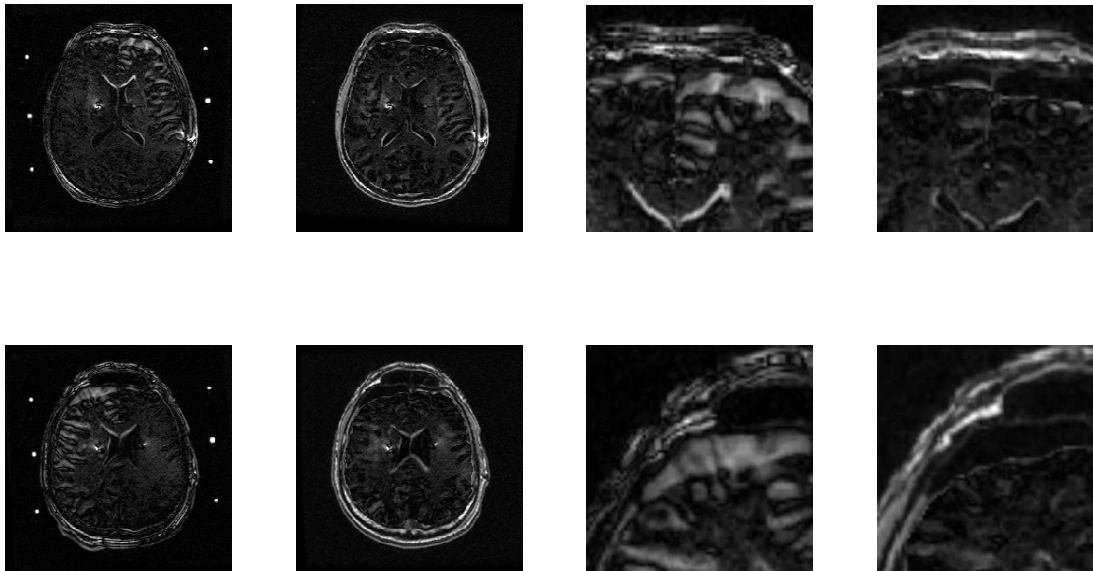


Figure 9. Non-Rigid Registration Combining Volumetric Biomechanical Model and Block-Matching: difference between pre- and post-operative images. 1st column: before registration. 2nd column: after registration. 3rd column: before registration zoom. 4th column: after registration zoom. Images courtesy of Pr. D. Dormont, the Neuroradiology Department, La Pitié Salpêtrière Hospital, Paris.

6.3.6. Intensity normalization within series of images

Key words: histogram matching.

Participants: Grégoire Malandain, Eric Bardinet [CNRS-LENA].

We address the problem of histogram matching in the context of medical image processing. Such a problem occurs while comparing two images of the same object, where intensity differences are due to different acquisition conditions. This can be compensated by histogram matching or equalization. To achieve this, we based our method on windowing techniques. This allows to match implicitly *continuous probability density functions*, yielding more robust results than the methods issued from *discrete histograms*. It is of great interest while reconstructing a 3-D image from a stack of 2-D sections (e.g. autoradiographs, optical images, histological slices, etc.) [74].

6.3.7. Multimodal image fusion

Key words: *Image fusion*.

Participants: Grégoire Malandain, Eric Bardinet [CNRS-LENA], Julien Dauguet [CEA, SHFJ].

The purpose of the fusion of a set of contiguous thin 2-D sections, with a 3-D image, e.g. an MR volume of the same individual, is to find the most exact correspondence in the MR volume for each 2-D section.

Reconstruction of a 3-D volume from a stack of 2-D images (histological slices or autoradiographs) has already been largely studied. It is done by registering each pair of consecutive images in the stack to recover a geometrically coherent 3-D alignment of the 2-D slices [123].

We addressed the fusion of 2-D autoradiographic slices with a 3-D anatomical MR image, when no intermediate modality, such as photographs, is available. We demonstrated that it is possible to achieve a satisfactory correspondence by using only linear transformations [73][93].

Such combination of linear transformations has also been applied to the reconstruction of optical images [68] within an informal collaboration with the Kent Institute of Medicine and Health Sciences (KIMHS).

During the acquisition protocol, more complicated transformations may be unavoidable. This is the case for histological sections, where first the brain manipulation (extraction, etc.) and the section staining lead to 3-D and 2-D deformations. In such a case, elastic deformations (e.g. splines) have to be used to fuse the histological data with 3-D imaging modalities [61].

6.3.8. Augmented Reality for Radio-Frequency Liver Surgery

This research project is conducted in close collaboration with L. Soler at IRCAD in Strasbourg.

Key words: *Augmented Reality, 3D/2D Registration, Uncertainty prediction, Calibration, Radio-Frequencies.*

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

The purpose of the augmented reality system we developed is to guide surgeon movements during radio-frequencies hepatic tumor destruction. 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) and 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 stuck 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. A careful evaluation of this criterion in terms of robustness, accuracy and computation time showed that our new criterion is much more robust and provides a target registration error up to 20% better than standard criteria for a 10 to 20 times larger computation time (that still remains compatible with real time) [77].

Accuracy being crucial for our application, we also led a theoretical study to predict the transformation uncertainty within the liver given any experimental setup and markers measurements. A validation step on phantom data (plaster cast of the human abdomen) showed that our prediction is correct within our clinical conditions (article submitted to ECCV'04).

In parallel, we carried out an interface that displays in real-time the models registered onto the video images, in addition to the virtual model of the needle when it has penetrated the skin (cf. Figure 10). Needle targeting experiments guided with our AR system showed that the surgeon is able to reach artificial hepatic tumor in the

phantom with a mean accuracy of 3 mm [76][75] We are currently improving the system ergonomy (automatic cameras and needle calibrations, robust detection of radio-opaque markers in the video images) to realize our first in-vivo experiment in the operating room.

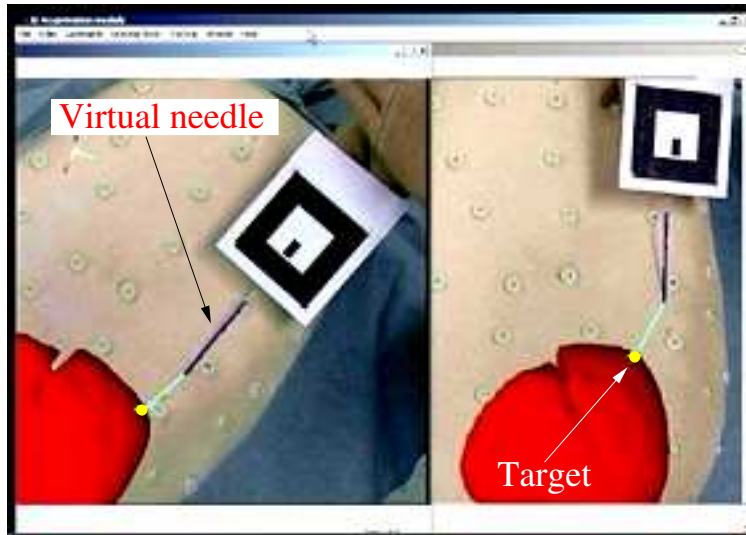


Figure 10. *Augmented Reality for Radio-Frequency Liver Ablation.* Example images displayed to the surgeon on its screen to guide the insertion of the needle towards the hepatic target center. Both video images contain the liver virtual model (in red), the target (in yellow) and the needle (in dark blue). The light blue line represents the distance between the needle top and the target.

6.4. Atlases, morphometry and statistical analysis

6.4.1. Generalized Image Models

Key words: *Statistical shape models, error propagation, registration, Kalman filter.*

Participants: Miguel Ángel González Ballester, Xavier Pennec, Nicholas Ayache.

We have introduced a novel Generalized Image Model (GIM) [65]. Images are represented as sets of 4-dimensional sites combining position and intensity information, as well as their associated uncertainty and joint variation. This model seamlessly allows for the representation of both images and statistical models, as well as other representations such as landmarks or meshes. A GIM-based registration method aimed at the construction and application of statistical models of images has also been developed. A procedure based on the iterative closest point (ICP) algorithm is modified to deal with features other than position and to integrate statistical information. Furthermore, we modify the ICP framework by using a Kalman filter to efficiently compute the transformation. The process of initialization and update of the statistical model was devoted careful consideration.

6.4.2. Learning object correspondences with the observed transport shape measure

This project was conducted in collaboration with Paul M. Thompson, from the LONI laboratory, within the framework of the associated team program.

Key words: *Reparameterization, Object matching, Shape measure.*

Participants: Alain Pitiot [EPIDAURE and LONI], Hervé Delingette, Arthur W. Toga [LONI], Paul M. Thompson [LONI].

We approached the issue of object matching by computing a dense correspondence field between objects elements that share particular similarities, in terms of shape, position, or both. The common drawback of most of the approaches from the literature lies in their lack of control over the used similarity measure, which is often defined a priori, once and for all, and uses only limited domain-based information (or information learned from examples). Typically, these matching processes can be reduced to optimizing a functional whose minimum corresponds to a “good” correspondence field. The difficulty of designing an adequate functional comes from the difficulty of characterizing an adequate correspondence field.

To overcome this issue, we proposed a learning method which introduced explicit knowledge to the object correspondence problem. Our approach uses an a priori learning set to compute a dense correspondence field between two objects, where the characteristics of the field bear close resemblance to those in the learning set. We introduced a new local shape descriptor we call the “observed transport descriptor”, whose properties make it particularly amenable to the matching problem. From the values of our descriptor obtained at every point of the objects to be matched, we compute a distance matrix which embeds the correspondence problem in a highly expressive and redundant construct and facilitates its manipulation. This matrix is both visually interesting (as it allows for visual inspection of the specific reparameterization problem at hand) and enables us to recast the matching problem as the search for a geodesic in another metrizable space: the space of reparameterizations (which is a group). We developed two learning strategies that rely on the distance matrix.

Discussions about their applications to the matching of a variety of 1-D, 2-D and 3-D objects, including the corpus callosum and ventricular surfaces can be found in [82] which also described the underlying theory. Figure 11 shows how our shape descriptor behaves on a few n-D objects. Figure 12 illustrates the learning matching of a series of corpus callosum delineations.

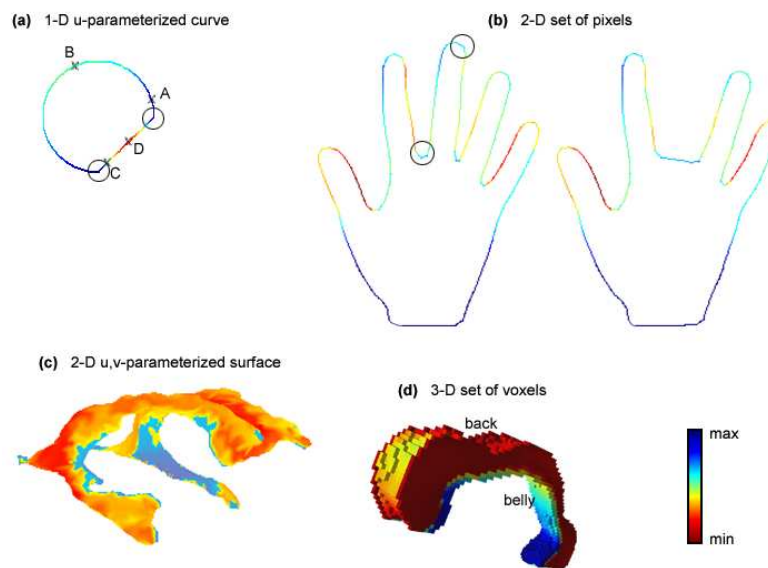


Figure 11. Observed transport descriptor computed over: (a) a u -parameterized 2-D curve (truncated circle), (b) a set of 2-D points (two hands), (c) a (u,v) -parameterized 2-D surface (ventricle) and (d) a set of 3-D points (corpus callosum). Black circles indicate a few high curvature areas.

6.4.3. Statistical Analysis of Sulcal Lines

This research action is done in close collaboration with our associated team, the Laboratory of Neuro Imaging (LONI) of the University of California, Los Angeles (UCLA).

Key words: Shape analysis, Brain images.

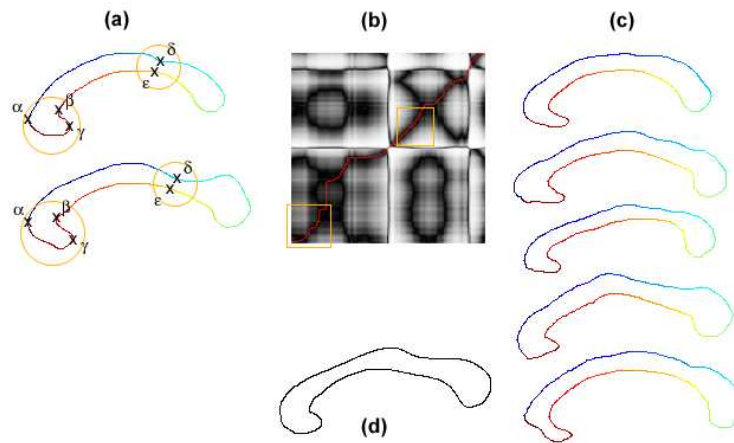


Figure 12. Pattern matching reparameterization of a few corpora callosa: (a) Two pairs of a priori parameterized callosa (greek letters indicate matching pairs of points); (b) their associated shape distance matrix with the corresponding path in red and the selected scenario/shape distance sub-matrices in orange; (c) a few reparameterized corpa callosa; (d) the overall point-by-point Euclidean average callosum.

Participants: Vincent Arsigny, Nicholas Ayache, Xavier Pennec, Paul Thompson [UCLA].

Sulcal lines are the roots of the sulci (valleys) present at the surface of the brain cortex. In this research action, we are developing new methods to analyze their anatomical variability in human brains. The database, provided by the LONI, groups manual delineations of 36 different sulcal lines, such as the central and lateral sulci. Around one hundred instances of each line is available, which is exceptionally large for such structures. Fig. 13 presents preliminary results showing mean shapes. We intend to infer from the analysis of the dataset new anatomical knowledge on the human brain, which could be useful for the study of neurological diseases such as Alzheimer's or schizophrenia. Also, the use of statistical models as *a priori* should improve the efficiency and robustness of non-rigid registration algorithms.

6.4.4. Statistical analysis of functional magnetic resonance images

This work is performed in close collaboration with the Service Hospitalier Frédéric Joliot, Unité de Neuro-Imagerie Anatomique et Fonctionnelle, CEA - Orsay, directed by Denis Le Bihan.

Key words: fMRI, Statistical analysis, Parcellation, Clustering.

Participants: Guillaume Flandin, Xavier Pennec, Grégoire Malandain, Nicholas Ayache, Jean-Baptiste Poline [CEA/SHFJ].

Functional Magnetic Resonance Imaging (fMRI) is a powerful tool to noninvasively address questions about activation effects in populations of subjects or to assess the functionality of neuronal networks. The most widely used method for the statistical analysis of fMRI data has been popularized by the SPM software¹ and relies on a voxel-by-voxel fitting of a linear model of the hemodynamic response function on smoothed data.

In previous work, we proposed a new framework in which functional data are embedded. It relies on an anatomical parcellation of the cortical ribbon. The corresponding algorithm is a spatial K-means using geodesic distances. We then obtain a representation of the data at any resolution between the voxel and the region of interest.

This parcellation framework has been successfully applied to the analysis of functional connectivity, and more specifically to the study of non-linear and/or asynchronous interactions between signals. Parcellation of

¹<http://www.fil.ion.ucl.ac.uk/spm/>



Figure 13. **Preliminary results on the statistical analysis sulcal lines.** Instances are displayed in yellow-green and mean shapes in red.

the cortex was used as a preprocessing to cope with the dimensionality of the data. This work, lead by P.-J Lahaye from CEA/SHFJ, was presented in [69] and [39].

Regional model estimation is another application of the anatomical parcellation of the cortex. Indeed a global model is widely used with signals observed at different brain locations, leading to questions of statistical efficiency and detection sensitivity. To overcome this, a response model is selected for each parcel using a multivariate model selection technique (MLM). This study, lead by A. Roche, CEA/SHFJ, was presented in [85] and the results suggest that the dynamic of the BOLD effect is region dependent, thus emphasizing the adequacy of a regional model based on a cortical parcellation.

Last but not least, we improved the parcellation algorithm leading to an anatomo-functional parcellation of the brain. Indeed we are looking for clusters of voxels with similar time series and similar position: this is spatio-temporal clustering. We chose to use a Gaussian mixture model in a feature space formed by the regression coefficients of a linear model and voxel positions in Talairach space. The model parameters are estimated using an EM algorithm. Furthermore, we extended this work to deal with multisubject analyses (see [38] for details on group analyses). In that case, the aim is to create clusters sharing similar functional values and similar positions among the subjects of an fMRI experiment. This can be seen as an attempt to bypass the badly defined precise coregistration of different subjects. Results were presented in [62].

6.4.5. Morphometric parameters of brain microvascular network

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.

Key words: Medical imagery, Confocal microscopy, Segmentation, Chamfer map, Skeletonization, Vascular network.

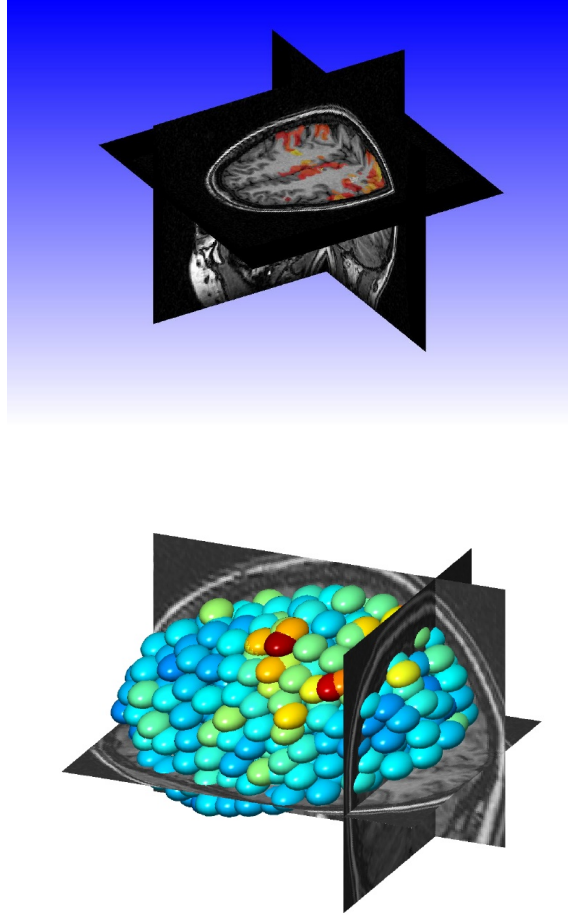


Figure 14. (a) Activation detection on a grasping task paradigm using an anatomical parcellation of the cortex. (b) Spatio-temporal mixture model fitted on a functional brain and reported on the anatomical scan.

Participants: Céline Fouard, Grégoire Malandain, Steffen Prohaska [INDEED], Malte Westerhoff [INDEED], Francis Cassot [INSERM U455], Christophe Mazel [TGS], Didier Asselot [TGS], Jean-Pierre Marc-Vergnes [INSERM U455].

The purpose of this study is to analyze vascular networks which are recorded using 3D confocal microscopy or other suitable 3D imaging techniques. This includes analysis of the network's topology, morphometry of individual vessels, and statistical analysis of morphometric properties on the network. To perform such analysis, we must extract a suitable discrete representation of the vascular network from the image data.

The images come from Duvernoy's collection: several sections of the brain have been injected with Indian ink. The sections are then observed by a confocal microscope. We obtain 3D images of the microvascular network of the brain where each slice corresponds to a focal plan of the microscope (see Fig. 15 left). The mean image size is $512 \times 512 \times 100$ voxels with $1.22 \times 1.22 \times 13\mu\text{m}$ per voxel.

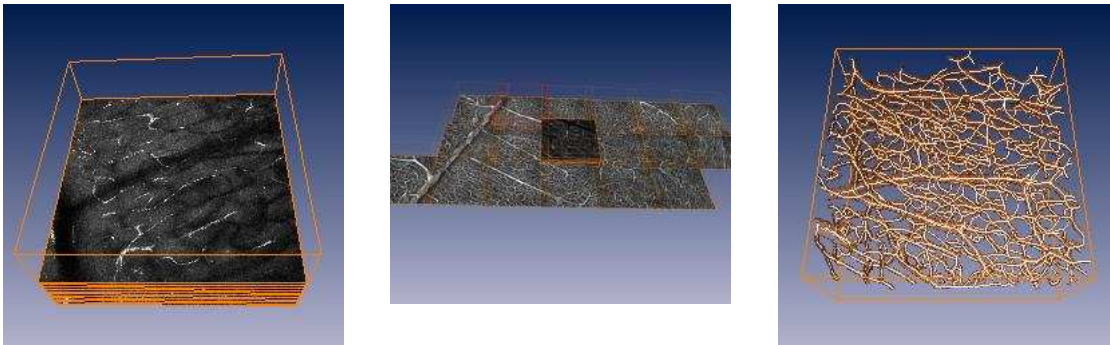


Figure 15. **Brain microvascular network.** *Left:* one of the multiple overlapping 3D confocal images. *Middle:* Example of a registered mosaic. *Right:* Extracted center-lines representing a part of the microvascular network.

Once an image is obtained, a micrometric screw moves the confocal microscope from some micrometers and we take another image. This leads to a mosaic of images (see Fig. 15 middle). It sometimes happens that, during the acquisition of the images, two image blocks are not exactly aligned. The first step of our treatment is to re-align mosaic blocks. We then perform median and Gaussian filtering on the images to remove impulsional noise and smooth borders, before thresholding them to obtain a binary image with the background pixels at 0 and the vessels pixels at 1.

The major morphometric parameters that we want to extract from the vessels network are vessels centerlines and vessels diameters. For both of these parameters, we need to compute the distance map inside vessels. Then, we extract the centerlines of the vessel by a thinning algorithm. (cf Fig. 15 right).

6.4.6. Automatic computation of chamfer mask coefficients for large masks and anisotropic lattice

Key words: *chamfer map, norm constraints, chamfer mask, anisotropic lattice.*

Participants: Céline Fouard, Grégoire Malandain.

Confocal microscope images contains a large volume of anisotropic data. Resampling these data would lead to an extremely high volume and time cost. This is why we adapted the chamfer map computation for anisotropic lattices. To do so, we proposed an automatic method to compute the chamfer mask coefficients in an anisotropic grid. This method takes into account Remy's norm constraints [127] and allows to foresee the error between the chamfer map and an Euclidean one. [63]

6.4.7. *Skeletonization by blocks for large 3-D datasets*

Key words: *skeletonization, block by block, large datasets.*

Participants: Céline Fouard, Grégoire Malandain.

Skeletons are compact representations that allow mathematical analysis of objects. A skeleton must be homotopic, thin and medial in relation to the object it represents. Numerous approaches already exist. The main focus is computational efficiency. However, when dealing with data too large to be loaded into the main memory of a personal computer, such approaches can no longer be used. We proposed a skeletonization algorithm that processes the data locally (in sub-images) while preserving global properties (medial localization). Our privileged application is the study of the cerebral microvascularization. [64]

6.4.8. *A unified tensor-based saliency model applied to the registration of curves and surfaces*

This research theme is done in close collaboration with the AREALL Company through a CIFRE PhD Fellowship.

Key words: *3D registration, Saliency, Statistical model, Curves, Surfaces.*

Participants: Sébastien Granger [AREALL/Epidaure], Xavier Pennec.

We have developed in this work a unified saliency model that can be used in various applications on noisy sets of points measured on curves or surfaces. Its goal is to provide an explicit equation for the probability of sampling a point on a curve or surface, knowing another point sampled on the same curve or surface, and taking into account the sampling errors (noise on point positions, outliers).

This is achieved by gathering and completing ideas from previous works on tensor voting and saliency completion field. First, we justify the use of a tensor field as an approximate but efficient way of making statistics on oriented points (e.g. for encoding the probable orientation of the surface normal). Then, we propose a unified generative model obtained by combining a sampling law on the curve/surface, a law on its shape (which behavior can be tuned between line/plane models, Stochastic Completion Field models and Medioni's Diabolo Field heuristic), and a third law that introduces the measurement noise. Moreover, we provide an explicit (yet approximate) equation for this unified model, which allows to efficiently fit the model to real data.

We demonstrate the validity of this saliency with a new application in this field: the rigid registration of surfaces. This is achieved through the enhancement of an ICP (iterative closest-point) algorithm. Experimental results show significant improvements in the result accuracy, and in the prediction of this accuracy.

This work was published in [24] and submitted to ECCV'04.

6.4.9. *Statistical Shape Analysis of the Human Ear Canal*

This study is performed in collaboration with the Department of Informatics and Mathematical Modelling, Technical University of Denmark and Oticon A/S.

Key words: *Human Ear Canal, 3D surface modeling, Active Shape Models, 3D point correspondence, 3D component placement.*

Participant: Rasmus R. Paulsen.

Hearing aids come in a number of different styles. The smallest of these styles is called CIC (completely in the canal) and it has a number of attractive properties. First of all the small size is cosmetically appealing because a well-produced CIC is as good as invisible in-situ. Secondly, the CIC has some acoustic advantages. The shell of a CIC must have size and shape that allows it to contain a microphone, an amplifier, a loudspeaker, and battery. On the other hand it is desirable to design these components in a way that makes it possible to minimize the size of the final hearing aid.

Today the design of components are based on intuition and skill and not on a systematic description of the ear canal. It is acknowledged that systematic knowledge of the geometry of ear canals and the variation thereof potentially could be extremely helpful in the mechanical design of new components for hearing aids. It is obvious that the systematic description of the variation of the shape of the ear canal must be done using statistical methods.

In the first part of a project a statistical shape model was built using laser scans of 29 ear canals.

During the period at INRIA (from February 2003) a Markov Random Field regularization method has been implemented. The method is used to enhance the quality of the shape model. Results are published in [79][67]

Also work on automated component placement has been performed. Some results are described in [80].

Future work includes writing an additional article describing the Markov Random Field approach and an article describing work on component placement.

6.5. Motion analysis and medical simulation

6.5.1. Breathing movement image correction for emission tomography

This study is performed in collaboration with the laboratory of biophysics of the Nice medical faculty, directed by Dr. J. Darcourt.

Key words: Nuclear medicine, Oncology, Image reconstruction, Emission tomography.

Participants: Mauricio Reyes, Gregoire Malandain, Nicholas Ayache, Jacques Darcourt.

In emission tomography, the process of image reconstruction has evolved since the utilization of the filtered back projection algorithm (FBP). Nowadays, iterative techniques incorporating statistical knowledge of the photon emission process has produced much interest among researchers, not only for the improvements achieved in image quality, but also by the possibility to incorporate correction factors, like scattering, attenuation, etc. One of the problems that has not been discussed in depth is the incorporation of correction methodologies due to patient breathing, which produces smearing of the reconstructed images. Solutions like respiratory gating, that synchronize the breathing cycle of the patient and the data acquisition process [121], or correlated dynamic PET techniques [122] that use external radioactive markers and list mode data. This type of techniques have been tested with improvements over the quantization of lungs lesions, but with the disadvantages of requiring extra hardware or more expensive scanner systems. The objective of this study is to incorporate breathing-movement corrections to the phase of image reconstruction. In this sense, two working lines have been developed according to the following two questions: What is the information that we can retrieve from the breathing cycle? How this information can be linked to the step of image reconstruction? For the former, a thorax phantom, called NCAT phantom [131] has been used to study the breathing cycle. For the latter, a procedure of correction inside the probability matrix in the MLEM and OSEM algorithms has been implemented which takes into account the spatio-temporal relationship of each voxel in the structure under study. The idea consists in modifying each value of the probability matrix, according to the relative displacement (using as base a reference frame) of each voxel along the breathing cycle. To get this transformation, the NCAT phantom can be used to retrieve the displacement vector field, or a couple of CT thorax images of the patient at full-exhalation and full-inspiration. The displacement vector field have been calculated using the PASHA algorithm [32] and now is being incorporated into the OSEM algorithm.

6.5.2. 4D tomographic reconstruction of coronary arteries from one rotational X-ray sequence

Key words: image reconstruction.

Participants: Christophe Blondel [Chir], Grégoire Malandain, Régis Vaillant [GEMS], Frédéric Devernavy [Movi, INRIA Rhône-Alpes], Eve Coste-Manière [Chir], Nicholas Ayache.

We develop a complete and fully automatic method to compute a tomographic 4D representation of coronary arteries from one single rotational monoplanar X-ray sequence [54]. The major steps of our method are the following: (1) images filtering, (2) arteries segmentation, (3) arteries matching and reconstruction, (4) parametric deformation field computation [53], and (5) deformation-compensated tomographic reconstruction [55]. Steps (2) and (3) involve only a few frames, acquired at the same cardiac cycle phase, while the steps (1), (4), and (5) use the frames acquired at all cardiac cycle phases. This method has been successfully applied to 4 patient data sets. The 4D representation allows the visualization of coronary arteries anatomy from any point of view, and at any cardiac cycle time.

6.5.3. Red blood cells velocity estimation in confocal microscopy imaging

This work is performed in close collaboration with the company Mauna Kea Technologies (Paris).

Key words: RBC velocity, Confocal microscopy.

Participants: Nicolas Savoire, Nicholas Ayache, Aymeric Perchant [MKT], François Lacombe [Observatoire de Paris].

Confocal microscopy imaging developed by Mauna Kea Technologies offers in vivo and in situ images of microcirculation in the small animal. The goal of our work is to estimate the red blood cell velocity in image sequences obtained through this new imaging modality.

The combination of the scanning process and red blood cell movement leads to deformations of the red blood cell shape in the images. By modeling this interaction, we are able, by analyzing the deformations, to retrieve the velocity [86].

The first part of our work consisted in modeling the shape deformations and then coming up with image processing techniques enabling the retrieval of deformations in image sequences and thus of the red blood cell velocity (see Fig. 16). Now we are trying to validate our methods by conducting experiments in controlled conditions.

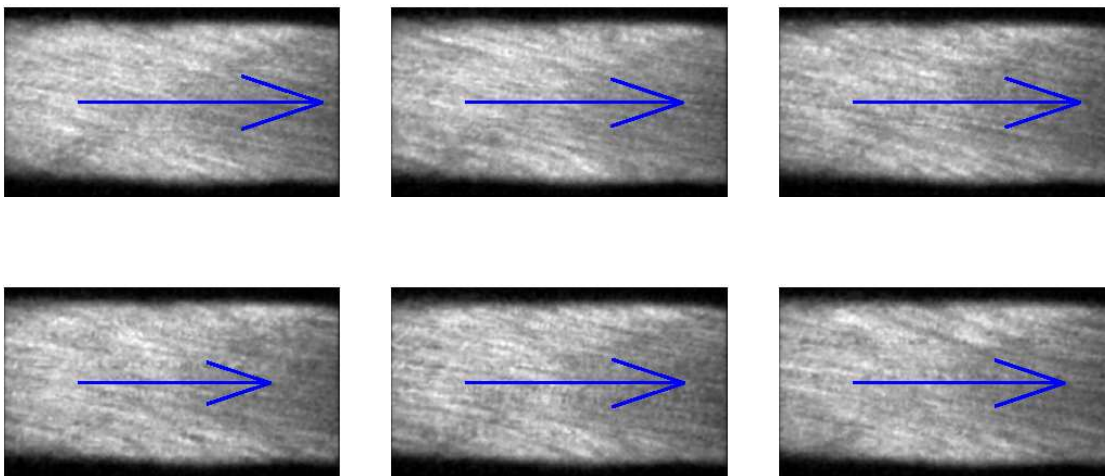


Figure 16. Mouse cremaster micro-vessel observed using a Cell-viZio™ (acquisition courtesy of Pr. E. Vicaut). The field of view is about 160x120 microns. Left: Example of ridge detection. Slanting segments are the ridge axes. Arrows are the raw velocities estimated from the ridge angles. Right: Median velocities of 6 randomly chosen images from a sequence of 40 images. Mean median velocity is 7.18 mm/s and standard deviation of the median velocity is 0.7 mm/s.

6.5.4. Patient-specific biomechanical model of the brain: application to Parkinson's disease procedure

This work has been realized in collaboration with the Neuroradiology Dept. and LENA UPR 640-CNRS, La Pitié-Salpêtrière hospital, Paris.

Key words: Biomechanical model, Brain, Finite element method.

Participants: Olivier Clatz, Eric Bardinet, Hervé Delingette, Nicholas Ayache.

Stereotactic neurosurgery for Parkinson's disease consists of stimulating deep nuclei of the brain. Although target coordinates are calculated with high precision on the pre-operative images, cerebrospinal fluid (CSF)

leakage during the procedure can lead to a brain deformation and cause potential error with respect to the surgical planning. We developed a patient-specific biomechanical model of the brain able to recover the global deformation of the brain during this type of neurosurgical procedure (see Fig. 17). The model includes different structures such as the brain, the skull, the cerebro-spinal fluid and the falx cerebri. This work has been presented in [50], [58], [59] and [33]. Such a model could be used to update the pre-operative planning and balance the mechanical effects of the intra-operative brain shift.

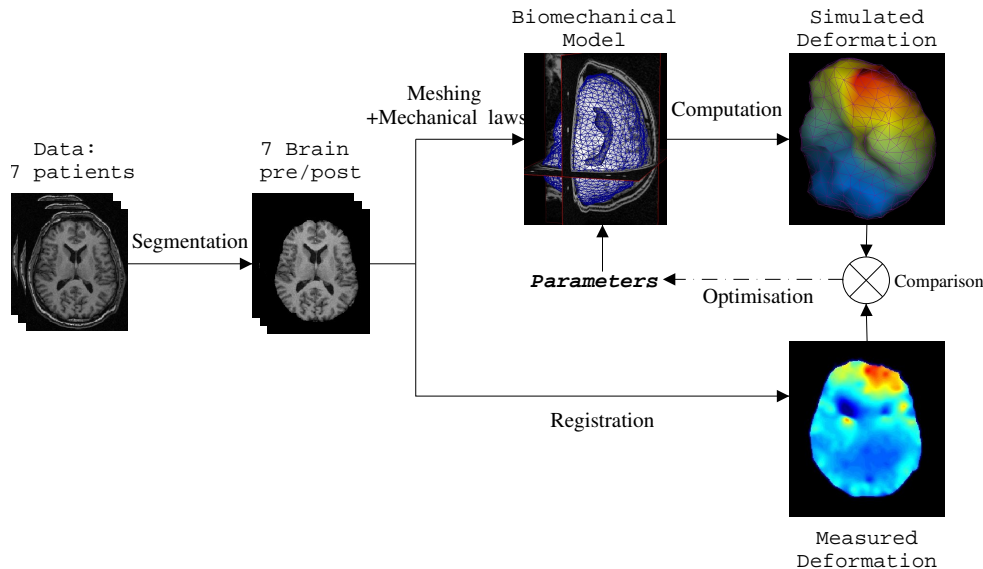


Figure 17. Overview of the biomechanical deformable model of the brain, including the model building and parameters optimization.

6.5.5. Modelling and Measuring the Cardiac Electromechanical Activity

An electromechanical model of the heart has been developed [26] and it is now validated with clinical measures through a collaboration with the Division of Imaging Sciences, Guy's Hospital, King's College London. This work was part of ARC ICEMA2.

Key words: Electromechanical model, cardiac activity, cardiac modeling, electrophysiology.

Participants: Maxime Sermesant, Hervé Delingette, Nicholas Ayache.

An electromechanical model of the heart has been proposed, which combines a realistic biomechanical model of the myocardium with the simulation of the action potential propagation and the mechanical contraction. This model has been specifically designed to enable interaction with cardiac images and a medical simulator [26].

This model is now validated on human clinical data in collaboration with the Division of Imaging Sciences, Guy's Hospital, King's College London. This team has access to a unique XMR facility allowing in vivo combined measurement of the electrical and mechanical activity of the heart [84], to an ESI² mapping system producing precise electrical mapping of the endocardial electrical activity (Fig. 18).

6.5.6. Parameter estimation of an electromechanical model of the heart using patient specific data.

Quantitative adjustment of an electrical model was performed using electrical data of team of Elliot Mc Veigh of National Institute of Health. This work was part of ARC ICEMA2.

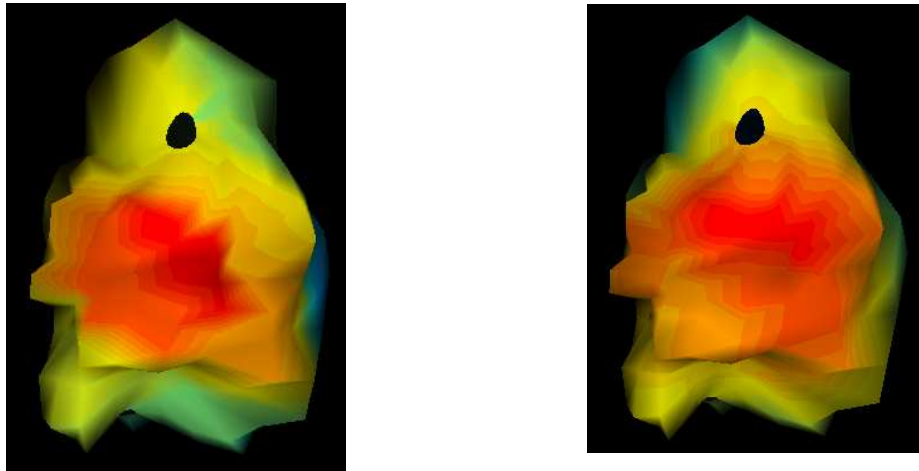


Figure 18. **Electrical isochrones on the endocardial surface.** *Left: isochrones measured by the ESI system. Right: isochrones computed with the electromechanical model (initialization prior to the automatic parameter estimation currently developed).*

Key words: *Parameter estimation, Data assimilation, Reaction-Diffusion models, Kalman filter, Quantitative comparison, Data/model comparison.*

Participants: Valérie Moreau-Villéger, Maxime Sermesant, Hervé Delingette, Nicholas Ayache.

In this project, which is part of ICEMA2 cooperative action, we intend to solve an inverse problem by estimating the parameters of an electro-mechanical model of the heart from a set of patient specific data such as time series of medical images (echography, or MRI) and electrical activity of the heart (ECG or VCG). This data consists of extracellular potential measured on the epicardium and endocardium of a canine heart from a basket of electrodes by the National Institute of Health, National Heart Lung and Blood Institute, Laboratory of Cardiac Energetics, Bethesda, Maryland. The electrical propagation model is based on a FitzHugh-Nagumo reaction-diffusion system of equations.

Figure 19 shows a first manual adjustment of the parameters to fit NIH experimental data that we performed in [88]. We are studying the feasibility of sequential approaches such as extended Kalman filter(EKF) to assimilate electrical information in the FitzHugh-Nagumo model.

6.5.7. Towards fast solution of non-linear mechanical problems based on algebraic methods

This work has been done in collaboration with the Galaad project (B. Mourrain) and University Paris VI (J-C. Faugère).

Key words: *Surgery Simulation, Algebraic methods, Gröbner bases.*

Participants: Thibaut Bardyn, Hervé Delingette.

During the DEA training period of Thibaut Bardyn, we have evaluated the use of algebraic methods such as Gröbner bases for solving non-linear systems of equations based on non-linear mechanics. This research activity is related to the simulation of soft tissue deformation. Indeed, the use of the St-Venant Kirchoff model (finite strain and linear stress-strain relationship) requires to solve a system of equations of order three.

Three basic algebraic method for solving such systems of equations have been studied including Gröbner bases and the resultant method. Given the computational complexity of those methods, we chose not to solve the global system but to iteratively solve the equation for each vertex (thus having only three unknowns). We have tested different software packages available in the Galaad project, and found that the package by

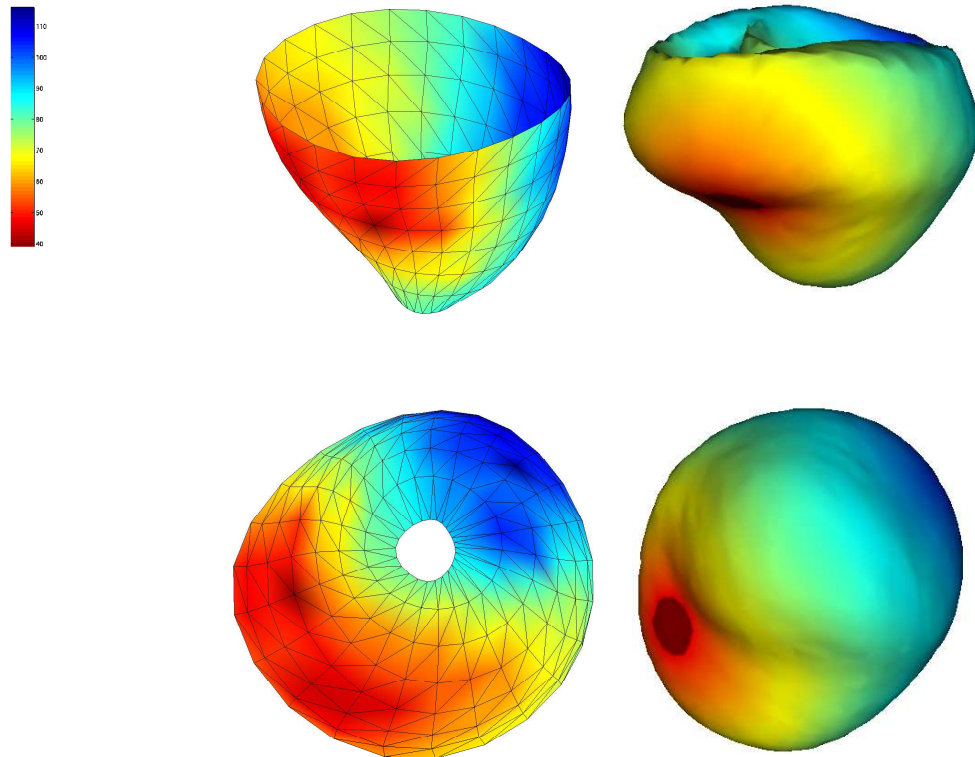


Figure 19. **Parameter estimation of an electromechanical model of the heart:** preliminary results showing the propagation of the depolarization wave on the endocardium of a canine heart. **Left:** isochrones measured in vivo by NIH. **Right:** isochrones extracted from the simulated model.

Jean-Charles Faugère (University Paris VI) was the most adequate for our problem. Our experiments have shown that non-linear relaxation techniques based on algebraic methods could be of high interest for surgery simulation provided that a dedicated version of this algebraic software package is created to tackle the specific nature of those equations.

6.5.8. Simulation of hepatic surgery

This research has been done in collaboration with the IRCAD center in Strasbourg (France)

Key words: *Surgery Simulation, Soft Tissue Modeling, Force-Feedback.*

Participants: Clément Forest, Hervé Delingette, Nicholas Ayache.

The effort in building a laparoscopic simulator for the practice of liver surgery has been pursued [23]. Our current prototype can simulate the action of two virtual instruments and one endoscope: both instruments are controlled through force-feedback systems. The resection of liver parenchyma with a cavitron may be simulated as well as the clamping and cutting of the main bifurcations of the portal vein. A dedicated data structure of tetrahedral meshes has been proposed to optimize the computation time of deformation and topological changes.

Since May 2003, the surgical simulator has been transferred to the IRCAD surgical training center for a first clinical validation.

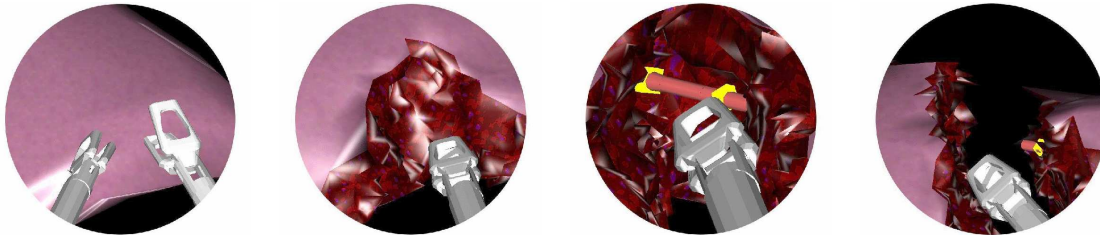


Figure 20. Simulation of hepatic resection based on a cavitron.

7. Contracts and Grants with Industry

7.1. QuantifiCare

Participants: Nicholas Ayache, Hervé Delingette, Grégoire Malandain, Xavier Pennec.

An exploitation license for several softwares (EpidaureLib, MecaMatch, EpiCard, démons de Maxwell, PFLib and PFRegister, Yasmina and YAV++) and three patents (EpiMatch, Volvar et Yasmina) has been delivered to QuantifiCare in June 2001.

7.2. CIFRE PhD Fellowships

7.2.1. TGS

The work of Céline Fouard on segmentation of brain microvascular networks from confocal microscopy images is supported by a CIFRE PhD fellowship from the company TGS.

7.2.2. GEMSE

The work of Christophe Blondel (Chir) on 3D reconstruction of coronary arteries from a single rotating C-arm acquisition is supported by a PhD fellowship from the company GMSE.

7.2.3. AREALL

The work of Sébastien Granger on a statistical approach to the rigid registration of surfaces for dental implantology was supported by a PhD fellowship from the company AREALL.

8. Other Grants and Activities

8.1. Regional projects

8.1.1. Regional PhD fellowships

Radu-Constantin Stefanescu and Guillaume Dugas-Phocion are partially supported by a “Région Provence-Alpes Côte d’Azur” PhD fellowship.

8.2. National projects

8.2.1. ARC ICEMA-2

Participants: Maxime Sermesant, Valérie Moreau-Villéger, Hervé Delingette [correspondant], Nicholas Ayache.

The Inria cooperative research action ICEMA-2 aims at creating an electro-mechanical model of the heart. More precisely, for the Epidaure project, a pro-active biomechanical model including both right and left ventricles was proposed in order to track the motion of those ventricles in time series of medical images such as 4D MRI images or 4D echographic images (see sections 6.5.5 and 6.5.6). This action is coordinated by the Sosso Inria project (F. Clément) and includes also several members of the Inria projects Macs, Caiman, Bang as well as Philips Research France. Its scientific achievements have been presented and discussed during the two plenary meetings that occurred on April 29th and October 20th 2003.

8.2.2. ACI Neurosciences Intégratives et Computationnelles

Participants: Éric Bardinnet, Nicholas Ayache [correspondant].

This is a collaboration between SHFJ (CEA), the La Pitié Salpêtrière Hospital (Neuroradiology unit), INSERM (U.289), Saint-Antoine Hospital (neurology unit) and INRIA (Epidaure project), for a duration of three years. The aim of this collaboration is to define an “Approach in fMRI of the anatomo-functional bases of the cortico-striatal relations in humans”. In particular, it focuses on the study of the anatomo-functional organization in humans of the fronto-striatal relations, in order to be able to determine the plastic modifications of these circuits as a result of dystonic pathologies, and those induced by the therapeutic treatments.

This project, established in October 2001 following a call for proposals of the Ministère de la Recherche (Neurosciences Intégratives et Computationnelles - thème “plasticité neuronale et adaptation fonctionnelle”), has effectively started at the end of 2002.

8.2.3. GIS Infections à Prions

Participants: Marius George Linguraru [correspondant], Éric Bardinnet, Xavier Pennec, Miguel Ángel González Ballester, Nicholas Ayache.

The GIS-PRIONS project (<http://www-sop.inria.fr/epidaure/Collaborations/GIS-PRIONS/indexNew.html>) involves a national collaboration between INSERM (Unit 360, Paris), the Neuroradiological Unit of the La Pitié Salpêtrière Hospital in Paris, the Centre for Magnetic Biological and Medical Resonance of CNRS in Marseille 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. Finding relevant signs of classification of the different types of CJD is another major goal of this project. The second year of the collaboration has already started and the first results are under clinical evaluation. Sections 6.2.3 and 6.2.4 expand on the undergoing work.

8.2.4. Specific Action on Non-Rigid Registration

Participants: Xavier Pennec [correspondant], Nicholas Ayache.

The Epidaure team participates to the specific action on non-rigid registration organized by the CNRS and coordinated by Nicolas Rougon (GET/INT) and Christian Heinrich (LSIIT). X. Pennec participated to the first meeting in October in Paris, where the objectives were refined. The goal will be to foster collaborative research between the different French groups working on non-rigid registration by providing a central repository for bibliographic references, preprints and finally a state of the art on the subject.

8.2.5. Scientific consulting

- 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 POP-SUD and of QuantifiCare. He is scientific consultant for the company Mauna Kea Technologies (Paris).
- Miguel Ángel González Ballester performed scientific consulting tasks for the company CEREVER, for the period January 2003 - April 2003.
- 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 Scientific council of the company Dosisoft (Paris), a subsidiary from the Gustave Roussy Institute and the Curie Institute (Paris).
- Xavier Pennec was a scientific consultant for AREALL up to April 2003.

8.2.6. Collaboration with national hospitals

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

8.2.6.1. IRCAD, hôpitaux de Strasbourg

Pr. Marescaux and L. Soler : hepatic surgery simulation (cf. section 6.5.8 and [23][45]) and augmented reality for guidance in hepatic surgery (see section 6.3.8 and [75][76][77][94]).

8.2.6.2. INSERM U455, Hôpital PURPAN, Toulouse

G. Malandain co-supervises the training period of Jean-Marc d'Angelo with Pr. J.-P. Marc-Vergnes (*Etude des possibilités de quantification semi-automatique des structures vasculaires*).

8.2.6.3. Hôpital de la Pitié-Salpêtrière, Paris

Dr. J. Yelnik (INSERM U.289) and Profs. D. Dormont and S. Lehéricy (neuroradiology unit) are our partners in the project ACI Neurosciences Intégratives et Computationnelles (see section 8.2.2 and [46][91]). Dr. J.P. Brandel (INSERM U.360) participates in the project GIS Infections à Prions (section 8.2.3).

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

Pr. Jacques Darcourt co-supervises the thesis of Mauricio Reyes, and was a co-supervisors of Jonathan Stoeckel's thesis [27]. Dr. Bondiau is doing a PhD within our project [30].

8.2.6.5. 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 [51][52][70].

8.3. European projects

8.3.1. EU Project MAPAWAMO

Participants: Grégoire Malandain [correspondant], Éric Bardinnet, Jonathan Stoeckel, Guillaume Flandin.

8.4. Hosting of foreign researchers

Angelo Zizzari (Marie Curie Fellowship) was hosted in the Epidaure project from September 2003 until May 2003. Angelo was granted a Marie Curie Fellowship in the context of the European project IMAVIS.

Rasmus Paulsen, a Danish Phd Student from the Technical University of Denmark in Lingby is staying at the Epidaure project since January 2003 as part of his PhD program. Rasmus is working on building a statistical shape model of the ear canal.

Stella Atkins, from Simon Fraser University (Canada) visited the group from 28 October to 5 November 2003.

8.5. Foreign associated team

Participants: Alain Pitiot, Xavier Pennec, Nicholas Ayache, Hervé Delingette, Vincent Arsigny, Eric Bardinet, Paul Thompson, Arthur Toga.

Since its inception 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 view of comparing and analyzing the performances and behaviors of image processing algorithms devoted to the building of brain atlases. As in 2002, the greater part of the interactions that took place in 2003 was in the form of data, software and expertise exchanges, all of which were facilitated by researcher visits.

Data: P. Thompson provided access to a large database of brain MRIs which helped to validate the automated segmentation system developed by A. Pitiot [81]. The variety of sulci lines delineated on these MRI data allowed V. Arsigny to test several approaches for a large scale statistical shape analysis.

A series of histological sections was also shared by J. Annese with A. Pitiot and V. Arsigny, to serve as tests for their registration techniques, reported respectively in [83] and [48].

Software: The reparameterization techniques developed by A. Pitiot and detailed in [82] helped complete the first phase of the Visual Cortex project (which already benefited in 2002 from the delineation software designed by A. Pitiot and the Baladin registration software developed at Epidaure). Details about this project, whose aim is the study of the human visual cortex from an architectonic point of view and conducted in collaboration with J. Annese from the LONI laboratory, can be found in [28] and [47].

Visits: Alain Pitiot spent his last month at the LONI in January before moving to Epidaure where he finished his Ph.D. thesis.

P. Thompson was invited to visit the Epidaure research group in November 2003. This was the opportunity to discuss with the program participants, give a seminar about his work, and attend A. Pitiot's Ph.D. defense.

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. The journal was awarded this year its first ISI impact factor (2.7).

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

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

9.1.2. Participation in the organization of conferences

- N. Ayache and H. Delingette organized the first International Symposium on Surgery Simulation and Soft Tissue Modeling (IS4TM'03) on June 12-13 2003 in Juan-Les-Pins, France. The objective of the symposium was to bring together the researchers of this emerging field and included three keynote speeches from Pr. David Hawkes of King's college (London), Pr. Simon Warfield of Harvard Medical School and Pr. Suzuki of Jikei University. The proceedings of this symposium [22] gather the contributions of researchers from 13 different countries and are published in the LNCS series. A sequel of this symposium will be organized in 2004 in Boston (USA).
- N. Ayache is a member since its creation in 1998 of the scientific board of the MICCAI conference (Medical Image Computing and Computer Assisted Intervention: <http://www.miccai.org>) held each year on a different continent. N. Ayache has been a member of the scientific board of several conferences held in 2003, including WBIR (Philadelphia, USA) and FIMH'03 (Lyon).
- G. Malandain was member of the scientific board of DGCI 2003, IPMI 2003, MICCAI 2003, DICTA 2003.
- H. Delingette was member of the scientific board of CFM 2003, MICCAI 2003, CASA 2003, Orasis 2003.
- X. Pennec was member of the scientific board of MICCAI 2003 and WBIR 2003.

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 assisting G. Kahn (Vice-President for Research of INRIA) on the topics related to "computer science for health care".

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. Bardinnet and J. Dauguet for the small classes. These 2 modules are common to the DEA MVA of ENS Cachan "Mathématiques, Vision et Apprentissage".
- 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) with the participation of Marius Linguraru.
- DEA IFA, Marne-la-Vallée G. Malandain is responsible of a module of 4 lectures on biomedical images, with the participation of E. Bardinnet, C. Barillot, and H. Delingette.
- IUT Nice Côte d'Azur V. Moreau-Villéger teaches mathematical analysis and probabilities at the computer science department(64 hours of discussion).
- DUT informatique, option imagerie numérique, université de Nice Sophia-Antipolis X. Pennec gave two introductive lectures on Medical Image Analysis (3 hours).

9.3. PhD Theses and Internships

9.3.1. PhD defended in 2003

1. Sébastien Granger, *Une approche statistique multi-échelle au recalage rigide de surfaces; Application à l'implantologie dentaire*, École des Mines de Paris, April 7 2003. Jury: Y. Rouchaleau (President), I. Bloch (Referree), R. Horaud (Referree), N. Ayache (Supervisor), X. Pennec (Co-supervisor), R. Derycke (AREALL, invited).
2. Alain Pitiot, *Segmentation automatique des structures cerebrales s'appuyant sur des connaissances explicites*, École des Mines de Paris, November 26 2003. PhD conducted jointly at Epidaure and at LONI, UCLA, USA. Jury: J.-P. Marmorat (President), J.-F. Mangin and D. Vandermeulen (Referees), P.M. Thompson (Supervisor at UCLA), N. Ayache (Supervisor at INRIA), H. Delingette and G. Malandain.
3. Maxime Sermesant, *Modèle électro-mécanique du cœur pour l'analyse d'images cardiaques*, University of Nice-Sophia Antipolis, May 26 2003, Jury : M. Barlaud (President), I. Magnin and D. Hill (Referees), N. Ayache (Supervisor), H. Delingette (Co-supervisor), O. Gérard, F. Clément.
4. Jonathan Stoeckel, *Outils statistiques d'aide au diagnostic d'imagerie fonctionnelle pour la maladie d'Alzheimer*, École des Mines des Paris, March 13 2003. Jury: J.-P. Marmorat (President), B. Gibaud and M. Zanca (Referrees), N. Ayache (Supervisor), J. Darcourt (Co-supervisor), G. Malandain, J.-P. Thirion.
5. Clément Forest, *Simulation de chirurgie par coelioscopie : contributions à l'étude de la découpe volumique, au retour d'effort et à la modélisation des vaisseaux sanguins*, École Polytechnique, May 19 2003, Jury : J.-J. Levy (President), Y. Payan and C. Chaillou (Referees), N. Ayache (Supervisor), H. Delingette (Co-supervisor), L. Soler.

9.3.2. Current PhD

1. Vincent Arsigny, *Analyse statistique de formes, application aux atlas anatomiques*, École Polytechnique.
2. Pierre-Yves Bondiau, *Utilisation et validation du recalage d'image dans l'élaboration du plan de traitement en radiothérapie*, Nice-Sophia Antipolis University.
3. Olivier Clatz, *Modélisation du comportement biomécanique du cerveau : application à la prédiction et à la simulation d'une intervention neuro-chirurgicale*, École des Mines de Paris.
4. 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.
5. Guillaume Dugas-Phocion, *Modélisation et segmentation des lésions de sclérose en plaques en IRM multi-séquences*, École des Mines de Paris.
6. Guillaume Flandin, *Utilisation d'informations géométriques pour l'analyse statistique des données d'IRMf*, Nice-Sophia Antipolis University. PhD in collaboration with J.-B. Poline at CEA/SHFJ, Orsay.
7. Céline Fouard, *Extraction de paramètres quantitatifs dans des images médicales 3D de réseaux vasculaires*, Nice-Sophia Antipolis University. CIFRE fellowship from the compagny TGS.
8. Valérie Moreau-Villéger, *Analyse d'images échocardiographiques multidimensionnelles*, ENS Cachan.
9. Stéphane Nicolau, *Construction d'un système de réalité augmentée pour la chirurgie hépatique*, Nice-Sophia Antipolis University. PhD in collaboration with L. Soler, IRCAD, Strasbourg.

10. Rasmus Paulsen, *Statistical Shape modeling of the human ear canal*. Technical University of Denmark.
11. Mauricio Reyes, *Fusion d'images CDET/PET avec des images tomodensitométriques pour la détection précoce des tumeurs pulmonaires*, Nice-Sophia Antipolis University. PhD in collaboration with J. Darcourt, CAL, Nice.
12. Radu-Constantin Stefanescu, *Thérapie guidée par l'imagerie médicale : Parallélisation et validation d'algorithmes de recalage*, Nice-Sophia-Antipolis University.

9.3.3. Participation to thesis committees

Nicholas Ayache participated to several thesis committees: Timo Makela in Helsinki (as opponent), Bertrand Thirion (as examiner, Sophia), Arnaud Cachia (as referee, Paris), Clément Forest, Sébastien Granger, Alain Pitiot, Maxime Sermesant and Jonathan Stoeckel (as supervisor).

Grégoire Malandain participated to several thesis committees: Jonathan Stoeckel (co-supervisor), Isabelle Corouge (referee, Rennes).

Hervé Delingette participated to several thesis committees: Maxime Sermesant (co-supervisor), Clément Forest (co-supervisor), Jean-Marc Schwartz (referee, Laval University, Canada), Jussi Tohka (referee, Tampere University of Technology, Finland)

Xavier Pennec participated to the PhD thesis committee of Sébastien Granger as co-supervisor, and Niels Holm Olsen (as opponent, IT University of Copenhagen, Denmark).

9.3.4. Training activities

Olivier Commovick [97]
 , *Utilisation d'atlas anatomiques numériques pour la cancérologie*, DEA Mathématiques, Vision, Apprentissage, École Normale Supérieure Cachan.

Thibaut Bardyn [96]
 , *Modèles biomécaniques déformables : introduction de méthodes algébriques pour le calcul de la déformation*, DEA Mathématiques, Vision, Apprentissage, École Normale Supérieure Cachan / École Polytechnique.

Heike Hufnagel *Robust deformable registration of medical images using block-matching*, diploma thesis, Institute of Mathematics, Medical University of Luebeck.

9.4. Participation to workshops, conferences, seminars, invitations

We only give here the invited participations. Readers are kindly asked to report to the references for the participation to conferences with a submission process.

- **Nicholas Ayache** gave invited lectures at Institut Pasteur (Paris), at a workshop on Image-guided Surgery in Nuremberg (Germany), at CARS'03 (Computer-Aided Radiology and Surgery) in London (UK), at CAIP'03 (Computer Analysis of Image Patterns) in Groningen (Netherlands), at SGI-Symposium and Jikei University in Tokyo (Japan), at DICTA'03 in Sydney, at ILIATECH (Rocquencourt).
- **Grégoire Malandain** gave invited lectures at the INSERM U594 unit (*NeuroImagerie Fonctionnelle et Métabolique*) in Grenoble (march 2003) and in the Copenhagen Image and Signal Processing *Warshop* (september 2003)

- **Hervé Delingette** gave an invited lecture at the Dimacs workshop on medical applications in computation geometry organized at Rutgers University (NJ, USA) in April 2003, at the Société Française de Physique Médicale conference in Rheims in June 2003, at the workshop on deformable models during the SCIA (Scandinavian Conference on Image Analysis) conference in Gothenburg (June 2003), at the Swiss CO-Me (Computer aided and image guided medical interventions) plenary meeting in Braunwald (Switzerland), at the Conférence Française de Mécanique in Nice (Sept 2003), at the European School of Surgical Robotics in Montpellier (Sept 2003) and at the Inria-Inserm meeting in Paris (October 2003).
- **Xavier Pennec** gave an invited lecture at the IT University of Copenhagen (Denmark) in January, a tutorial talk on validation in medical image processing at MICCAI'03 (Medical Image Computing and Computer Assisted Intervention) in Montreal (November), and was invited to participate to the *Imaging, Medical Analysis and Grid Environments (IMAGE)* workshop organized by the National e-Science Center in Edinburgh in September.

9.5. Scientific prizes

- **Vincent Arsigny** obtained one of the *5 best student paper award* at the MICCAI'03 conference for a work with X. Pennec and N. Ayache entitled *Polyrigid and Polyaffine Transformations: A New Class of Diffeomorphisms for Locally Rigid or Affine Registration* [48].
- **Maxime Sermesant** received the second prize from the french association SPECIF for his research work performed during his thesis entitled "An electromechanical model of the heart for medical image segmentation and the simulation of cardiac pathologies" supervised by N. Ayache and H. Delingette. He was also awarded a label from the Telecom Valley association for the the best Ph.Ds in computer science prepared in Provence-Alpes-Côte d'Azur Region.

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