Previous Activities and Results of CREATIS 2005-2009

General presentation

1. Presentation

CREATIS (Centre for Research and Applications in Image and Signal Processing), Centre de REcherche et d'Applications en Traitement de l'Image et du Signal, is a research Unit common to the National Institute for Applied Sciences (INSA) in Lyon, University Claude Bernard Lyon 1, CNRS (since 1987) and Inserm (since 2004). The presence of 18 members of hospital staff meant that in 2005 the Hospices Civils de Lyon (HCL) became full partners in the Unit. Since 2007, The Centre Leon Berard (CLB) is also present with 1 Hospital staff member.

CREATIS, Inserm U630 has been recognized by Inserm on January 01, 2004. The Unit belongs to the "Institut National des Technologies pour la Santé". It is assessed by Specialized Scientific Commission (CSS) n°3, entitled "Sciences et Technologies Appl iquées à la Médecine (STAM)".

CREATIS, UMR CNRS 5220, has been associated with the CNRS for 24 years. The LRMN, UMR CNRS 5012, joined CREATIS in 2007. The laboratory is attached to the CNRS "Institut des sciences et technologies de l'information et de l'ingéniérie (INST2I)" and to the "Institut des Sciences Biologiques" (INSB). The main evaluation sections are 7 (main), 30 and 09.

CREATIS is a laboratory at the INSA in Lyon. It is attached to the Electrical Engineering department and, thanks to the researcher-lecturers of which is composed, there is also a link with the department of Telecommunications, Computer Science and the Undergraduate Studies cycle.

It is a laboratory at the University Claude Bernard Lyon 1. It is partly attached to the "Faculté des Sciences et Technologies"(ST) in the department GEP and in part to the health sector thanks to its researcher-lecturers in science and medicine.

The laboratory is composed of 190 members of staff, distributed as follows:

- 60 researchers and researcher-lecturers, including 13 full time researchers and 18 physicians
- 23 Research engineers and technicians
- 67 doctoral students including 12 physicians
- 11 post-doctoral students
- 20 master students
- 9 guest researchers from abroad and trainees.

2. Scientific objectives and missions

The mission of CREATIS is to push away the frontiers of knowledge in medical Imaging. To succeed, CREATIS promotes and develops new imaging techniques, instrumentation, algorithms and softwares to solve unanswered biological and medical questions. This is achieved by means of the association of three scientific communities, attached to the information and communication science and technology, instrumentation and methodology and life sciences.
The Life Science researchers and clinicians (HCL) of CREATIS have the mission to enhance and select major unanswered questions in their field of competence. The specialists of the imaging acquisition devices must develop the adapted tools and new imaging modalities (XRay, MRI, MRS, RF US, optics) to provide significant and quantitative observation data. The researchers in signal and image processing propose new algorithms to extract quantitative models from such front edge multi-physical data to help answering the initial biological and medical questions.

3. Specificity of the laboratory: an interface between Imaging Science and Life Sciences

It is this specificity that can both explain and justify the fact that the unit is located on both academic and clinical sites that are the Doua campus in Villeurbanne, the Groupement Hospitalier Pôle Est (GHPE) in Bron, the Centre Leon Berard (CLB) in Lyon and the European Synchrotron Research Facility (ESRF) in Grenoble.

4. Functional organization

In order to make this scientific project a success, and making optimal use of its resources, the unit is composed of a board of management, a board of directors and a Unit Council.

The Unit's board of management

The Unit is headed by a Director, I. Magnin, and 2 vice Directors D. Revel (clinics) and D. Graveron (NMR). The priority of the Unit's board of management is to encourage and facilitate encounters and interactions between the researcher-lecturers and researchers belonging to the three communities. This strong political volition can be seen through the teams' composition described in the structural organization part.

The Board of management

The board of management receives advices with regard to its strategic choices from a board of directors including the managers of the scientific teams, the manager of the computing team, the communications adviser and the development adviser. The board of directors meets at least every two weeks, on Monday. The decisions of each meeting are compiled on one page that is spread out to every member of the unit.The Unit also has a Training adviser, an IT security adviser and a Hygiene and Safety adviser.

The Unit council

Statuory affairs are dealt with in a regulatory manner by the Unit Council.

5. Structural organization

The research teams

The Unit is composed of various kinds of teams designed to facilitate the pluri-disciplinary and trans-disciplinary researches at the interface between Sciences and Life Sciences.

Two mixed life sciences and image processing and modeling teams which objectives are two folds: 1) The life sciences researchers raise important, unanswered, questions in the fields of life sciences and health covered by their fields of expertise, Heart-Vessel-Lung and Brain, 2) the information processing researchers contribute to solve such biomedical questions by adapting or developing new algorithms and digital processing methods and models in close interaction with the life sciences researchers

Team 1: Imaging of the Heart-Vessels-Lungs
Team 6: Brain Imaging

Two information and communication science and technology teams which objectives is to produce new knowledge in digital processing, modelling, inverse problems and quantification for the aid for diagnosis or therapy focused towards dedicated biological and medical application fields.

Team 2: Images and Models
Team 7: Tomographic Imaging and Therapy with Radiation

Three engineering and methodology teams produce new data and images acquisition strategies, signal processing techniques for US image formation, MRI excitation sequences, new methodology in spectroscopy often involving new contrast agents.

Team 3: Ultrasound imaging
Team 4: Imaging and exploring methodologies in NMR
Team 5: Methods and systems in MRI and optics

Team 8: cellular and molecular Imaging: a particular case

This very small team includes 2 researcher-lecturers M. Janier, PUPH and C. Billotey, MCUPH who recently recruited D Kryza as a MCUPH. This team performs interesting researches in molecular imaging but with very few interactions with the others teams of the Unit the last 3 years. On the contrary, the team progressively increased its research interactions with the laboratory of physico-chimie des matériaux luminescents (LPCML) so it was jointly decided that it would be more fruitful for the future that this team joins the LPCML. The Team main results and context are briefly summarized by M. Janier, head of the team, as follows :

"Although a molecular imaging approach had been identified within CREATIS, it was not developed as expected for several reasons (in particular a lack of shared vision within CREATIS, the CERMEP is almost exclusively oriented neurology and was not willing developing the synthesis of the tracers we proposed, unexpected ending of the Genopole fundings). Therefore our small group could not develop a coherent

strategy on all the activities planned. We then refocused on the development of nanoparticles as diagnostic or therapeutic agents, and have strengthened our links within local and national network. It allowed us to obtain more fundings (ANR APTAPROBE, CancerNanoTransfert canceropole CLARA, OSEO FUI) to carry out these specific developements. Our work aims to validate experimentally and clinically nanoparticles developed by LPCML (UCBL1-CNRS). The project OSEO-FUI is on pre-clinical validation (models of glioblastoma and peritoneal carcinomatosis) of Holmium particles activated using medical cyclotron. The CancerNanoTransfert project covers the validation of particles of gadolinium as radiosensitizer. The first proof of concept will target melanoma and chondrosarcoma. The APTAPROBE project aims to provide these various nanoparticles with targeting properties by functionalizing them with aptamers specific to different cell or tissue targets. The first approach involves the targeting of MMP9, but other aptamers will be developed. D Kryza, as a pharmacist, is involved in pre-clinical validations but he also plays a key role in facilitating the study of bio-distribution in labelling the nanoparticles with dedicated radioactive isotopes. Other small ancillary projects are undergoing in order to consider future collaborations in molecular imaging using nuclear and MR imaging. Three patents have been filled(HCL- UCB), several publications in journals of very high level are released." The major publications of the team can be found on http://www.creatis.insa-lyon.fr/site/fr/publications.

The Common departments

Computer science

The computing department is transversal for the entire Unit so that the developments initiated in the research teams can easily be transferred, validated and evaluated by the researchers in the Life Sciences domain.

Administration

The secretarial and administration department is also transversal for the entire Unit. It is responsible for managing the credits received from our trustees and their subsidiaries, that is, INSA, Insavalor, UCB, Ezus, LST, CNRS and Inserm, with the software specific to each partner, particularly Nabucco,SIFAC, X-Lab and Safir.

Transfer

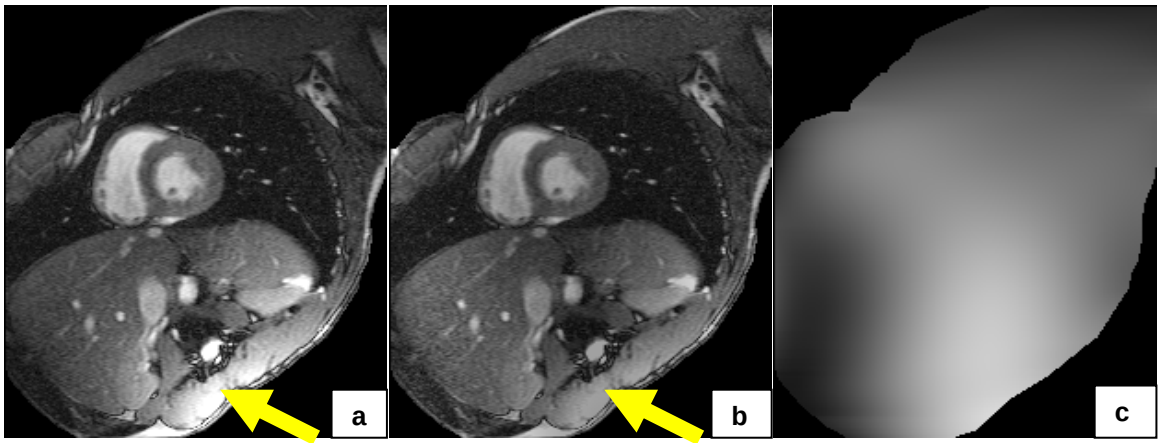
The Development unit was strengthened in 2005 by the appointment of an INSA IR at its head. The unit's mission is to assist the transfer and industrial development of our research (sale of software and licences, image processing services for industry).

6. Key results

The main scientific results obtained during the last four years are given below. These key events provide a good overview of the main contributions of the laboratory during this period, without exhaustivity. The first three ones have been selected as national key events by the Inserm or the CNRS.

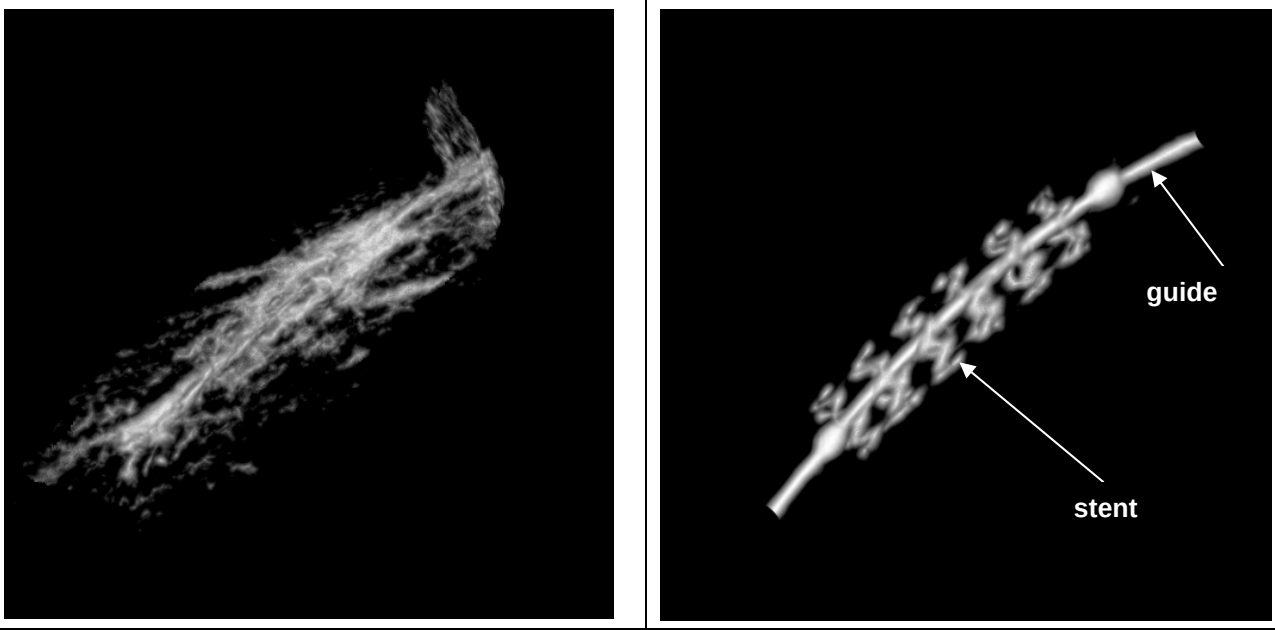
Team 1: Artefactless quantitative MRI

Three researchers of the laboratory and a Chinese collaborator proposed a new processing technique to suppress MRI artefacts from medical images. The method is based on a mathematical model of the spectra using a decomposition of the signal into a linear combination of singular functions. The result is the elimination of the noisy low spatial frequencies containing field inhomogeneities (noise) without distorting the useful signal within the image [LUO-05]. **Elected « Inserm Key event » of the year 2005**



Legend: (a) Image before correction, (b) image after correction, (c) Inhomogeneity of the intensity background.

Teams 1,2,7 : 3D reconstruction of a "stent" in a coronary artery of a patient
with Hospices Civils de Lyon and General Electric Healthcare.



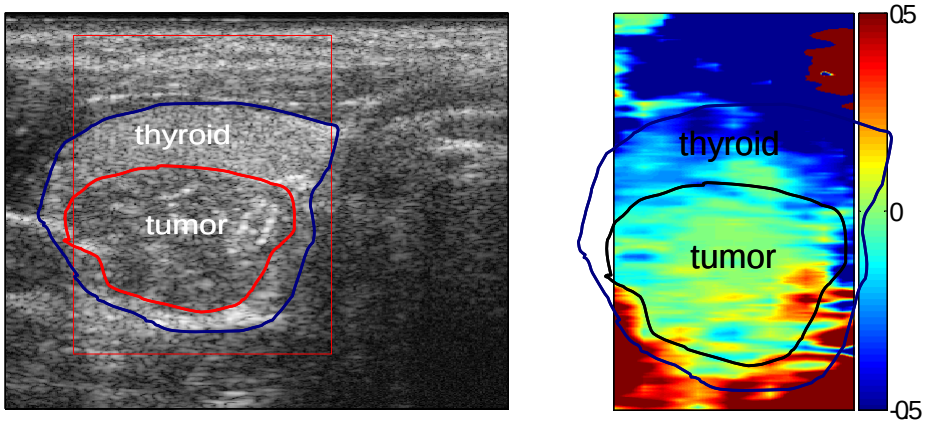
a **b**

Legend: 3D tomographic reconstruction of a stent deployed in a coronary artery of a pig (voxel of 0.1 mm3 voxels, size of images: 2563, stent diameter: 3mm) a) without motion correction, b) after our algorithm has corrected the local cardiac and breathing motion.

The problem was to control the deployment of a stent (metal prosthesis) in the treatment of stenosis in a coronary artery. To this aim, we proposed a new motion correction method for tomographic reconstruction in X-ray cardiac rotational angiography. This technique allows the visualization of the stent in a coronary artery in three dimensions, without blurring artefacts. It is then possible to see the mesh of the stent and perform measurements in order to monitor its deployment. The first results obtained in pigs in vivo are remarkable (see figure). This technique, which has a major interest for the patient is currently undergoing clinical evaluation[Perrenot-07]. http://www.creatis.insa-lyon.fr/web2/fr/General/ **Elected « CNRS Key event » of the year 2008.**

Team 5. HR-MRI of articular cartilage using small animal dedicated array coils
Due to limited size of small animal joints, cartilage assessment is very challenging. Based on modeling methods, a two-channel phased array coil for High spatial Resolution MR Imaging (HR-MRI) of the articular cartilage (rat, guinea pigs) [RENG-09, IEEE TBE] considerably improving the SNR (2.2 gain) as well as the signal uniformity was designed for 7T. These later parameters are mandatory for image segmentation and to quantify cartilage morphology (thickness, volume). Gain in SNR was used to decrease voxel size down to 51 x 51 x 94 µm3. The spatial resolution value achieved in similar conditions (in vivo at 7T) has never been reported in the literature before. Moreover, HR-MRI of both joints performed simultaneously significantly increase throughput [GOEB-08, *Biomed Mater Eng*]. These results obtained in collaboration with UMR 7561 have been retained as key result 2009 by the CNRS INST2I http://www.cnrs.fr/inst2i/recherche/faits-marquants/2009/imagerie-teslas.htm. **Elected «CNRS Key event » of the year 2009**

Team 3: real time compression estimation of thyroid based on deformable mesh controlled with a bilinear parametric motion model.
When an external compression is applied on thyroid, complex soft tissue deformations appear in the concerned region. Deformation analysis is a mean to collect information about tissue stiffness and pathology. The ultrasound imaging team of Creatis developed a local motion estimation method to map the thyroid tumour. The method uses a deformable mesh controlled with a bilinear parametric motion model to compute a map of the Local Direction of the Displacement (LDD parameter). [A. Basarab et al, 2008; A. Basarab et al 2009]

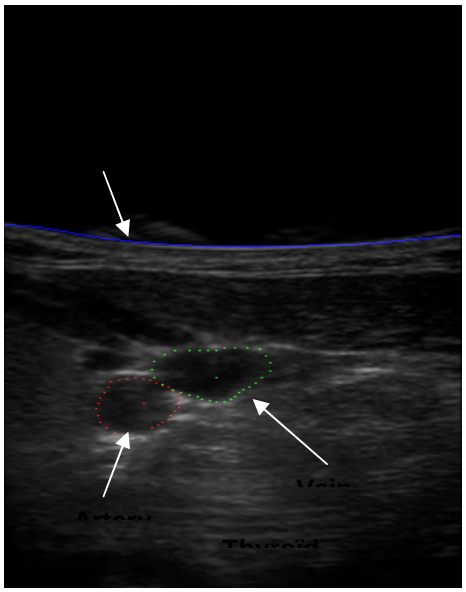


Legend: ultrasound B-mode image (left) and the proposed image of a thyroid tumour (right). Contours are plotted by the radiologist. The map of the Local Direction of the Displacement (LDD parameter) shows a homogeneous region inside the thyroid corresponding to the malignant tumour.

Team 3 with Theraclion company

Patented algorithm for real time anatomic monitoring in ultrasound imaging – application to monitoring of thyroid pathologies treatment by High Focused Utrasound (HIFU)

The ultrasound imaging team of Creatis has developed an algorithm which enables to follow in real time, i.e. at the ultrasound images acquisition rate, different anatomical structures (artery, vein, skin) during the treatment by HIFU of the thyroid gland pathologies. The efficiency of the algorithm comes from its extreme simplicity and its robustness despite the low signal to noise ratio of the ultrasound images speckle as well as the numerous parasite movements (carotid artery pulsatility, breathing, therapy by HIFU). The originality of the algorithm has been patented in co-propriety with the company Théraclion, expert in treatment of thyroid pathologies by HIFU. National and International Patent DPI 02154-01-N°2008/54572-PCT/FR2009/051305 – D. VRAY et al., Co-property CREATIS, Theraclion, CNRS, INSA-Lyon.



Legend : Ultrasound image of the thyroïd during HIFU treatment. The algorithm enables to follow in real time the vessels and the skin.

Teams 4, 6: Neuroinflammation in Cerebral Ischemia and Stroke

Validation of USPIO-enhanced MRI to monitor post-ischemic neuroinflammation in a murine model of focal cerebral ischemia (Wiart et al 2007, Desestret et al 2009) and translation of the approach into the clinics in stroke patients (Nighoghossian et al 2007, Cho et al 2008).

Team 5 : Patented endoluminal coil for human

The development of endoluminal radiofrequency (RF) coils removes the obstacles inherent to the investigation of deep organs. This technique is particularly useful in the diagnosis of ano-rectal pathology. The high spatial resolution achievable with endoluminal coil provides detailed information on the local

anatomy and pathology. In this context, a patented endoscopic coil [BEUF-07, PCT/FR2008/052248], fully developed by team 5 and dedicated to the exploration of the anal sphincter, is undergoing clinical evaluation. This study aims to compare high spatial resolution MR imaging performed at 1.5T with echo endoscopy in anal incontinence diagnosis.

Team 6: Micro-coils

A new concept of implantable micro-coils (500x1000 mm²) fabricated by electroplating technique has been developed [Baxan et al. 2008] for biomedical applications (spectroscopy and imaging). This work was particularly noted in David Bradley's article 'A brainy approach to NMR coils', on the NMR Knowledge Base. See http://www.spectroscopynow.com at NMR : A brainy approach to NMR coils .

7. Grid computing for distributed medical imaging

To support the ever-growing computing needs of medical image analysis software produced at the lab, an in-house cluster has been exploited for years already and collaborations with computing centers (e.g. CC-IN2P3 Lyon and Pleiades cluster at EPFL) have been established. Foreseeing the need for computing power and data management at a larger scale, CREATIS has been implied in grid projects since their early ages (regional: RAGTIME project ; national: ACI Medigrid 2003-2005, ACI AGIR 2005-07 and ANR Gwendia 2006-2009; international: DATAGRID (2000-2003), EGEE-I/II/III, ICT-Asia Oncomedia) and pioneered the deployment of biomedical applications on those platforms. The SHARE European program (share-roadmap.jpg) recently drew a roadmap of the research challenges in the field of grids. It appears clearly that CREATIS that began to work on that topic in 1997 was among the visionaries. CREATIS (pilot of the medical imaging application in EGEE WP4) was the first laboratory to study the potentialities of medical Imaging on the grid.

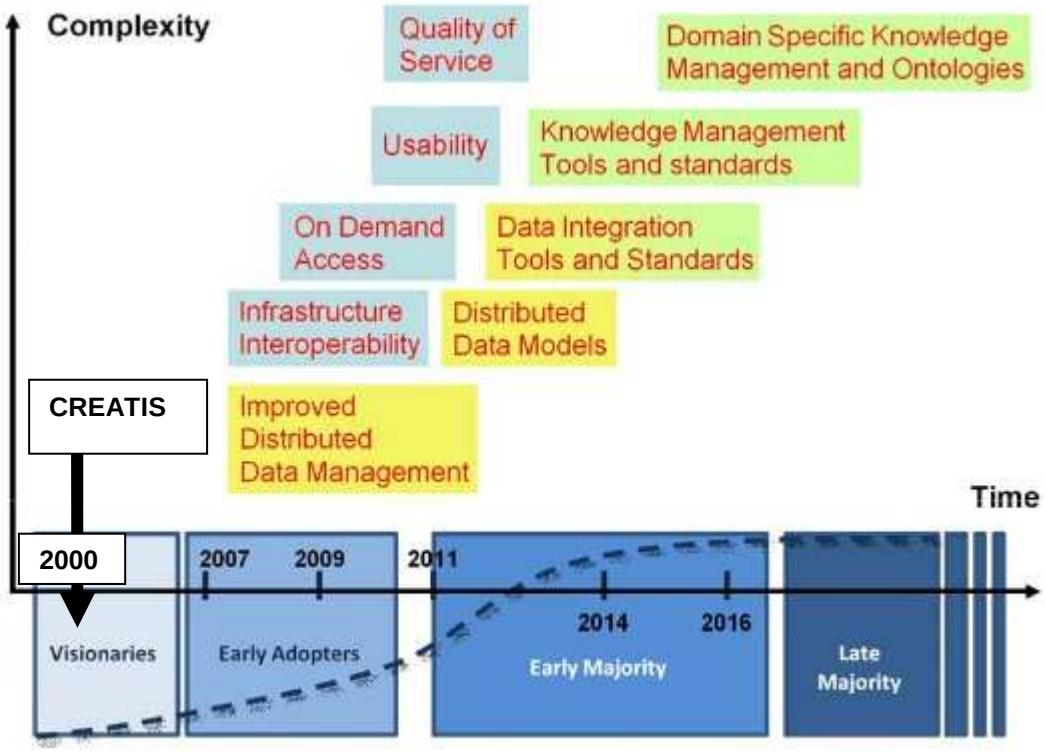


Figure 2: research challenges as a function of time and complexity

With the end of the EGEE project and the birth of a European Grid Initiative (EGI), production grids are now at the crossroads of development and exploitation phases. Ensuring the sustainability of a grid infrastructure for biomedical applications in Europe is a major challenge to which we plan to contribute by a strong implication in the French National Grid Initiative through the CNRS Grid Institute, adopting grids and other distributed systems as scientific instruments for research.

Production exploitation of computing and data storage platforms is targeted for the coming years. Several applications, such as simulation of the imaging process and radiotherapy have already been deployed on the Grid by CREATIS such as (SIMRI (magnetic resonance imaging simulator, author CREATIS), FIELD

(ultrasound imaging simumator, author Jensen), Sorteo (PET imaging simulator, authors: CERMEP, Mc Gill), GATE (PET imaging simulator, author external), cardiac image analysis (segmentation and motion estimation, author CREATIS) and fluid simulation for aneurism stroke (author CREATIS) are now deployed either on EGEE or on clusters. Their planned integration in an integrated environment for distributed execution will further facilitate daily access to computing and data storage resources. Heavy experiments such as multi-modality simulations of the beating heart or large-scale studies on patient databases are targeted, reducing computation time from years to hours. New methods for model adaptation (patient-specific parameter tuning), algorithms evaluation and validation could then been envisaged. Besides, exploiting dedicated parallel machines such as Graphical Process Units (GPUs) is expected, bringing computation times closer to clinical constraints (from hours to minutes).

Teams 2 and 7: Grid computing for simulation Elected at a European level

ThIS (Therapeutic Irradiation Simulator) is a Geant4 based software dedicated to the Monte-Carlo simulation of irradiations of living tissues with photons, protons or light ions beams for cancer therapy developed by the teams 2 and 7. It was selected as a User success story and future challenge by Vangelis Floros, GRNET; Cal Loomis, LAL/CNRS during the NA4 Activity EGEE'08, 22-26 September 2008, Istanbul, Turkey.

8. Transfer / Development / Software licence/ Patents/Start'up

Software developments

Free licence software http://www.creatis.insa-lyon.fr/NEW/General/Logiciel.php

Among the most important common software developments, we can mention:

- Gdcm (http://www.CREATIS.insa-lyon.fr/Public/Gdcm): Library written in C++ with a free BSD licence. It has all the functions necessary for reading and writing images in the DICOM format, which is indispensable for all applications that handle medical images. Since January 2005, it has been distributed with the ITK library developed by the company Kitware.
- DaVaW (http://www.CREATIS.insa-lyon.fr/Public/DaVaW): Library written in Python with a free BSD licence. It provides highly interactive software components (2D, 3D and sequence visualization, drawing tools for regions of interest, curve displays and so on), as well as a pattern for designing applications that define observation, cooperation and synchronization models, thus guaranteeing the stability and reliability of large software packages [REGR-05-ICIP'05].
- CreaTools: Evolutive software integration platform written in Python and C++. It is based on the components and pattern of the DaVaW library. There are currently three modules integrated into CreaTools, one for analyzing brain perfusion, one for analyzing cardiac perfusion and one for analyzing atheromatous plaques.

2005 Licensed Software: Maracas in 2005 licensed to Medasys, under licensed to Hitachi Japan.

jMRUI Software Package

The software package jMRUI with Java-based graphical user interface enables user-friendly time-domain analysis of Magnetic Resonance Spectroscopy (MRS) and Spectroscopic Imaging (MRSI), and HRMAS-NMR signals. It is presently developed in the context of the European Marie Curie project 'FAST' (Team 6). This software, considered as one of the 'Gold Standards' in MRS, is free for Academia and currently used by more than 1200 research groups and hospitals worldwide. Licenses have been sold to the main pharmaceutical companies. See http://www.fast-mariecurie-rtn-project.eu.

2008 a new start'up (the 3rd) was initiated by Creatis in 2008. Its name is CIRMA, headed by MJ Seurin (IR CNRS) devoted to PET MRI diagnostic Imaging

9. CREATIS behind the international FIMH (Functional Imaging and Modeling of the Heart) conferences.

In 2001, CREATIS was behind the organization of a series of workshops on functional imaging and modeling of the heart (FIMH) with Finnish partners from the LBE at the Technology University of Helsinki in Espoo and the departments of radiology and cardiology from the Central hospital in Helsinki. CREATIS organized FIMH'01 with its Finnish partners in Helsinki, then FIMH'03 in Lyon. and intends to organize FIMH'13 with its Chinese partners from the LIA Project in 2013.

10. The Unit and training in research

In order to respect the main disciplines that make up the basic skills of the laboratory, the unit is composed of 3 "équipes d'accueil doctorants (EAD)", attached to 3 different écoles doctorales (ED). These three EAD are in the fields of Signal and Image Processing, Electrotechnics, Electronics, Automatics ED (EEA # 160) Acoustics, Mechanics, Energetics, Civil engineering, Acoustics ED (MEGA # 162) and Medical imaging, Interdisciplinary Science-Health ED (EDISS # 205).

Most of the researchers and researcher-lecturers in the Unit intervene in the teaching of the initial training modules (Master) as a complement to these three doctoral schools. Some take part in the organization or

are responsible for a course of study within these different doctoral schools: masters SIDS EEA school and Master IMB EDISS school. D.Revel assumes the directorship of the EDISS doctoral school since 2006.

11. Platforms

CREATIS has its own plateforms common to the all the teams of the Unit
- Optical devices
- RF Echographs (6 devices)
- NMRI systems (2T and 4.7T) and 3,3T magnet

Imaging platforms

- CREATIS is a very important user and also provider for the external “Centre d'Exploration et de Recherche Médicale par Emission de Positons” CERMEP platform headed by G. Gimenez including 4 departments TEP, MRI 1.5 T Imaging (D Sappey-Marinier) and Animage Multimodal imaging in small animals (HF US, high field MRI 7T, microPET, microCT X-ray) are the more important for CREATIS
- ESRF X-ray synchrotron imaging – line 19 – Grenoble.

12. Regional projects

In the scope of the “Doua plan Campus”, CREATIS intends to develop collaboration with the LIRIS on 3D Imaging (meshing).
CREATIS is a partner in the Hadronthérapie/Etoile project supported by UCB. This national project involves the IPNL, LIRIS and IN2P3 Lyon laboratories.
CREATIS has strengthened its ties with the Institut Fédératif des Neuro-Sciences de Lyon (IFNL)
CREATIS is a member of the Institut de Médecine Théorique (IMTh) directed by J.P. Boissel.

13. National and international opening

The laboratory plays a role at the national level in its field. In synergy with Grenoble, it coordinated the State-Region plan contract (CPER) in Engineering for Health 2000-2006 (I. Magnin).
The laboratory is well integrated into the French community thanks to its participation in several research groups attached to the CNRS among them ISIS. It also promoted the GDR STIC Santé common to both the CNRS and INSERM EPST with I. Magnin and F.Peyrin currently vice directors.
At the international level, the laboratory is recognized by each community. The following table (annex) summarizes the Unit’s international collaborations resulting in publications.

14. European projects

Y. Cremillieux and D. Graveron manage 2 Marie Curie European networks: FAST and PHELINET (2006-2009) and the laboratory belongs to a 3rd one: Warthe.
D. Revel is the correspondant of the (EIBIR) European Institute for Biomedical Imaging Research (2006 - 2009).
CREATIS is in the core group of the European NoE VPH (Virtual Physiological Human) (2008-2012).
CREATIS is promoting medical applications into the European grid projects: EGEE 2 (2005 -2007), EGEE 3(2008-2010) (Enabling Grid for E-science in Europe) includes 27 countries.
CREATIS is also in STREPs I-Know (N Nighoghossian) (2005–2008) and COST P19 (2006–2010 G Courbebaisse, MC members and WG4 leader).

CREATIS - LRMN
Centre de Recherche et d'Applications en Traitement de l'Image et du Signal
31 Mai 2009

Directeur : I. Magnin
Directeurs adjoints : D. Graveron et D. Revel

Assistante de Direction : Christiane Jeanguillaume
Secrétaire de Direction : Fatima Berkaï (50 %)

Eméritat : R. Goutte

Equipe 1
Imagerie cœur-vaisseaux-poumons

Resp. P. Clarysse
Adj. L. Boussel
P. Croisille
Ph. Douek
C. Guerin
I. Magnin
M. Orkisz
D. Revel
J.C.Richard
Y.M. Zhu
G. Courbebaisse* (50%)

Equipe 2
Images et Modèles

Resp. R. Prost
Adj. D. Friboulet
H. Benoit-Cattin
O. Bernard
T. Glatard
T. Grenier
C. Lartizien
C. Muller
C. Odet
S. Valette
F. Bellet* (50%)
S. Camarasu-Pop* (50%)

Equipe 3
Imagerie ultrasonore

Resp. : D. Vray
Adj. P. Delachartre
O. Basset
E. Brusseau
C. Cachard
D. Vray
G. Gimenez (50%)
F. Duboeuf* (50%)

Equipe 4
Imagerie et methodologies Exploratoires en RMN

Resp. Y. Cremillieux
Adj. E. Canet
B. Montcel
B. Neyran
M. Wiart
S. Gaillard ** (75%)
F. Foulon* (50% CDD UE)

Equipe 5
Méthodes et systèmes en IRM et optique

Resp. O. Beuf
Adj. F. Pilleul
S. Cavassila
V. Detti
P. Girard
A. L. Perrier
E. Perrin
H. Ratiney
D. Grenier* (50%)
R. Sablong (80%)

Equipe 6
Imagerie cérébrale

Resp. D. Graveron*
Adj D. Sappey Marinier
Y. Berthezene
F. Cotton
L. Derex
F. Durand Dubief
L. Fakri Bouchet
J.C. Froment
M. Hermier
N. Nighoghossian
F. Di Cesare* (CDD UE)
F. Foulon* (50% CDD UE)

Equipe 7
Imagerie tomographique et thérapie par rayonnements

Resp. F. Peyrin
Adj. D. Sarrut
C. Carrie
V. Maxim
M. Robini
C. Olivier*

Equipe 8
Imagerie cellulaire et moléculaire

Resp. M. Janier
C. Billotey
D. Kryza

Service Administratif & logistique : Resp. B. Barchasz*

Site INSA

Accueil : M. Lissac
Secrétariat Unité & Master : F. Berkaï (50%)
Gestion: U. Max, (CDD)
G. Pequay (CDD)
Logistique : J. Barat

Site CPE

Gestion-Secrétariat : F. Larregain
I. Thévenoux (80%)

Site hospitalier Est

Gestion-Secrétariat: S. Boudjema (50 %) (CDD)

Services Informatiques

Développement : Resp. M. Orkisz
Adjoint D. Sarrut
L. Guigues*
J.P. Roux*
E. Davila*
V. Chenavier*(50%)
S. Camarasu-Pop*(50%)
F. Cervenansky * (CDD UE)

Réseaux et matériel : Resp. F. Bellet*(50%)
P. Ferrier

Plateformes IRM : Resp. D. Grenier* (50%)
V. Mazon* (CLD)

Plateforme Ultrasons
F. Duboeuf*(50%)

Logistique
B. Azazi
S. Basset (50%)
S. Gaillard** ACMO (25%)

Valorisation et Communication
G Courbebaisse* (50%)

Start'up CIRMA
Directeur M.J. Seurin*

** IR ou IE* ***Assistant ingénieur*

ANNEXE - CREATIS - INTERNATIONAL COOPERATION - *Period 2005 to 2009*

Forcin country	People in charge in the lab.	Forsign correspondant	Laboratoire étranger	Project title	Beginning year	Ending year	Publications	Ph.D with co-direction
Belgium	FRIBOULET Denis	D'HOOGE Jan	Medical Image Computing, Université Catholique de Leuven	Segmentation and motion estimation in echocardiography	1998	on	ALES-09a, LIEB-09b, BERN-07, BERN-06a, BERN-06d, BERN-06c, BERN-06e, DYDE-06, BERN-05	
Belgium	CAVASSILA Sophie RATINEY Hélène	ANTOINE JP	Institut de physique théorique (FYMA), Université catholique de Louvain, Louvain-la-Neuve.	Morlet wavelet analysis in Magnetic Resonance Spectroscopy	2007	on	SUVI-09	
Belgium	GRAVERON-DEMILLY Danielle	J.P. Antoine Pr. S. Van Huffel Pr. U. Himmelreich	Université Catholique de Louvain, Louvain la Neuve Catholic University of Leuven, Electrotechnic, SISTA Catholic University of Leuven, Biomedical NMR	Signal Procesing for in vivo Spectroscopy	1993	on	Marie Curie European Network FAST	
Canada	VRAY Didier	FOSTER Stuart	Sunnybrook and Women's College Health Sciences Centre, Toronto	High frequency echographic ingoing	2001	on	AOUD-06, AOUD-05b, AOUD-05c, AOUD-05a	1
Canada	BRUSSEAU Elisabeth	Cloutier Guy	LBUM, Université de Montéal, Montréal	Imaging elastic vascular properties by ultrasound imaging ; 3D elastography.	2004	on	MAUR-05, MAUR-07 DEPR-07 DEPR-09	
Canada	SAPPEY-MARINIER Dominique	Dr. D. Arnold	University Mc Gill, Montreal	Magnetic Resonance Spectroscopy	2005	on	NARA-06	
China	ZHU Yue Min	LUO Jianhua YANG Jie	Departments of Biomedical Engineering, Inst. Image Proc. & Pattern Recog., Shanghai Jiaotong University, Shanghai, Chine	MRI image reconstruction, and processing	2000	on	LUO-09a, b, LUO-08, MIAO-07, LUO-05, QIN-08a,b, XIE-08[a], XIE-07a,b,c LI-06a,b, YU-06	
China	MAGNIN Isabelle	LIU Wanyu	INSA Sino French Research Centre for Biomedical Imaging, Harbin Institute of Technology, Harbin, China	Cardiac diffusion tensor magnetic resonance imaging	2006	on	BAO-09a, b, LIU-08, BAO-08, LIU-07 BAO-07	2
Colombia	ORKISZ Maciej	FLOREZ VALENCIA Leonardo	Departamento de Sitemas y Computacion, Pontificia Universidad Javeriana	Vascular segmentation and quantification from 3D médical images.	2001	on	SCHA-09, ORKI-08, CANT-07c, CARR-07, FLOR-07b, CARR-06d,	1
Colombia	ORKISZ Maciej	HERNANDEZ HOYOS Marcela , HERNANDEZ José Tiberio	Centre d'Informatique et d'automatique en production, Université de los Andes, Bogota	Vascular segmentation and quantification from 3D médical images.	2001	on	HERN-06a, HERN-06b, HERN-05	1
Czech Republic	CACHARD Christian	HLAVAC Vaclav	Centre for Machine Perception, Dept. of Cybernetics, Faculty of Electrical Engineering, Czech Technical University, Prague	Localization of chirurgical instruments in 3D RF	2003	2007	BARV-05b, BARV-05, CACH-05, BARV-07, BARV-08	1
Czech Republic	CACHARD Christian BRUSSEAU Elisabeth	KYBIC Jan	Centre for Machine Perception, Dept. of Cybernetics, Faculty of Electrical Engineering, Czech Technical University, Prague	real-time localization of metallic tools in tissues from 3D RF ultrasounds Numerical methods for strain	2007	on	UHER-09, UHER-09a, UHER-09b BRUS-08 VAND-08, VAND-09	1

	CLARYSSE Patrick SARRUT David			imaging Image guided radiotherapy				
Czech Republic	GRAVERON-DEMILLY Danielle	Starcuk Z.	Institute of Scientific Instruments, NMR, Brno	Magnetic Resonance Spectroscopy, Quantum Mechanics	2006	on	STARC-09A,STARC-09b	
Denmark	DELACHARTRE Philippe	JENS Wilhjelm	Centre for Arteriosclerosis with Ultrasound, Technical University of Denmark	Beamforming methods for ultrasound elastography	2002	on	LIEB-05, LIEB-07	1
Finland	MAGNIN Isabelle CLARYSSE Patrick	KATILA Toivo	Laboratory of Biomedical Engineering, Helsinki University of Technology	Multimodal cardiac imaging	1994	on	DELH-05	1
Germany	PEYRIN Françoise	RAUM Kay	Univ. Halle-Witemberg	Synchrotron Radiation micro-CT and Scanning acoustic imaging	2005	on	RAUM-05, RAUM-06a, RAUM-06b, HOFM-06, RAUM-07	
Germany	GRAVERON – DEMILLY Danielle	Moeller H.	Max Planck Institut, Leipzig	Magnetc Resonance Spectroscopy	2006	on	FAST	
Germany	RICHARD Jean-Christophe	I. Frerichs	Univ. Schleswig-Holstein	Measurement of regional lung ventilation	2008	on	RICH-09	
Germany	GLATARD Tristan	Krefting D.	Institute of Medical Informatics, Charite – Universitätsmedizin Berlin	Interoperability between EGEE and German D-Grid	2008	on	OLAB-2009	
Greece	GRAVERON – DEMILLY Danielle	Fotinea E. Karras D.	Institute of Language and Speech Processing, Athènes, Chalkis Institute of Technology, Pr.	Medical MRI	2001	on	FAST	
Italy	PEYRIN Françoise	CANCEDDA Ranieri	Istituto Nazionale per la Ricerca sul Cancro, & Dipartimento di Oncologia, Biologia e Genetica dell Universita di Genova	Studying biomaterials for bone tissue engineering	2004	on	MAST-05, KOML-06, MAST-07, PAPA-07, PEYR-07, CANC-07, KOML-09	
Italy	CACHARD Christian	TORTOLI Piero	Dipartimento di Electtronica e Telecomunicazioni, Università, Di Firrenze	3D ultrasound models of biological tissues for the evaluation of engineering imaging techniques	2003	on	BALO-05, BALO- 05b, BALO-06 BALO-06b, BALO-07, BALO-08	1
Italy	CACHARD Christian	TORTOLI Piero	Dipartimento di Electtronica e Telecomunicazioni, Università, Di Firrenze	Imagerie ultrasonore non-linéaire. Focalisation fréquentielle pour l'amélioration de l'imagerie harmonique de contraste	2008	on	VARA-09	
Japan	PROST Rémy	KANAI Takashi	Kanai Lab, Keio University, Tokyo, Japan	Meshes for medical images	2003	2008	GELA-06c, GOUA-05b	1
Korean	PROST Rémy	JUNG Ho-Youl	Laboratoire Multimedia Signal Processing, Yeungnam Univ., South Korean	Lossless image compression. Digital Watermarking 3D meshes Deformation and motion 3D meshed models	2000	on	CHO-07b, LEE-06a,b, CHO-06,-06b, KIM-05,-06a,b, CHO-05,	3
Liban	CACHARD Christian	KHACHAB Maha	Département de Siences Biomédicales, Université de Balamand	Imagerie paramétrique des agents de contraste ultrasonore, application à l'échocardiographie	2004	2009	GHAZ-07a, GHAZ-07b, GHAZ-09	1
Liban	PROST Rémy	DIAB Chaouki KHALIL Mohamad	Lebanese University	Compressive sensing	2009	on		1
Netherlands	CACHARD Christian	DEJONG Nico VAN DER STEEN Ton	Thorax Centre, Erasmus University	Ultrasound coded emission for contrast imaging and tissue characterization	2005	on	PASO-09	1
Netherland	CAVASSILA	Van	Applied Physics Department, Delft University of	Analyse quantitative des signaux	2005	on	CUDA-08	

s	Sophie	ORMONDT Dirk	Technology, Delft	de spectroscopie de résonance magnétique				
Netherlands	GLATARD Tristan	Silvia D. Olabarriaga	Academic Medical Centre, Amsterdam	Environnement d'exécution d'applications de traitement d'images médicales sur grille de calcul.	2008	on	GLAT-09b, OLAB-2009	
Netherlands	CLARYSSE Patrick	ARTS Theo	Cardiovascular Research Institute Maastricht (CARIM), Universiteit Maastricht (T. Arts)	Traitement des séquences d'images par RM de marquage tissulaire	2003	on	article en révision 2009	
Netherlands	GRAVERON Danielle	Van Ormondt D.	Université Technique de Delft	MR reconstruction in medicine	1993	on	GRAV-09, STEF-09, CUDA-08, RABE-08b, RAB-07ª, RATI-05, CUDA-06	
Netherlands	GRAVERON Danielle	Heerschap A.	Radboud University Nijmegen	Magnetic Resonance Spectroscopy	1998	on	FAST	
Norwey	CANET-SOULAS Emanuelle	LARSON H.	MRI Center, Trondheim	Myocardial perfusion modeling and quantification by MRI	2002	2006	WIAR-06a	
Poland	CREMILLIEUX Yannick	DOHNALIK Tomasz	Jagiellonian University, Cracovia	IRM de l'hélium3	2003	on	CIES-06a, CIES-05	
Poland	ORKISZ Maciej	Ewa Piatkowska-Janko	Université Technique de Varsovie	analyse du réseau vasculaire et de la perfusion	2003	on	HERN-05a, HERN-05b, HERN-06a, ORLO-09	
Romania	PEYRIN Françoise	BUZULOIU Vasile	Polytechnic University of Bucarest	Segmentation de structures filaires 3D dans un contexte bruité : application à des images synchrotron nanotechnologiques de réseaux cellulaires.	2008	2011	PACU-09a, PACU-09b	1
Roumania	DELACHARTREPhilippe	BUZULOIU Vazile, GRAVA Cristian	Ecole Polytechnique de Bucarest et Université d'Oradea	Estimation de mouvement pour l'élastographie	2005	on	BASA-06	1
Singapore	BEUF Olivier	WANG Shih-Chang SWEE HIN 'Teoh	National Univerity of Singapore	MRI tracking of stem cell using iron oxide nanoparticles	2005	on	LEE-09	1
Singapore	PROST Rémy	NOWINSKI Wieslaw	Biomedical Imaging Laboratory, Singapore	Surface Meshing	2006	2008	GELA-06d, GELA-09	
Spain	GRAVERON-DEMILLY Danielle	CABANAS Miquel	Autonoma University of Barcelona	Magnetic Resonance Spectroscopy, jMRUI	1993	on	STEF-09a, STEF-09b	
Switzerland	WIART Marlène	DESVERGNE Béatrice	Centre Intégratif de Génomique Unité Sciences, université de Lausanne, Suisse	Evaluation de l'effet neuro-protecteur des PPAR en IRM haute résolution dans un modèle murin d'ischémie cérébrale	2004	2007	WIAR-05a, PIAL-07a	
Switzerland	BERNARD Olivier	UNSER Michael	Biomedical Imaging Group, Ecole Polytechnique fédérale de Lausanne	Segmentation par ensembles de niveaux paramétriques	2007	on	BERN-09a, BERN-08	
Switzerland	COURBEBAISSE Guy	CHOPARD Bastien	CUI – Université de Genève	Méthode de Boltzmann sur Réseau pour la simulation de phénomènes physiques complexes	2003	on	OUAR-07	

Switzerland	COURBEBAISSE Guy	DEVILLE Michel	LIN – EPFL (Ecole Polytechnique Fédérale de Lausanne)	Méthode de Boltzmann sur réseau pour la mécanique des fluides	2004	on	MALA-08, BOUF-09	1
Switzerland	CACHARD Christian	HUNSER Michaël	Biomedical Imaging Group, Ecole Polytechnique Fédérale de Lausanne, Suisse	Localisation échographique d'inclusions fortement échogènes en tissus mous, application à la détection d'électrode	2000	2004	MARI-09	MARI_04
Switzerland	Nighoghossian Norbert		Centre intégratif de génomique, Université de Lausanne,	MRI, Stroke	2005	on	PIAL-07a	
Switzerland	GRAVERON-DEMILLY Danielle		Ecole Polytechnique de Lausanne, CIBM, LIFMET	Magnetic Resonance Spectroscopy	2006	on	FAST	
Switzerland	GLATARD Tristan	MÜLLER Henning	Hôpitaux Universitaires de Genève	Interopérabilité entre les grilles EGEE et NorduGrid	2009	on	GLAT-09a	
UK	GRAVERON-DEMILLY Danielle	Williams S.	University of Manchester, Imaging and Biomedicine Department	Magnetic Resonance Spectroscopy, temperature measurement	1998	on	STEF-09b	
USA	GRAVERON-DEMILLY Danielle	Boska M.	Ohama University,	Magnetic Resonance Spectroscopy, jMRUI	2009	on		1
USA	ZHU Yue Min	GUTTMAN Charles	Departments of Radiology, MRI and Neurology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA	Cerebral segmentation in MRI.	1998	on	MILL-05	2
USA	PEYRIN Françoise	MAJUMDAR Sharmila	Dept Radiology, University of California, San Francisco	Evaluating the role of the growth factor IGF-I on the bone structure of foetus of mice at the micrometric scale.	2004	on	BURG-05, BURG-07	
USA	REVEL Didier CROISILLE Pierre	SAEED Maythem	University of California San-Francisco –Department of Radiology	MRI caracterization of Myocardial ischemia	2004	on	CROI-06, SAEE-06 MEWT-08, JACQ-08a	1
USA	CROISILLE Pierre	WEN Han	NIH-NHLBI (Washington, DC)	Myocardial tissue tracking with displacement-encoded MR imaging	2006	on	WEN-08	
USA	RATINEY Hélène	Pelletier Daniel	University of California San Francisco- Department of Neurology	MRSI of Multiple sclerosis	2007	on	RATI-07a	
USA	RATINEY Hélène	Nelson Sarah	University of California San Francisco Department of Radiology	Metabolite Relaxation Times in Gliomas	2007	2008	LI-08	
USA	RATINEY Hélène	Kurhanewicz John	University of California San Francisco Department of Radiology	Quantification of HR-MAS data from prostate Tissue	2006	on	ZHA-08	
USA	PROST Rémy, MAXIM Voichita	ZOGLAUER Andreas	Space Sciences Laboratory, University of Californiaat Berkeley, Berkeley, CA 94720 USA	Compton-scattering based Imaging System for Hadron Therapy Monitoring	2008	on	FRAN-08, FRAN-09a, FRAN-09b	
USA	BENOIT-CATTIN Hugues	PAULY J.	Stanford Univ, Magneic Resonance Sytems Research Lab Molecular MRI	MRI Simulation	2008	on	ADDY-09, CHAR-08b	
USA	CLARYSSE Patrick	AXEL Leon	New York Langone University	Tagged MR Image processing				

Team n°1 - Imaging of the Heart/Vessels/Lungs

Previous activity: Period 2005-2009

Key words: cardio-vascular diseases; acute lung injury; multi-modality imaging; medical image analysis; anatomical, architectural and functional modelling; multi-scale imaging and modelling; Integrative imaging;

Team leader	CLARYSSE Patrick	CR1 CNRS-HDR
Vice-team leader	BOUSSEL Loïc	PHU UCB
	CROISILLE Pierre	MCUPH-HDR UCB
	DOUEK Philippe	PUPH UCB
	GUERIN Claude	PUPH UCB
	MAGNIN Isabelle	DR Inserm
	ORKISZ Maciej	PU UCB
	REVEL Didier	PUPH UCB
	RICHARD Jean-Christophe	MCUPH-HDR UCB
	ZHU Yue-Min	DR CNRS
ETP : 5		
Engineers	COURBEBAISSE Guy	IR, HDR
Invited professors	LUO J. H.	Shangai Jiaotong Univ.
	LIU W. Y., Co-dir HIT-INSA Lab.	Harbin Inst. Tech. (HIT)

Post doc		University	Financial support
	BERNARD Sophie, PHR	UCB Lyon1-HCL	CNRS-HCL
	BREGEON F., MCU-PH Physiologie	Université de Marseille	Marseille

Ph.D students		Financial support	
	BAO Lijun	Chinese Gvt.	Joint PhD with HIT, China
	BERKANE Mohamed	Algerian Gvt.	
	FRINDEL Carole	CIFRE Siemens	
	LOFFROY Romaric	UCB Lyon1-HCL	JHU, USA
	MEWTON Nathan	UCB Lyon1-HCL	Kings College London
	MILLON Antoine	UCB Lyon1-HCL	Surgeon
	POUZOT C.	Ecole vétérinaire, Marcy l'étoile	Veterinary
	RAPACCHI Stanislas	ENS Grant	NIH, USA
	SCHILLING Tanja	Marie-Curie Grant	Joint PhD with Pragues
	SONG Xin	South China Univ. Tech.	SCUT, China
	STEPHANT Eric	UCB Lyon1-HCL	Physician
	VANDEMEULEBROUCKE Jef	Marie-Curie Warthe	Joint PhD with Pragues
	ZHANG Nan	Chinese Gvt.	Tsinghua Univ, Chine
	ZHANG Yanli	Chinese Gvt.	HIT, China
	ZHU-YANG Feng	Chinese Gvt.	
	ZULUAGA Maria A.	Colombian Gvt.	BioMedIA Lab, CSIRO, Brisbane, 8 months,

Defended HDR		Year of defense
	CLARYSSE Patrick	2005
	CROISILLE Pierre	2008
	RICHARD Jean-Christophe	2009

Defended Theses		Nationality	Year of defense	Future
	SCHAERER Joël	French	2008	Post-Doc
	JACQUIER Alexis	French	2008	Marseille APHP:PH
	ATTIA Cherif	Egyptian	2007	PH Guadeloupe
	HADDAD Rana	Syrian	2007	Assist. Prof. Damas
	BOUSSEL Loic	French	2006	PHU
	DELHAY Bertrand	French	2006	Engineer BioClinica SAS
	FLOREZ VALENCIA Leonardo	Colombian	2006	Assist. Prof. Bogota
	YANKAM NJIWA Josiane	French	2007	Post-Doc
	XIN Huamei	Chinese	2008	Assist. Prof., Jinan China

Per-reviewed Publications: 116 **Conference papers : 99** **Patents : 0**

1. Résumé

Les réalisations de l'équipe vont du développement de nouvelles techniques ciblées d'acquisition et d'agents de contraste (nouvelles séquences IRM et USPIO pour l'imagerie haute résolution de la plaque d'athérosclérose et de l'inflammation) à des études cliniques (i.e. étude du remodelage post-infarctus) et fondamentales (études de l'architecture fibreuse du cœur chez l'homme) en passant par des développements méthodologiques en post-traitement d'images (segmentation de structures vasculaires et du cœur en IRM) ou plus fondamentaux (reconstruction à partir de données bruitées et investigation de nouvelles représentations d'images dites 'éparses ').

2. Objectives

The team is a multidisciplinary team composed of researchers in image processing and modelling and medical researchers specialists of cardio-vascular and lung diseases. Our approach is therefore to start from clinical questions to develop novel medical imaging methodologies (acquisition and post-treatment) and assess their efficiency through clinical trials. We present the main achievements of the last 4 years organised into 6 scientific actions that are (1) vessel lumen and wall, (2) myocardial ischemia, (3) response to lung injury, (4) spatio-temporal image analysis, (5) Organ or modality dependent modelling and simulation, (6) Representation of nD signals and optimization.

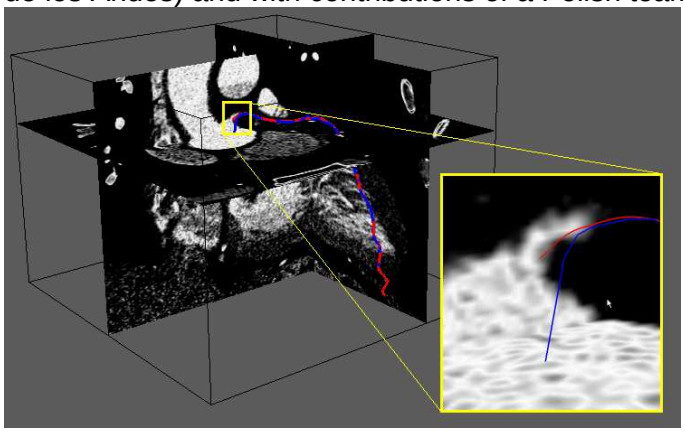
3. Research activity

Vessel lumen and wall (L. Boussel, G. Courbebaisse, P. Douek, M. Orkisz, interaction with team 8)

Action 1: High resolution imaging and contrast agent targeting inflammation [SIGO-09, Radiology, in Press]. In this work we evaluated the use of a new fast-clearance ultrasmall superparamagnetic particles of iron oxide (USPIO, P904) for detection of vascular inflammation in atherosclerotic plaque. P904 (Guerbet Laboratories) and a reference USPIO (Ferumoxtran-10) were tested in a rabbit model of induced aortic inflammation (hyperlipidemic New Zealand white rabbits, N=26). In vivo MR angiography and T2*-weighted plaque imaging were performed at baseline and after administration of the contrast agent (J2 and J3 for P904 and J7 and J10 for Ferumoxtran-10). We demonstrated that plaque analysis was possible as early as 48 hours after P904 injection in rabbits. A 27.7% increase in vessel wall area due to susceptibility artifacts was obtained with P904 at day 2 (p=0.04) and a 38.1% increase at day 3 (p=0.04), compared to +44.5% at day 7 (p=0.04) and +34.8% at day 10 (p=0.22) with Ferumoxtran-10. These susceptibility artifacts were correlated with intraplaque iron uptake in corresponding histological slices. In conclusion, plaque inflammation can be detected in rabbits using P904 earlier than with Ferumoxtran-10, thanks to a faster blood pharmacokinetics and an early uptake in the reticulo-endothelial system.

Action 2: Development of a MR sequence improving contrast on post-gadolinium high-resolution carotid plaque imaging [BOUS-08b, JMRI]. We developed an EKG-triggered double inversion-recovery (DIR) turbo spin-echo (TSE) sequence with an extra saturation (90°) radio frequency (RF) pulse placed immediately after the DIR module, shortening the repetition time to a fixed value of 400 ms. We compared, in ten patients with carotid plaque, the intra-plaque gadolinium contrast uptake for the new sequence in comparison with the standard one (i.e. the same sequence but without the extra pulse). Post-gadolinium-injection intra-plaque contrast was 31.7+/-12.8% with the

standard sequence, and 45.3+/-17.2% with the new one, showing a significant contrast enhancement of 13.6% ($p<0.001$) without significant image quality modification. In conclusion, the addition of a RF pulse to the standard EKG-triggered T1-weighted TSE sequence increased intra-plaque contrast without increasing sequence acquisition time. Furthermore, it appeared to be a robust technique, easy to implement on clinical scanners.
Action 3: Model-based enhancement and segmentation of 3D vascular structures. Despite the use of contrast agents, the intensity range of the vascular lumen often overlaps the intensities of other neighbouring structures. The segmentation of the vascular lumen therefore requires the use of prior knowledge via shape models [ORKI-08, Mach Graph Vision], and often involves an enhancement filter. We proposed a computationally efficient framework for the filters based on the eigen-analysis of matrices such as Hessian [ORLO-09, IRBM]. Our segmentation framework is based on an elastic model of the centreline [HERN-05c, Mach Graph Vision],[HERN-06ab, Int J Comput Assist Radiol Surg] using a multi-scale analysis of the inertia matrix. Inertia moments and a bifurcation model were used to segment vascular trees from a single seed point [CARR-06d, Int J Comput Assist Radiol Surg],[CARR-07a, Rev Col Radiol]. The method based on the elastic model was classified 7th among the participants of the final stage of the MICCAI Workshop - Grand Challenge Coronary Artery Tracking [SCHA-09, MedIA] that were able to provide the results in real time. This work was carried out in a close collaboration with the Colombian partners (Universidad de los Andes) and with contributions of a Polish team (Politechnika Warszawska).



Extraction of coronaries in a 3D-CT image in the context of the MICCAI challenge in 2008.

Myocardial ischemia (P. Clarysse, P. Croisille, D. Revel, Y-M. Zhu, interaction with teams 8, 5)

Action 1: MR imaging monitoring of reperfused myocardium and of cardioprotective strategies. Although reperfusion is undoubtedly beneficial, it has detrimental effects, including myocardial stunning, ventricular arrhytmias, and microvascular dysfunction. Microvascular obstruction (MVO) is an additional factor of adverse outcome in patients after myocardial infarction. We showed that even after acute non-ST-elevated myocardial infarction (NSTEMI), MVO was detected in 32% of the patients, and the presence of MVO comes with significantly larger infarct size [MEWT-09, Cardiology]. We used MR to monitor one of the recently proposed strategy to limit ischemia-reperfusion injury using cyclosporine as a potent inhibitor of mitochondrial permeability transition and showed in a pilot trial, that administration of cyclosporine at the time of reperfusion was associated with a smaller infarct (collaboration M.Ovize, INSERM U886).
Action 2: Left ventricular post-infarction remodeling. Although structural changes in the remodeling myocardium have been well described, the functional differences between regions and the impact of structural modifications on regional function are not clearly defined. MRI enables the study of myocardial deformation and strain evolution in precise regions of the myocardium with high level of reproducibility and accuracy with MR tagging. The data combination obtained with delayed enhancement and MR tagging allows a precise monitoring of the functional variations in the different regions. In an experimental setup in pigs (n=8) studied in the acute and chronic phase after ischemia-reperfusion (Sabbatical period of D.Revel in collaboration with M.Saeed, UCSF), we confirmed the hypothesis that scared myocardium imposes additional functional burden to the peri-infarcted myocardium [MEWT-08, Invest. Radiol.]. This work is one example of the added value of MR tagging that can, with the help of strain quantification, provide additional information on the deleterious remodeling occurring in the post-ischemic myocardium.
Action 3: Myocardial architecture with Diffusion Tensor Imaging in humans (DTI). To better understand and describe the characteristics of normal ventricular architecture and changes

occurring in various pathological processes involving cardiac remodeling (hypertrophic and ischemic cardiomyopathy), we studied 20 human samples with ex-vivo DT-MRI of both normal and hypertrophic human samples in collaboration with the Lyon Forensic Institute (UMRESTTE Lab) using acquisition conditions that could be compatible with in-vivo imaging. The distribution of MR diffusion indexes (fraction anisotropy (FA), mean diffusivity (MD), and Coherence Index (CI) are significantly different when comparing hypertrophic and normal regions [STEPH-09, ISMRM]. The use of regularization methods is useful to better describe fiber architecture and changes among groups [FRIN-09, MEDIA], [BAO-09, PMB].

Response to lung injury (C. Guérin, J-C. Richard, interaction with teams 8, 2)

Action 1: Regional lung ventilation measurement. We measured regional lung ventilation in vivo in pigs by developing an original method which consists of: 1) a continuous administration of $^{13}NN_2$ produced by a cyclotron into a ventilator via an open-circuit, 2) measurement of lung ventilation by using Positron-Emission Tomography (PET) from the ^{13}NN washout modelling [RICH-05, J. Nuclear Med]. This method was validated over a wide range of regional lung ventilation.

Action 2: Effects of prone position and Positive End-Expiratory Pressure on the distribution of lung ventilation, lung perfusion and lung recruitment [RICH-08, Crit. Care Med]. In 6 pigs whose lung were injured by oleic acid, PEEP of 0 and 10 cmH_2O were set in prone or supine position to each animal in a random order. Lung ventilation ($^{13}NN_2$ washout after $^{13}NN_2$ inhalation), lung perfusion (intravenous injection of H_2O_{15}) and lung recruitment (transmission scan) were measured by using PET. PEEP of 10 cm H_2O redistributed ventilation and perfusion towards the dependent parts of the lung along a gravitational gradient in both supine and prone positions. The lung was totally recruited in prone position at 10 cm H_2O PEEP.

Action 3: Effect of ACP on lung ventilation & perfusion [GUER-07a, Intensive Care Med]. In this study, we investigated the effects of Activated C Protein (ACP), an anticoagulant which had been able to increase survival in patients with septic shock, on lung ventilation and perfusion in a porcine model of oleic acid-induced acute lung injury. We hypothesized that ACP may recruit lung perfusion by reopening damaged lung vessels and, hence improve ventilation/perfusion mismatch and oxygenation. In this placebo-controlled study of 9 animals per group, we found that ACP worsened oxygenation and did not change significantly the distribution of perfusion. This result can be explained by an early use of ACP (full coagulation abnormality not yet established in the model) and insufficient PET resolution to detect more subtle changes in the ventilation/perfusion distribution.

Action 4: Regional ventilation from EIT. In the study conducted in [RICH-09, Critical Care] study done in 7 pigs, we validated Electrical Impedance Tomography against PET to measure regional ventilation. We found a strong unbiased correlation between the two techniques.

Spatio-temporal image analysis (P. Clarysse, I. Magnin, M. Orkisz, interaction with teams 3, 8)

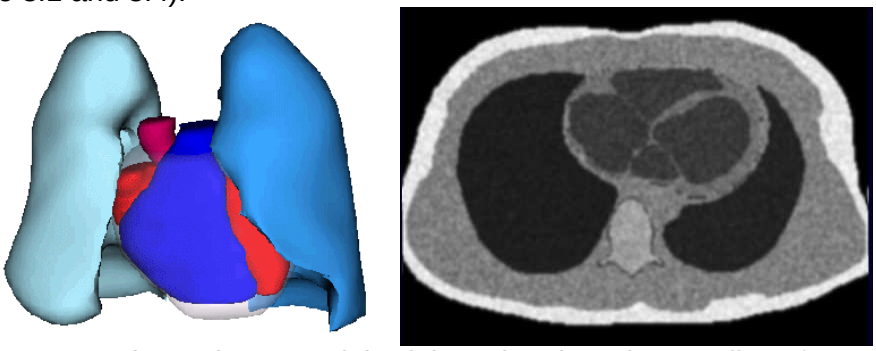
Our main developments concern the spatio-temporal segmentation and motion estimation within cardiac and thoracic image sequences.

Action 1: dynamic segmentation. We proposed an extended version of our previous deformable elastic template model (DET) developed by our group to 1) handle non-linear elastic law [ROUC-07, Inv. Pb.] and 2) a spatio-temporal formulation [SCHA-08b, thesis]. This latter method is able to segment and track the heart throughout the whole image sequence and has been demonstrated on 2D dynamic cine-MRI sequences or the segmentation of the LV myocardium. The demonstration of convergence of this new dynamic DET model has been done in collaboration with ICJ, Lyon (Prof. J. Pousin).

Action2: motion estimation. We have developed the Spatio-Temporal EstimAtor of Motion (STEAM) based on non-rigid registration cascade controlled over time by a Kalman filter [DELH-06e, thesis]. STEAM estimator has been successfully demonstrated on both cardiac and thoracic image sequences [SARR-07, IEEE Trans. MI]. Moreover, we have ported as a plug-in the inTag software (co-developed with Maastricht Univ, Prof. T. Arts) from MATLAB to the widely used OsiriX Dicom imaging software (http://www.osirix-viewer.com/). The inTag plug-in allows the straight and fast analysis of short and long-axis cardiac tagged MR images. It will be soon released to the community in the context of a scientific collaboration agreement.

Organ or modality dependent modelling and simulation (P. Clarysse, G. Courbebaisse, I. Magnin, M. Orkisz, interaction with teams 2, 8)

Action 1: Virtual imaging of a breathing thorax and beating heart model. The model, called ADAM (A Dynamic Anthropomorphic Model of the breathing thorax and the beating heart), [HADD-05c, IRBM] provides a multi-structure, mesh-based representation of thoracic structures animated with realistic movements. It offers structure shapes, volumes, functional parameters and a set of virtual MR (SIMRI simulator) and PET (SORTEO simulator, coll. CERMEP, Lyon) image sequences of a reference thorax. In the future, simulation of real clinical image acquisition protocols will be facilitated by the virtual multimodality imaging platform [CAMA-08b], which is under development. Ongoing work also aims at the inclusion of morphological and functional inter-patient variability, to adapt it to various patient-specific anatomies, as well as to normal and pathological behaviours (see 3.1 and 3.4).



Left - ADAM thorax-heart model. Right - Virtual MR image slice of ADAM (computed with SIMRI)

Action 2: numerical vascular simulation. Lattice Boltzmann method is an efficient alternative to the well-established numerical simulation methods, such as finite elements or particles. We study its implementation for the simulation of visco-elastic flow [COUR-06][MALA-08, Modern Physics C], and more specifically of the thrombosis in aneurysms. The first results provide an estimate of the thrombus volume within the aneurysm [OUAR-08]. This work is carried out in collaboration with the Scientific and Parallel Computing Group (University of Geneva) and the Laboratoire d'Ingénierie Numérique (EPF Lausanne), and is a part of the European project COST P19. Moreover, a previously developed deformable cylindrical simplex model has been used to simulate the deployment of arterial stents, based on patient-specific angiographic data [FLOR-07b, ITBM].

Representation of n-D signals and optimization (Y-M. Zhu, interaction with team 2)

Action 1: Optimization. We addressed the problem of reconstructing an ideal n-D signal from indirect measurements corrupted by noise. Stabilization of this ill-conditioned inverse problem leads to a challenging optimization task. To overcome this difficulty, we introduced a new class of hybrid algorithms that combine simulated annealing with deterministic continuation. We call this class of algorithms stochastic continuation (SC). We proved that SC inherits the finite-time convergence properties of generalized simulated annealing under mild assumptions, and we showed that SC can be successfully applied to 3-D reconstruction from a very limited number of projections [Robi-07a, IEEE Trans. Image Processing]. Our numerical experiments using both synthetic data and real radiographic testing data [Robi-07b, IEEE Trans. Nuclear Science] show that SC outperforms standard simulated annealing.

Action 2: Sparse representation. We addressed the sparse representation of images using two different approaches. The first approach is based on the conventional idea of using an overcomplete dictionary. By combining sparse representation with a segmentation scheme based on the nonstationarity degree (NSD) detector, we showed that the generation of the dictionary can be made more adaptive, thus improving the denoising of human cardiac DTI and the calculation of diffusion tensors as well as the principal eigenvector field, and fibre tracking of the myocardium [BAO-09, PMB]. The second approach is based on the development of singularity function model. We demonstrated that singularity function representation can be used for several MR image processing problems. When applied to the correction of intensity inhomogeneity, such approach gets rid of the commonly used assumption that anatomical information in MR images occurs at higher spatial frequencies than bias field, and requires no initialization or a prior models, nor image preprocessing such as brain masking or presegmentation [Luo-05, *IEEE Trans. Med Imaging*]. Likewise, when used for denoising MR images, the approach presents the non-distortion

advantage of the multiple observed images averaging technique, but only requires one single observed image [Luo-09a, *IEEE Trans. Biomedical Engineering]*.

4. Plateforms

- Preclinical: CERMEP-Animage.
- Clinical: Hospices Civils de Lyon: 3T and 1.5 T MRI. 64 slices MDCT.

5. Interactions

- Team 2: D. Friboulet, O. Bernard, cardiac US Image analysis ; R. Prost, Multiplanar coronary stent reconstruction from DSA images.
- Team 5: D. Grenier, Cardiac DT-MRI

6. Technological transfer

- Development of the inTag plugin (Integrated Analysis of MR-Tagged Images) into the OsiriX imaging software (http://www.osirix-viewer.com/) by the Axinoe company.

7. Grants

National projects

- Simed Project (Simulation en Imagerie Médicale pour le diagnostic et le Thérapie, http://www.creatis.insa-lyon.fr/Simed) of the ISLE Cluster of the Région Rhônes-Alpes, coordinated by P. Clarysse and E. Promayon (TIMC, Grenoble), 30k€/year + Thesis grant, 2009-2012
- Ragtime Project (Rhône-Alpes – Grille pour le traitement d'informations médicales), Thématique prioritaire: Calculs Scientifiques Logiciels, Région Rhônes-Alpes, 2003-2005.
- Action IMPEIC (Initiative Multicentrique pour une Plateforme d'Evaluation en Imagerie Cardiaque, http://stic-sante.org/), piloted by F. Frouin (LIF, Paris) 2008-2009
- ANR MDCA GWENDIA (Grid Workflow Efficient Enactement for Data Intensive Applications), coordinated by I3S-Nice, 48k€, 2007-2010.
- ANR INFLAM (2007-2010), Principal Investigator Y Berthezène : INFLAMmation in brain and vessels with iron nanoparticles and cell trafficking: a multi-scale approach of tissue microenvironment, iron nanostructure and iron biotransformations. 9 partners (7 academics, 2 industrials), 849 kEuros.
- ACI-MD AGIR (Analyse Globalisée de Données d'Imagerie Radiologique), coordinated by LRI-Orsay, 54k€, 2004-2006.

European projects

- PAI Polonium 09182YG, mobility: 5.5 k€, 2005-2006
- European Network of Excellence VPH (Virtual Physiological Human, http://www.vph-noe.eu/), 2008-2012
- European (IST) EGEE2 (Enabling Grids for E-SciencE) project, 2006-2008; EGEE3 project, 2008-2010
- European COST P19 (European Cooperation in the field of Scientific and Technical Research) Multiscale Modeling of Materials. Guy Courbebaisse is coordinator of Workgroup 4 (Hybrid Methods of Simulation) and member of the COST P19 Management Committee, 2006-2010.

International projects

- ECOS-Nord Colombia C07M04, mobility: 13.5k€, 2007-2009

Industrial contracts

- PHILIPS Healthcare, Best, The Netherlands: Research contract
- SIEMENS Medical, Erlangen, Germany: Research contract
- SEGULA Technologies, Nanterre, France.

8. Publishing collaborations

National collaborations

- LIRIS, CNRS UMR 5025, Lyon [SARR-07]
- Institut Camille Jordan, CNRS UMR 5208, Lyon [ROUC-07]
- CEA-LETI, Grenoble [ESCO-08]
- I3S, CNRS UMR 6070, Nice [FLOR-07b], [MAGN-06a, b], [GERM-05], [PIER-05], [MONT-05a, b]

- LAL, Orsay [GERM-05]
- CEREMADE, Paris [BENM-09]

International collaborations

- China: Shanghai Jiaotong Univ, Harbin Institute of Technology. [LUO-09a], [LUO-08], [MIAO-07], [LI-06a,b], [YU-06], [LUO-05]
- Colombia: Universidad de los Andes, Bogotá, [ORKI-08], [CARR-07], [CANT-07c], [CARR-06a, b, d], [HERN-06b], [DOUE-05x], [HERN-05]
- Germany: Univ Schleswig-Holstein [RICH-09]
- Poland: Technical Univ. Warsaw [HERN-06a], [ORLO-09]
- Switzerland: EPFL – LIN, University of Geneva – CUI [MALA-08], [COUR-08]
- The Netherlands: T. Arts, Maastricht Univ., [MILL-04a]
- USA: NY Langone Univ. [WANG-07], [SCHA-06]; University of California, San Francisco (UCSF), [BOUS-09a,c], [BOUS-08c,d], [JACQ-08a,b], [RAYZ-08a,b], [BOUS-07a], [CROI-06b], [SAEE-06]

9. Expertise and consulting

- P. Clarysse has been reviewers for NOW (The Netherlands Organization for Scientific Research), Division for Physical Sciences (The Netherlands, 2009), NIHR (National Institute for Health Research,10th Call, 2008, UK), French ANR DEFIS 2009. He is part of program committees of FIMH, ISPA, SURGETICA conferences
- G. Courbebaisse: VPH 7FP expert, COST MPNS expert, ANR expert
- P. Douek is part of INSERM CSS 3
- C. Guerin has been reviewer for ANR 2009 and PHRC 2006
- I. Magnin was expert at the EC, 1996-2006, Member of the 'Comité National' of CNRS (2005-2008). She is part of CA of Inserm (2006-2009). President of AERES Committee.
- D. Revel belongs to the Scientific committee of EIBIR (European Institute of Biomedical Imaging Research).

10. Distinctions

- I Magnin, 1st French laureate of the Chang Jang professorship, Tech. Univ. Harbin, China, 2008-2010.
- premio Gonzalo Esguerra for a presentation at Congreso Colombiano de Radiologia [CANT-07b]
- premio Otto de Greiff for Michael Baltaxe co-supervised by M. Orkisz et M. Hernandez Hoyos [BALT-07]

11. Research training

- Master 'Images & Systems', ED EEA. P. Clarysse is responsible of the Module #5 (image registration and motion estimation)
- IMAVI (Imaging of the living bodies) INSA Option. P. Clarysse is responsible of this transversal option of the last year of the engineering School
- Marie Curie Early Stage Training in the FP6 Human Resource programme 'Wide Area Research Training in Health Engineering (WARTHE)', multi-sites program of research training in the Biomedical Engineering field piloted by INSA with University of Ulster and Czech Technical University, 2006-2010
- D. Revel is the Chairman of the ED 205 (EDISS). School of PhD students
- P. Douek is the co-ordinator at the Regional level of the inter-university diploma in 'diagnostic and therapeutic cardio-vascular imaging' and of the courses in MRA of the ESMRMB.

12. Congress organisation and committees

- P. Clarysse is IEEE Member, part of the program committees of FIMH, ISPA, SURGETICA, AMINA 2008 (http://www.ltim.org/amina2008)
- M. Orkisz: program committee of ICCVG and MIT (Poland)
- Clinical Update on MRI and CT in coronary artery disease. 2009. P. Douek, D. Revel, P. Croisille, L. Boussel.

Scientific Production Team #1
Imaging of the Heart/Vessels/Lungs

Articles in peer reviewed international journals (ACL)

[BERK-09] M. Berkane, P. Clarysse, J. Yankam Njiwa, Y-M. Zhu, and I. E. Magnin. Spatio-temporal summarizing method of periodic image sequences with Kohonen Maps. Neural Network World, pp (in press), 2009.
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[BOUS-09a] **L. Boussel**, S. Arora, J. Rapp, B. Rutt, J. Huston, D. Parker, C. Yuan, H. Bassiouny, and D. Saloner. Atherosclerotic Plaque Progression in Carotid Arteries: Monitoring with High-Spatial-Resolution MR Imaging--Multicenter Trial.. ***Radiology***, pp in-press, 2009.
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[GUER-09] **C. Guerin** and **J.C. Richard**. On the randomized trial of activated protein C in acute lung injury. ***Am J Respir Crit Care Med***, 179(2):172-3; author reply 173, 2009.
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Previous activity: Period 2005-2009

Keywords : Modeling, simulation, meshing, segmentation, detection, grid computing

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Résumé. Nous avons contribué à l'aide au diagnostic médical par des travaux amont, en modélisation et simulation de la formation de l'image, en modélisation géométrique, en détection et segmentation. L'application de ces travaux se fait en collaboration avec d'autres équipes de CREATIS et concerne principalement les domaines de l'oncologie, la rhumatologie et la cardiologie. Les masses de données à traiter et la complexité des calculs ont nécessité des travaux d'implémentation sur grille.

1. Aims

In order to contribute to diagnosis aid by quantitative medical imaging we used an appropriate mathematical framework: image formation models and simulations, shape models, estimation and detection theory, segmentation by active contour. Applications of this work were performed through collaboration with CREATIS teams and concern mainly oncology, rheumatology, cardiology, and phenotyping. The amount of data to be processed and the complexity of the calculations required implementation on grid architectures.

2. Research activity

Estimation, Detection (C. Lartizien)

Positron Emission Tomography (PET) using fluorine-18 deoxyglucose (FDG) has become an increasingly recommended tool in clinical whole-body oncology imaging. To assist the clinicians facing the difficult cases of residual or low contrast lesions, we are investigating different schemes of computer aided detection (CAD) systems. The original CAD strategy that was proposed as part of the PhD of S. Tomei combines two supervised classifiers, the linear discriminant analysis [LART-07b] [TOME-07b] and the non linear Support Vector Machine (SVM), which have never been applied to lesion detection task in PET imaging. The image feature sets that serve as input data for these classifiers consist of the coefficients of an undecimated wavelet transform. Detection performances are assessed based on simulated normal and pathological whole body PET images [TOME-08b]. This CAD strategy indicates promising classification performances with couples sensitivity/FPI of 80%/25 for the lungs and 81%/14 for the liver [TOME-08a].

Segmentation

Parametric level sets (O. Bernard, D. Friboulet, R. Prost)

We proposed a novel approach, which relies on a continuous parametric representation of the level set, based on radial basis functions (RBF) [GELA-07, IEEE TIP, 2007] (fig. 1a) and B-splines functions [BERN-09a, IEEE TIP, 2009] (fig. 1b). Such formulation provides many advantages over the usual finite difference scheme: (i) It allows an overall control of the level set over the whole computational domain (ii) It avoids the usual shape reinitialization step, yielding topologically more flexible solutions (which may easily develop new contours, i.e., new zero level components) (iii) - The smoothness of the solution is implicitly enforced, and thus the use of the costly curvature term in the propagation equation may be avoided in most cases. Moreover, this intrinsic smoothness allows for large propagation steps and thus much less iterations.

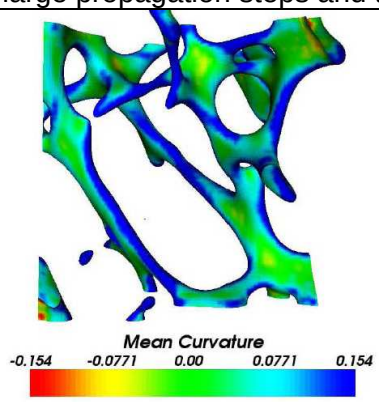

Fig. 1a RBF based level set image segmentation of a 100^3 micro-CT image of a calcaneus bone. The continuous implicit function provides analytical access to the differential properties of the interface, such as Gaussian and mean curvatures.

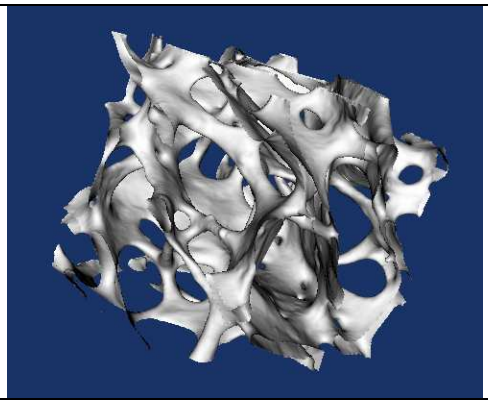

Fig. 1b B-splines based level set image segmentation of a 256^3 micro-CT image of a calcaneus bone. Due to the overall control and the large propagation steps of the level set, the result is obtained in 19 iterations.

Active contour regularized by smoothing B-Spline (H. Benoit-Cattin, C. Odet)
During the PhD of J. Velut, we explored the regularization of active contour by using smoothing B-Spline. First, we proposed a 2D active contour model that enables a local regularization [VELUT-07, JASP,2007]. Then we extended this model in 3D to propose a Smoothing B-Spline active surface [VELUT-06a]. By adapting locally the cut-off frequency of the IIR filter used in our regularization model to the mesh geometry, we proposed an IIR filtering of surface meshes [VELUT-08a]. In collaboration with Servier Company (with team 5), we considered the segmentation by active contour of the knee cartilage in the context of osteoarthritis longitudinal study of animal model using high resolution MRI [BOLB-08, NMR in Biomedicine 2008] [BOLB-07, OAC, 2007] [DU-08].

Multiparametric segmentation (T. Grenier, C. Muller)
We focused on multidimensional filtering and segmentation methods, which take into account the whole set of information, benefit from the complementarities of the parameters and achieve a robust segmentation. These methods are based on the “feature space”, a multidimensional space particularly well-adapted for representing a whole set of observations. In this space, we explored the “Mean Shift” filtering procedure and proposed some optimizations (about the whole process of Mean Shift [GREN-6a], adaptive scale parameters [GREN-5a]. These approaches were successfully applied to multi-parametric ultrasound data [DAVI-05, GREN-05b].

Region growing (C. Muller, T. Grenier, C. Odet)
We proposed a robust adaptive region growing method [GREN-06b] based on local parameters (fig. 2a) http://www.creatis.insa-lyon.fr/site/fr/node/31246. We provided a solution to set automatically initial seeds of the region growing in whole-body 3D NaF PET images [GREN-05c, IEEE TNS]. We developed an unsupervised region growing method in the feature space in order to segment multi-parametric images stemmed from multidimensional Mean Shift filtering. We integrated shape prior in region growing [ROSE-07]. We proposed a solution to adapt automatically the degree of shape prior [ROSE-08]. Shape prior was represented by distance map or by shape descriptors such as 3D Tchebychev’s moments. We also described region growing by a variational approach [ROSE-09]. A discrete derivation is applied to a region-based criterion in order to get an evolution rule for the evolving region. This equation guides the evolving region towards a minimum of the criterion. We highlighted the relevance of this approach to shape prior integration (fig. 2b). http://www.creatis.insa-lyon.fr/site/fr/node/31243

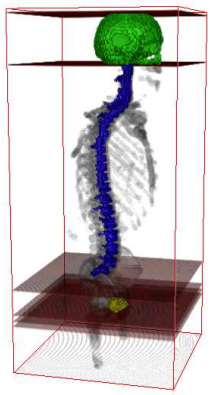

Fig 2a Adaptive region growing segmentation in a whole-body 3D NaF PET image.

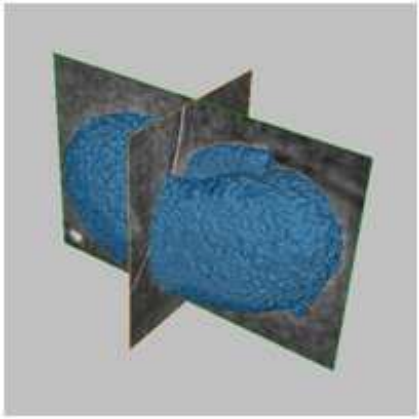

Fig. 2b Variational region growing integrating shape prior for mouse kidney segmentation in a 3D micro-CT image.

Geometric Modeling
Implicit modeling of surfaces by radial basis functions (R. Prost)
An alternative to the usual approximation and interpolation methods of surfaces using Cartesian products of parametric spline bases, is the use of a sum of radial basis functions (RBF). These basis functions make a fully 3D approach because they are inseparable functions of x, y, z. In his PhD thesis A. Gelas proposed a hybrid method combining interpolation (or approximation) by radial basis functions with bounded support and the partition of unity technique [GELA-06 a,b,c,d]. (fig. 3a)This work has being carried out in collaboration with T. Kanai, Tokyo Univ., and Y. Ohtake,

RIKEN, Tokyo. This approach has been successfully applied for segmentation by the level set approach (see 2.2.1). http://www.creatis.insa-lyon.fr/site/en/levelsetRBF

Variational implicit surface meshing (S. Valette, R. Prost)
We have proposed an algorithm for meshing implicit surfaces (defined by f(x,y,z)=0), with the assumption that we also have access to the gradient of f. This allows us to mesh the surface adaptively to the local curvature. The vertices placement is driven by the Quadric Error Metrics formalism, improving the accuracy of our algorithm over previous isotropic mesh generation approaches. This work in collaboration with A. Gelas, Harvard Medical School and W. L. Nowinski, Biomedical Imaging Lab., Singapore [GELA-09, Computers and Graphics, 2009] (fig. 3b).http://www.creatis.insa-lyon.fr/site/en/variationalimplicitmeshing

Meshes Watermarking (S. Valette, R. Prost)
Watermarking provides a mechanism for copyright protection by embedding information, called a watermark, into host data. In the PhDs of M. S. Kim and J. W. Cho, both in joint supervision with Yeungnam Univ., Korea (H. Y. Jung) we proposed two blind watermarking methods for 3-D triangular mesh models, which modify the distribution of vertex norms according to the watermark bit to be embedded [JUNG-06 Patent] [CHO-07, IEEE TSP]. These approaches are remarkably robust against distortionless attacks and fairly robust against various distortion attacks. We have derived a wavelet based watermarking approach in the PhD of M. S. Kim. It reduces the visibility of the watermark but is less robust again attacks than Cho method [KIM-06-b-c]. We have also investigated dynamic meshes watermarking in [KIM-06-a].
Meshes Compression (S. Valette, R. Prost)
In order to extend our previous works on wavelet based static mesh compression (see Valette and Prost, IEEE TVCG, 2004) we have investigated with success dynamic mesh compression [CHO-06b, CHO-07b]. Recently we proposed a progressive lossless static mesh compression algorithm based on our concept of Incremental Parametric Refinement. The algorithm starts with a coarse version of the original mesh, which is further refined by means of a refinement scheme driven by a geometric criterion, in spirit with surface reconstruction algorithms, aiming at generating uniform meshes. The vertices coordinates are quantized and transmitted in a progressive way, following a geometric criterion, efficiently allocating the bit budget. With this assumption, the generated intermediate meshes tend to exhibit a uniform sampling. [VALE-09, Computer Graphics Forum 2009, with LIRIS lab. Lyon]

Surface Remeshing (S. Valette, R. Prost)
We proposed a generic approach 3D meshes remeshing and simplification. This approach is based on a variational clustering algorithm. The clustering is carried out directly on the input mesh. It is fast due to its discrete nature and its convergence is guaranteed. The definition of a generic energy term allows several use cases: isotropic meshing (well suited for usual numerical simulations) or anisotropic meshing, when geometric accuracy is of first concern [VALE-08, IEEE TVCG, 2008] (fig. 3c) http://www.creatis.insa-lyon.fr/site/en/acvd

Variational tetrahedral meshing from labeled voxel volumes (S. Valette, R. Prost)
During J. Dardenne's PhD (with Ampère Lab. in Lyon, ANR BioRFmod), we proposed an algorithm for converting a segmented volume of voxels into a tetrahedral mesh, with the goal to numerically simulate the effects of electromagnetic radiations on the human body. A variational clustering step is used to evenly distribute the mesh vertices in the volume, and an optimization step increases the quality of the generated tetrahedra, which is critical for the accuracy and efficiency of the Finite Elements Simulations [DARD-09, The Visual Computer, 2009] (fig. 3d).http://www.creatis.insa-lyon.fr/site/en/tvc

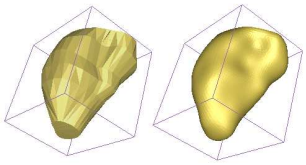	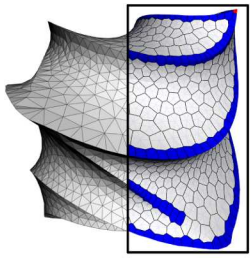	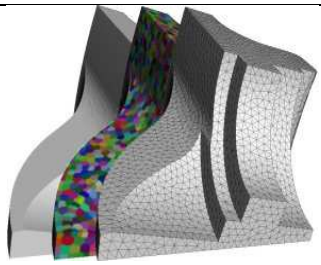	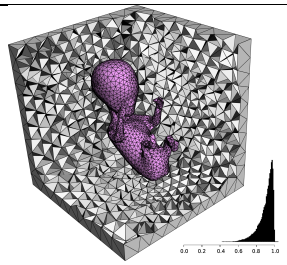
Fig. 3a Left: triangulated surface.Rigth: interpolated by RBFs.	Fig.3b Twisted octahedron meshed with our approach, with some parts showing the underlying Voronoï diagram approximation.	Fig. 3c Illustration of remeshing steps (original, clustering, remeshed) preserving edges.	Fig.3d Tetrahedral mesh of a fetus into a cube. Tetrahedron quality histogram (right)

Image formation modeling

Parametric modeling of US image statistics (O. Bernard, D. Friboulet, with team 3)

Based on the K-distributions model, we have developed a statistical distribution - called K_{RF} - allowing reliable modelling of the statistics of radiofrequency (RF) echographic images in blood and myocardial regions [BERN-06a, IEEE TUFFC, 2006]. Applying the K_{RF} model in the context of segmentation raises a certain number of problems: the consistency of the parameter estimators is not guaranteed and the complexity of the model makes efficient implementation difficult for a segmentation task. In order to overcome these difficulties, we have shown that efficient approximation to K-distributions and development of more stable estimators is feasible through the Generalized Gaussian distribution [BERN-07, IEEE TUFFC, 2007], yielding stable segmentation [BERN-06d].

Quantitative MRI and MRI simulation (H. Benoit-Cattin, C. Odet)

During the PhD of B. Belaroussi, we studied MRI artifacts that make quantitative imaging difficult [BELA-06, MedIA, 2006]. We focused specifically on the susceptibility artifact and we proposed an original scheme to correct such artifact that exploits MR simulation [BELA-06a]. Our approach is the first one that permits the correction of the susceptibility artifact in gradient echo MR images [BELA-06b]. In this work, we manage the development of an MRI simulator named SIMRI that is able to simulate realistic MR images including artifacts [BENO-05, JMR 2005]. This work has been done in collaboration with team 5 and the CEMAGREF, Rennes and is available as an open source project [http://simri.eu]. In collaboration with the CEA Neurospin, we added into SIMRI new functionalities on RF fields and antenna network [AMA-08]. We continued our collaboration with the CEMAGREF by participating to the PhD Thesis of F. De Guio. We considered the susceptibility artifact induced by air bubble as a source of information. We proposed a quantitative approach based on the signal decay observed in gradient echo MR imaging [GUIO-08, MAGMA, 2008] and its application to bread dough during proving [GUIO-09, MRI 2009]. At each step of this work, we use SIMRI simulations [GUIO-07]. Susceptibility is one of the main effects induced by iron oxide nanoparticles that widely contribute to the development of Molecular MR imaging. We address this field with the D. Charpigny PhD. Our objective is to propose an image processing technique that enables the quantization of iron oxide nanoparticles from MR acquisitions. We proposed a deconvolution approach of the default field map to retrieve the susceptibility values [CHAR-09] that are directly linked to the particles concentration.(fig. 4a) During this PhD, we have initiated collaboration with the Stanford Univ. MRSR Lab (J. Pauly) [CHAR-08] [ADDY-09] through a France-Stanford ICA project. This work is part of the ANR INFLAM project driven by team 6.

Monte Carlo Simulation for PET (C. Lartizien)

Our first objective was to develop and evaluate Monte Carlo simulations for 3D PET. Two projects have been conducted toward that goal: 1) the simulation tool PET-SORTEO was validated against the geometries of the two widely distributed microPET systems [LART-07, Phys. Med. Biol., 2007].

This validation was carried out against actual measurements performed by two international collaborators in Canada and Austria. 2) As part of the fGATE project funded by the ANR CIS grant (2006-2009), we have developed new mechanisms to simulate realistic scans in efficient computation time with the OpenGATE simulation plat-form. This project is done in collaboration with team 1. Our second objective was to generate a 3D database of human realistic PET images. The oncoPET-DB (http://www.creatis.insa-lyon.fr/oncoPET_DB/) is the first addressing the need of simulated FDG PET oncology images by providing a series of whole-body patient images with well controlled inserted lesions of calibrated uptakes [TOME-08b] (Fig 4b).

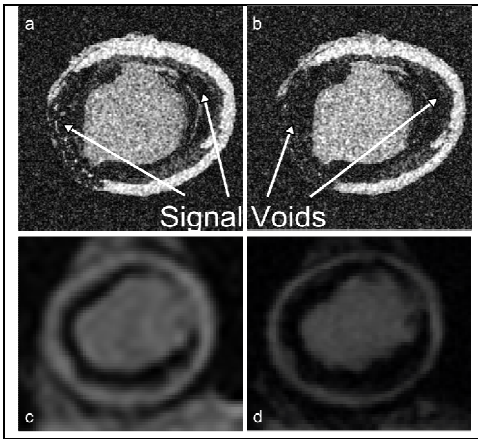

Fig 4a Simulated and ex vivo images. GE Simulated images for (a) TE = 4ms (b) TE = 9ms. Ex vivo GE images for (c) TE = 4ms (d) TE = 9ms. For both sets of images, in areas around the USPIO regions, we see the signal voids which result from the B_0 field inhomogeneities. This is caused by signal dephasing which is a function of TE. We see that the signal void area increases with TE (images on right) both in the simulated and ex vivo images.

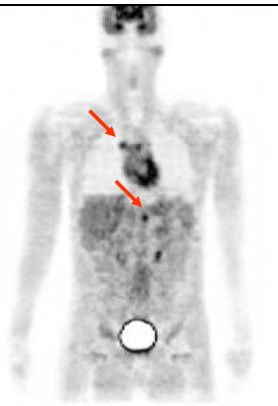

Fig. 4b Simulated PET image of the oncoPET_DB with two lesions pointed by the arrows.

Collaborative Topics

Reconstruction of coronary stents (R. Prost, with F. Peyrin team 7, P. Douek team 1)

We have developed a 3D tomographic reconstruction method in rotational angiography to monitor stenting in the treatment of cardiovascular diseases (PhD of B. Perrenot, CIFRE grant, General Electric Health Care). The difficulties come with cardiac motion and both the small stent size and its low contrast in the radiographic image. We have developed a motion correction method based on the markers positioned on the guide wire of the stent. This method was evaluated on synthetic stent models and in animal experiments. [PERR-07b, IEEE TMI], [PERR-07a,c]. Finally, the method was applied to 12 patients and compared to conventional methods (IVUS and scanner). This work was selected as a "Fait Marquants du CNRS, STIC 2008". http://www.cnrs.fr/st2i/recherche/faits-marquants/2008/deploiement-stent.htm

3D Image reconstruction for Compton camera (R. Prost with V. Maxim team 7)

A carbon ion hadrontherapy centre (ETOILE) will being operating in Lyon (2013). It will use up to 400 MeV/amu carbon ^{12}C ions and 220 MeV protons beams. Our work is motivated by the striking necessity of monitoring the radiation dose. Relating it to nuclear fragmentation gamma particles produced during irradiation is a promising way. We proposed the use of an imaging system based on a combined Compton scattering and pair creation camera. In the PhD of M. Frandes we showed by Monte Carlo simulations that the proposed system provides the required dose location capabilities [FRAN-09a, IEEE TNS] (with A. Zoglauer, Univ. of California at Berkeley). Reconstruction of images from Compton projections is still an issue. Currently available analytical image reconstruction algorithms ignore the largest part of the data or suffer from numerical deficiencies. We proposed an exact analytical reconstruction of the image that allows the use of

the entire set of data [MAX-09, Inverse Problems]. This work will be now partly supported by the EU FP7 project ENVISION WP3.4 (2010-2014).

Grid computing for distributed applications (T. Glatard, with team 1 and 7)
Several efforts were conducted to enable the exploitation of large-scale distributed computing infrastructures. In particular, our long-term implication in the European EGEE project (EGEE, EGEE-II, EGEE-III) and local initiatives (ACI Medigrid 2003-2005, RAGTIME project) allowed early production exploitation of grids, with applications to cardiac image segmentation and motion estimation (in collaboration with team 1, [MAHE-2009], ANR Gwendia), MRI simulation ([BELL-06], [MONT-05d]), content-based image retrieval ([CAMA-08a], ICT-Asia Oncomedia, collaboration with D. Racoceanu from IPAL Singapore [RACO-07]) and hadrontherapy (collaboration with team 7, [CAMA-08c], collaboration with J. Mosciki at CERN Geneva [CAMA-09]). Those applications and associated tools were demonstrated several times in grid user forums ([CAMA-08d], [CAMA-09], [GLAT-09]) and set the basis for an integrated virtual imaging platform [CAMA-08b] (see the team project).

3. Interactions

Interaction with team 3 [DYDE-05],[GREN-05], team 7 (see section 2.5) [PERR-07-a-b-c, FRAN-08, LART-07], team 1, team 4 [BOLB-08, BOLB-07, DU-08], team 5 [ADDY-09]
Common papers and conferences writed with the other CREATIS team:

Team #	1	3	4	5	6	7	8
papers	3	2	0	4	1	5	4
conferences	7	9	1	9	0	7	3
total	10	11	1	13	1	12	7

4. Technological transfer

Open source software: SIMRI http://simri.eu, [BENO-05 JMR, 2005]. Patent [JUNG-06 Patent]

5. Grants

National projects
ACI Medigrid (2003-05). Région Rhône Alpes, project RAGTIME (2003-05). ANR BioRFmod (2006-09) with Ampère lab. Lyon. ANR Fgate (2007-09) with team 7. ANR Gwendia (2007-10) with team 1. ANR INFLAM (2007-10) with team 5. ANR ProstaFluo (2008-10) with team 3. Cluster 'Région Rhône Alpes ISLE, Informatique, Médecine et Santé' projects I3M (2005-08), SIMED (2009-12). PEPS Tagging-US (2008-09) with team 3. BQR INSA 2006 with team 5.

European projects
EGEE (2004-06), EGEE 2 (2006-08), EGEE 3 (2008-10), NoE Virtual Physiological Human (NoE VPH) (2008-2012).

International projects
Momarisp France-Stanford ICA project, Stanford University MRSR Lab (J. Pauly) [CHAR-08, ADDY-09], ICT Asia Oncomedia [RACO-07].

Industrial contracts
Cifre General Electric Health Care with teams 1 and 7 [PERR-07-a-b-c], Cifre Philips Medisys 2008-2011.

6. Collaborations

National collaborations
CEMAGREF Rennes [GUIO-07-08-09], CEA NeuroSpin [AMA-08], I3S Nice Sophia-Antipolis [LING-09], [MAHE-09] [LING-09], LRI Orsay [GERM-09], Ampere Lyon [DARD-09], [LIRIS Lyon [VALE-09].

International collaborations
Medical Image Computing Leuven Univ. Belgium: [DYDE-06, BERN-06a, BERN-07]. Biomedical Imaging Group Ecole Polytechnique Fédérale de Lausanne Suisse: [BERN-09]. Dept. of Information and Com. Eng., Yeungnam University Gyongsan Korea [CHO-07, CHO-07b, JUNG-06 Patent, CHO-06a-b, KIM-06-a-b-c ,CHO-05, KIM-05]. Computer Graphics Lab. Tokyo Univ., Tokyo Japan [GELA-06c]. Space Sciences Lab., Univ. of California at Berkeley USA [FRAN-08]. Harvard Medical School, Boston [GELA-09]. Biomedical Imaging Lab., Singapore [GELA-09]. IPAL Singapore [RACO-07], HUG Genève [RACO-07], Univ. of Amsterdam [OLAB-2009], MTA SZTAKI Budapest: [GLAT-07], Univ. Berlin: [OLAB-2009].

7. Expertise and consulting
ANR : AAP DEFIS 2009, BLANC 2008,09

Journals: IEEE Trans. on Signal Processing, IEEE Trans. on Image Processing, IEEE Trans. on Medical Imaging, IEEE Trans. on Information Technology in Biomedicine, IEEE Trans. on Biomedical Engineering, IEEE Trans. on Visualization and Computer Graphics, IEEE Trans. on Circuits and Systems for Video Technology, IEEE Trans. on Sensors, Inter. Journal on Mathematical Modelling of Natural Phenomena, MedIA, Image and Vision Computing, SIAM Journal on Imaging Science, The Visual Computer, Future Generation Computer Systems (FGCS), Physics in Medicine and Biology, Acad. Radiology, Medical Physics.

Conferences: IEEE Inter. Ultrasonic Symposium, IEEE Inter. Symposium on Biomedical Imaging (ISBI), IEEE Inter. Conf. on Image Processing (ICIP), IEEE Engineering in Medicine and Biology Society (EMBS), Functional Imaging and Modelling of the Heart Workshop (FIMH), Siggraph, Eurographics, Symposium on Geometry Processing, Siggraph Asia, MICCAI and MICCAI–Grid, Workflow Systems in eScience (WSES).

Miscellaneous: C. Odet: AERES expert (CRESTIC 2007, LAGIS 2008, ERT E. Valdes 2007), member of the CNU section 61 from 2004.

8. Awards
The work of O. Bernard was awarded by the Biomedical Engineering PhD prize by the "Engineering in Medicine and Biology Society" (EMBS) of the French IEEE France section and the "Société Française de Génie Biologique et Médical". (28 may 2008). The work of J. Dardenne was awarded by JCGE'2008.

9. Research training
H. Benoit-Cattin: Head of Telecom Department INSA-Lyon, C. Odet : Head of Teaching Management at INSA-Lyon, T. Grenier: Head of International Master of Embedded Systems and Medical Image Engineering, INSA-Lyon, R. Prost: Signal and Image Processing topic manager at Dep. Electrical Engineering (Master 2 level) INSA-Lyon.

10. Congress organisation and committees
CCGRID Health 2009, Shanghai 2009, Singapore Workshop 2006, 2007

Articles internationaux avec comité de lecture répertoriés par l'AERES (ACL)
Per-reviewed journal papers
[BERN-09a] O. Bernard, D. Friboulet, P. Thevenaz, and M. Unser. **Variational B-Spline Level-Set: A Linear Filtering Approach for Fast Deformable Model Evolution**. *IEEE Transactions on Image Processing*, 18(6):1179-1191, 2009.

[BABO-09] L. Baboi, F. Pilleul, L. Milot, C. Lartizien, C. Roche, G. Poncet, J.Y. Scoazec, and O. Beuf. **MRI follow-up of liver growth of neuro-endocrine tumors in an experimental mouse model**. *Magnetic Resonance Imaging*, pp (in-press), 2009.
[DARD-09b] J. Dardenne, S. Valette, N. Siauve, N. Burais, and R. Prost. **Modélisation adaptative 3D de structures anatomiques pour la simulation électromagnétique et thermique**. *European Journal of Electrical Engineering*, pp in press, 2009.
[DARD-09a] J. Dardenne, S. Valette, N. Siauve, N. Burais, and R. Prost. **Variational tetraedral mesh generation from discrete volume data**. *The Visual Computer*, 25(5):401-410, May 2009.
[GUIO-09] F. De Guio, M. Musse, H. Benoit-Cattin, T. Lucas, and A. Davenel. **Magnetic resonance imaging method based on magnetic susceptibility effects to estimate bubble size in alveolar products: Application to bread dough during proving**. *Magnetic Resonance Imaging*, 27:577-585, 2009.
[GELA-09] A. Gelas, S. Valette, R. Prost, and W.L. Nowinski. **Variational implicit surface meshing**. *Computers and Graphics (proceedings of IEEE Shape Modeling International SMI 2009)*, 33(3):312-320, June 2009.
[MAXI-09] V. Maxim, M. Frandes, and R. Prost. **Analytical inversion of the Compton Transform using the full set of available projections**. *Inverse Problems*, pp (in-press), 2009.
[ROSE-09a] J.L. Rose, A. Lalande, O. Bouchot, E. Bourennane, P.M. Walker, P. Ugolini, C. Revol-Muller, R. Cartier, and F. Brunotte. **Optimized automatic detection of vessel wall contours from cine-MRI for routine aortic distensibility determination**. *Magnetic Resonance Imaging*, pp in-press, 2009.
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[FRAN-09a] M. Frandes, A. Zoglauer, V.a Maxim, and R. Prost, A Tracking Compton-scattering Imaging System for Hadron Therapy Monitoring, IEEE Trans. On Nuclear Science, pp (in press), 2009
[BABO-08] L. Baboi, L. Milot, C. Lartizien, D. Grenier, C. Roche, J.Y. Scoazec, F. Pilleul, and O. Beuf. **Characterization of liver lesions in a mouse model of endocrine tumors using MRI**. In *International Society of Magnetic Resonance in Medicine*, Toronto, Canada, pages 2809, April 2008.
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[CHO-09] J.W. Cho, H.K. Kim, S. Valette, H.Y. Jung, and R. Prost. **A Compression Method for 3-D Mesh Sequences Combining Wavelet-based Multi-resolution Analysis and Multi-order Differential Coding**. In *International Conference on Image Processing, Computer Vision, and Pattern, IPVC'09*, Las Vegas, USA, pages in-press, July 2009.
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[FOLI-05] S. Philipp-Foliguet and L. Guigues. **Critères multi-échelle d'évaluation de la segmentation**. In *GRETSI'05*, Louvain-la-Neuve, Belgium, pages 885-888, 2005.

Conférences données à l'invitation du Comité d'organisation dans un congrès national ou international(INV)

Invited Conferences

[LIEB-09] H. Liebgott, A. Basarab, P. Gueth, D. Friboulet, and P. Delachartre. **Transverse oscillations for tissue motion estimation**. In *World Congress on Ultrasonics*, Santiago, Chile, 2009.
[BEUF-08a] O. Beuf and H. Benoit-Cattin. **Contraste de susceptibilité: analyse et correction**. In *12ème Congrès du GRAMM*, Lyon, France, 26-28 mars 2008.
[BENO-06] H. Benoit-Cattin and G. Collewet. **Numerical implementation of the Bloch equation to simulate magnetization dynamics and imaging**. In *International CONFERENCE ISMRM'06*, Seattle, USA, May 2006.
[MAGN-06b] I.E. Magnin, H. Benoit-Cattin, and J. Montagnat. **Medical grids**. In *AIRS'06 Asia Information Retrieval Symposium*, Singapore, Singapore, October 2006.
[BENO-05] H. Benoit-Cattin. **SIMRI: A versatile and interactive MRI simulator**. In *Workshop COST B21*, Lödz, Pologne, October 2005.

[NIST-05] I. Nistoreanu, F. Bellet, C. Pera, and H. Benoit-Cattin. **SIMRI at WEB: An MRI simulation service on EGEE Grid architecture**. In *4th EGEE CONFERENCE*, Pisa, Italia, Sept 2005.

Brevet (AP)

Patents

[JUNG-06] J.W. Jung, H.Y.and Cho, M.S. Kim, and R. Prost. **Brevet N. 10-2006-0080755 - Coréen**. Encoding and Decoding Method for Watermarking Using Statistical Analysis, 2006.

HDR

Defended HDR thesis

H. Benoit-Cattin. **Contributions en segmentation d'images, simulation et correction en imagerie par résonance magnétique**. H.D.R., INSA Lyon, 2006. Jury: Pr. J.P. Coquerez (rap.), Pr. J. Demongeot (rap.), Pr. M. Revenu (rap.), Pr. P. Bolon , Pr. J. de Certaines, Pr. C. Guttmann, Pr. M. Janier, Pr. C. Odet, Pr. J.G. Postaire.

Thèse de doctorat soutenues

Defended Ph D thesis

C.S. Coello. **Traitement de signal, matériel et logiciel, pour nouveaux détecteurs de radiologie médicale numérisée**. Doctorat, 6 Mars 2009. Jury: BARBIER Daniel Président, ODET Christophe Directeur de thèse, BRASSE David Rapporteur, MOREL Christian Rapporteur, DINTEN Jean-Marc Examinateur, ARQUES Marc (Invité), ROH Pierre (Invité).

Y. Khadra. **Méthodologie de réalisation de modèles anatomiques maillés : application à l'imagerie du petit animal**. Doctorat, INSA Lyon, 2008. Jury: F Mériandeau (rap.), J.-C. Pinoli (rap.),M. Janier (prés.), H. B. Cattin, C.Odet (dir.)

B. Perrenot. **Reconstruction tomographique 3D de stent coronaire avec prise en compte du mouvement en angiographie rotationnelle cardiaque par rayons X**. Doctorat, INSA Lyon, 2008. Jury: G. Finet (co-dir.), L. Desbat (rap), J. Felblinger (rap.), F. Peyrin (dir.), M. Gilard, G. Malandain, R.Prost, R. Vaillant.

J.L. Rose. **Croissance de région variationnelle et contraintes géométriques tridimensionnelles pour la segmentation d'image**. Doctorat, INSA Lyon, 2008. Jury: M. Revenu (rap.), F.Truchetet (rap.),P.Bolon (prés.), M.Jourlin , C.Revol-Muller,C.Odet(dir.).

J.W. Cho. **Watermarking, Compression, and Their Combination for 3-D Triangular Meshes**. Doctorat, INSA Lyon, Yeungnam University, 2007. Jury: M. Antonini (rap.), K.R. Kwon (rap.), K.Y. Yoo, I.E. Magnin (prés.), H. S. Kang, F. Preiteux, K. Y. Yoo, H.Y. Jung (dir.), R. Prost (dir.).

M.S. Kim. **Wavelet transform based digital watermarking for 3-D surface meshes and mesh sequences**. Doctorat, INSA Lyon, Yeungnam University, 2007. Jury: F. Schmitt (rap.), K.R. Kwon (rap.), K.Y. Yoo, I.E. Magnin (prés.), H.Y. Jung (dir.), R. Prost (dir.).

J. Velut. **Segmentation par modèle déformable surfacique localement réularisé par spline lissante**. Doctorat, INSA Lyon, 2007. Jury: J.-O. Lachaud (rap.), J. Montagnat (rap.),O. Coulon(prés.), H. B. Cattin, C.Odet(dir.).

O. Bernard. **Segmentation en imagerie échocardiographique par ensembles de niveaux paramétriques évoluant à partir des statistiques du signal radiofréquence**. Doctorat, INSA Lyon, 2006. Jury: Jan D'Hooge, Denis Friboulet (dir.), Alain Herment (rap.), Rémy Prost, Philippe Réfrégier (rap.), Mickael Unser (prés.).

A. Gelas. **Compactly supported radial basis functions: multidimensional reconstruction and applications**. Doctorat, INSA Lyon, November 2006. Jury: Michel Barlaud (rap.), Jean-Marc Chassery (prés.), Olivier Devillers (rap.), Denis Friboulet, Takashi Kanai (co-encadrant), Yutaka Ohtake et Rémy Prost (dir.).

S.W. Lee. **Enrichissement de la régularité de la triangulation de l'isosurface des images volumiques. Application à l'imagerie médicale et à la compression sur une base d'ondelettes**. Doctorat, INSA Lyon, December 2006. Jury: Marc Antonini (rap.), Ho-Youl Jung, Isabelle Magnin (prés.), Frédéric Truchetet (rap.) et Rémy Prost (dir.).

B. Belaroussi. **Correction par traitement d'images de l'artéfact de susceptibilité magnétique dans les images IRM**. Doctorat, INSA Lyon, October 2005. Jury: Saint-Jalmes, H. and Revenu, M. (rap.) and Bolon, P. (rap.) and Davenel, A. and Zaim-Wadghiri, Y. and Benoit-Cattin, H. and Odet, C. (dir.).

A. Gouaillard. **Contexte générique bi-multirésolution basé ondelettes pour l'optimisation d'algorithmes de surfaces actives**. Doctorat, INSA Lyon, October 2005. Jury: GU X.D., Morvan J.M. (rap.), Delingette H. (rap.), Janier M., Benoit-Cattin H. et Odet C. (dir.).
T. Grenier. **Apport de l'espace des caractéristiques et des paramètres d'échelle adaptatifs pour le filtrage et la segmentation d'image**. Doctorat, INSA Lyon, December 2005. Jury: P. Refregier (prés.), D. Comaniciu (rap.), J.M. Nicolas (rap.),M.

Team n°3 : Ultrasound Imaging – Imagerie Ultrason ore

Previous activity : Period 2005-2009

Key words : Ultrasound image formation, radio frequency (RF) signals, synthetic aperture, elastography, motion estimation, blood flow, ultrasound contrast agents, 3D ultrasound.

Team leader	Vray Didier	PU Insa
Vice-team leader	Delachartre Philippe	MCU-HDR Insa
	Basset Olivier	PU UCB
	Brusseau Elisabeth	CR CNRS
	Cachard Christian	PU UCB
	Gimenez Gérard (50%)	PU Insa
	Liebgott Hervé	MCU UCB

ETP : 3,75

Engineers	Duboeuf François	IE Inserm

Invited professors	Kybic Jan	Tchec Rep., Assistant Prof., Prague Tech ; Univ	Center for Machine Perception (CMP), 2 months in 2005, 2006

Post doc	Saroul Laurent	France, EPFL Thesis	Convention CEA
	Basarab Adrian	Roumanie, Creatis Thesis	ATER
	Aoudi Walid	Tunisie, Creatis Thesis	ATER

Ph.D student	Ghazhal Bilal	Bourse Liban	Co-tutelle Liban
	Liu Yang	Bourse Chine	
	Pasovic Mirza	All. Menesr	Erasmus center Rotterdam
	Marion Adrien	All. Menesr	
	Gueth Pierre	All. ENS	
	Uhercik Marian	Prog Europ Marie Curie	Co-tutelle Prague
	Varray François	All. Menesr	Co-tutelle Florence

Defended HDR	Delachartre Philippe	2006

Defended Theses

Liebgott Hervé	France	2005	MCU
Mari Jean-Martial	France	2005	Chercheur Imp. College
Durning Bruno	France	2006	MCU
Balocco Simone	Italie	2006	PostDoc Barcelone
Said Ghada	Syrie	2006	Ens/cherch Syrie
Barva Martin	Tchéquie	2007	
Aoudi Walid	Tunisie	2008	ATER
Basarab Adrian	Roumanie	2008	MCU
Deprez Jean-François	France	2008	PostDoc Oxford
Ghazhal Bilal	Bourse Liban	2009	Ens/cherch Liban

Per-reviewed Publications: 37 ; book chapters: 2.
Conference papers : 61 ; invited talks: 5
Patent : 2

Résumé: Notre équipe développe des méthodes de traitement du signal et de l'image qui permettent de caractériser un milieu biologique imagé avec un système d'imagerie ultrasonore.
Nous travaillons suivant 3 axes complémentaires : la maitrise du système d'imagerie à la fois en émission et en réception, l'estimation du champ de déformation du milieu, et l'estimation des caractéristiques géométriques et statistiques des images ou des séquences d'images ultrasonores pour remonter aux propriétés des milieux. Les méthodes que nous développons s'appuient sur des modèles physiques pour estimer les paramètres d'élasticité, de mouvement ou de non linéarité des milieux biologiques. La formation de l'image est adaptée aux méthodes qui reposent sur l'acquisition des signaux Radio Fréquence (RF) indispensables en entrée des traitements. Chaque fois que cela est possible, les méthodes sont implantées pour fonctionner en temps réel, c'est-à-dire au rythme de l'acquisition des images par le système et sont étendues aux données 3D.

1. Objective

The aim of our work is to develop signal and image processing methods that can characterize biological media imaged with ultrasound imaging system.
We work on 3 complementary axes: the control of imaging system in both transmission and reception, the estimation of deformation field of the medium and the estimation of geometrical and statistical characteristics of ultrasound images or image sequences. The methods we develop are based on physical models to estimate the parameters of elasticity, movement or non-linearity of biological media. The image formation is adapted to the methods based on the acquisition of radio frequency signals (RF). Whenever possible, the methods are developped to operate in real time, ie the rate of acquisition of images by the system and are extended to 3D data.

2. National and international context

Ultrasound medical imaging covers a wide range of fields in medicine and technology. We have chosen to focus our work on the development of signal and image processing methods devoted to motion estimation and tissue characterization so as to provide a diagnosis aid to medical doctors. The main challenge is to provide robust estimation (motion, low deformation, contour, segmentation, quantitative characterization…) despite the noisy nature of ultrasound images and taking into account the real-time acquisition of image sequences. The applications of our methods in medicine or biology are established via collaboration with the doctors in Creatis or other laboratories. Through exchange of doctoral students, co-supervision thesis, research visit or common research grants, we have collaborations with the teams recognized by the scientific community and publishing in the field of ultrasound medical imaging. Of these teams, we can mention at the national level P. Laugier and L. Bridal (LIP, Paris), A. Bouakkaz (Inserm, Tours), J.Y. Chapelon (Inserm, Lyon) and M. Fink (LOA, Paris). At the international level, we can mention S. Foster (Univ. Toronto) for high frequency ultrasound imaging, T. Van Der Steen and N. De Jong (Thorax center, Rotterdam) for non linear imaging, G. Cloutier and R. Maurice (LBUM, Montréal) for the imaging of vessels, J. Jensen and J. Wilhjelm (DTU, Copenhagen) for image formation and P. Tortoli (Univ. Florence) for flow estimation.

3. Research activity

Control of the imaging system (O. Basset, P. Delachartre, C. Cachard, H. Liebgott)
Joint adaptation of the excitation signals and image formation (P. Delachartre, H. Liebgott)
In order to improve motion estimation in the direction perpendicular to beam axis a specific receive beamformng method has been developped based on the production of transverse oscillations [LIEB-05, *Eurasip J Appl Signal Process*]. Experimental validation of the approach for elastography has been studied [LIEB-07a, *IEEE Trans Ultrason Ferroelectr Freq Control*] showing improvement compared to more conventional methods as speckle tracking. The possibility to use combined transmit/receive beamforming enables to produce faster oscillations and higher spatial resolution leading to improve even more the accuracy of the transverse estimated motion field [LIEB-08a, *IEEE Trans Ultrason Ferroelectr Freq Control*] compared to the initial receive only approach.
New approaches for ultrasound imaging with contrast agents (C. Cachard, D. Friboulet)
Ultrasound contrast agents (UCA) are intravenously injected to improve the identification of perfused areas. A spectral autoregressive method dedicated to the detection of UCA from radio frequency (RF) data, based on second order autoregressive (AR) modeling of the RF signal has been developed. The results obtained on numerical simulation and on in vitro data show that the

proposed parameter SM2 which quantifies the second harmonic peak enables to detect correctly the contrast agent, in particular at low concentration and mechanical index [DYDE-05, *Ultrasonic Imaging*].

3D RF imaging (C. Cachard, H. Liebgott)

In clinical practice, line-segment shape micro tools are frequently used to perform diagnosis or therapeutic tasks. From 3D ultrasound RF data [MARI-07a, *Technical Acoustics*].we show that the micro tool axis can be found through maximizing the Parallel Integral Projection transform that is a form of the Radon transform. Once the axis position is known, localization of the micro tool tip is performed. Localization accuracy is of the order of hundreds of micrometers and is comparable to the ultrasound system axial resolution [BARV-08, *IEEE Trans UFFC*].

Elastography – Estimation of the displacement field (O. Basset, E. Brusseau, P. Delachartre)

The work in elastography is to develop new models for estimating displacement and 3D deformation in real time. The “free hand” compression of the organ studied with the ultrasound probe will also be taken into account.

Estimation based on a dynamic spatiotemporal approach (P. Delachartre)

Two ways were followed to estimate the subpixel displacement in elastography. At first a new bilinear deformable mesh method was developed to estimate complex tissue motion [BASA-08a, *Med Image Anal*]. Then, the bilinear method was extended and encapsulated in a tracking algorithm for free hand tissue compression in elastography [BASA-09c, *J Signal Process Syst*]. The second way was to develop subpixel strain and displacement estimators based on close-form solutions. A 1D strain estimator was first published [FROM-07, *Eurasip J Adv Signal Process*]. Then, we focussed on 2D approches of subpixel displacement estimation via phase images. The analytic estimation and its characteristics were described in [BASA-09a, *IEEE Trans Image Proces*]. A phase based matching method was detailled in [BASA-09b, *IEEE Trans Ultrason Ferroelectr Freq Control*] and implemented for real time processing on Ultrasonix imaging system (Elavisu, Lyon Science Transfert, 2009)

Estimation based on a 3D model of deformation (E. Brusseau, O. Basset)

Contrary to commonly used strain estimation techniques, a method based on an original deformation model, adapted to the highly anisotropic character of RF ultrasound data was developed [BRUS-08, *IEEE Trans Med Imaging*]. This method has first been proposed to estimate 2D strain fields [BRUS-07, *J Radiol*], and was then extended to the 3D strain distribution computation [DEPR-09, *Med Image Anal*]. Deformation parameter estimation was initially performed independently [SAID-06, Ultrasonics] and then jointly through constrained optimization [DEPR-09, *Med Image Anal*]. This approach remains efficient for large strains (>10%) and freehand acquisition conditions.

Exploration of flow dynamics (O. Basset, C. Cachard, D. Vray)

Estimation of the properties of the vessel wall and the distribution of flow rate (O. Basset, C. Cachard)

A 3D model reproducing the biomechanical behaviour of human blood vessels has been proposed. It is based on a multilayer geometry and enables the representation of different vessel structures such as stenoses, bifurcations and the associated pathologies. Different vessel structures, including bifurcations, with associated pathologies such as local arterial wall thickening, aneurysms, stenosis and atherosclerotic plaques can be simulated. Each region is acoustically characterized using FIELD II software, which produces the RF echo-signals corresponding to echographic scans [BALO-06, Ultrasonics]. M-mode, B-mode and color Doppler images derived from these phantoms can be provided. The model can be used as a tool for the preliminary evaluation of ultrasound signal processing and visualization techniques [BALO-08, Med Phys]. It can also be used for the quantification of tissues stiffness [BALO-07, *IEEE Trans Ultrason Ferroelectr Freq Control*] using ultrasound Doppler measurement.

High frequency ultrasound imaging (D. Vray)

Motion and flow estimation need the developpement of specific methods when high frequency ultrasound (>30MHz) images are processed. In collaboration with the team of S. Foster, Toronto, Canada, we proposed a quantification of flow with a method based on the spatio-temporal decorrelation of the US images [AOUD-06, Ultrasonics]. In the same way, we have proposed the

spatio-temporal filtering of sequence of US images to estimates low velocities (<1mm/s) in thin vessel (<1mm) with a high spatial resolution (~20µm) [MARI-09a, Pattern Recognition]. These methods have been evaluated with experimental and simulated data. At this occasion, we developed a very efficient simulation method to simulate sequence of ultrasound images [MARI-09b, IEEE Trans. UFFC]

Characterizing the response of perfused tissues (O. Basset)
The acoustical properties of investigated tissue and in particular the scatterer density are related to the statistical distribution of backscattered signals. A segmentation tool, based on the local measurement of the Nakagami distribution parameters was proposed to segment ultrasound data [DAVI-05, Ultrasonics].
To increase the contrast of images during harmonic or contrast tissue imaging, we propose to work on the nonlinear propagation in the tissue which produces second harmonic. In a first step, a specific multifrequency signal is emitted to reduce the second harmonic component due to the propagation. Then, different approaches are tested to extract the nonlinearity parameter of tissue. This work is made in the frame of an ANR Tecsan project MONITHER.

Biological and medical application (P. Delachartre, E. Brusseau, F. Duboeuf, D. Vray)

Characterization of the pathologies of the thyroid (P. Delachartre)
Ultrasound elastography is a promising imaging technique that can assist in diagnosis of thyroid cancer. However, the complexity of the tissue movements under freehand compression requires the use of a parametric displacement model and a specific estimation method adapted to sub-pixel motion. Therefore, a motion estimation method, referred to as Bilinear Deformable Block Matching (BDBM), was applied to thyroid gland analysis. The proposed method uses a bilinear model with eight parameters for controlling the local mesh deformation and includes an iterative multi-scale process [BASA-08a, *Med Image Anal*]. The free-hand compression also requires motion analysis with image sequences. A registration method using a technique of compression orientation detection led us to introduce a new parameter based on the local angle map of estimated motion vectors [BASA-09c, *J Signal Process Syst*].
Tissue mimicking fantom and ultrasound image simulation (D. Vray, F Duboeuf)
In collaboration with CEA LETI, Grenoble, France, we have developed an original optic and ultrasound phantom for the quantitative evaluation of time resolved fluorescence imaging controlled with ultrasound imaging [BOUT-09, Journal of Biomedical Optics]. We acquired a large experience in realization of phantoms with complete control of physic properties [DUBO-09, J. Med Phys] and mimicking biological tissues. In the frame of ANR TecSan PROSTAFLUO, we developed a bimodality US/Optic phantom for mimicking prostate tissue which conducted to a patent [VRAY-09, French Patent]
Imaging of vessels (E. Brusseau)
A severe complication of arterial atherosclerosis is thrombosis, a consequence of plaque rupture or fissure, which might lead to myocardial infarction and sudden ischemic death. Plaque rupture is a complicated mechanical process, correlated with the plaque morphology, composition, mechanical properties and with the blood pressure. In the context of extracting information on the plaque local mechanical properties, ultrasound elastography was applied to examine pathological arterial walls, of a carotid artery ex vivo ([MAUR-05, Ultrasound Med. Biol.]) and coronary arteries in vivo ([MAUR-07, Ultrasound Med. Biol.]). Results demonstrated the ability of the technique to differentiate between different vascular tissue structures, namely hard and soft materials, for a better understanding of the plaque composition.

4. Plateforms
An experimental US platform has been built by our team at Creatis. It is equipped with a fully programmable Ultrasonix imaging scanner (emission, reception, real time processing). Linear, cardiac and 3D probes enable the acquisition of RF signals.

5. Interaction
Collaborations with several teams of Creatis for methodological aspects : D. Friboulet and O. Bernard for motion estimation and ultrasound image segmentation [BERN-06a, *IEEE Trans Ultrason Ferroelectr Freq Control*], [BERN-06b, MedIA]. G. Courbebaisse for modeling and

simulation of vascular dynamics [BALO-06, Ultrasonics], [BALO-08, Med Phys], [BALO-07, *IEEE Trans Ultrason Ferroelectr Freq Control*]. O. Beuf and D. Grenier for MR/US elastography.

6. Grants

National projects
Prostafluo, ANR Tecsan 2008-2010,
Monither, ANR Tecsan 2008-2010
Elavisu, Lyon Science Transfert, 2009.
US Tagging, PEPS CNRS ST2I, 2008-2009
Elasto US In vitro, BQR INSA, 2004-2006
Cancer diagnosis and Treatment by Ultrasound, CDTU
European projects (NoE, Réseaux Marie Curie, STREP, IP, …)
Marie Curie Early Stage Training in the FP6 Human Ressource Program Wide Area Research Training in Health Engineering (WARTHE), multi sites training in the Biomedical Ingeneering field piloted by INSA with University of Ulster and Czech Technical University, 2006-2010.
Industrial contracts
Theraclion, Real-time tracking of vessels in US image sequence, 2007-08. 1 brevet, [VRAY-08 French and international patent]
CEA-LETI, US/Optic imaging for Prostate Cancer disgnosis, 2007-08, 1 ANR Tecsan Prostafluo, 1 publication [BOUT-09 J. Biomed. Opt.], 1 brevet [VRAY-09 French patent]

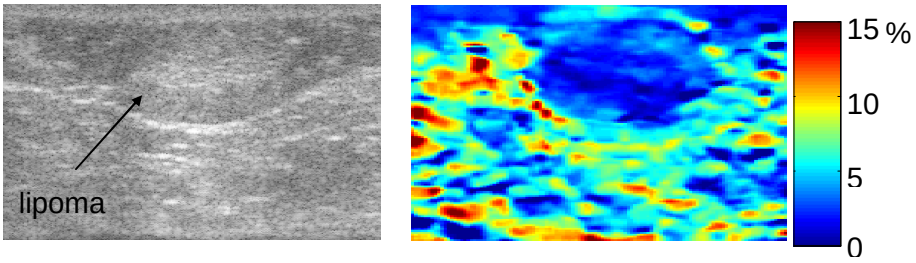
7. Collaborations (uniquement publiante)
National collaborations
- LAMCOS Laboratory, INSA, 2 publications
- Institut des Sciences cognitives, Lyon, 1 publication
- ENVL : Ecole National Vétérinaire de Lyon, France, 1 congrès international.

International collaborations
- LBUM : Laboratoire de Biorhéologie et d'Ultrasonographie Médical, Montréal, CANADA, 3 publications
- Center for Machine perception, Prague University, Czech Republic, 2 publications
- Microelectronics Systems Design Laboratory, Firenze University, Italie, 3 publications
- Center For Fast Ultrasound, Copenhaghen, Danemark, 2 publications
- Departement of Medical Biophysic, Toronto, Canada, 1 publication
- Biomedical Imaging Group, EPFL, Lausanne, Switzerland, 1 publication
- Bucarest Technical University, Romania, 1 publication

8. Expertise and consulting
- Experts for ANR Tecsan 2008 and 2009.
- C. Cachard is member of CNU 61, 2007-2011
- D. Vray was an elected member of the Scientific Committee of INSA Lyon 2003-2007
- C. Cachard was an elected member of the Scientific Committee of Université lyon 1, 2007-2008
- G. Gimenez is the Director of the multimodality imaging platform Cermep-Imagerie du vivant

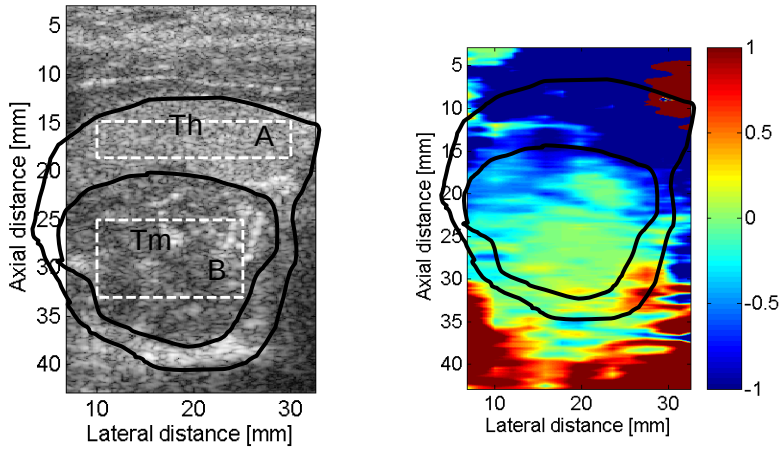
9. Research training
Olivier Basset is head of the specialty "Systems and Images" of the Master GEGP (Génie Electrique, Génie des Procédés)
Olivier Basset is a member of the scientific committee of "Ecole Doctorale EEA".
Christian Cachard is in charge of the yearly Ultrasound session of EUROPEAN SCHOOL for MEDICAL PHYSICS (ESMP), Archamps (Haute Savoie)

10. Congress organisation and committees
- O. Basset is member of technical committee of the IEEE International Ultrasonic Symposium
- E. Brusseau has been a member of the national technical committee of the IEEE EMBC 07



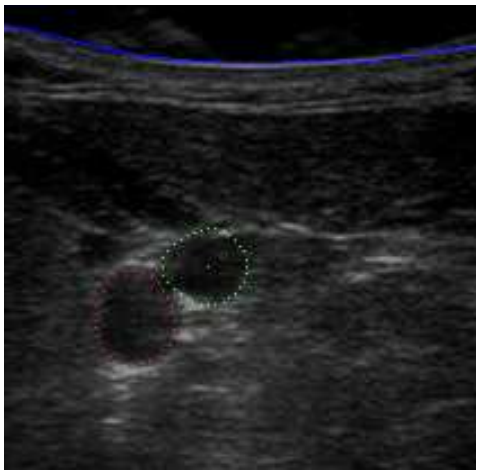
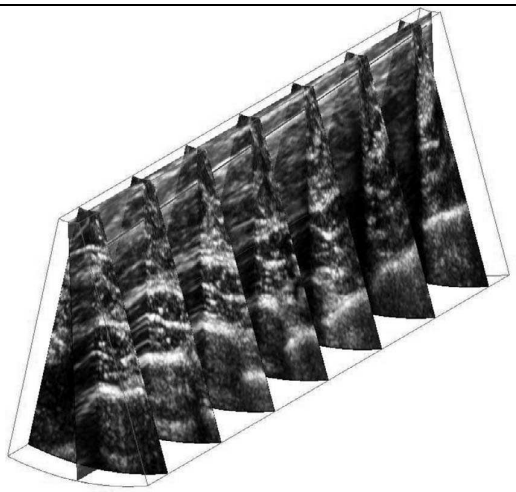
(a) (b)

2D in vivo elastography. Data acquired from a volunteer suffering from the Roch-Leri mesosomatous lipomatosis. (a) conventional B-mode image and (b) estimated axial strain. Reported strain values are up to 15% of deformation. We can observe that the lipoma is harder than the surrounding tissues and appears mechanically homogneous. [BRUS-09, IEEE *International Symposium on Biomedical Imaging*], [BRUS-08a, *IEEE Trans Med Imaging*]



(a) (b)

B-mode image (a), Th - thyroid gland, Tm - malignant tumor. CNR calculated in regions A and B gives 0.53. (b) colormap of the local orientation parameter. CNR, calculated in regions A and B, is increased by 3 on this map (1.6) compared to the B-mode image (0.53). [BASA-09c, J Signal Process Syst]

	
Real-time tracking of skin and vessels during HIFU thyroid treatment. Collaboration with Theraclion company (Paris) which conducted to a patent [VRAY-08 International patent]	3-D view of data from breast biopsy. The boundary geometry of 3-D data is marked by thin lines. There is one planar section with a needle in the upper part and seven perpendicular planar sections. [BARV-08, *IEEE Trans Ultrason Ferroelectr Freq Control*],

Team n°3 : Ultrasound Imaging – Imagerie Ultrason ore

References: period 2005-2009

Indicateurs, indicators
33% of publications in the frame of international collaborations
33% of publications in the frame of team interaction at Creatis

ALC : Articles dans des revues internationales avec comité de lecture
Original International and National articles in specialized journals with review committee

[BASA-09b] A. Basarab, P. Gueth, H. Liebgott, and P. Delachartre. **Phase-based block matching applied to motion estimation with unconventional beamforming strategies**. *IEEE Trans Ultrason Ferroelectr Freq Control*, 56(5):945-957, 2009.
[BASA-09a] A. Basarab, H. Liebgott, and P. Delachartre. **Analytic estimation of subsample spatial shift using the phases of multidimensional analytic signals**. *IEEE Trans Image Proces*, 18(2):440-447, 2009.
[BASA-09c] A. Basarab, A. Lyshchik, C. Grava, V. Buzuloiu, and P. Delachartre. **Ultrasound image sequence registration and its application for thyroid nodular disease**. *J Signal Process Syst*, 55(1-3):127-137, 2009.
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[DEPR-09] J.F. Deprez, E. Brusseau, C. Schmitt, G. Cloutier, and O. Basset. **3D estimation of soft biological tissue deformation from radio-frequency ultrasound volume acquisitions**. *Med Image Anal*, 13(1):116-127, 2009.
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OS : Ouvrages scientifiques (ou chapitres de ces ouvrages)
[BASS-07] O. Basset and C. Cachard. **Ultrasound Image Post-Processing: application to segmentation**. In *Physics for Medical Imaging Application*, pages 227-239. Y. Lemoigne, A. Caner, and G. Rahal, editors. Springer - NATO Science Series, Publ., Dordrecht, The Netherlands, 2007.
[CACH-07] C. Cachard and O. Basset. **Ultrasound Contrast Agents**. In *Physics for Medical Imaging Application*, pages 137-150. Y. Lemoigne, A. Caner, and G. Rahal, editors. Springer Verlag - NATO Science Series, Dordrecht, The Netherlands, 2007.

OV : Ouvrages de vulgarisation (ou chapitres de ces ouvrages)
[VRAY-05] D. Vray. **Des souris et des ondes**. Pour la Science. pp 118-121, 2005.

AP : Autres productions : Brevets
[VRAY-09] D. Vray, N. Djaker, L. Guyon, L. Saroul, F. Duboeuf, D. Friboulet, and J. Boutet. **Brevet N. 09 - Français.**. Fantome bi-modalité destiné à simuler les propriétés ultrasonores et optiques de la prostate, 2009.
[VRAY-08] D. Vray and T. Pechoux. **Brevet N. 08 54572 - Français, N. PCT/FR2009/051305 - International**. Méthode de traçage du contour vraisemblable d'un élément anatomique sur une image de coupe, 2008.

HdR et thèses soutenues
Defended thsesis
[GHAZ-09] B. Ghazal. **Traitement d'image ultrasonore de contraste : modélisation autorégressive et classification**. Doctorat, Université Claude-Bernard Lyon I, Université de Balamand (Liban), 2009. Jury: Ayache BOUAKAZ (rapporteur, CR INSERM,)Tours; Christian CACHARD (Co-directeur, PU 61, Université Lyon 1) ; Chaouki DIAB (Professeur associé, Beyrouth) ; - Denis FRIBOULET (Président, PU 61, INSA de Lyon) ; Elie KARAM (Rapporteur, Professeur, Université de Balamand) ; Maha KHACHAB (Co-directeur, Professeur associé, Université de Balamand) ; Chafik MOKBEL (invité, Professeur associé, Université de Balamand).
[AOUD-08] W. Aoudi. **Methodes d'estimation des flux en imagerie ultrasonore haute fréquence. Application à l'étude de la microcirculation**. Doctorat, INSA Lyon, 2008. Jury: D. Kouamé (Rap.), J.L. Dillenseger (rap.), M. Janier, N. Gache, D. Friboulet, D. Vray.
[BASA-08] A. Basarab. **Estimation du mouvement dans des séquences d'images échographiques : application à l'élastographie de la thyroide**. Doctorat, INSA Lyon, 2008. Jury: V. Buzuloiu (co-dir.), P. Delachartre (dir.), P. Flandrin (prés.), C. Grava, A. Herment (rap.), C. Jutten (rap.), C. Vertan (rap.) et D. Vray.
[DEPR-08] J.F. Deprez. **Estimation 3D de la déformation des tissus mous biologiques par traitement numérique des données ultrasonore radiofréquences**. Doctorat, INSA Lyon, 2008. Jury: O. Basset (dir.), E. Brusseau (co-dir.), D. Cathignol (Prés.), D. Colin, C. Gehin (inv.), C. Fernandez-Maloigne (rap.)et M. Tanter (rap.).
[DELA-06b] P. Delachartre. **Méthodes d'estimation paramétrique pour l'imagerie de l'élasticité**. H.D.R., INSA Lyon, 2006. Jury: J. Duchène (rap.), C. Jutten (rap.), F. Patat (rap.), M. Fink, G. Gimenez, D. Vray. [BALO-06] S. Balocco. **Modèle dynamique ultrasonore 3D d'artère pathologique, application à l'estimation des paramètres mécaniques de la paroi artérielle**.

Doctorat, Université Claude-Bernard Lyon I, 2006. Jury: Garreau M. (rap.), Herment A. (rap.), Basset O., Cachard C., Diciotti S., Palombo C., Ricci S., Tortoli P.
[DURN-06] B. Durning. **Simulation, estimation spectrale et imagerie des agents de contraste ultrasonore**. Doctorat, Université Claude-Bernard Lyon I, 2006. Jury: Ayache Bouakaz (rap.), Christian Cachard, Dominique Cathignol (prés.), Denis Friboulet, François Guillet (rap.), Lori Bridal.
[SAID-06] G. Said. **Elastographie ultrasonore tridimensionnelle : de l'estimation des déformations au module d'Young des tissus biologiques**. Doctorat, INSA Lyon, 2006. Jury: O. Basset, C. Lafon, S. Mensah, L. Pourcelot (rap.), J.P. Tasu (rap.), D. Vray.
[LIEB-05] H. Liebgott. **Synthèse de réponse impulsionnelle en imagerie ultrasonore pour l'estimation vectorielle du déplacement**. Doctorat, INSA Lyon, 2005. Jury: P. Delachartre., R. Harba, J.A. Jensen, C. Jutten, L. Pourcelot (prés.), D. Vray, J.E. Wilhjem.
[MARI-05] J.M. Mari. **Localisation échographique d'inclusions fortement échogènes en tissus mous, application à la détection d'électrode**. Doctorat, Université Claude-Bernard Lyon I, 2005. Jury: Duchene J. (rap., prés.), Bou Matar O. (rap.), Cachard C., Duhamel J.R., Gimenez. G., Unser M. et Basset O. (inv.).

Team n° 4 Title : Imaging and exploratory method ologies in NMR

Previous activity : Period 2005-2009

Key words : MRI methodology, animal models, polarized nuclei, contrast agents, function and metabolism, perfusion, diffusion, ventilation.

Team leader	Crémillieux Yannick	DR CNRS-HDR
Vice-team leader	Canet-Soulas Emmanuelle	PU-UCB-HDR
	Wiart Marlène	CR CNRS
	Montcel Bruno	MCU UCB
	Neyran Bruno	MCU UCB

ETP : 3,5

Engineers	Gaillard Sophie	AI
Invited Professor	Boesch Chris	PU-PH, University of Bern (1 month, 2005)

Post doc	Stupar Vasile	Industrial funding
	Cieslar Katarzyna	European funding
	Fissoune Rachida	Contract funding
	Rouffet David	Contract funding

Ph.D student	Bannier Elise	Ministry funding	
	Zurek Magdalena	European funding	
	Alsaid Hasan	Rhone-Alpes Region funding	
	Al-Faraj Achraf	Ministry funding	
	Sigovan Monica	Ministry funding	3 months, Stanford, CA, USA
	Brisset Jean-Christophe	Ministry funding	
	Goutailler Florent	Ministry funding	
	Bessaad Amine	Contract funding	

Defended Theses	Nom prénom	Nationality	Defended	Devenir
	Fissoune Rachida	Morocco	2005	Post-doc (1 year), private activity (Morocco)
	Abdulrazzaq Sulaiman	Irak	2008	Surgeon (St Etienne Hospital)
	Bannier Elise	France	2009	IR (Rennes)
	Alsaid Hasan	Syria	2008	Researcher, GSK, USA
	Al-Faraj Achraf	Lebanon	2009	Postdoc (Paris)
	Sigovan Monica	Roumania	2009 (October)	Post-doc (San Francisco, CA)

Contractuel	Frédérique Foulon	Assistante coordinatrice Projet Européen

Per-reviewed Publications: 37

1. Résumé

L'imagerie et la spectroscopie RMN constituent des techniques de référence pour le diagnostic médical chez l'homme et pour l'investigation non-invasive de modèles physio-pathologiques chez l'animal. Ces techniques permettent de réaliser des caractérisations tissulaires fines et d'établir des images fonctionnelles et métaboliques des principaux organes (cerveau, cœur, poumons, muscles) avec une excellente résolution spatiale et temporelle. Les objectifs généraux de l'équipe thématique portent sur le développement, la mise en œuvre et l'application de techniques, méthodes et protocoles innovants en IRM et SRM in vivo sur des modèles animaux et chez l'homme. Les thèmes de recherche de l'équipe seront centrés sur des problématiques médicales liées pour l'essentiel aux pathologies cardio-vasculaires et pulmonaires où existent des besoins importants en développements méthodologiques et pour la réalisation de protocoles d'imagerie pré-cliniques originaux.

2. Objectives

NMR imaging and spectroscopy are the reference techniques for medical diagnosis in human and for the non invasive investigation of physiopathological models in animals. These techniques make it possible to both produce precise tissue characterizations and establish functional and metabolic images of the main organs (brain, heart, lungs, muscles) with excellent spatial and temporal resolution. The general objectives of this topic's team are the development, implementation and application of innovative techniques, methods and protocols in MRI and MRS in vivo on animal models and in human. The team's research themes will be focused on the medical questions associated essentially with cardiovascular and lung pathologies where there are major needs in terms of methodological development and to produce original pre-clinical imaging protocols.

3. National and international context

The use of MRI for diagnostic or therapeutic purposes in cardiovascular or lung pathologies requires the implementation of innovative and highly multi-disciplinary approaches. The main problems to be resolved in this field, concern on the one hand the sensitivity and specificity of the techniques in relation to a given pathology and, on the other hand, the complexity involved in analyzing and interpreting the images or signals acquired. The solution to these problems lies in using innovative MRI markers (polarized nuclei, intelligent contrast agents), in developing imaging protocols on animal models and finally in extracting parameters that are pertinent from a medical point of view. In this field, the team members of this theme have acquired skills that are recognized both nationally and internationally (participation in, and coordination of, national and European programs, prizes), thus allowing them to respond to current and future questions in these biomedical imaging fields.

4. Research activity

MRI and MRS of Hyperpolarized Nuclei
Permanent staff members involved: Yannick Crémillieux (in charge), Emmanuelle Canet-Soulas, Bruno Montcel
Interactions: Morphological and functional imaging (medical team)

Key Results

This research activity line exploits the enhancement of MR sensitivity obtained with techniques of hyperpolarization of nuclear spins. Our group is developing the polarization techniques and the related applications in two research areas.
The first domain concerns the polarization of rare gas (helium, xenon) with applications in the field of lung MRI. Research activities are performed within the framework of a European Network (RTN) gathering 11 academic groups and 7 industrial partners throughout Europe. Our group is involved in small animal studies (methodological developments and animal models) and in clinical

investigations with cystic fibrosis patients. The second research axis is focusing on dynamic nuclear polarization (DNP) technique and its application. The group has developed a low temperature (1.2 K) and high field (3.35 T) system aiming at polarizing molecules labeled with long-lived T1 nuclei (carbon13, nitrogen15, etc). This program has been funded by a “programme Blanc” ANR Polarim coordinated by Y. Crémillieux.
The research group is currently composed of one research associate (Bruno Montcel) and one engineer assistant (Sophie Gaillard). During the period 2005-2009, two postdocs were recruited on industrial contract and European grant and five students were enrolled in PhD programs (3 thesis defended). The researches run on European grant (Phelinet) and ANR programs (Programme blanc Polarim, programme SEST Respinttox, programme Biotec GR-ARA) and industrial contracts (Novartis, Boehringer Ingelheim, Bracco). 14 papers in international review board journal and book chapters were published during this period.

Tissue and molecular characterization: non invasive approaches

Permanent staff members involved: Emmanuelle Canet-Soulas (in charge), Bruno Neyran, Marlène Wiart
Interactions: Morphological and functional imaging (medical team), Dynamic imaging
Key Results
Imaging biomarkers are envisioned for longitudinal follow-up of complex pathologies, such as cardiovascular and metabolic diseases. The hope of this competitive field is to combine imaging markers with blood biomarkers to enable personalize treatment, and a better use of new targeted drugs. A consensus on the définition of Imaging Biomarkers for cardiovascular and metabolic diseases has recently been achieved. We have been working for two specific purposes : MRI markers of atherosclerosis and MRI/MRS lipid pool characterization (intracellular lipid muscle, and subcutanuous and visceral fat depot). Our objective was to evaluate and standardize the imaging procedure (contrast agent, in-vivo MRI follow-up and post-processing) to enable progression and regression protocols for both pre-clinical and clinical therapeutic trials.

Imaging biomarkers of atherosclerosis
For atherosclerosis, the ideal imaging marker would define a lesion prone to rupture. First generation of imaging markers included morphological and functional parameters, extracted by robust post-processing algorithms, that enables plaque characterization, i.e. composition and architecture. For example, the presence of a large lipid core and a thin fibrous cap, as measured by image analysis, is a marker of vulnerable plaque (clinical application in collaboration with the clinical team, Philippe Douek & Loïc Boussel) [Boussel, J Magn Reson Imaging, 2008].
Second generation of imaging biomarkers are molecular and cellular agents. In this category, pre-clinical and clinical validation are still ongoing. As inflammation has been recognized as a major process in plaque destabilization, imaging markers to follow non invasively vascular inflammation are essential.
First, we developed multicontrast MRI sequences, together with cardiac and respiratory gating to characterize plaque components in the aortic arch of atherosclerotic mouse models [Alsaid, Magnetic Resonance in Medecine, 2007]. We then validated two markers of inflammation. The first one is targeted to the adhesion molecule, P-selectin and the other to macrophages. They have been validated respectively in mice and rabbit models of atherosclerosis [Alsaid, Investigative Radiology, 2009] [Sigovan, Radiology, 2009] (PhD thesis of Hasan Alsaid and Monica Sigovan, Guerbet contract). The macrophage marker, i.e. iron oxide nanoparticles, is now entering the clinical phase.
We also showed that it was possible to evaluate various inflammatory status during plaque progression using iron oxide nanoparticles. Two labelling strategies were respectively evaluated, in situ labelling by intravenous injection of iron nanoparticles or direct cell labelling in cell culture followed by macrophage imaging after their intravenous injection (collaboration with Guerbet and Genfit, and academic partners, consortium ANR Health Technology, 2008-2010)

Imaging and Spectroscopic biomarkers of lipid storage and metabolism
Cardio-vascular diseases are closely related to metabolic disorders, as lipid transporters are among the first blood biomarkers of cardiovascular risk.

Magnetic Resonance Spectroscopy (MRS) is complementary to MRI to non invasively evaluate lipid storage. MRI can measure the lipid depot volume in different locations, i.e. sub-cutanuous, visceral and liver fat. MRS provides a quantification of mobile lipids, and can differentiate intracellular from extracellular triglycerides under certain circumstances. For example, the anisotropy of the skeletal muscle separates extracellular and intracellular lipids into two distinct resonances. We performed intramyocellular lipid measurements in physically active elderly men (> 65 years) to evaluate their ability to use these metabolic reserve during an aerobic exercise. This lipid consumption has been shown to decrease with age and insulin resistance, whereas lipid accumulation in muscle increased. In contrast, endurance athletes have both an increased lipid storage capacity in muscle fibers, but also an increased lipid oxidation during exercise. This has been called the metabolic paradox. We showed non invasevely by MRS that metabolic flexibility is preserved in physically active seniors, and that confirmed the metabolic paradox (lipid accumulation, but preserved lipid turn-over in exercising muscle) in this population (PhD thesis and post-doctorate of Rachida Fissoune, 1 presentation at the ISMRM [Rouffet, ISMRM, 2009], manuscript in preparation) (ANR Young Researcher, 2006-2008).

Cardiovascular applications of these biomarkers are ongoing for dedicated purposes:
biodistribution and biological effects of iron nanoparticles and carbon nanotubes (ANR RespiNNTox, collaboration with INERIS, ANR Health Technology),
progression and regression studies of atherosclerotic inflammation (macrophage imaging) in mice for drug testing (ANR Health Technology, collaboration with Genfit and Guerbet, PhD exchange program with the University of Stanford),
vascular inflammation (adhesion molecule expression) in a mouse model of sickle cell disease after hypoxia modulated by physical training or pharmacological intervention (ANR Biotec GR-ARA, collaboration with Erytech Pharma and CRIS, laboratory of Sports of University Lyon 1, PhD of Emeline Aufradet),
lipids storage and metabolism by MRI/MRS in pre-clinical and clinical applications, i.e. peri-vascular fat in mouse models of atheroclerosis, muscle triglyceride turn-over and visceral fat depot in active elderly men (Fondation Caisse d'Epargne, collaboration with the Army lab. CRSSA in Grenoble, with CRIS and with two teams of the future Cardio-Metabolism, Diabetes and Nutrition Research Institute of Lyon, PhD of Clément Villars)
follow-up of aerobic training in mice with cardiac MRI markers (validated against end-stage muscle enzymes) (collaboration with CRIS, PhD of Emeline Aufradet)

From 2005 to 2009, these activities were granted by 4 ANR projects with multidisciplinary academic and industrial collaborations (chemistry, physics, pharmacy, bio-engineering), an international PhD exchange program with the University of Stanford, 5 PhD defenses and after PhD, either post-doctorate or research positions in the pharmaceutical industry (Glaxo-Smith-Kline).

Title action n°3 MRI of experimental models of cere bral ischemia

Permanent staff members involved: Marlène Wiart (in charge), Emmanuelle Canet-Soulas, Bruno Neyran

Interactions: Morphological and functional imaging, Dynamic imaging
Background
Ischemic stroke is the most frequent cause of persistent neurologic disability in modern Western societies. Therapeutic intervention through systemic thrombolysis is currently only possible in a narrow time window of 3 hours. Unfortunately, in most cases stroke patients reach hospital treatment beyond the early time window for thrombolysis therapy. A growing body of evidence suggests that inflammatory processes are involved in the pathophysiology of stroke, causing delayed expansion of the infarct. In this context, noninvasive imaging of inflammation associated with ischemic stroke lesions could have a predictive value and may be helpful for the development of cytoprotective drugs.
Cellular imaging of inflammation with MRI using ultrasmall superparamagnetic nanoparticles of iron oxides (USPIO) has recently emerged as a promising non-invasive technique for experimental and clinical studies of several inflammatory diseases. When injected intravenously, USPIOs are

phagocytosed by macrophages within the blood-pool (circulating monocytes) or locally at the site of inflammation (tissue macrophages). They thus become magnetic and can be monitored by MRI. Based on this hypothesis, we have developed and validated a USPIO-enhanced MRI approach to study neuroinflammation in a mouse model of focal cerebral ischemia and translated the technique into the clinics to assess neuroinflammation in stroke patients

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Pre-clinical studies

We first validated a method allowing the MR tracking of phagocyte cells in stroke-induced mice [WIAR-07a]. Imaging data correlated with histochemical analysis showing inflammation remote from the lesion and uptake of USPIO by macrophages.

While MR signal changes after intravenous USPIO injection were indisputably related to inflammatory cells at the subacute stages after focal cerebral injury, the interpretation of USPIO-related MR signal alterations at the acute stages remained controversial. We then compared MR signal changes with the histological iron and macrophage distribution during the first 24 hours in the same mouse model of acute stroke [DESE-09a]. Our results suggested that early reproducible USPIO-related MR signal changes were mainly caused by passive diffusion of free USPIO after blood–brain barrier leakage and by intravascular trapping, rather than by peripheral phagocyte infiltration.

Finally, we measured the relaxation properties of macrophages labelled with two types of USPIOs (Ferumoxtran-10 and AMNP), at 4.7T and 7T using multi-parametric (T1, T2 and T2*) quantitative MRI in vitro and in vivo [BRIS-09a], thus moving the technique towards potential quantitative follow-up of neuroinflammation.

One limitation of direct administration of USPIO, though, is the potentially confounding effects of free iron oxide nanoparticles on the MR signal. In the future, we therefore aim to develop alternative cellular MRI techniques, involving administration of ex vivo magnetically labelled cells and subsequent tracking of their trafficking in the inflamed brain, as part of the INFLAM project (ANR TecSan).

Clinical studies

We have been amongst the first to propose the use of USPIO-enhanced MRI to assess neuroinflammation in stroke patients. In brief, no USPIO enhancement was observed 2 days after stroke onset [CHO-07a], whereas MR signal changes were consistently observed in studies performed at 6 days after stroke [NIGH-07a]. In this small series (10 patients), USPIO-related MRI enhancement was heterogeneous and not related to blood-brain barrier disruption.

Given the heterogeneity of inflammation response in human stroke, further larger clinical studies are needed to demonstrate the clinical benefit associated with the use of USPIOs as an MRI surrogate marker for brain inflammation. However, there are still several limitations to overcome for a widespread application of the technique, including a better understanding of USPIO biotransformation and the development of new MR strategies allowing unambiguous discrimination of free USPIOs versus USPIO-labeled cells. Both issues are currently adressed in the INFLAM projet.

5. Plateforms

Use of CERMEP platforms : MRI (pre-clinical and clinical)

Members of the CERMEP scientific committee: Y. Crémillieux, E. Canet-Soulas.

6. Grants

National projects (ANR, BQR, PEPS, …)

ANR LIMC (coordinator Emanuelle Canet-Soulas) (2006-2008)

ANR Polarim (coordinator Yannick Crémillieux)

ANR Respinttox. Investigation of pulmonary toxicity of carbon nanotubes (2007-2009)

ANR GR-ARA. (2009-2010) Assessment of therapeutic approaches for sickle cell diseases

“Vaincre la Mucoviscidose” Helium3 lung imaging in asymptomatic young patient with cystic fibrosis

Rhône-Alpes Region MIRA grant. (Y. Crémillieux) Alveolar pO2 imaging using polarized Helium3.

Fondation Caisse d’Epargne (E. Canet-Soulas) Lipid turn-over in exercising muscle in elderly men

Cluster 11 (2007-2008), principal investigator (PI) N Nighoghossian: Etude physiopathologique de l'ischémie cérébrale à l'aide de l'IRM
Fondation pour la Recherche sur le Cerveaux (2007), PI N Nighoghossian: Imagerie de la dynamique inflammatoire au cours des affections neurologiques
BQR INSA (2007), PI M. Wiart: Etude de l'effet neuroprotecteur d'une nouvelle forme de l'acide docosahexaénoïque (AceDoPC) dans un modèle murin d'ischémie cérébrale focale
ANR INFLAM (2007-2010), PI Y Berthezène : INFLAMmation in brain and vessels with iron nanoparticles and cell trafficking: a multi-scale approach of tissue microenvironment, iron nanostructure and iron biotransformations.
ANR NEUROPROTECT (2007-2011), PI M Lagarde, PI at Creatis-LRMN N Nighoghossian : Métabolisme chez l'Homme d'un phospholipide d'origine marine structuré et action neuronale.

European projects (NoE, Réseaux Marie Curie, STREP, IP, …)
Research Training Network (RTN) Phelinet (coordinator Yannick Crémillieux): Polarized Helium lung imaging network www.phelinet.eu

European project I-KNOW (2006-2009), PI L Oestergaard, PI at Creatis-LRMN N Nighoghossian : Integrating Information from Molecule to Man: Knowledge Discovery Accelerates Drug Development and Personalized Treatment in Acute Stroke (www.i-know-stroke.eu)

International projects (avec la Chine, les USA …)
PhD exchange program (2008-2009) with the University of Stanford (E. Canet-Soulas, K. Butts-Pauly)

Industrial contracts
Novartis (Y. Crémillieux)
Boehringer Ingelheim (Y. Crémillieux)
Bracco Research (Y. Cremillieux)
Guerbet (3 contracts, E. Canet-Soulas & M. Wiart)
Ineris (Y. Crémillieux)

7. Collaborations (uniquement publiante)

National collaborations
University Joseph Fourier, Grenoble (Yannick Crémillieux)
Ineris, Verneuil-en-Halatte, Oise & ANR RESPINTTOX consortium (E. Canet-Soulas, Y. Crémillieux)
Erytech Pharma & ANR GR-ARA consortium (E. Canet-Soulas, Y. Crémillieux))
U698 INSERM, Paris & Guerbet, Aulnay-sous-bois & Genfit, Lille & ANR INFLAM consortium (9 partners: molecular Imaging of inflammation in atherosclerosis and stroke) (E. Canet-Soulas, M. Wiart)
CRSSA, Grenoble & Cemagref, Lyon : In-vivo MAS spectroscopy of daphnies (environmental biomarkers and metabolomics) (E. Canet-Soulas, D. Graveron)
U842 Inserm, Neurooncologie et neuroinflammation, Lyon (M. Wiart): [BRIS-09a], [DESE-09a], [WIAR-07a]
UMR CNRS 5180, Laboratoire des sciences analytiques, Lyon (M. Wiart): [BRIS-09a]

International collaborations
Yannick Crémillieux
University of Mainz, Germany
Novartis Research Center, Basel, Switzerland
University Complutense, Madrid
Siemens AG, healthcare sector
University of Krakow, Poland

Emmanuelle Canet-Soulas
University of Stanford (PhD exchange program, 2008-2009)

Marlène Wiart
Centre intégratif de génomique, Université de Lausanne, Lausanne (Suisse): [PIAL-07a]

8. Expertise and consulting (Expert européen, Comité scientifiques, internationaux, nationaux, CA ; …)

Elected secretary of study group ISMRM « Hyperpolarized nuclei » (Yannick Crémillieux)
Consulting Boehringer Ingelheim (Yannick Crémillieux)
Comité scientifique congrès du GRAMM 2008 (Yannick Crémillieux, Emmanuelle Canet-Soulas)
Member of the Contrast Media Resarch group (2007-2008), of the selection committee for « Molecular Imaging at the European Society of Radiology (2006-2008), of the selection committee for « Molecular Imaging of the Immune System at the World Molecular Imaging Congress (2009) (Emmanuelle Canet-Soulas)
Expert for Excerpta medica, Univadis website (Emmanuelle Canet-Soulas)
Expert pour l'ANR (Yannick Crémillieux, Emmanuelle Canet-Soulas)

9. Distinctions

2005. Best scientific presentation CMR meeting (Contrast Media Research). Vasile Stupar. "spontaneous breathing imaging in small animals". Evian, France.

Marlène Wiart:
Young Investigator Award of Lyon city (Prix du jeune chercheur de la ville de Lyon), Juin 2007
Young Investigator Award of the International symposium Contrast Media Research: Magnetic resonance imaging of cerebral ischemia with ultrasmall superparamagnetic particles of iron oxide in mice, Octobre 2005

10. Research training (éléments pertinents : responsabilités dans un Master, une école Doctorale)

Emmanuelle Canet-Soulas in charge of Master 2 Recherche « Ingénierie Biomédicale et Pharmaceutique », member of Ecole Doctorale EDISS (ED205), member of Conseil Scientifique de l'Ecole Nationale Vétérinaire de Lyon

References : period 2005-2009

Articles dans des revues internationales avec comité de lecture

Bannier E, Neyran B, Cieslar K, Rivoire J, Heidemann RM, Gaillard S, Sulaiman AR, Canet-Soulas E, Cremillieux Y. Free breathing hyperpolarized 3He lung ventilation spiral MR imaging. Invest Radiol. 2009 Apr;44(4):185-91. PubMed PMID: 19252441.

Al Faraj A, Cieslar K, Lacroix G, Gaillard S, Canet-Soulas E, Crémillieux Y. In vivo imaging of carbon nanotube biodistribution using magnetic resonance imaging. Nano Lett. 2009 Mar;9(3):1023-7. PubMed PMID: 19199447.

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Alsaid H, Sabbah M, Bendahmane Z, Fokapu O, Felblinger J, Desbleds-Mansard C, Corot C, Briguet A, Crémillieux Y, Canet-Soulas E. High-resolution contrast-enhanced MRI of atherosclerosis with digital cardiac and respiratory gating in mice. Magn Reson Med. 2007 Dec;58(6):1157-63. PubMed PMID: 17969010.

Beckmann N, Cannet C, Karmouty-Quintana H, Tigani B, Zurbruegg S, Blé FX, Crémillieux Y, Trifilieff A. Lung MRI for experimental drug research. Eur J Radiol. 2007 Dec;64(3):381-96. Epub 2007 Oct 10. Review. PubMed PMID: 17931813.

Cieślar K, Alsaid H, Stupar V, Gaillard S, Canet-Soulas E, Fissoune R,Crémillieux Y. Measurement of nonlinear pO2 decay in mouse lungs using 3He-MRI. NMR Biomed. 2007 May;20(3):383-91. PubMed PMID: 17451167.

Cieślar K, Stupar V, Canet-Soulas E, Gaillard S, Crémillieux Y. Alveolar oxygen partial pressure and oxygen depletion rate mapping in rats using 3He ventilation imaging. Magn Reson Med. 2007 Feb;57(2):423-30. PubMed PMID: 17152086.

Stupar V, Canet-Soulas E, Gaillard S, Alsaid H, Beckmann N, Crémillieux Y. Retrospective cine 3He ventilation imaging under spontaneous breathing conditions: a non-invasive protocol for small-animal lung function imaging. NMR Biomed. 2007 Apr;20(2):104-12. PubMed PMID: 16998954.

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Invited conferences

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Investigation of ozone exposure on rat pulmonary function using hyperpolarized Helium3. CMR Meeting, Evian, France, October 2005. Yannick Crémillieux

Non invasive hyperpolarized helium3 imaging studies in rats under spontaneous breathing conditions using retrospective Cine imaging technique. CMR Meeting, Evian, France, October 2005. Vasile Stupar

Quand la physique rencontre l’imagerie médicale par Résonance Magnétique Nucléaire : voyage à l’intérieur du poumon. Conférence « Année Mondiale de la Physique », Lyon, Octobre 2005. Yannick Crémillieux

Lung ventilation imaging : a new tool for the evaluation of drug therapies in animal models ? 20th Germ Congress, Blankenberge, Belgium, March 2006. Yannick Crémillieux

Mesure de la décroissance non linéaire de la pO2 alvéolaire chez la souris par IRM de L’hélium3. Journées scientifiques Imagerie du Petit Animal Marseille, October 2006. Yannick Crémillieux

He-3 lung MR imaging: a new tool for the evaluation of drug therapies in animal models ? Institute of Physics Seminar, Jagiellonian University, Krakow, January 2007. Yannick Crémillieux

Hyperpolarized Helium-3 MRI : principles and biomedical applications. Bern University Seminar, February 2007. Yannick Crémillieux

Dynamic nuclear polarization : applications to Carbon13 MRS/MRI. Sheffield University Seminar. August 2007. Yannick Crémillieux

Longitudinal 3-Helium and Proton imaging of magnetite biodistribution in a rat model of instilled nanoparticles. 4th Krakow - Winnipeg Workshop On MR Imaging Technology. October 2007. Yannick Crémillieux

Méthodologie pour l’IRM cardiovasculaire et pulmonaire chez le petit animal. Colloque AFSTAL. Reims, November 2007. Yannick Crémillieux, Emmanuelle Canet-Soulas.

Imagerie des noyaux hyperpolarisés. GRAMM. Lyon, March 2008. Yannick Crémillieux

Helium3 MRI in small animal studies. Advanced course of magnetic resonance imaging of the lung using magnetic resonance imaging. Madrid, May 2008. Yannick Crémillieux

ESMRMB school. Marseille, 2008. “Polarized nuclei for small animal imaging”. Yannick Crémillieux

Congrès du GRAMM. Marquage cellulaire pour l’IRM de l’inflammation vasculaire, Lille, 2009. Emmanuelle Canet-Soulas

Molecular imaging of inflammation in atherosclerosis and stroke. Stanford University seminar, 2008. Emmanuelle Canet-Soulas

European Congress of Radiology. Molecular imaging of atherosclerosis (mini-course), Vienne, 2008. Emmanuelle Canet-Soulas
Société Francophone de Nutrition Clinique et Métabolique SFNEP. Apport de la spectroscopie RMN
sur l'évaluation des réserves lipidiques et de leur mobilisation : applications potentielles dans l'obésité sarcopénique. Montpellier, 2007. Emmanuelle Canet-Soulas
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European Congress of Radiology. Molecular imaging of atherosclerosis (mini-course), Vienne, 2007. Emmanuelle Canet-Soulas
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Journée Interface INSERM « Imagerie Moléculaire ». Nouveaux traceurs polyfonctionnels en IRM et Imagerie Optique (E. Canet-Soulas, D. Letourneur), Paris, 2006. Emmanuelle Canet-Soulas
Laboratoire CNRS de RMN, Professeur Cozzone. Ciblage moléculaire pour l'imagerie de la plaque d'athérosclérose, Marseille, 2006. Emmanuelle Canet-Soulas
Atelier du Savoir CNRS « Imagerie Médicale ». Produits de contraste en RMN : application à la plaque d'athérome, Lyon, 2006. Emmanuelle Canet-Soulas
Séminaire « Review and current status of cardiovascular and brain physiology and diseases », CERIMED (projet de creation d'un centre de recherche en imagerie biomedicale). Molecular imaging of atherosclerosis with bi-modal markers. Rome, 2006. Emmanuelle Canet-Soulas
Club Angio MR. Experimental Models and High Resolution MRI for Atherosclerotic Plaque, Marrakech, 2005. Emmanuelle Canet-Soulas
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Team nº: 5 Title : Methods and systems in MRI an d optics

Previous activity: Period 2005-2009

Key words: RF engineering ; EM simulations; methodology; MR sequence development ; RF heating; scattering light; NMR and optics coupling ; MC simulations; MRS quantification; digestive wall and liver dysfunction; cartilage structure; pre-clinical and clinical applications.

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Vice-team leader	Pilleul Frank	PUPH-HDR UCB
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ETP: 4.7

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PhD students	Brouillon Guillemette	CIFRE	joint PhD with cIRMa
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	Lee Shoo Ming	Singapore	joint PhD with Singapore
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	Tailhades Emmeline	MESR	
Defended HDR	Beuf Olivier	2006	
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	Pilleul Frank	2006	

Defended Thesis	Baboi Loredana	Roumaine	2008	Post-doctorant Hôpital Genève
	Falconet Julie	Française	2007	ATER UCB
	Bolbos Radu	Roumaine	2006	Chercheur Institut Myologie
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	Pilleul Frank	Française	2005	PUPH HCL

Per-reviewed Publications: 92
Conference papers: 130
Patents: 2

Résumé
Les objectifs généraux de l'équipe sont de mieux comprendre des phénomènes complexes obtenus en champ proche dans le cas du magnétisme pour l'IRM (champ radiofréquence) ou au contraire en champ lointain en imagerie optique. Les applications directes de ces travaux sont l'imagerie morphologique, fonctionnelle et interventionnelle pour l'exploration du foie et des parois digestives. La difficulté demeure la faible interaction avec le milieu observé en optique comme en RMN, et donc un très faible rapport signal sur bruit qu'il s'agit constamment d'améliorer par le développement de nouveaux systèmes et de nouvelles méthodes. Les méthodes employées comprennent la modélisation, la simulation, l'expérimentation et la quantification de paramètres d'intérêt. Les travaux menés dans cette thématique sont pour l'essentiel des développements instrumentaux et méthodologiques dans le domaine de l'imagerie biomédicale. En RMN, l'objectif est d'améliorer la quantité et la qualité des informations recueillies tout en permettant des explorations in vivo sur des modèles animaux ou sur l'homme. Ainsi, l'accent est porté sur le développement de capteurs (réseau ou endoluminaux) qui nous permettent de mettre en œuvre de

nouvelles méthodes d'imageries ou de spectroscopies. De même, post acquisition, des méthodes de quantification des signaux de spectroscopie sont développées, et mises en œuvre en étroite interaction avec les contraintes expérimentales. Dans le domaine de l'optique des milieux diffusants, une caractérisation optique préalable de ces milieux est indispensable à la mise au point de techniques d'imagerie optiques efficaces. Ces dernières présentent l'avantage d'être remarquablement compatibles et complémentaires des modalités de RMN.

1. Objectives

The overall objectives of the team are to improve the understanding of some complex phenomena obtained in the near-field in the case of magnetism for Magnetic Resonance (RF field) or in the far-field in the case of optical imaging. Morphological, functional and interventional imaging are developed for liver and gastro-intestinal wall exploration. The challenge remains the weak interaction with the observed environment in optics as well in Nuclear Magnetic Resonance (NMR), and thus the very low signal-to-noise ratio (SNR) which have to be improved through the development of new systems and methods. The methods used include modeling, simulation, in vitro and in vivo experimentations up to the quantification of relevant parameters. The work carried out in this team is mainly focused on new instruments and methodology developments in the domain of biomedical imaging. In NMR, the goal is to improve the quantity and quality of acquired information from in vivo in animal models and humans. Thus, the accent is put on the development of miniaturized coils (array and endoluminal) for new imaging and spectroscopic methods. Signal processing quantifications methods are designed in tight interaction with the experimental constraints. In the field of optics of scattering media, optical characterization is essential prior to the development of optical imaging techniques which are, in addition, compatible with NMR modalities.

2. Research activities

Tissue and metabolic characterization using MR (D. Grenier, O. Beuf, S. Cavassila, H. Ratiney, F. Pilleul), interactions with team 3 (E. Brusseau) and team 6 (D. Graveron)

MR Elastography (MRE) and Spectroscopy (MRS) were developed and used in a clinical environment for non invasive diagnosis and characterization of diffuse liver diseases.

MRE: Viscoelastic properties changing very significantly between healthy and pathological tissues, MRE opens new perspectives in the early detection of diseases such as breast, liver or some visceral cancers. Starting from scratch four years ago, our team developed a MRI compatible mechanical driver to generate the wave within the targeted organ together with a dedicated MRI sequence with Gradient Sensitive Motion (GSM). This sequence, based on a phase contrast flash sequence (developed on 1.5T Siemens Symphony system), included several specific features such as 2D and 3D acquisitions, automatic increment delay with external excitation as well as a fully operational triggering module [IC1]. The phase images obtained are processed, using inversion algorithms, to locally determine the propagation rate and the attenuation of mechanical shear waves (MRE-View, courtesy of R. Ehman, Mayo clinic, Rochester, USA). The advantage of this dynamic technique over static methods is to generate absolute viscoelastic 2D, 3D maps without having to know the applied constraint. After validation on agar-agar phantoms [MILO-08b, J Radiol; SOUC-08, *Magn Reson Med*], the driver and the sequence are currently used on patients with suspected fibrosis or cirrhosis (Fig 1). In vitro experiments were also performed with endoluminal coil coupled with an endoluminal driver.

MRS: Localized in vivo MRS provides metabolic information resource and offers the unique ability to non-invasively identify and measure intrinsic biomarkers. Primarily applied on the brain, the liver spectroscopy requires specific adaptation of the acquisition protocol. In contrast to what has been usually proposed by the ten or so groups working on liver MRS worldwide, our advanced MR spectroscopy sequences is respiratory gated to account for the body movements and is included in a clinical 1.5T protocol [IC3]. The originality of our approach consists in using water suppressed spectrum to assess metabolic and lipid contents. Thanks to a home-made dedicated algorithm [RATI-08c, *IEEE ISBI*], we are able to derive quantitative profiles for human liver spectroscopic data which have been compared with fat content measured by MRI (Fig. 2). With this approach, our team is in the lead pack having investigated the hepatic proton MRS signals at this level of refinement [CAVA-08, ISMRM].

Concerning preclinical studies on small animal, new competencies and knowledges for in vivo localized MR Spectroscopy have been acquired and developed [CUDA-06g, C.R Chimie]. They gave rise to collaborations with neurologists and neuro-biologists from the "Institut Federatif des

Neurosciences de Lyon", studying the brain metabolism by localized MRS [CUDA-08a, C.R Chimie]. These studies enabled to validate all MRS links going from the in vivo acquisition and subsequent metabolite concentration quantification to biological outcomes, such as early detection of metabolism alterations [BUCU-08, ISMRM][NP8].

NMR instruments: RF coils and optical-based synchronization device (O. Beuf, R. Sablong, E. Perrin, V. Detti, A-L. Perrier), interactions with team 2 (H. Benoit-Cattin)

Human endoluminal coil: The development of endoluminal radiofrequency (RF) coils removes the obstacles inherent to the investigation of deep organs. This technique is particularly useful in the diagnosis of ano-rectal pathology (Fig. 3). The high spatial resolution achievable with endoluminal coil provides detailed information on the local anatomy and pathology. In this context, an endoscopic coil, fully developed by our team and dedicated to the exploration of the anal sphincter, is currently undergoing clinical evaluation [NP9]. This study aims to compare high spatial resolution MR imaging performed at 1.5T with echo endoscopy in anal incontinence diagnosis [BEUF-07, PCT/FR2008/052248]. Security aspects, regarding RF heating in presence of metallic materials are investigated at the same time.

Small animal array coil: In the field of small animal, modeling methods are applied to the development of array coils for High spatial Resolution MR Imaging (HR-MRI) of the articular cartilage (rat, guinea pigs) [RENG-09, IEEE TBE] and spectroscopy in the brain mouse [IC2]. Due to limited size of small animal joints, cartilage assessment is very challenging. A two-channel phased array coil considerably improving the SNR as well as the signal uniformity was designed for 7T. These parameters are mandatory to segment and to quantify cartilage morphology (thickness, volume). The spatial resolution value achieved with this coil has never been reported in the literature [NP4]. Moreover, HR-MRI of both joints performed simultaneously significantly increase throughput [GOEB-08, *Biomed Mater Eng*]. These results obtained in collaboration with UMR 7561 [NP14] have been retained as key result 2009 by the CNRS INST2I (http://www.cnrs.fr/inst2i/recherche/faits-marquants/2009/imagerie-teslas.htm).

Optical-based synchronization device: Synchronization of NMR sequences on the cardio-respiratory movements of small animal remains an issue. The main difficulties are related to the environment of the object, strongly confined and noisy from the electromagnetic point of view. These constraints are increasing with image spatial resolution, the small space available and the intensity of B0. An optical fiber-based device, used to monitor the macroscopic movements of the small animal chest, was developed. Full fiber optical-based signal derived from heart and respiratory motion was suitable for prospective triggering for heart and liver MR imaging on rats and mice (Fig. 4). The fiber optic-based device performed as well as the ECG and air pressure sensors. The optical fiber-based device is an attractive alternative to commercially available triggering devices for small animal MRI in challenging environments such as small volume available and fast gradients switching [RENG-09b, ISMRM]. This device is the first concrete demonstration made by the team to use optics with MR [NP1]. Anne-Laure Perrier joined the team in September 2008. She brings her skills on simulation, design and realization of microwave devices (impedance transformer [JRAD-05, *Electronics Letters*], power divider [PERR-08, *MOTL*], RFID tags) to study new RF coil designs for MRI/MRS application [NP15].

NMR Spectroscopy and Imaging Methodology (H. Ratiney, S. Cavassila, O. Beuf), interactions with team 2 (C. Lartizien) and team 1 (P. Douek)

MRS: Fundamental and experimental researches aimed to develop entire methodologies to investigate the molecular contents (potential biomarkers) of living tissues (brain, liver) going from novel acquisition strategies to dedicated quantification algorithms. Developments targeted the measurement and the accurate and reliable quantification of macromolecules and metabolites present in the brain of small animals (Fig. 5) as well as the identification of MRS biomarkers measured in human livers. The following key results were obtained: a) In vivo single and multiple voxels edition sequences of the macromolecules and news dedicated quantification algorithms [CUDA-09, *J Signal Process Syst;* RATI-08a1, ISMRM][NP12]; b) Assessment of the accuracy of the metabolite concentration estimates using experimentally measured or theoretically simulated prior knowledge [CUDA-08, NMR in Biomed 2008]; c) Dedicated quantification algorithms for HR-MAS data from liver and prostate biopsies [ZHA-08, ISMRM; RATI-08d, ESMRMB][NP15].

MRI: Though working at high magnetic field B0 is of particular interest for functional imaging and spectroscopy, changes due to T1, T2, T2* relaxation time modifications with field strength have to

be addressed to control image contrast and spectrum quality. New acquisition strategies are required, especially in abdominal imaging for which classical imaging sequences do not allow to control image contrast independently of the respiratory period [BABO-07, BIIJ][NP3,6]. Moreover, for anatomical imaging, the SNR gain with the field strength increase is limited by the magnetic losses in living tissues. Thus an original alternative performing multiple animal acquisitions simultaneously using medium field strength and a large imaging volume was demonstrated on a clinical 1.5T system [BEUF-06a, *Magn Reson Mater Phy*].

Optical characterization of scattering media (R. Sablong, E. Perrin)
Optical biopsy is expected to become a non-invasive diagnosis technique but methodological development and evaluation for probing scattering media as tissue models are still needed. In this context, we have first successfully compared the in-lab spatially resolved method (called Reflectance Integral) using non-polarized illumination, to a standard temporally resolved method to measure global absorption (μa) and scattering (μ's) coefficients of calibrated samples [FALC-08a, *Appl Opt*]. Secondly we have used linearly polarized incident light to improve characterization by estimating the anisotropy factor g. This method is based on the Fourier analysis and statistical processing of the backscattering images (azimuthal intensity profiles of the Q-element of Stokes vectors), obtained by Monte Carlo simulation [FALC-08b, *Appl Opt*]. The experimental setup has been adapted to validate the method on calibrated phantoms (Fig. 6). Fibered elements are being used on the optical bench as a first step to enable endoscopic applications [NP13].

3. Platforms

Developed inside the laboratory:
- Optical bench for characterization of turbid media (polarized light)
- Multi-channel spectrometer for hyper-spectral optical imaging
- RF measurement bench with network analyzer, 500 MHz oscilloscope, chemical etching…
- ^{1}H dual channel imaging modulus on the laboratory 4.7T system

Access in Lyon to Animage platform (7T MRI; μPET) and MRI department (1.5T) of CERMEP, 3T clinical MRI of Hôpital Neuro-Cardiologique and 1.5T clinical MRI of Hôpital Edouard Herriot as well as 500 MHz vertical MRI system at CRMBM (CNRS UMR 6612) in Marseille.

4. Interactions

- With Volume imaging team 2 (C. Lartizien, H. Benoit-Cattin): Co-registered PET/MRI abdominal imaging for the characterization of liver growth of endocrine tumors in an experimental mouse model [NP7][BABO-09, Magn Reson Imaging]. Knee cartilage thickness quantification on a guinea pig model of OA [BOLB-07, Osteoarthritis Cartilage; BOLB-08, NMR Biomed].
- With Ultrasound imaging team 3 (E. Brusseau, H. Liebgott): MR and US Elastography comparison, engineering of a dynamic excitation driver for USE [GREN-09, ESMRMB].
- With team 6 (D. Graveron): MRS signal processing algorithms [NP8][CUDA-08, NMR Biomed].
- With team 4 (E. Canet, M. Wiart): MRS muscular lipid quantification [FISS-06, C R Chimie]. Bi-modal optics-MR imaging of the atherosclerotic plaque on the mouse [NP5]. MRI monitoring of neuro-inflammation in mouse cerebral ischemia [WIAR-07a, Stroke; PIAL-07a, NMR Biomed].
- With medical team 1 (P. Croisille, P. Douek): Diffusion tensor imaging of the heart (joint PhD). Stent-graft placement with real-time MR fluoroscopy [ATTI-08, *J Vasc Interv Radiol*].
- With info team: C++ class writing for Bruker data reading. CreaContour software improvements.

5. Technological transfer

Start'up
M-J. Seurin left the team to create in March 2008 a start'up named cIRMa (Centre d'Imagerie de Résonance Magnétique pour Animaux). The team is supporting cIRMa to develop dedicated RF coils and 3D sequences for imaging of domestic animal (Convention CNRS n°20499).
Software
Software dedicated to the advanced quantification of MRS data (HR-QUEST) has been freely distributed in a context of cooperation agreements at 3 academic centers (CRMBM, CNRS UMR 6612, Marseille; IFR1, Grenoble; Department of Radiology, University of California San Francisco).
Patents
- N. 0759652. PCT/FR2008/052248. Sonde endocavitaire pour l'imagerie et/ou la spectrométrie par résonance magnétique nucléaire, 2007.

- N. 0757654. PCT/EP2008/062480. Acquisition de signaux dans un espace hypercomplexe, 2008.

6. Grants

National projects

[NP1] Abondement ANVAR 2005 (12 mois, 20 k€) : H. Saint-Jalmes.
[NP2] BQR conjoint HCL/UCB 2005 (24 mois, 20 k€) : O. Beuf.
[NP3] Programme Interdisciplinaire IPA CNRS-CEA 2005 (24 mois, 15 k€) : O. Beuf.
[NP4] Programme Interdisciplinaire IPA CNRS-CEA 2005 (24 mois, 12 k€) : P. Gillet.
[NP5] Programme Interdisciplinaire IPA CNRS-CEA 2005 (24 mois, 19,5 k€) : R. Sablong
[NP6] Action Jeune Chercheur du Département SPI CNRS 2005 (24 mois, 50 k€) : O. Beuf.
[NP7] BQR INSA-Lyon 2006 (24 mois, 20 k€) : C. Lartizien.
[NP8] BQR 2006 Université Lyon 1 (12 mois, 12 k€) : D. Graveron.
[NP9] Action Incitative Hospices Civils de Lyon 2006 (24 mois ; 60 k€) : F. Pilleul.
[NP10] ANR 2007 (36 mois, 420 k€) :P. Litaudon.
[NP11] INCA 2007 (36 mois, 200 k€) : J. Hasserodt.
[NP12] PEPS INST2I-CNRS 2008 (12 mois, 10 k€) : H. Ratiney.
[NP13] PEPS CNRS 2009 (24 mois, 20 k€) : R. Sablong.
[NP14] ANR Blanche 2009 (36 mois, 550 k€) : P. Gillet.
[NP15] 2 Soutiens Jeune chercheur IFNL (12 mois, 2 k€) : H. Ratiney (2008), A-L. Perrier (2009).

Industrial contracts

[IC1] SIEMENS Medical Solutions, Erlangen, Germany; Dr. B. Kiefer.
[IC2] Bruker Biospin, Ettlingen, Germany; Dr F. Hennel.
[IC3] Philips Medical Systems, Best, Netherland.
[IC4] GE HealthCare, Muenchen, Dr T. Schirmer.

7. Collaborations with common publications

National collaborations (15)

CNRS UMR 6612 (P. Cozzone), Marseille: Y. LeFur, M. Sdika [RATI-09, ISMRM]; CNRS UMR 5182 (P. Sautet), ENS Lyon: J. Hasserodt [STAV-08, *New J. Chem*]; CNRS UMR 5161 (J. Samarut), ENS Lyon: L. Canaple [CANA-08, *NMR Biomed*]; CNRS UMR 7551 (J. Magdalou), Université Nancy 1: P. Gillet, A. Pinzano [GOEB-08, *Biomed Mater Eng*]; CNRS UMR 5020 (R. Gervais), Université de Lyon: N. Ravel, P. Litaudon [MART-07, *Neuroimage*]; CNRS UMR 8165 (P. Lanièce), Paris IX, Orsay: P. Lanièce [DESB-05, *IEEE Trans Nucl Sci*]; CNRS UMR 6232 (B. Mazoyer), GIP Cyceron, Caen: F. Lamberton [LAMB-07, JMRI]; Inserm U642 (L. Senhadji), Université Rennes 1: H. Saint-Jalmes [RENG-09, IEEE TBE]; Inserm U842 (J. Honnorat), Université de Lyon: A. Bernard, M. Touret [BUCU-08, ISMRM]; Hospices Civils de Lyon, Université Lyon 1 : Ph. Ryvlin [CUDA-07f, C.R. Chimie]; Inserm U855 (G. Mithieux), Université Lyon 1: F. Rajas; Inserm U865 (J-Y. Scoazec), Université Lyon 1: C. Roche [BEUF-08, *Gastroenterol Clin Biol*]; Inserm U556 (J-Y. Chapelon), Université Lyon 1: O. Rouvière, R. Souchon [SOUC-08, *Magn Reson Med*]; LETI - CEA Grenoble: A. Laidevant, J.M Dinten [FALC-08a, *Appl Opt*].

International collaborations (6)

- National Singapore University, Pr S-C. Wang, joint PhD thesis of L.S. Ming [LEE-09, *Stem Cells*].
- Université Technique de Delft, D. van Ormondt [CUDA-08, NMR in Biomed].
- Institut de physique, Université de Louvain, Belgique. JP. Antoine [SUVI-09, *Meas. Sci. Technol*].
- University of California San Francisco, J. Kurhanewicz, S. Nelson [ZHA-08 ISMRM; LI-08, *JMRI*].
- University of California San Francisco, USA, D. Pelletier [RATI-07a, *Magn Reson Mater Phy*].
- University of Veterinary Medicine Hannover, Germany, M. Joly.

8. Expertise and consulting

- Expertise: ANR TecSan (2006 et 2008) ; ANR programs PCV (2008) and PIRIbio (2009) ; PEPS CNRS INST2I 2009; « Transfert de Technologie » Program (2006) for Conseil Régional de Bourgogne; Euro-Trans Bio (2006) of EURA-NET (European Commission funded); CIFRE Grants Committee (Industrial PhD Grants) (2008); European Expert FP7 - Call 4 - ICT for Health - Chapter 5.2 Patient Safety (2009); Member of the Administration Council of AGBM (Alliance for BME)
- Consulting: Animage-CERMEP platform (O. Beuf, D. Grenier); Group of discussion NEVAMET on the brain (NEurones), Vascular systems and MEtabolisms (S. Cavassila, H. Ratiney).

- Journal's reviewing: Osteoarthritis & Cartilage, JBMR (Part A), J Neuroscience Methods, J Biomechanics, Biomed Imaging and Intervention Journal, Magn Reson Mater Phy, MR Imaging, J Magn Reson Imaging, Magn Reson Med, IEEE Trans Signal Proc, IEEE Signal Proc Letters.

9. Distinctions

1 GRAMM price 2008 (Bucur), 5 ISMRM student stipends (Rengle, Bucur, Cudalbu x2, Armenean), 1 GERM student stipend (Cudalbu), 2 ESMRMB student stipends (Cudalbu, Armenean).

10. Research training

- Head of Health Engineering Master Degree (2006-) & Biomedical Department of ISTIL (E. Perrin).
- Evaluation of training activities in BME & Medical Physics (130 practical courses/year) (E. Perrin).
- Board Member of Electrical Engineering department of Univ. Lyon1 (2001-2008) (S. Cavassila).
- Head of "Embedded systems and Computer Science" teaching staff joining 7 associated professors and 170 students (2004-) (S. Cavassila).
- Head of the comity in charge of the recruitment of the assistant and full professors in the "Electrical Engineering" department at Université Lyon 1 (section 61) since 2008 (S. Cavassila).
- Members of comities in charge of the recruitment of assistants and full professors section 61 (2), section 63 (4), section 31 (1), section 29 (1), section 39 (1), section 85 (1).
- Students trained for research: 10 TER M1 GEP, 2 M1 GBM, 11 M2R GBM, 5 M2R EEA, 2 M2R.

11. Congress organization and committees

Member of the organizing comity of the 12th Congress of GRAMM 2008 (O. Beuf).

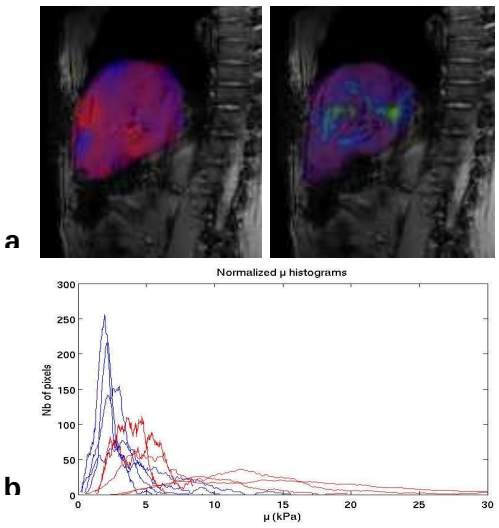

Fig. 1: a) False colors phase image and shear modulus map of the liver superimposed on modulus MR image; b)

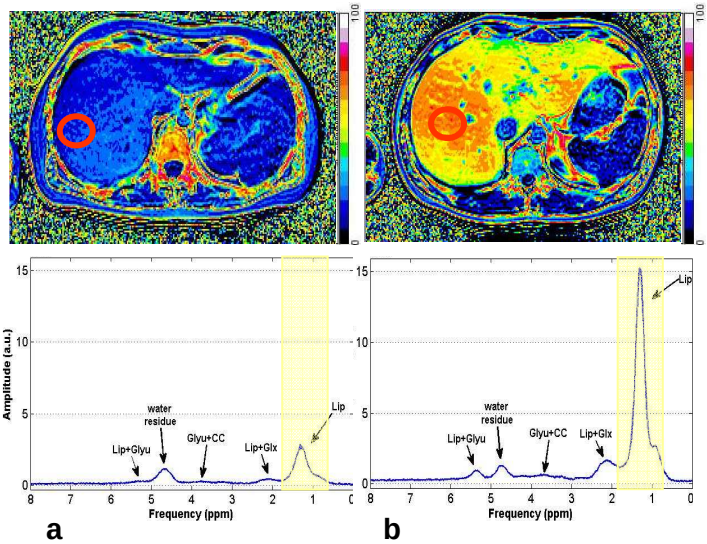

Fig. 2: Colored maps of the percentage of steatosis estimated from in and out of phase images for two patients a) with low (<30%) and

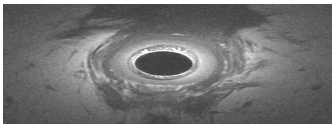

Fig. 3: High-resolution axial T1-weighted MR image (100 mm FOV; pixel = 223 x 298 μm^2; 2 mm slice thickness; 3 min scan time) of the anal sphincter acquired on a patient with the developed prototype. The Internal and external sphincter muscles are clearly visible.

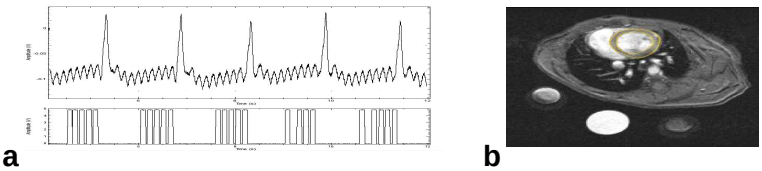

Fig. 4: a) Optical-based signal (largest peaks = respiration; small oscillations = heart beats) and output trigger signal. b) Cardiac MR image acquired on a mouse using a CINE FLASH with prospective triggering using the optical device.

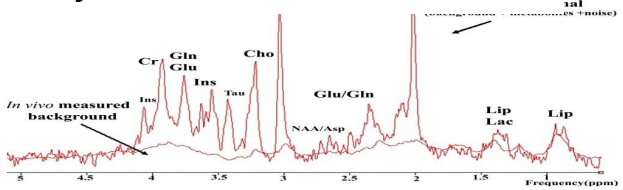

Fig. 5: In vivo short echo time MRS spectrum acquired at 7T in a rat brain superimposed on measured in vivo macromolecule spectrum.

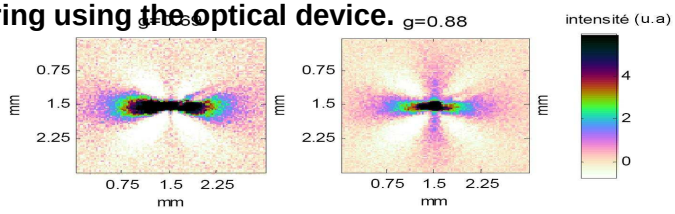

Fig. 6: Experimental images of calibrated scattering media illumination by a PM fiber. The anisotropy factor g is 0.69 and 0.88 respectively.

Team nº: 5 Title : Methods and systems in MRI an d optics

ALC : Original International and National articles in specialized journals with review committee

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[CUDA-09] C. Cudalbu, O. Beuf, and S. Cavassila. In vivo short echo time localized 1H MRS of the rat brain at 7T: influence of two strategies of background-accommodation on the metabolite concentration estimation using QUEST. J Signal Process Syst, 55:25-34, 2009.
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Team n°6 Title : Magnetic Resonance Spectrosco pic Imaging

Previous activity : Period 2005-2009

Key words: Magnetic Resonance, MRS/MR(S)I/MRI, signal processing, quantification, metabolism, stroke ; inflammation, contrast agent, neurodegenerative diseases, cancer.

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Peer-reviewed Publications: 83; Conference papers : 111

Cette thématique concerne la Spectrométrie (SRM), l'Imagerie Spectroscopique (ISRM) et l'Imagerie (IRM) multimodale de Résonance Magnétique. Les objectifs sont : 1) la recherche de techniques innovantes d'acquisition rapide des données ISRM conjuguée à l'utilisation de l'Imagerie de tenseur de Diffusion, 2) L'utilisation de nanoparticules super paramagnétiques (USPIO) pour le suivi de la neuro-inflammation, et de micro antennes pour augmenter la sensibilité du signal, 3) le développement de méthodes avancées de quantification automatique permettant l'identification et l'imagerie *in vivo* des métabolites (bio-marqueurs des pathologies), 4) Le développement d'un 'imageur virtuel' fondé sur la Mécanique Quantique pour la modélisation de séquences d'acquisition et de signaux spectroscopiques, 5) L'implantation et la validation des techniques proposées pour : le suivi du métabolisme lors de processus physiologiques chez l'homme et l'animal; les applications cliniques concernant principalement la caractérisation et le suivi thérapeutique de l'ischémie cérébrale, des maladies neuro-dégénératives (maladie d'Alzheimer, sclérose en plaques), le cancer et les tumeurs cérébrales.

1. Objectives

This research concerns Magnetic Resonance Spectroscopy (MRS), Spectroscopic Imaging (MRSI) and multimodal Imaging (MRI). The aims are: 1) the search for innovative fast acquisition techniques for MRSI data linked to diffusion tensor imaging (DTI); 2) use of ultra small super paramagnetic nanoparticules of iron oxides (USPIO), and of micro coils to enhance the signal; 3) the development of advanced methods for automatic quantification enabling identifying and imaging of metabolites (bio-markers for pathologies) in vivo, 4) the development of a "virtual scanner" based on quantum mechanics for modelling acquisition sequences and spectroscopic signals, 5) the implantation and validation of the techniques proposed for monitoring metabolism during physiological processes in humans and animals; the clinical applications concern mainly the characterization and therapeutic follow-up of several brain diseases including stroke, neurodegenerative diseases (mainly multiple sclerosis), aging pathologies such as Alzheimer's disease, cancer and brain tumours.

2. National and international context

Understanding of metabolic processes is a key element in diagnosis and therapeutic follow-up for medical exploration in man and/or for studying experimental models in animals. It is, however, currently difficult to obtain this metabolic information under ultra-fast examination conditions.

Although MRSI enables to obtain the spatial distribution of metabolites of major importance for the follow-up of physio-pathological processes, there are still many major obstacles before MRSI can be applied routinely in clinical practice: 1) acquisition times that are too long; 2) low spatial resolution and the low signal-to-noise ratio of metabolic images; 3) the complexity of signal processing, analysis and visualization of the data.

Few international groups have recently demonstrated the feasibility of rapid MRSI. As for the quantification aspect, the jMRUI software developed in the context of our European network is considered to be one of the "gold standards" in MRS/MRSI.

Concerning the applications, brain diseases including stroke, neurodegenerative diseases (multiple sclerosis), aging pathologies such as Alzheimer's disease represent research priorities in heath.

3. Research activity

MR Methodology - Signal Processing (D. Graveron-Demilly)

The aim is to develop advanced signal processing methods for in vivo Spectroscopy, Spectroscopic Imaging and High Resolution Magic Angle Spinning (HR-MAS) NMR. This research exploits the powerful synergy between signal processing and MR methodology and is carried out in the context of the European Project FAST.

Quantitation: method QUEST for automatic quantification of MRS/MRSI/HR-MAS-NMR signals

Quantitation of in vivo signals is a daunting and difficult task for many reasons: 1) MRS(I) signals contain a strong non-parametric part from `macromolecules' that perturbs the wanted, parametric, part from metabolites. This requires a semi-parametric approach which is still under development, worldwide. 2) Many spectral peaks (several hundreds) of the parametric part overlap strongly. 3) Low signal-to-noise ratio of the signals, 4) All processing needs to be fully automatic and

numerically stable. Reliance on starting values will be reduced by development of genetic algorithms. 5) Reliable error bars on metabolite concentrations that accommodate the non-parametric part must be provided.
The automatic and reliable quantification of proton spectra obtained in vivo at short echo-times, is a current challenge in research and in clinical practice. Indeed, these spectra enable to observe several metabolites, markers of pathologies. Our quantitation algorithm 'QUEST' (QUantitation based on QUantum ESTimation) [RATI-05, RABE06a, RABE-08b, POPA-09] is based on a time-domain semi-parametric approach and on a priori knowledge of a metabolite basis-set, obtained by quantum mechanics or measured in vitro. It has been implemented in the jMRUI Software Package. So, since 2006, the first publications reporting quantification results obtained with our method QUEST have been appearing in the international literature.
QUEST has been recently applied for the quantification of about twenty metabolites present in HR-MAS NMR spectra obtained at 9.4T from biopsies of mouse/rat brains [RABE-08b], in collaboration with the Laboratory of the CRSSA in Grenoble (Dr. F. Fauvelle). Together, we recently proposed the very first in vivo proton HR-MAS NMR profiles of freshwater cladoceran Daphnia magna [BUNE-09a], "Research highlights" in Chemical Biology, 2009, in press.

Virtual Scanner based on the programme NMR-SCOPE

With this 'Virtual scanner', based on the quantum mechanical formalism of density matrix and the products of operators, we can simulate signals of metabolites in response to any experimental protocol, for different fields and for a range of nuclei (^{1}H, ^{13}C, ^{31}P, etc.) and in particular, the metabolite basis-sets used in QUEST. This algorithm was implemented in the jMRUI software package. Three types of users are supposed: 1) 'quantitators' (i.e. users of jMRUI quantitation tools), 2) pulse-sequence developers, and 3) data-processing developers.
Thanks to ab initio calculations, estimation of spin parameters is quite feasible once the equilibrium geometrical structure of the molecule has been determined. Note that no in vitro experiment is needed! Nevertheless, such cutting-edge calculations require a huge amount of computation time [ALLO-08a, ATIE-09 and "Research highlights" in Chemical Biology, July 2007, Vol. 2, Issue 7).

Development of the jMRUI Software Package, http://www.mrui.uab.es, Coordination Danielle Graveron-Demilly,

In the context of FAST, we develop of a ground-breaking Software Package jMRUI enabling estimation, analysis and visualization of multi-parametric metabolite images based on 1) our algorithms, 2) Object-oriented, Java-based graphical user-interface (GUI), 3) Web distance-collaboration between remote clinical experts as well as researchers. Multiple clients world-wide will learn, train, interpret interactively through their computers by remote real-time sharing signal processing and visualization actions.
Version 4.0 of jMRUI with Plug-ins is now ready [STEF08a, STEF-09].

Methodology – Instrumentation : Micro-coil for MR Spectroscopy (L. Fakri-Bouchet)

A new concept of receiver planar micro-coil (1000 X 500µm^{2}) operating at 200 MHz (proton at 4.7Tesla) fabricated by electroplating technique has been developed [BAXA-08, SORL-05, CHER-05, BAXA-06a, b, c]. The innovative part of this work concerns:
- Implemented MR instrumentation at micro-scale,
- Restricted volume detection by MR spectroscopy and imaging (about the micro mole/litre).

The micro coil performance improvement opens the way to highly spatially resolved explorations on animal models and developments in NMR micro-spectroscopy are moving apace. is promising for the metabolic or functional investigation of particular lesions and for the monitoring and studying of specific diseases like (epilepsy, tumours, Parkinson's disease, Alzheimer and sclerosis).
This work was particularly noted in David Bradley's article 'A brainy approach to NMR coils', on the NMR Knowledge Base website dedicated to Nuclear Magnetic Resonance Spectroscopy. See http://www.spectroscopynow.com/coi/cda/detail.cda?id=17742&type=Feature&chId=5&page=1

Preclinical development

Ischemic stroke (Y. Berthezène, N. Nighoghossian)

A growing body of evidence suggests that inflammatory processes are involved in the pathophysiology of stroke, causing delayed expansion of the infarct. In this context, noninvasive imaging of inflammation associated with ischemic stroke lesions could have a predictive value and may be helpful for the development of cytoprotective drugs.

Cellular imaging of inflammation with MRI using ultrasmall superparamagnetic nanoparticles of iron oxides (USPIO) has recently emerged as a promising non-invasive technique for experimental and clinical studies of several inflammatory diseases. When injected intravenously, USPIOs are phagocytosed by macrophages within the blood-pool (circulating monocytes) or locally at the site of inflammation (tissue macrophages). They thus become magnetic and can be monitored by MRI. Based on this hypothesis, we have developed and validated a USPIO-enhanced MRI approach to study neuroinflammation in a mouse model of focal cerebral ischemia and translated the technique into the clinics to assess neuroinflammation in stroke patients

We first validated a method allowing the MR tracking of phagocyte cells in stroke-induced mice [WIAR-07a]. Imaging data correlated with histochemical analysis showing inflammation remote from the lesion and uptake of USPIO by macrophages.

While MR signal changes after intravenous USPIO injection were indisputably related to inflammatory cells at the subacute stages after focal cerebral injury, the interpretation of USPIO-related MR signal alterations at the acute stages remained controversial. We then compared MR signal changes with the histological iron and macrophage distribution during the first 24 hours in the same mouse model of acute stroke [DESE-09a]. Our results suggested that early reproducible USPIO-related MR signal changes were mainly caused by passive diffusion of free USPIO after blood–brain barrier leakage and by intravascular trapping, rather than by peripheral phagocyte infiltration.

Finally, we measured the relaxation properties of macrophages labelled with two types of USPIOs (Ferumoxtran-10 and AMNP), at 4.7T and 7T using multi-parametric (T1, T2 and T2*) quantitative MRI in vitro and in vivo [BRIS-09a], thus moving the technique towards potential quantitative follow-up of neuroinflammation.

Neurodegenerative diseases (Alzheimer models) (L. Fakri-Bouchet, F. Cotton)

Due to its low sensitivity, NMR analysis of small volume samples of a few nano litres is rather difficult and use of micro-coils is promising, One interesting application in the field of neurosciences will be the direct observation of individual amyloidal plaques observation in Experimental animal of Alzheimer diseases (AD). AD and neurodegenerative processes are also studied by MRS/MRSI (NAA quantification), DTI with tractography (uncinate fascicule and temporal connections) and susceptibility weighted imaging (amyloidal plaques detection) in collaboration with Dr Pierre Krolak-Salmon and Pr. Y. Zaim Wadghiri, NYU School of Medicine, USA.

Action 3 : Clinical development

Stroke (Y. Berthezène, N. Nighoghossian)

We have been amongst the first to propose the use of USPIO-enhanced MRI to assess neuroinflammation in stroke patients. In brief, no USPIO enhancement was observed 2 days after stroke onset [CHO-07a], whereas MR signal changes were consistently observed in studies performed at 6 days after stroke [NIGH-07a]. In this small series (10 patients), USPIO-related MRI enhancement was heterogeneous and not related to blood-brain barrier disruption.

Given the heterogeneity of inflammation response in human stroke, further larger clinical studies are needed to demonstrate the clinical benefit associated with the use of USPIOs as an MRI surrogate marker for brain inflammation.

Multiple Sclerosis (F. Durand-Dubief, D. Sappey-Marinier, F. Cotton)

Multiple sclerosis (MS) includes both inflammation and neurodegenerative processes, leading to irreversible neurologic impairments. MRI has emerged as the most important paraclinical tool for diagnosis and monitoring of MS. Initial inflammation is not fully understood and a better understanding of the natural history of plaque formation is necessary. For this purpose, a project was developed at 3T to weekly follow up new active lesions with DTI, MR perfusion and MRSI.

However, metrics from conventional contrasts MRI (lesion load) are modestly correlated with disability outcomes measured by clinical index (EDSS or MSFC), leading to a so-called “clinico-radiological paradox”. Further, the paradigm understanding MS as a primary inflammatory disease has been challenged by the neurodegenerative hypothesis as described by Confavreux et al.. Thus new functional and quantitative MRI techniques have been developed such as MRS and DTI to provide new biomarkers of disease evolution and prediction [SAPP-07].

1. On one hand, MRS provides metabolic information (decrease of NAA (neuronal marker), increase of choline (myelin and inflammation marker), increase of creatine and myoinositol (gliosis) which is better correlated with clinical status. However, this technique suffers from limited spatial resolution and processing. Developments in quantification and signal processing with QUEST were

investigated using 1) a « global » approach (large brain VOI) to test the hypothesis of detecting general and absolute metabolic changes between MS clinical forms, and 2) a « focal » approach by using MR spectroscopic imaging (CSI) to characterize different brain regions [BAGO-09].
2. On the other hand, DTI has proved to be a very sensitive method to detect micro-structural tissue damage occurring in MS. Investigation of white matter (WM) and gray matter (GM) using a ROI approach has shown decreased fractional anisotropy (FA) associated with greater change in radial diffusivity (λr) compared to axial diffusivity (λa). In contrast, deep gray matter nuclei are characterized by increased λa and decreased λr leading to an increased FA. These alterations are significantly different between the clinical forms and particularly greater in patients with primary progressive form demonstrating that diffusivity parameters may constitute an early marker of neurodegenerative processes. A second approach using voxel-based statistical analysis of WM (using TBSS) and GM (using VBM). These measurements will be correlated with the clinical informations to better evaluate their impact on the prediction of the disease evolution and the therapy follow-up [HANN-09].

4. Platforms

- The Laboratory CREATIS-LRMN is actually equipped with 2T and 4.7T Bruker preclinical (30 cm bore) system.
- The CERMEP-Imagerie du vivant (GIE labelled RIO) provides several MRI equipments such as a 7T Bruker preclinical (20 cm bore) system, a 1.5T Siemens system and a 3T system will be installed en 2011.
- The unit of Radiology at the neurological hospital provides a 1.5T Siemens Avanto system and a 3T Philips system. Both systems have DTI and spectroscopy modules.
- Access to the FAST scanner platforms (7T for human, 9.4T and 14T for animals).

5. Interaction

Team 4: strong collaboration with M. Wiart concerning the development of ischemic stroke in animal models [WIAR-07a, DESE-09a, BRIS-09a) and in human to assess neuroinflammation in stroke patients using USPIO-enhanced MRI [CHO-07a, NIGH-07a]; and with E. Canet (lipid metabolism) [BUNE-09].

6. Technological transfer

jMRUI Software Package

D. Graveron-Demilly has been coordinating since 1997, the development of jMRUI software package for MRS/MRSI/HRMAS-NMR quantification of in vivo data [STEF-09a, STEF-09b]. This software, considered as one of the 'Gold Standards', is currently used by more than 1200 research groups and hospitals worldwide. Licenses have been sold to pharmaceutical companies.

7. Grants

National projects

Région Rhône-Alpes, Cluster 11, 2006-2008, 26 k€, D.Graveron-Demillly, D. Sappey-Marinier.
Région Rhône-Alpes, Cluster 11, 2008-2009, 15k€, R. Cespuglio, L. Fakri-Bouchet.
Région Rhône-Alpes, Cluster 11, 2007-2008, 30k€, N. Nighoghossian.
Région Rhône-Alpes, Cancérologie, 2004-2007, 28k€, D. Graveron-Demillly.
BQR UCB, 2006, 12 k€, D. Graveron-Demilly.
BQR INSA, 2007, 15 k€, M. Wiart.
BQR UCB, 2006-2007, 14 k€, L. Fakri-Bouchet.
Fondation pour la Recherche sur le Cerveaux, 2007, N Nighoghossian.
HCL, 2009-2010, F. Cotton.
ANR INFLAM, 2007-2010, 155k€, Y Berthezène.
ANR NEUROPROTECT, 2007-2011, 85k€, M Lagarde, N Nighoghossian and D. Sappey-Marinier.
ANR Neurosciences, Neurologie et psychiatrie, 2006-2009, 70 k€, D. Pelisson, D. Sappey Marinier.

European projects

European project I-KNOW, 2006-2009, STREP, 305 k€, PI L Oestergaard, PI at CREATIS-LRMN N Nighoghossian : Integrating Information from Molecule to Man: Knowledge Discovery

Accelerates Drug Development and Personalized Treatment in Acute Stroke (www.i-know-stroke.eu)
European Project 'FAST', Marie Curie Research Network (MRTN-CT-2006-035801), 01-11-2006 au 01-11-2010, 3 Millions €, 'Advanced Signal-Processing for Ultra-Fast Magnetic Resonance Spectroscopic Imaging, and Training', 16 Partners among Philips Medical Systems, Siemens Healthcare et Sanofi-Aventis, Coordinator D. Graveron-Demilly (www.fast-mrs.eu)

Industrial contracts
- Philips Medical Systems, Best, Hollande (BDI CNRS/Philips, H. Rabeson, 2004-2007, 27k€ ; E. Popa, 2006-2009, 12k€), Dr. R. de Boer.
- Siemens Health Care, FAST project.
- General Electric, Dr T. Schirmer, NDA in the context of the jMRUI Software Package.
- Merck and Covance, jMRUI Software Licences, 50 k€.

8. Collaborations

National collaborations
U842 Inserm, Neurooncologie et neuroinflammation, Lyon: [BRIS-09a, DESE-09a, WIAR-07a]
UMR CNRS 5180, Laboratoire des sciences analytiques, Lyon: [BRIS-09a]
CRSSA, Grenoble, Dr. F. Fauvelle [RABE-06, BUNE-09].
- Unité INSERM EA 3734, Neurobiologie des états de vigilance, UCB, Lyon 1, Dr. Raymond Cespuglio [BQRs, 2006].
- Unité CNRS UMR5579, LASIM, Dr. Monique Frécon [ALLO-07, ALLO-08, ATIE-09a, ATIE-09b].
- LENAC EA 3730, Université Claude Bernard Lyon1, Dr. Pierre Morin [CHER-05, SORL-05,BAXA-06a, BAXA-06b, BAXA-06c].

UMR CNRS 6600, Laboratoire de Biomécanique et de Génie Biomédical, Université Technologique de Compiègne, Dr. Odette Fokapu [SABB-06, ABDA-06].

International collaborations
Belgium, Catholic University of Leuven, Electrotechnic, SISTA, Pr. S. Van Huffel [STEF-07]; Catholic University of Leuven, Biomedical NMR, Pr. U. Himmelreich; Université Catholique de Louvain, Inst. of Theoretical Physics, Pr. J.P. Antoine (EU Project, FAST).
Canada, University Mc Gill, Montreal, Dr. D. Arnold [NARA-06].
Czech Republic, Institute of Scientific Instruments, NMR, Brno, Dr. Z. Starcuk (EU Project FAST) [STARC-09a, STARC-09b].
Germany, Max Planck Institut, Leipzig, Dr. H. Moeller; Siemens Medical Solutions, Erlangen, Dr. S. Röll ; Sanofi-Aventis, Frankfurt, Dr. H.P. Juretschke (EU Project FAST).
Greece, Institute of Language and Speech Processing, Athènes, Dr. E. Fotinea ; Chalkis Institute of Technology, Pr. D. Karras (EU Project FAST).
Romania, Université de Cluj, Pr. O. Cosar [DEA C. Cudalbu, N. Baxan, A. Bucur, S. Gutoiu].
Spain, Autonoma University of Barcelona, M. Cabanas (EU Project FAST, [STEF-09a, STEF-09b]).
Switzerland, Ecole Polytechnique de Lausanne, Pr. R. Gruetter (EU Project FAST). Centre intégratif de génomique, Université de Lausanne, Lausanne [PIAL-07a].
The Netherlands, Delft University of Technology, Dr. D. van Ormondt [RATI-05, CUDA-06,RABE-06a, RABE-06b, RATI-05b, CUDA-05a, CUDA-05b, KARR-05, STEF-09A, STEF-O9b, POP-09] ; Radboud University Nijmegen, Pr. A. Heerschap; Philips Medical Systems, Best, Dr. R. de Boer, MR Clinical Science Director (EU Project FAST).
United Kingdom, University of Manchester, Imaging and Biomedicine Department, Pr. S. Williams (EU Project FAST, [STEF-09b]).
USA, NIH, Bethesda, Dr. J.W. van der Veen; Department of Radiology, University of California-San Francisco, USA, Dr. John Kurhanewicz, Dr. D. Pelletier, Dr. S. Nelson [RATI-06c]; NYU, School of Medicine, Department of Radiology, Dr. Y. Zaim Wadghiri [joint PHD]; Ohama University, Dr. M. Boska [joint PhD].

9. Expertise and consulting

D. Graveron-Demilly: Expert/Evaluator EU FP4/FP5/FP6; Biomedical Engineering Panel of Finish Research Projects, Academy of Finland, 16-17 June 2008, Helsinki, Finland; INSERM 2009, Projet de Maturation. L. Fakri-Bouchet: Evaluator ANR Jeunes chercheurs.

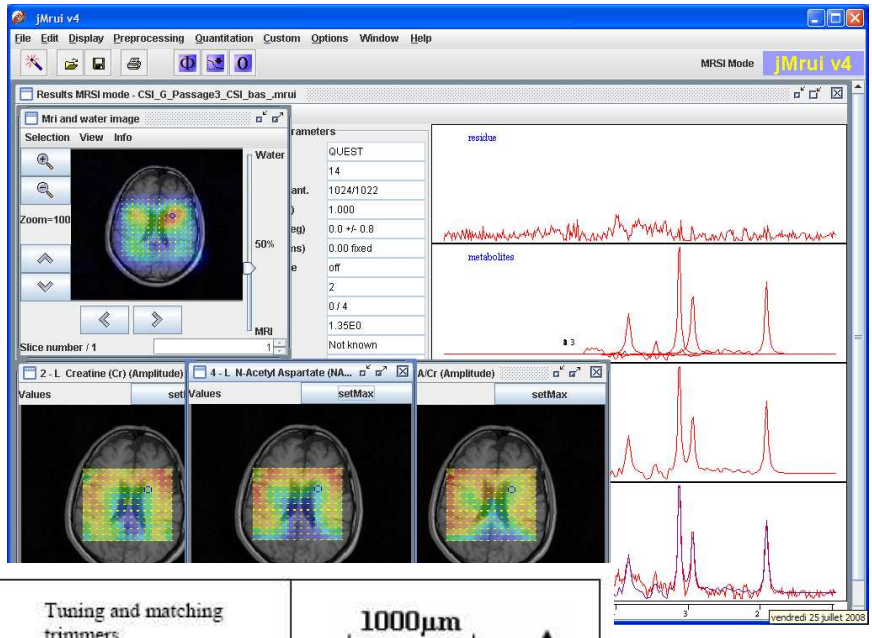
Team members are reviewers for Magnetic Resonance in Medicine; Journal of Magnetic Resonance; NMR in Biomedicine; Magn. Reson. Mater. Phy; Stroke; Cerebrovascular Diseases (Editorial Board); BMJ; JNNP; JMRI, Europ. Radiol.

10. Distinctions

Salem Hannoun, Prix du poster du GRAMM, 2008.
Danielle Graveron-Demilly, Chevalier des Palmes académiques, Oct 2007.

11. Congress organisation and committees (FIMH, IEEE, ISMRM, …)

jMRUI User Meetings (in the context of ISMRM), 23 Mai 2007, Berlin, Allemagne; 7 Mai 2008, Toronto, Canada ; 22 Avril 2009, Honolulu, USA ; 100 participants, organisation D. Graveron-Demilly.
jMRUI Demos (in the context ISMRM) in Philips booth, Miami, 8-12 Mai 2005 ; Seattle 7-11 Mai2006 ; in Philips et Siemens booths, 20-24 Mai 2007, Berlin, Allemagne; 4-8 Mai, 2008, Toronto, Canada; 19-23 Avril 2009 Hawaii, USA; 100 participants, organisation D. Graveron-Demilly.
FAST jMRUI Training Course, 11 September 2008, Chania, Greece, organisation D. Graveron-Demilly.
jMRUI Demos during Info Reso, ESMB2008, 2-4 Octobre 2008, Valencia, Espagne.
Danielle Graveron, member of the NEMA Task force concerning the advanced DICOM standard; SCAR05, Orlando, 2005 and RSNA, Chicago, 2005.
European projects FAST/Phelinet : non scientific course (Intellectual property, ethics, etc.), 28-11-2008, Lyon, France, 40 participants.
IEEE-IST-2008, IEEE International Workshop on Imaging Systems and Techniques – IST 2008, 12 Septembre, 2008, Chania, Crete, Greece. Special Sessions on MRS Methodologies organized by Prof. D. Karras, Dr. D. Graveron-Demilly , D. van Ormondt.
GRAMM2008, 12ème Congrès du GRAMM, 26-28 mars 2008, Lyon, France, Président D. Sappey-Marinier; D. Graveron-Demilly, Comité d'organisation.
FAST Kick-off Meeting, 5-7/02/2007, Université Claude Bernard, Lyon 1, France, Organisation D. Graveron-Demilly, 36 participants.
Interaction with the European Network Health Agents, 'Agent-based Distributed Decision Support System for Brain Tumour Diagnosis and Prognosis', FP6, STREP, Coordinator Magi Lluch-Ariet, MicroArt (SME), in the context of the jMRUI software package.



Quantitation with QUEST of ^{1}HMRSI data (32 × 32 voxels, PRESS sequence with an echo-time of 136 ms) of a human brain of a patient with multiple sclerosis, obtained at 1.5 T. Metabolic images of NAA and Cr, and of the ratio NAA on Cr superimposed on the anatomic image, and quantitation results in a selected voxel in plaques; from bottom to top, raw (red) and estimated (black) spectra, estimated spectrum, individual metabolites and the residue.

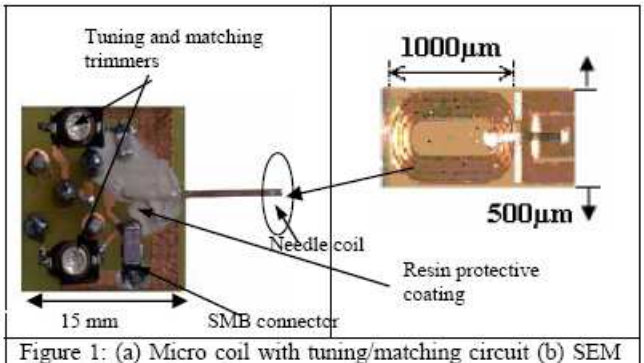


Figure 1: (a) Micro coil with tuning/matching circuit (b) SEM view of the needle coil.

Team n°: 6 Title : Magnetic Resonance Spectroscop ic Imaging

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ALC : Articles dans des revues internationales avec comité de lecture

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[GRAV-08a] D. Graveron-Demilly. **Méthodes et logiciels de traitement en Spectroscopie cérébrale**. In *Journées Françaises de Radiologie*, Paris, Octobre 2008.
[GRAV-07] D. Graveron-Demilly. **Magnetic Resonance Spectroscopic Imaging, Toward Non-Invasive In Vivo Assessment of Metabolic Content**. In *ProRISC 2007*, Veldhoven, The Netherlands, November 2007.
[GRAV-06] D. Graveron-Demilly. **Quantitation for NMR Spectroscopy**. In *Advanced Spectroscopies on Biomedical and Nanostructured Systems*, Cluj-Napoca, Romania, Sept 3-6 2006.
[GRAV-06a] D. Graveron-Demilly. **jMRUI Quantitation Methods & Application to MRS, MRSI & HRMAS-NMR**. In *International Society of Magnetic Resonance in Medicine, ISMRM Workshop, Data Processing for MR Spectroscopy and Imaging*, Warrenton, Virginia, USA, Nov 11-13 2006.
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[GRAV-09a] D. Graveron-Demilly. Magnetic Resonance Spectroscopic Imaging, Science, Technology and Innovation Projects, Celebrating Research and Development in Europe, 10, 114-115, 2009. Article invité.

Team n°7 Title : Tomographic Imaging and Therapy with Radiation

Previous activity : Period 2005-2009

Key words: Tomography, ionizing radiation, Image guided radiation therapy, bone imaging, three-dimensional imaging, cellular imaging

Team leader	**Peyrin Françoise**	**DR-HDR INSERM**
Vice-team leader	Sarrut David	CR-HDR CNRS
	Maxim Voichita	MCU Insa
	Robini Marc	MCU Insa
	Carrie Christian	MD CLB (Léon Bérard cancer center)

ETP : 3,3

Engineers	Olivier Cécile	IE

Post doc	Name	Nationality or University PhD	Funds
2004-2005	Apostol Lian	UJF, Grenoble	Projet RNTS
2005-2008	Peter Zsolt	Univ. Bordeaux	CNRS + ANR Vascos
2007-2008	Boldea Vlad	Univ Lyon	Miniara
2007-2009	Frisson Thibault	Univ. Paris X11	ANR fGate/Simca2
2009	Langer Max	Swedish	ANR Vascos
2009	Schaerer Joel	Univ Lyon	Philips
2009	Pery Emilié	Univ Nancy	CEA-Carnot

Ph.D student	Name	Support	Stay abroad
	Larrue Aymeric	Cluster 11	
	Ducros Nicolas	Cluster ISLE	EPF Lausanne
	Joita-Pacureanu Alexandra	MENRT	Bucarest (Roumanie)
	Lecordier Ludovic	CEA	
	Vandemeulebroucke Jef	EU Marie-Curie	Prague (7 months)
	Grèzes-Besset Louise	CIFRE	

Defended HDR	Sarrut David	2008

Defended Theses	Name	Nationality
2006	Lamotte Thomas	French
2007	Valton Solène	French
2008	Perrenot Béatrice	French
2008	Langer Max	Swedish

Two PhD students, Vlad Boldea and Simon Rit were supervised by Serge Miguet (LIRIS, UMR CNRS 5205) and David Sarrut. When the latter joined Creatis in 2006, the students stayed at LIRIS but kept the same supervisors

Per-reviewed Publications: 66
Conference papers: 94
Invited conferences : 16

Résumé
Ce bilan regroupe les activités liées à l'imagerie par rayons X, la tomographie et le calcul de dose, pour la thérapie par rayonnement et l'imagerie du tissu osseux.
Les activités en reconstruction tomographique ont concerné des méthodes de reconstruction pour l'imagerie de la microarchitecture osseuse à partir d'un nombre limité de vues, pour l'imagerie du petit animal, la prise en compte du mouvement cardiaque pour le contrôle de la pose de stents coronaires ou encore la prise en compte des mouvements pulmonaires pour les imageurs

tomographiques embarqués en radiothérapie. Des méthodes de reconstruction en holo-tomographie reposant sur un problème d'estimation de phase ont également été développées.
Les activités en imagerie du tissu osseux sont basées sur un savoir-faire reconnu en microtomographie par rayonnement synchrotron à l'ESRF de Grenoble. Nous avons développé de nouvelles méthodes d'analyse et de segmentation pour l'os trabéculaire ou cortical à l'échelle d'une dizaine de micromètres. Nous avons également débuté des études à l'échelle micrométrique, en particulier pour l'investigation tridimensionnelle de microfissures dans le tissu osseux humain.
Les activités en radiothérapie guidée par l'image et en simulation reposent sur la collaboration depuis plusieurs années avec le centre de lutte contre le cancer Léon Bérard. Nous avons ainsi proposé une méthode de quantification des mouvements pulmonaires par recalage déformable, validée sur données cliniques, dans le cadre du traitement du cancer du poumon. Nous avons également proposé des méthodes accélérées de simulations de calcul de dépôt de dose en radiothérapie et hadronthérapie.

12. Objectives

The general objectives of the team are the development of new reconstruction algorithms methods for limited data or data corrupted by motion, new analysis methods for the quantification of bone tissue, and new methods for image-guided and simulation-guided radiation therapy.

13. Research activity

Tomographic reconstruction (M. Robini, V. Maxim, F. Peyrin, interaction team 2)
Stochastic optimization (Marc Robini)
The objective of this work was to investigate the possibilities offered by generalized simulated annealing theory for solving difficult optimization issues such as those that arise in Bayesian reconstruction. We introduced a new class of hybrid algorithms which combines the theoretical advantages of simulated annealing with the practical advantages of deterministic continuation (both of which are well-known generic optimization approaches to global optimization) and we performed successful experiments in the context of 3-D reconstruction from a very limited number of line-integral projections [ROBI-07, IEEE TNS] [ROBI-07b, IEEE TIP].
3D reconstruction of bone micro-architecture from a limited number of views (F. Peyrin)
We investigated tomographic reconstruction from a limited number of views in the context of 3D imaging of bone micro-architecture, which is still limited in vivo because of dose problems (PhD Thomas Lamotte, coll. with CEA-Grenoble). We investigated an approach based on a Markov binary prior. Due to the limitation of standard Ising models to reflect the complexity of bone micro-architecture, a new model based on two sets of cliques, reflecting close and remote interactions was developed. Determinist minimization algorithms coupled to morphological filtering provided satisfying results for reconstruction from only 18 projections [LAMO-05a] [LAMO-05b].
3D reconstruction for small animal imaging (F. Peyrin)
This work (PhD Solene Valton), concerned the study of a new micro- PET/CT for small animal imaging (IPA project, collaboration CPPM, Marseille, ANIMAGE Platform and IPNL). The originality was to propose a simultaneous PET/CT acquisition thanks to new detectors (XPAD) developed at CPPM. However CT acquisition was performed in a non-standard geometry with an excentred X-ray cone-beam source, requiring adapted reconstruction techniques. We first proposed an extension of the well known Feldkamp algorithm to this geometry [VALT-06a, IEEE TNS]. Due to missing data in the Radon domain, different correction techniques were evaluated [VALT-06b, Int J Biomed Imag] both on simulated data and on real data acquired at CPPM [VALT-07a, Nucl Inst Meth Phys] [DELP-07a, Nucl Inst Meth Phys]. Finally, new reconstruction algorithms were also proposed for another PET/CT developed at Sherbrooke University, Canada (collaboration with Pr. R. Lecomte). This work led to 4 publications in peer reviewed journals.
3D reconstruction of coronary stents (F. Peyrin, coll with R. Prost team 2, P. Douek, team 1)
The goal was to study three-dimensional reconstruction from rotational angiography data to prepare and monitor stenting in the treatment of cardiovascular diseases. (PhD Beatrice Perrenot, CIFRE grant with GEMS (General Electric Medical System)). The difficulties were on the one hand, cardiac motion and on the other hand, the small stent size and its low contrast in the radiographs.. We developed an original motion correction method based on the identification of markers positioned on the guide of the stent. This method was extensively evaluated on synthetic stent models and in animal data. Finally, it was applied to 12 patients and compared to conventional

methods (IVUS and scanner). This work yielded to 5 papers in international conferences and 2 in peer-reviewed journals [FINET-07, EuroIntervention] [PERR-07b, IEEE TMI]. It was selected as a "Fait Marquants du CNRS" in the STIC department in 2008 (cf. Figure 1).

Holotomography of hard tissue (F. Peyrin)

We worked in the phase retrieval problem in holotomography (tomography coupled to phase contrast imaging) in the context of the PhD of Max Langer (ESRF grant) in collaboration with P. Cloetens (ESRF). The phase retrieval problem is a non linear ill posed inverse problem. Different approaches based on the linearization of the problem were studied and evaluated on numerical simulations. A regularization scheme based on some homogeneity of the object was proposed, with a specific procedure based on the L-curve to set the regularization parameter. The method was particularly to the imaging of scaffolds in bone tissue engineering. This work led to 4 publications [GUIG-07, Optics Letters] [LANG-08, Med Phys], [LANG-09, J Opt Soc Am A], [PRAD-09, PNAS]. This action will be pursued in future.

Image reconstruction for Compton camera (V. Maxim, coll. with R. Prost team 2)

This work was done in the context of the ETOILE (European Light Ion Oncological Treatment) centre that will be operating in 2013. It will use up to 400 MeV/amu carbon 12C ion and 220 MeV protons beams. It was motivated by the striking necessity of monitoring the irradiation dose in hadrontherapy. We proposed the use of an imaging system based on a combined Compton scattering and pair creation camera. We showed by Monte Carlo simulations that the proposed system could provide the required imaging and dose location capabilities [FRAN-08]. This work is part of the PhD of M. Frandes and was done with A. Zoglauer (Space Sciences Laboratory, Univ California, Berkeley). Reconstruction of images from Compton projections is still an issue, since analytical reconstruction algorithms ignore the largest part of the data or suffer from numerical deficiencies as arbitrary truncation of infinite series. We proposed a reconstruction method that allows the use of the entire set of data for an exact analytical reconstruction of the image [MAXI-09, Inverse Problems]. The continuation of this work will be supported by the EU, FP7 project ENVISION WP3.4 (2010-2014).

Fluorescent Diffuse Optical Tomography (F. Peyrin)

We began to work on reconstruction problems in Fluorescent Diffuse Optical Tomography (FDOT) in coll. with CEA-LETI. The goal of the PhD of Nicolas Ducros was to extract relevant information from Time-resolved acquisitions which opens interesting perspectives for diagnosis. In this context, theoretical works allowed to obtain new results on the modelisation of such acquisition as well as on the use of temporal signal methods [DUCR-08, J Opt Soc Am A].

Micro-imaging of bone tissue (F. Peyrin)

Osteoporosis is responsible of fractures and vertebral compression and is a major source of expense for public health. Its early diagnosis is an important goal to act at an early stage of the disease and prevent severe complications. However, the understanding of bone fragility is still partial and is a topic of active research worldwide.

In previous works, we developed a synchrotron based micro-CT device with the ESRF (European Synchrotron Radiation Facility) in Grenoble. The setup allowed 3D imaging with an isotropic voxel size with spatial resolution up o the micrometer level [Salomé, Med Phys 1999]. We pointed out for the first time that SR micro-CT had the advantage over standard micro-CT to enable the simultaneous analysis of bone micro-architecture and mineralization.

Research actions based on this almost unique technique, used as a reference both for fundamental studies on bone tissue and for the validation of emerging techniques for the diagnosis of osteoporosis are described below.

Segmentation of osteons in cortical bone (F. Peyrin)

Although less studied than trabecular bone, cortical bone has an important role in bone strength. In earlier works, we showed for the first time, the possibility of obtaining qualitative and quantitative data on cortical bone by 3D SR micro-CT [BOUS-04, J Bone Min Res]. In cortical bone, 3D.SR micro-CT allows visualizing osteons (cf Figure 2, right), but their contrast with respect to interstitial bone is weak and close to the standard deviation of noise, and so far no quantification had been proposed. We proposed an automatic segmentation method based on a customized region growing approach taking into account biological prior to segment osteons [PETE-08, Pattern Recognition]

Geometric analysis of trabecular bone (F. Peyrin)
We developed various methods for calculating model independent morphometric parameters from 3D images of trabecular bone samples. In addition, we developed an original method to characterize locally the type of geometry ("plate" or "rod") of bone trabeculae. New micro-architecture parameters such as the percentage of "plate" or "rod" voxels, or even the thickness of the "plate" or "rod" structures were defined [PEYR-07b, *Image Anal Stereol*]

Micro-CT coupled to SAM (Scanning Acoustic Microscopy) (F. Peyrin)
In a joint work with P; Laugier (LIP, Paris) and K. Raum (Q-BAM university), we showed that the fusion of SR-micro CT and Scanning Acoustic Microscopy (SAM) allowed to derive mechanical properties of bone tissue. This is related to the quantitative nature SR-micro-CT providing maps of the degree of mineralization and that of SAM for providing acoustic impedance maps. Site-matched SR-micro-CT and 200-MHz SAM maps were used to derive the elastic coefficient in cross sections of bone. The technique was applied both to human cortical bone [RAUM-05, Phys Med Biol] and mice femoral bone [RAUM-06, Bone] and opens many perspectives for the mechanical modelisation of bone.

Imaging of trabecular bone micro- cracks (F. Peyrin)
Micro-cracks have an important role in bone fragility which is not completely elucidated. While micro-cracks study is topical, their observation is difficult and limited to 2D observations. In the PhD of A Larrue, coll. L. Vico (Inserm U890, Saint-Etienne), we proposed to use SR micro-CT at the micrometer scale. Even at this spatial resolution, the segmentation of micro-cracks is not straightforward due to low contrast, partial volume and ring artifacts. A dedicated method based on steerable filters and non-linear filtering allowed us to observe for the first time the complexity of the 3D morphometry of micro cracks [LARR-08]. For this work, A Larrue, received the Young Investigator Award at the 18th Int Bone Densitometry Workshop (in June 2008). The results are under publication.

Micro-vascularization in a rat model (F. Peyrin)
The goal of this work was to quantify the microvascular bone network in a rat model by SR micro-CT (VASCOS ANR project in coll. with MH Lafage-Proust, Inserm U890, Saint-Etienne). The interest of using SR micro-CT is to image microvascularization simultaneously to bone at a micrometric spatial resolution. A procedure was developed in order to segment the two structures and identify the different compartments necessary for quantification. First statistical results show significant differences between rats treated with PTH and normal rats [LANG-09a]

Action n°3: Image guided radiation therapy and simu lation for treatment planning (D. Sarrut, C. Carrie, P. Clarysse (now with team n°1)

Image guided lung cancer treatment
Lung cancer is the first cause of death by cancer in the world and radiation therapy is largely used as therapy, in particular when surgery is not eligible. Breathing motion makes lung cancer treatment by radiation therapy highly difficult: the main challenge consists in taking into account such motion both in the planning phase and the therapy phase. In this context, we proposed an original deformable registration method to accurately quantify breathing motion from 3D and 4D CT thorax images. It has been validated on real data with accuracy around 2mm [SARR-06a, Med Phys 2006, SARR-07, IEEE TMI 2007, SARR-08 & BOLD-08 Med Phys 2008] (Boldea PhD). Such work is a fundamental basis for patient specific lung cancer treatment strategies, in particular, it allows to personalized margins to each patient (planning phase).In the same context, we also proposed and validated a motion compensated reconstruction method allowing better image quality for on-board Cone-Beam CT [RIT-09 IEEE TMI 2009] (Rit PhD). Such work is performed in strong collaboration with physicians and physicist of the radiotherapy department at the CLB. Improving targeting by imaging is fundamental since hypo-fractionated treatments (few sessions, high dose), could be an alternative to surgery.

Monte-Carlo simulation for radiation therapy
Predicting patient dose distribution resulting from an irradiation session is the main challenge of the radiation therapy treatment phase. It is specially challenging in hadrontherapy where ion beams (proton, carbon) is used instead of photon beams, with different particle-matter interactions. Among different types, Monte-Carlo simulations are recognized as the most accurate but still very computer intensive. We proposed a method allowing significant speed up (up to factor 4) of Monte-Carlo simulations for computing patient dose distribution [SARR-08, Med Phys 2008](cf. Figure 3).

We also proposed a mathematical model and a simulation-based method to predict optical density for dosimetry with radiochromic films under carbon ion irradiation [FRIS-09, NIM A 2009] (Frisson post-doc). Since the fGATE ANR project, we are now active participants to the OpenGate collaboration: a “radiation therapy module” including all these methods will be publicly proposed to the community in the next IEEE MIC conference (end 2009).

14. Plateforms

The research actions are based on two main collaborative institutes:
- The ESRF (European Synchrotron Radiation Facility) in Grenoble with Synchrotron Radiation micro-CT device (beamline ID19)
- The radiation therapy department of the Léon Bérard cancer center located in Lyon (6 LINAC, 4D CT, CT-PET, 6 DOF robotic table, video system for patient positioning)

15. Interaction

Team n°1 : P. Clarysse : lung motion model, T. Glat ard and S. Pop-Camarasu : Gate project on the EGEE grid
Team n°2 : R Prost, .tomographic reconstruction, C. Muller, image segmentation, L. Guigues : Monte-Carlo simulation

16. Technological transfer

GATE. We actively participate to the development of the GATE software inside the OpenGate international collaboration (http://opengatecollaboration.healthgrid.org**)**
VV. Development of software dedicated to 4D images visualization and analysis. http://www.midasjournal.org/browse/publication/288
Rec3Dana, 3D cone-beam reconstruction software based on Feldkamp method (CPPM, Marseille, Sherbrooke)

17. Grants

National projects (ANR, BQR, PEPS, …)
- VASCOS, Bone vascularization, ANR Blanche , 2006-2009, F. Peyrin
- PET/CT Smal animal imaging, Projet IPA, 2004-2006, F. Peyrin
- MICROTOMOS, Cellular bone imaging, Projet FRM, 2009-2011, F. Peyrin
- SIMCA2, Simulation Cancer Carbone, ANR Blanche, 2007-2010, D. Sarrut
- fGate, Simulation speedup for imaging and radiation therapy, ANR calcul intensif et simulation, D. Sarrut
- RIO, Rayonnement, Images, Oncologie, PPF (Projet Pluri-Formation), 2007-2010, D. Sarrut with LIRIS, CNDRI, IPNL
- Miniara, Registration for cancer treatment in radiation therapy, http://www.medicen.org, 2007-2010, D. Sarrut

European projects (NoE, Réseaux Marie Curie, STREP, IP, …)
- WARTHE, Lung motion model for lung cancer, FP6 Human Resource
- PARTNER, Monte-Carlo simulations for hadrontherapy, FP7 Marie Curie Initial Training Networks, 2008-11, D. Sarrut
- ULICE, Union of Light Ion Cancer Centers in Europe. Treatment of moving organs, FP7 Capacities Research Infrastructure, D. Sarrut, Accepted, kick off oct 2009
- ENVISION, European NoVel Imaging Systems for ION therapy, FP7 Cooperation, 2010, V. Maxim, D. Sarrut
- BONE QUALITY, Long Term Project ESRF, 2006-2009, F. Peyrin

International projects (avec la Chine, les USA …)
- SRCT, Synchrotron micro-CT, France-Berkeley, 2006, F. Peyrin with UCSF San Francisco, USA

Industrial contracts
- ELEKTA, Motion-compensated Cone-Beam reconstruction for radiation therapy, CIFRE, 2004-07, D. Sarrut
- ELEKTA, On-line registration of fluoroscopy images for lung cancer treatment, CIFRE, 2007-10, D. Sarrut
- PHILIPS, Ventilation image from 4D CT scan, Post-doc, 2007-10, D. Sarrut
- DOSISOFT, 4D lung cancer planning, Post-doc, 2007-10, D. Sarrut
- IBA, Monte-Carlo simulation in hadrontherapy, Marie-Curie, 2009-12, D. Sarrut

- GEMS, Stent reconstruction in rotational angiography, CIFRE, 2006-08, F. Peyrin
- CEA-LETI, Diffuse Optical tomography, Post-doc, F. Peyrin

18. Collaborations

National collaborations

Institut de Physique Nucléaire de Lyon, UMR CNRS 5822 (ANR Simca2 project)
The OpenGate collaboration : SHFJ CEA (Orsay), IMNC U8165 CNRS (Orsay), LATIM INSERM (Brest), CPPM, Centre de Physique des Particules de Marseille (fGate ANR project)
ASCLEPIOS-INRIA, Nice (Miniara project)
ESRF (European Synchrotron Radiation Facility), Grenoble. [LANG-09]
CNRS Laboratoire GIPSA-Lab, UJF Grenoble. [PEYR-07b]
Département Système (DSYS), CEA-LETI, Grenoble. [DUCR-08]
Inserm U890 (LBTO), L. Vico, Saint-Etienne. [RAUM-07]
Inserm U678, Dr. Benhamou, Orléans. [CHAP-06a]
CNRS, LIP (Lab. Imagerie Paramètrique) UMR 7623Paris, Dr. P. Laugier. [PADI-08]
CNRS, UMR7052 et Hôpital Lariboisière, Paris, Dr. Bergot, Dr. Bousson, Pr. Larédo [PETE-08]
CNRS MAP5, UMR8145, Paris (S. Sevestre) (work in progress)

International collaborations

The NKI (The Netherlands Cancer Institute), with joint work following the PhD of Simon Rit.
The MGH (Massachusetts General Hospital), with G. Sharp on lung image registration [Boldea et al. Med Phys 08]
With Dietmar Georg from univ. Wien and Guido Baroni from univ. Milano on lung cancer 4D treatment (European ULICE project, starting mid 2009).
EPFL Lausanne, Suisse, Biomedical Imaging Group, Pr. Unser. [DUCR-09b]
Univ Vienne, Autriche, Dept de mécanique, Pr. Zysset [HENG-03]
Magnetic Resonance Science Center, San Fransisco, CA, Dr. Sharmila Majumdar. [BURG-07]
Univ. Gênes, Inst de Recherche sur le Cancer, Pr. Cancedda. [CANC-07]
Univ. des Marches, Pr. Rustichelli. [CANC-07]
Univ. Halle-Witemberg, Pr. Kay Raum. [RAUM-06a]
Russian Academy of Sciences, A.A Baikov Inst. Metal. and Material Science, Dr. V. Komlev. [KOML-09]

19. Expertise and consulting (Expert européen, Comité scientifiques, internationaux, nationaux, CA ; …)

- IEEE BISP International (Biomedical Image ans Signal processing) Tech committee
- Reviews for IEEE ICASP 06, IEEE ISBI 06, IEEE ICASP 07, IEEE ISBI 07, IEEE ICASP 08, IEEE ISBI 08, IEEE ICASP 09, IEEE ISBI 09, , IEEE TMI, Med Phys, MICCAI
- 2006-2009 : GDR 2647 CNRS/Inserm STIC-Santé, F. Peyrin, Direction Committee and Resp Working Group
- 2008-2011 : GDR CNRS Mécanotransduction, F. Peyrin, Resp Working Group
- 2008-2010 : Scientific Committee ENVL Blois imaging, F. Peyrin
- Since 2006 : Scientific Committee Annual Bone Quality Seminar
- Reviewer of Ant projects (D Sarrut, F Peyrin)

20. Distinctions

Revue CNRS "Faits Marquants du département STIC", « Contrôle du déploiement 3D d'un stent dans une artère coronaire d'un patient », 2008.
Larrue (doctorant) Young Investigator Award, 18th Int Bone Densitometry Workshop, Italie, 2008
F. Peyrin, « L'insoutenable légèreté de l'os », in « Voir l'invisible », Ed Omniscience (dec. 2007), ISBN-10: 2916097139.
Images used for an exposition at Cité des sciences, Paris, Juin 2008

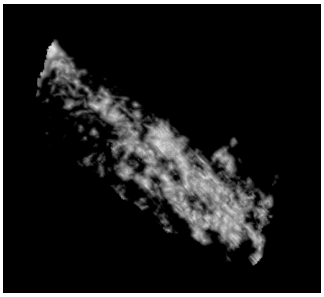
21. Research training

- Ecole Internationale de printemps, Bucarest, Mai 2009

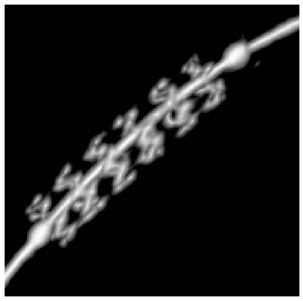
22. Congress organisation and committees (FIMH, IEEE, ISMRM, …)

2006, 45e « journées scientifiques de la SFPM » (Société Française de Physique Médicale), Lyon, local org. D. Sarrut,
2006, Franco-Japanese workshop on hadrontherapy, org D. Sarrut
2006, Workshop “Tomographic imaging”, GDR STIC-Santé and GDR ISIS, org F. Peyrin, I. Buvat, Z. Yue Min,
2006, Workshop “MicroTomographic imaging”, GDR STIC-Santé and GDR ISIS, org. F. Peyrin, I. Buvat, Z. Yue Min,
2006, Workshop “Segmentation with geometrical prior”, GDR STIC-Santé and GDR ISIS, org. C. Muller, F. Peyrin, Z. Yue Min,
2007 : X-ray CT”, IEEE EMBC, Lyon, F. Peyrin, Track chair
2008, Workshop n°1 on respiratory motion in radiotherapy and imaging, GDR STIC-Santé, org D. Visvikis, D. Sarrut
2008, Workshop “Tensor Imaging”, GDR STIC-Santé and GDR ISIS, F. Peyrin, I. Buvat, Z. Yue Min
2009, Workshop n°2 on respiratory motion in radiotherapy and imaging, GDR STIC-Santé, org D. Visvikis, D. Sarrut
2008, Workshop “ MRI : a quantitative imaging technique ?” GDR STIC-Santé and GDR ISIS, org G. Collewet, J. Idier, F. Peyrin, L. Blanc-Féraud

Illustrations



a



b

Figure 1: Three-dimensional tomographic reconstruction of a coronary stent in an animal model : a) without motion correction . b) with the proposed motion correction algorithm [Perrenot et al., IEEE TMI, 2007]

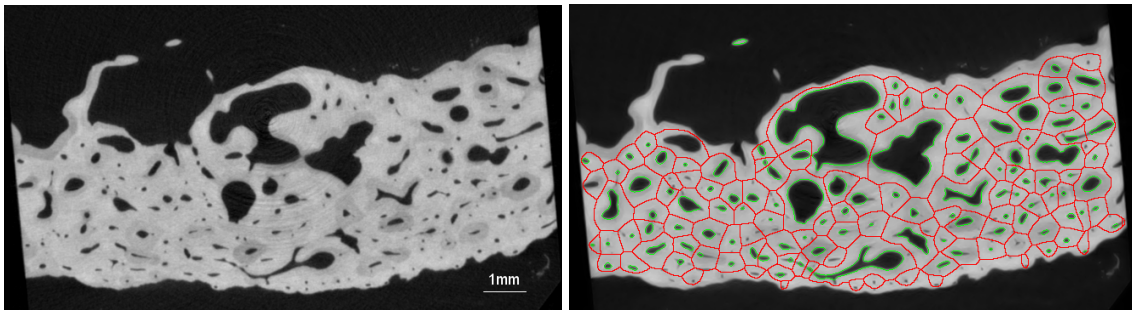
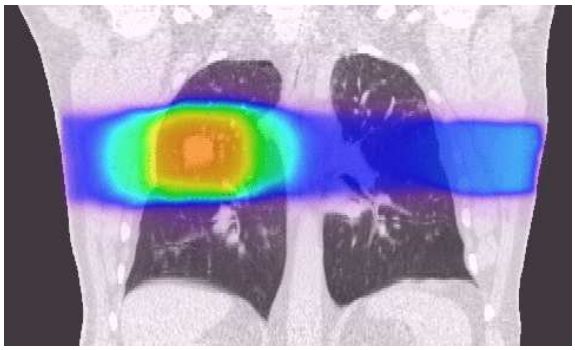


Figure 2: right: slice in cortical bone allowing to observe different degree of mineralization, Left : segmentation (in green) with the proposed approach [PETE-08, Pattern Recognition]



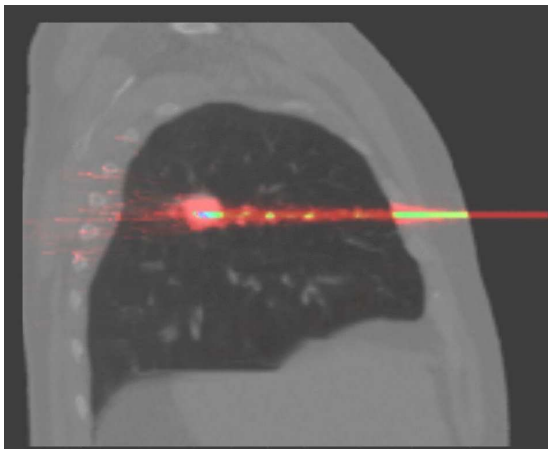


Figure 3, left: photon dose distribution (12 beams) computed by taking into account lung motion thanks to the deformable registration method developed in [SARR-06, Med Phys]. Right: Monte-Carlo simulation of carbon ion beam [SARR-08, Med Phys].

Team n°: 7 Title : Tomographic Imaging and Thera py with Radiation

References : period 2005-2009

Book chapters : 3 + vulgarisation
Dissertations/HDR : 1
Thesis : 4
Articles in journal : 68 (66 + 2)
Invited Conferences : 16
Communications Proceedings : 94
Publications inter-équipes : 12/60

(ALC) Articles dans des revues internationales avec comité de lecture
Original international articles in specialized journal with review committee

1. [FRAN-09a] M. Frandes, A Zoglauer, V. Maxim, and R. Prost. A Tracking Compton-scattering Imaging System for Hadron Therapy Monitoring. IEEE Trans Nucl Sci, pp (in-press), 2009.
2. [BAO-09] L.J. Bao, Y.M. Zhu, W.Y. Liu, P. Croisille, Z.B. Pu, M. Robini, I.E. Magnin., "Denoising human cardiac diffusion tensor magnetic resonance images using sparse representation combined with segmentation," Physics in Medicine and Biology, 2009, vol. 54, no. 6, pp. 1435-1456.
3. [CAR-09b] C. Carrie, J. Grill, D. Figarella-Branger, V. Bernier, L. Padovani, J. Louis Habrand, M. Benhassel, M. Mege, M. Mahe, P. Quetin, J.P. Maire, M.H. Baron, P. Clavere, S. Chapet, P. Maingon, C. Alapetite, L. Claude, A. Laprie, and S. Dussart. Online Quality Control, Hyperfractionated Radiotherapy Alone and Reduced Boost Volume for Standard Risk Medulloblastoma: Long-Term Results of MSFOP 98. J Clin Oncol., pp (in-press), 2009.
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6. [FRIS-09] T. Frisson, N. Zahra, P. Lautesse, and D. Sarrut. Monte-Carlo based prediction of radiochromic film response for hadrontherapy dosimetry. Nucl Instr Meth Phys Res A, 606(3):749-754, July 2009.
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10. [CAR-09a] R. Mazeron, B. Etienne Mastroianni, D. Perol, D. Arpin, M. Vincent, L. Falchero, I. Martel Lafay, C. Carrie, and L. Claude. Predictive factors of late radiation fibrosis: a prospective study in non-small cell lung cancer. J Clin Oncol., pp (in-press), 2009.
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