Creatis

Scientific Committee

27 September 2013

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Scientific report
Scientific Committee of the 27th of September 2013

1. Context

The Scientific Committee and its mission

CREATIS is in the middle of the 5 years' period (2011-2015). The scientific evaluation for renewing the national labels will take place at the beginning of 2015. The objective of CREATIS, by inviting this international scientific committee, is to have an external and internal appreciation of the teams' international scientific visibility and competitiveness. The meeting will give us the opportunity to discuss and get advice on the future trends and strategies of CREATIS and of each team separately.

The document

This report is deliberately a synthetic scientific report that highlights the most exciting and recent scientific results of each team. The Vision at the laboratory level and the perspectives of each team will be deepened during the oral presentation of Friday 27th where the main results will be presented through three transversal projects.

2. Presentation

CREATIS (Centre de Recherche pour l'Acquisition et le Traitement d'Image pour la Santé) is a biomedical imaging research laboratory (200 people). The Director is Isabelle E. Magnin (DR Inserm) and the deputy Director is Pierre Croisille (PUPH). CREATIS is co-labeled by the Institutes INSIS (Systems engineering), INS2I (Computer science) and INSB (Biological sciences) of the CNRS (UMR 5220), by the Inserm (Unit 1044) and by the University of Lyon (University Lyon 1 and INSA).

3. Scientific objectives and missions

The main areas of excellence and international influence of CREATIS are linked to two fundamental objectives:

- Identification of major health issues that can be addressed by imaging
- Identification of new challenges in biomedical imaging related to signal and image acquisition, processing, modelling and numerical simulation.

The mission of CREATIS is to go beyond the frontiers of knowledge in biomedical Imaging. This is achieved by associating three scientific communities working together:

1. Life Science researchers and clinicians (HCL): their mission is to enhance and select major unanswered questions in their field of competence.
2. Specialists of imaging acquisition techniques: their mission is to develop the adapted tools and new imaging modalities (X Ray, MRI, MRS, RF US, optics) able to accurately image the disease targeted by the Life Science researchers
3. Researchers in signal, image processing and computer science: their mission is to extract quantitative information from the data and to develop new models, algorithms and simulation to help answering the initial biological and medical questions.

4. An interface between Imaging Science and Life Sciences

The laboratory is located on both academic and clinical sites namely the Campus LyonTech La Doua, the Groupement Hospitalier Est (GHE) and the Centre Leon Bérard (CLB) in Lyon, the Saint-Etienne Hospital and the European Synchrotron Research Facility (ESRF) in Grenoble.

5. Research Organization

The strong pluridisciplinarity of our research is facilitated by a matricial organization

The research teams

Team 1: Imaging of the Heart-Vessels-Lungs (P. Clarysse)
Team 2: Images and Models (D. Friboulet)
Team 3: Ultrasound Imaging (P. Delachartre)
Team 4: Tomographic Imaging and Therapy with Radiation (F. Peyrin)
Team 5: MRI and Optics: Methods and Systems (O. Beuf)
Team 6: Brain Imaging (N. Nighoghossian)

The transversal projects

A. Ischemic disease and consequences: vascular, cardiac and cerebral
B. Hybrid and multi-physics Imaging (MRI/PET, US/optics, PET/CT,..)
C. Reconstruction, modelling and simulation

6. A selection of 2012-2013 successful realizations

CREATIS is laureate of the France Life Infrastructure (new spectral CT prototype from Philips in 2013), is a major actor in the EQUIPEX LILI (clinical device MRI/PET), the Pilot of the LABEX PRIMES (Physics, radiobiology, medical imaging and Simulation) and a member of LABEX CeLya (acoustics). The last start-up of CREATIS is CIRMA in 2011 (PET diagnosis imaging). CREATIS is also the pilot of 1 European project and Involved in 8 others. CREATIS participates at the committee of the VPH European Institute and was deeply involved in the governance of the National Institute for Technology for Health (2009-2013).

7. Highlights

For many years CREATIS has been promoting experimental, preclinical and clinical researches in the fields of ischemic and inflammation pathology and their consequences in both cardio-vascular and cerebral systems. Research on cancer, pulmonary disease (SARS), bone ultrastructure and gastro-intestinal exploration are also strongly supported. In the same time, CREATIS encourages theoretical and methodological approaches for imaging acquisition and quantification with the emergence of new bio-markers. To make effective realistic large scale studies, CREATIS has been investing in grid computing for 15 years, being a pioneer by introducing medical Imaging on the European Grid (CREATIS is a core member of the NoE VPH (Virtual physiological Human)).

The main scientific highlights are detailed for each team.

8. Challenges and perspectives

Quantitative Imaging is a very powerful tool to help understanding human physio-pathology.
In the future, CREATIS will pursue its efforts to develop

- Multiscale multiphysics quantitative imaging : from nanometer (synchrotron) to whole body (clinics)
- Fast dynamic imaging : acquisition and processing (compressive sensing, GPU,…)
- Virtual radiology: imaging simulators (US, MRI, PET, CT) and patient avatars (grid computing)
- Large scale longitudinal studies (cohorts) (big data)

Our next challenge will be to acquire and be able to compare accute experimental and/or clinical data with simulated/virtual data
CREATIS will consolidate both

- its multimodal Imaging and experimental platform
- Its computing infrastructure and facilities (European Grid access)

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Team 1 : Imaging of the Heart-Vessels-Lungs

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

1. People : 15 permanent staff

Team leader	CLARYSSE Patrick	DR CNRS	
Vice leader	BOUSSEL Loïc	PU PH	
COURBEBAISSE Guy	IR INSA, Ph.D, HDR	CROISSILLE Pierre	PU PH
DOUEK Philippe	PU PH	FOULON Frédérique	IR (50%)
GUERIN Claude	PU PH	MAGNIN Isabelle	DR Inserm
NEYRAN Bruno	MCU UCB	POUZOT-NEVORET Céline	MCU UCB
ORKISZ Maciej	PU UCB	Didier REVEL	PU PH
RICHARD Jean-Christophe	PU PH	VIALLON Magalie	IR (50%)
Yue-Min ZHU	DR CNRS		

and 2 invited professors, 4 post-docs, 16 PhD students, 7 master students, 2 software engineers

2. Scientific objectives

Cardio-vascular and pulmonary diseases, responsible for more than 40% of death in the developed countries, constitute the target of our research. Our objective is to develop new-dedicated acquisition techniques and model based quantification methods to better assess 3D organ anatomy, tissue and function at various scales from human examinations and animal experiments. More specifically, we aim at 1) confronting simulated flows from extracted 3D shapes to experimental flow MRI measurements in vessels and vessel networks 2) confronting *in vivo* human heart shape and fibre architecture to heart dynamics to better understand the cardiac remodelling process and 3) characterizing ventilator-induced lung injuries from PET imaging and at the bedside EIT.

3. International and national context

Thanks to multidisciplinary competences, Team 1 conducts a translational research in cardio-vascular and lung imaging to bring new developments to the clinics for the benefit of the patient. In the fields of interest, worldwide leading groups are (groups with which we have on-going collaboration are in bold):

France: **INRIA Sophia & Rocquencourt groups** (D. Chapelle, N. Ayache): modelling of the cardiac electro-mechanical coupling, DTI analysis; **Inserm Paris** (F. Frouin): analysis of the heart dynamics in MRI and US imaging; LTSI, Rennes Univ (M. Garreau): 4D-CT imaging and processing; ENST, Paris (E. Angelini): 3D ultrasound ; **ISIT Clermont-Ferrand** (L. Sarry): cardiac image processing; Nancy Univ. (J. Felblinger): dynamic MRI ; CEREMADE Paris (L. Cohen) : 3D vascular tree segmentation; **TIMC, UJF Grenoble**: Imaging of the heart fibre architecture (Y. Usson, P-S. Jouk)

Europe: UK, Imperial College London (D. Rueckert): dynamics of the heart, image registration; UK, Oxford Univ. (P. Kohl, A. Noble): cardiac cell modelling / cardiac US image processing; UK, CMIC-UCL (David Hawkes); The Netherlands, Maastricht Univ & Eindhoven Univ (T. Arts, P. Bovendeerd): cardiac electric and mechanics modelling; Leiden Univ. (J. Reiber, B. Lelieveldt): cardiac image segmentation and analysis; The Netherlands, Biomedical Imaging Group Rotterdam (W.J. Niessen): vascular image analysis; Spain, Univ Pompeu Fabra (A. Frangi): vascular and cardiac image analysis and modeling; Germany: Kiel (Frerichs) : Electrical Impedance Tomography; Sweden, CMIV, Linköping Univ. (Ö. Smedby): medical image analysis, visualization and simulation; **Switzerland, EPFL LTS5** (J.Ph. Thiran), **Université de Genève CUI** (B. Chopard); **Belgium, ULB – CHU Charleroi** (K. Zouaoui).

World: USA, NY Langone Univ. & Rutgers Univ. (L. Axel/D. Metaxas): cardiac dynamics estimation and modelling; Bethesda, NIH (H. Wen): Phase contrast imaging and Cardiac DT-MRI; Baltimore, JHU (E. McVeigh): cardiac imaging; University of California, San Francisco (UCSF, David. Saloner); UCSD (A. McCullogh): cardiac modelling; Boston, Harvard Medical School (J.G. Venegas, G.Gardena) : Pulmonary PET imaging, iPS; **New-Zeland, Univ. Auckland** (P. Hunter, A. Young): cardiac modelling and image analysis; Brasil, Univ. Sao Paulo (M.B.P. Amato) : Electrical Impedance Tomography

Industrial companies: **Siemens Princeton** (M-P. Joly, D. Comaniciu), Philips Medisys (N. Villain, C. Lorentz) and GE (R. Vaillant)

4. Imaging platform / experimental platform / computing infrastructure

Team 1 relies on the imaging platforms available at HCL-Lyon Est, Lyon Croix-Rousse, CHU St Etienne Nord. It uses small animal imaging infrastructure at Cermep, is involved in the Lili EquipEx project for the installation of a MRI-PET coupled imaging system in Lyon (2014) and leads the Lyon node of the FLI national project (PI: P. Douek, Installation of a new Spectral-CT setting at INSA).

5. Scientific Coordination and Outreach

- G. Courbebaisse leads the european FP7 STREPS Thrombus project (2011-2014)
- P. Croisille is in the board of the SCMR Society
- I. Magnin was until recently deputy director of the national Institute of Technology for Health (ITMO TS) (2009-2013)
- Y-M. Zhu leads the ANR MOSIFAH project (Modèles numériques, 2013-2017)
- P. Clarysse colleads WP4 of the LabEx PRIMES.

Technology transfer: The group developed and releases the inTag-OsiriX plugin (integrated analysis of cardiac tagged MRI), used in more than 200 clinical and academic centers.

6. Five most significant journal publications

- Millon A, Boussel L, Brevet M, Mathevet JL, Canet-Soulas E, Mory C, Scoazec, JY, Douek P. Clinical and histological significance of gadolinium enhancement in carotid atherosclerotic plaque. Stroke. 2012 Nov;43(11):3023-8.
- H. Wei, M. Viallon, B. Delattre, L. Wang, V. Pai, H. Wen, H. Xue, C. Guetter, P. Croisille, and Y. Zhu, "Assessment of cardiac motion effects on the fiber architecture of the human heart in vivo," IEEE Trans Med Imaging, Jun 19 2013.
- F. Yang, Y. M. Zhu, I. E. Magnin, J. H. Luo, P. Croisille, and P. B. Kingsley, "Feature-Based Interpolation of Tensor Fields and Applications to Human Cardiac DT-MRI," Medical Image Analysis, vol. 16, pp. 459–481, 2012.
- T. Arts, F. W. Prinzen, T. Delhaas, J. R. Milles, A. C. Rossi, and P. Clarysse, "Mapping Displacement and Deformation of the Heart With Local Sine-Wave Modeling", IEEE T Med Imaging, vol. 29, no. 5, pp. 1114-1123, 2010
- Guérin C, Reignier J, Richard JC, Beuret P, Gacouin A, Boulain T, Mercier E, Badet M, Mercat A, Baudin O, Clavel M, Chatellier D, Jaber S, Rosselli S, Mancebo J, Sirodot M, Hilbert G, Bengler C, Richecoeur J, Gainnier M, Bayle F, Bourdin G, Leray V, Girard R, Baboi L, Ayzac L; PROSEVA Study Group. Prone positioning in severe acute respiratory distress syndrome. N Engl J Med. 2013;368(23):2159-68.

7. Perspectives : towards theragnostic imaging

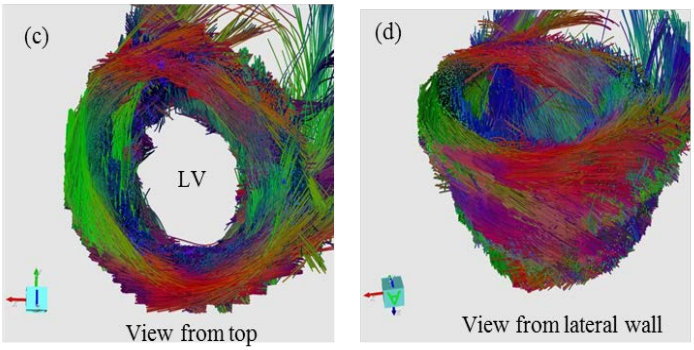
Within these 3 application domains, team 1 aims at developing integrated non-invasive multimodal imaging approaches for understanding the physiopathological processes at multiple scales via preclinical studies and physical/numerical simulations, establishing accurate diagnosis through new biomarkers, identifying and conducting optimal patient specific therapies taking into account organ's motion. For vascular diseases, we propose to combine morphology, 4D hemodynamic analysis and inflammation detection as well as biological priors. For cardiac diseases, the objective is to better understand the 'normal' relationship between tissue architecture and dynamics and its impairment in pathologies from dynamic hybrid acquisitions. For ARDS, the aim is to better explain the impact of mechanical ventilation on lung stress, strain and inflammation from lung imaging and at the bed side imaging.

8. Highligths

A quantitative model of thrombosis in intracranial aneurysms. The aim of our project is to define novel imaging bio-markers of arterial diseases (atherosclerosis and aneurysms) in order to identify, in a reliable and non-invasive manner, patients at high risk of negative outcomes, such as atherosclerosis plaque or aneurysm rupture. Rupture risk of intracranial aneurysms (IA) has been studied at length. However, very little is known about the healing mechanism, namely the formation of a clot inside the cavity after insertion of a stent. The core of the European STREP THROMBUS project (PI: G. Courbebaisse, CREATIS) is to develop and validate a biological model of spontaneous or stent-induced thrombosis in IA.

This illustration shows a deployed flow diverter in a model of IA, used for validation of the modeling. *[Chen et al., Med Image Anal, in press]*, *[Patent submitted March 2013]: 'Test Bench for In Vitro study of Aneurysm and Blood Vessels*'

Toward subject specific fiber architecture of the heart. The medical objective is to refine our understanding of structural/functional changes involved in remodelling processes that occur in several cardiomyopathies from patient specific cardiac models. In particular, one of our main goals is to infer the subject specific 3D heart fiber architecture both from new *in-vivo* free-breathing DT-MRI technique applicable in experimental and clinical setups and a priori *ex-vivo* atlases. Our recent studies of the impact of the motion on DWI/DT-MRI [Delattre et al., Invest Radiol, 2012] have lead to improved *in vivo* whole heart DTI acquisitions [Wei et al., IEEE TMI, 2013]. Also, a first statistical atlas of the 'normal' cardiac fiber architecture has been proposed from ex vivo DTI data in the context of a collaboration [Lombaert et al., IEEE TMI, 2012].



Two views of fiber tracts with the PCATMIP approach from in vivo whole heart DTI in free-breathing, *[Wei et al., IEEE TMI, 2013]*

Further insights into the Ventilator-Induced Lung Injury

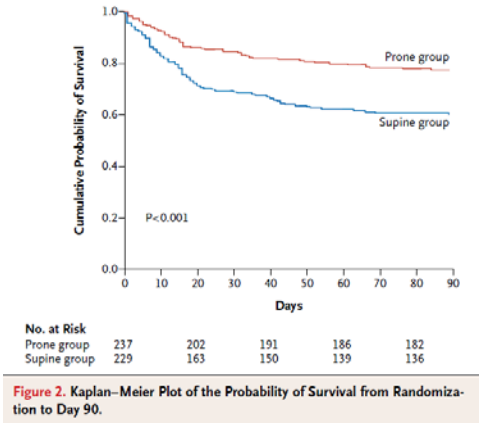


Figure 2. Kaplan–Meier Plot of the Probability of Survival from Randomization to Day 90.

Preventing ventilator-Induced Lung Injury (VILI) is a real challenge for clinicians. We have recently shown that the survival was markedly and significantly increased by using prone positioning in patients with severe ARDS *[Guerin, Regnier, Richard et al. N Engl J Med, 2013]*.

Publications in International Journals 2010-2013
Team 1 : Imaging of the Heart-Vessels-Lungs

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4. [AMAN-13] C. Amanieu, I. Sanchez, S. Arion, E. Bonnefoy, D. Revel, P. Douek, and L. Boussel, "Acute myocardial infarction: early CT aspects of myocardial microcirculation obstruction after percutaneous coronary intervention.", European radiology, vol. 23, issue 9, pp. 2405-12, 2013 Sep .
5. [Mill-93] A. Millon, E. Canet-Soulas, L. Boussel, Z. Fayad, and P. Douek, "Animal models of atherosclerosis and magnetic resonance imaging for monitoring plaque progression.", Vascular, 2013 Mar 14 .
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7. [PORO-13] V. Porot, and C. Guérin, "Bench assessment of a new insufflation-exsufflation device.", Respiratory care, vol. 58, issue 9, pp. 1536-40, 2013 Sep .
8. [BARB-13] T. Barba, J. Karsenty, L. Boussel, and T. Ferry, "Brain abscess associated with persistent left superior vena cava in a 58-year-old man.", BMJ case reports, vol. 2013, 2013 .
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Creatis

Team 2: Images and Models

Key words: Segmentation, Computer Aided Diagnosis, Distributed computing, Reconstruction and sparsity, Registration, motion estimation, Geometry processing

1. People: 13 permanent staff

Team leader	FRIBOULET Denis	PU	
Vice leader	LARTIZIEN Carole	CR CNRS	
BENOIT-CATTIN Hugues	PU	PROST Rémy	PU
BERNARD Olivier	MCU	VALETTE Sébastien	CR CNRS
FANTON Laurent	PHU	BELLET Fabrice	IR CNRS
GLATARD Tristan	CR CNRS	POP Sorina	IR CNRS
GRENIER Thomas	MCU	SDIKA Michaël	IR CNRS
ODET Christophe	PU		

And 10 PhD students, 3 master students

2. Scientific objectives (ou Research activity)

The aim of team 2 “Images and Models” is the identification and tackling of methodological/theoretical and computational barriers. As such, this team thus mainly performs upstream research, yielding the development/design of advanced image processing and modeling methods. This research is performed in close collaboration with all the other teams of Creatis as well as national and international collaborators, by proposing novel and competitive solutions to medical or scientific issues. The main domains of expertise of the team are the following:

- Segmentation and feature extraction
- Computer Aided diagnosis (CAD) systems
- Distributed computing and data
- Reconstruction and sparsity
- Registration and motion estimation
- Geometry processing

3. International and national context

The design of advanced image processing and modeling methods adapted to medical imaging implies covering a wide field of expertise. As a consequence, our research is often performed in collaboration with international collaborators (exchange of doctoral students, co-supervised thesis, common research grants, etc.). Our main international collaborations are given in the following table.

Country	Laboratory/University	Topic
Belgium	Medical Image Computing, Katholieke Universiteit Leuven	Segmentation and motion estimation in echocardiography
Canada	Montreal Neurological Institute, McGill University	Distributed computing systems for neurologic image processing
China	Sino-French Research Center for Biomedical Image, Harbin Institute of Technology	Placement and replication of files on distributed systems
Germany	Institute of Medical Informatics, Universitätsmedizin Berlin	Interoperability between EGEE and German D-Grid
Korea	Laboratoire Multimedia Signal Processing, Yeungnam University	Lossless image compression, Digital Watermarking 3D meshes, Deformation and motion 3D meshed models
Liban	Lebanese University	Compressive sensing
Netherlands	Academic Medical Centre, Amsterdam	Grid execution environment for image processing applications
Romania	Polytechnic University of Bucarest	Simplification of shapes with complex geometry and topology
Switzerland	LTS5, EPFL	Fast US acquisition
UK	School of Computer Science and Informatics, Cardiff University	Interoperability among workflow systems
USA	Research Lab Molecular MRI, Stanford University	MRI Simulation
USA	Space Sciences Laboratory, University of California at Berkeley	Compton-scattering based Imaging System for Hadron Therapy

4. Imaging platforms / experimental platforms / computing infrastructures

- VIP: Virtual Imaging platform – A grid enabled, multimodality, web accessible medical images simulation platform – 440 registered users since 2011. http://vip.creatis.insa-lyon.fr/
- Creaseg: A level-set based segmentation platform – More than 5200 downloads since 2010. http://www.creatis.insa-lyon.fr/~bernard/creaseg/
- Desk: Desk exposing server kit - HTML5 solution for remote processing and visualization. https://desk.creatis.insa-lyon.fr/
- OncoPET_DB: A Freely Distributed Database of Realistic Simulated Whole Body 18F-FDG PET Images for Oncology – 50 registered users since 2010. https://www.creatis.insa-lyon.fr/oncoPET_DB/

5. Scientific Coordination and Outreach

5.1. Research, academic and administrative responsibilities

- Associate editorship for IEEE trans. Image Processing and Area chairmanship for ICIP
- Coordination of the European Life-Science Grid Community of the European Grid Infrastructure
- Co-management of the biomedical infrastructure (VO) of the European Grid Infrastructure

5.2. National ANR projects

- 2 INCa projets : Cartographix, LYRIC, 7 ANR projects as Leader, Workpackage Leader or Partner)

5.3. European projects

- ENVISION - European NoVel Imaging Systems for ION therapy (Partner)
- THROMBUS - A quantitative model of thrombosis in intracranial aneurysms (Partner)
- ER-flow - Building an European Research Community through Interoperable Workflows and Data (Partner)
- N4U - Expansion of NeuGRID services & outreach to new user communities (Partner)
- VPH NOE - Virtual Physiological Human (Local Coordinator)
- SHIWA - Sharing Interoperable Workflows for large-scale scientific simulations (Partner)
- EGEE III - Enabling Grids for E-sciencE (Local Coordinator)

5.4. Industrial collaborations

- OneFit Medical – Segmentation of knee bone structure for prosthesis surgical implant planning
- CCITI – 3D Registration of MRI slices in radical prostatectomy
- Philips Medisys Healthcare – TEP image processing for oncology – 3D US image simulation
- CEA – X-ray tomography simulation

6. Five most significant journal publications

- R. Kéchichan, S. Valette, M. Desvignes, and R. Prost, "Shortest-Path Constraints for 3D Multiobject Semiautomatic Segmentation via Clustering and Graph Cut", IEEE trans. on Image Processing, in press, 2013
- E. Niaf, O. Rouvière, F. Mèger, F. Bratan, and C. Lartizien, "Computer-aided diagnosis of prostate cancer in the peripheral zone using multiparametric MRI", Phys. Med. Biol., vol. 57, no. 12, pp. 3833-3851, 2012
- S. Camarasu-Pop, T. Glatard, J. T. Moscicki, H. Benoit-Cattin, and D. Sarrut, "Dynamic partitioning of GATE Monte-Carlo simulations on EGEE", Journal of Grid Computing, vol. 8, no. 2, pp. 241-259, 2010.
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7. Perspectives

We will tackle the problem of segmenting «Big Data» (multi-organs approach) by developing multi-scale and multi-objects representation, as well as the real-time segmentation of 3D data using B-spline explicit surfaces. Concerning CAD systems, we will explore the introduction of a priori (in particular spatially) in the learning phase of SVM. Reconstruction will be oriented toward the design of new sparse dictionaries (Transform learning) and dynamic aspects in image sequences (sequential compressed sensing) and we will study motion through the design of diffeomorphic spline registration and monogenic signal-based motion estimation. In terms of computational models, we will develop scheduling methods and self-healing loops to control applications online and under non-clairvoyant assumptions for distributed computing.

8. Highlights

8.1. Virtual Imaging platform (VIP)

While distributed computing used to be a tool of a scientific few, it has now become a daily instrument for researchers in various disciplines, including medical image processing and simulation. This evolution creates new challenges for distributed systems which now have to accommodate unpredictable loads executed on dynamic infrastructures with uncertain characteristics. Our Virtual Imaging Platform (VIP) [GLAT-2013] is a web portal hosting medical image simulation applications deployed on the European Grid Infrastructure (EGI). It includes new task scheduling methods [CAMA-2013] and self-healing loops [FEIR-2013] to control applications online and under non-clairvoyant assumptions. VIP is now used by 440 users from 49 countries, which makes it one of the most used computing robot on EGI.

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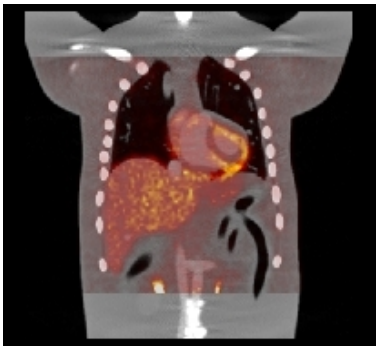

Example of a PET/CT acquisition simulated with VIP from the XCAT body model. The image displays overlaid the results of CT and FDG-PET simulations (simulated 0.5 s CT acquisition and simulated static 224 s FDG-PET acquisition)

8.2. Real time 3D segmentation of the heart

One of the major challenges in medical image analysis is the design of near real time tools that allow the specialist detecting anatomical structures in an intuitive manner. In this context, we have developed a dedicated variational segmentation formalism based on the equivalence between explicit and implicit functions. The interest of such model resides in its ability to deal with a segmentation problem in a lower dimensional space, making the underlying algorithm very efficient in terms of computational time. This model has been recently successfully applied for the automatic segmentation of the heart in 3D near real time in ultrasound (obtained from a dataset composed by 24 patients having different pathologies). Results show that our algorithm produces comparable quality of segmentation with manual references produced by 3 experts for a mean computational time of 45 ms per volume.

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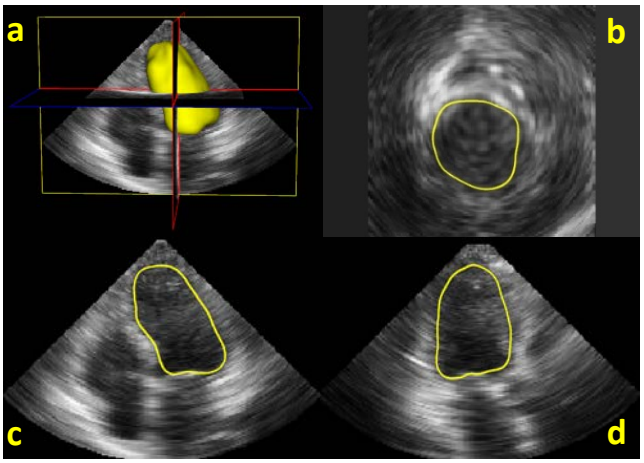

Segmentation results from 3D cardiac US data. The corresponding computational time needed to perform the segmentation is 51 ms. (a) Display of the segmented volume along with of 3 slices of the data volume. (b) Short axis and (c-d) long axis views, along with the intersection with the segmented volume.

Publications in International Journals 2010-2013
Team 2: Images and Models

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Team 3 : Ultrasound Imaging

Key words : Control of the imaging system; Tissue and flow motion estimation; Parametric imaging and multimodality imaging

1. People : 8 permanent staff

Team leader	DELACHARTRE Philippe	PU INSA	
Vice leader	LIEBGOTT Hervé	MCU HdR UCB	
BASSET Olivier	PU UCB	BRUSSEAU Elisabeth	CR CNRS
CACHARD Christian	PU UCB	DETTI Valérie	MCU UCB
VARRAY François	MCU UCB	VRAY Didier	PU INSA

and 13 PhD students, 2 invited researchers of Canada

2. Scientific objectives (ou Research activity)

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 ultrasound images or image sequences in order to get back to the medium properties owing to 3 complementary axes: the control of imaging system in both transmission and reception, the estimation of motion field of the medium (soft tissue or blood) and the parametric or multimodality imaging (US/MRI and US/optic). The developed methods 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 developed to operate in real time, ie the rate of acquisition of images by the system and are extended to 3D data.

3. International and national context

Ultrasound medical imaging covers a wide range of medical and technological fields. We have chosen to focus our works on the development of imaging techniques and 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 doctors in Creatis or in other laboratories. Through exchange of doctoral students, co-supervised thesis, research visit or common research grants, we have developed collaborations with the several research groups recognized by the scientific community and publishing in the field of ultrasound medical imaging. Among 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), M. Fink (Institut Langevin, 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) and M. D. Verweij (TU Delft) for nonlinear imaging, G. Cloutier,R. Maurice (LBUM, CRCHUSJ Montréal) for the imaging of vessels, J. Jensen and J. Wilhjelm (DTU, Copenhagen) for image formation and for flow estimation, P. Tortoli (Univ. Florence).

4. Imaging platform / experimental platform / computing infrastructure

Experimental US platform at Creatis, equipped with fully programmable scanners: UlaOP and Ultrasonix imaging scanners with DAQ box (emission, reception, real time processing, fast imaging).

5. Scientific Coordination and Outreach

(Grants, technology transfer, industrial collaborations, conference organisation, research, academic and administrative responsibilities)

European Projects

2013-2016 : partner of FP7 ITN Oiltebia project concerned with photoacoustic imaging (277 k€)

2007-2010: leader ITN Warthe

ANR projects

2012-2015 : Porteur du projet ANR Tecsan BBMUT (Broad Band ultrasound imaging using a CMUT probe). Le montant s'élève à 772 K€ pour les 5 partenaires dont 260 k€ pour Creatis

2011–2013: **Young Researcher ANR project, 204 k**€. "US Tagging". Following PEPS "US Tagging" project. Functional imaging and cardiac structure tracking using transverse oscillation images.

2008-2011 : Partner ANR Tecsan MONITHER. Il portait sur l'imagerie ultrasonore de contraste à l'aide de transducteurs capacitifs micro-usinés (CMUT). Le montant dévolu à Creatis s'élevait à 98 k€.

2010-2012: partner **ANR Cosinus project, 271 k**€ for the Virtual Imaging Platform (VIP). The objective was to develop a virtual radiology platform

2008-2011: partner ANR Tecsan ProstaFluo

Other projects

2013-2015: FFCR (Fonds France Canada pour la Recherche) **15 k$ (~11 k€)** Ultrafast ultrasound Tagging, in collaboration with Damien Garcia from the University of Montreal.

2011–2012: CNRS PEPS project from INSIS department, 20 k€. 3D ultrasound imaging by compressive sensing.

2011-2013: PEPS CNRS INSIS, project dedicated to developing magnetic resonance elastography and combining ultrasound and MR elastographic information (20 k€).

2011-2013: BQR INSA Lyon - project dedicated to breast elastography (15 k€).

2011-2013: BQR INSA Lyon ImaQuat, (20 k€).

Research responsibilities

2011-2014 : member of the evaluation committee of ANR TecSan granting research projects in the field of biomedical engineering

2000- : scientific committee "IEEE International Ultrasonics Symposium".

Academic responsibilities

2011-2014, Head of the academic department "Génie Industriel et Maintenance", IUT Lyon 1

Administrative responsibilities

2010- : Membre du bureau de l'Ecole Doctorale EEA de Lyon (5membres) depuis 2010 et membre de son conseil (25 membres);

2011- : Management committee of labex Celya

2010-2014: member elected of education council at INSA-Lyon

6. Five most significant journal publications

F. Varray, O. Basset, P. Tortoli, and C. Cachard, "CREANUIS: A Nonlinear Radio Frequency Ultrasound Image Simulator", Ultrasound in Medicine and Biology, accepted, 2013.

G. Zahnd, M. Orkisz, A. Sérusclat, P. Moulin, and D. Vray, "Evaluation of a Kalman-based block matching method to assess the bi-dimensional motion of the carotid artery wall in B-mode ultrasound sequences", Medical Image Analysis, vol. 17, no. 5, pp. 573?585, 2013 .

G. Zahnd, D. Vray, A. Serusclat, D. Alibay, M. Bartold, M. Durand, L. M. Jamieson, K. Kapellas, L. J. Maple-Brown, K. O'Dea, et al., "Longitudinal displacement of the carotid wall and cardiovascular risk factors: associations with aging, adiposity, blood pressure and periodontal disease independent of cross-sectional distensibility and intima-media thickness", Ultrasound in Medicine & Biology, vol. 38, no. 10, pp. 1705-1715, 2012.

F. Varray, O. Basset, P. Tortoli, and C. Cachard, "Extensions of Nonlinear B/A parameter imaging methods for echo mode", IEEE Transactions on Ultrasonics, Ferroelectrics and Frequency Control, vol. 58, no. 6, pp. 1232-1244, 2011.

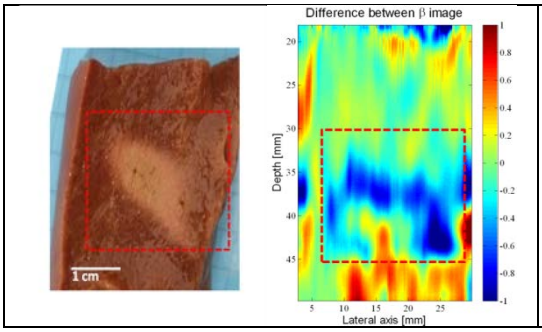
7. Perspectives

The team turns on main ways such as **the nonlinear imaging** with studies on the emission of ultrasounds (generalized pulse inversion, CMUT based methods), **the motion imaging** by studies concerning the image formation (US-Tagging), the motion estimation by the local phase, **the 4D ultrasound imaging** with advances on fast image formation (plane-wave imaging), the compressive sensing, the optimization of 2D probes, the breast cancer elastography, and finally **the multi-modality imaging** by combining several modalities: US/optics, photoacoustic, US/IRM.

8. Highligths

Nonlinear parameter imaging in echo mode configuration

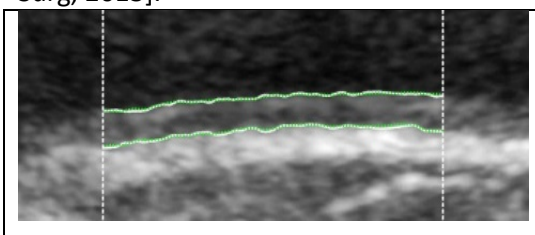
The literature shows that the nonlinear parameter of tissue, which is mainly responsible for the harmonics increase during the ultrasound wave propagation, is related to the healthy or pathological behaviour of tissues. Using the new nonlinear propagation simulator, CREANUIS, such situations have been investigated from images exhibiting heterogeneous coefficient of nonlinearity. The measurement strategy of the local non linearity is very effective when only the pressure field is considered. However, in echo mode imaging, more complex strategies have been investigated such as the alternative sequential morphological filtering or more specific signal and image processing techniques to decrease the backscattering impact on the RF image in view to emphasize the pressure field information. [IEEE Transactions on Ultrasonics, Ferroelectrics and Frequency Control, 2011], [Eurasip Journal on Image and Video Processing, 2011], [Ultrasound in Medicine & Biology, 2013]



Nonlinear parameter measurements on a porcine liver after an HIFU therapy. The burned area is highlighted in the difference nonlinear images.

Motion estimation for vessel wall characterization

Alterations in vascular dynamics, including arterial stiffening, appear to be predictive of cardiovascular events. Furthermore, in the atherosclerosis process, significant changes of the mechanical properties of the vascular wall may occur before the anatomical changes of the intima-media thickness (IMT) become visible. Early detection of this pathology is, therefore, an important issue. However, the performance of traditional risk markers as Pulse wave velocity (PWV) or Arterial distensibility (i.e. cross-sectional diameter change) as screening tests for subclinical atherosclerosis remains relatively poor. We have developed a novel segmentation method for localizing the contours of the intima-media complex in the carotid artery wall combined with a block matching method using a pixel-wise Kalman filter for assessing the 2D motion i.e. radial and longitudinal (in the same direction as the blood flow) of the intima-media complex. Our method was evaluated *in vivo* on several cohorts of healthy volunteers and patients at high cardiovascular risk, providing a relevant diagnosis aid for atherosclerosis screening in clinical studies [Ultrasound in Medicine & Biology, 2011] [Ultrasound in Medicine & Biology, 2012] [Medical Image Analysis, 2013] [Int J Comput Assist Radiol Surg, 2013].



By combining a novel filter bank with an appropriate dynamic-programming strategy, the segmentation method is providing reproducible, robust and accurate results, in a reasonable computational time, for clinical images of variable geometry and/or quality. By successively processing all frames of a sequence, the temporal variation of the IMT during the heart beat can be assessed.

Publications in International Journals 2010-2013
Team 3: Ultrasound Imaging

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2. [DIAR-13] B. Diarra, M. Robini, P. Tortoli, C. Cachard, and H. Liebgott, "Design of optimal 2-D non-grid sparse arrays for medical ultrasound", *IEEE Transactions on Biomedical Engineering*, 2013, In Press.
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4. [ZAHN-13b] G. Zahnd, M. Orkisz, A. Sérusclat, P. Moulin, and D. Vray, "Simultaneous extraction of carotid artery intima-media interfaces in ultrasound images - Assessment of wall thickness temporal variation during the cardiac cycle", *Int J Comput Assist Radiol Surg*, In Press.
5. [LIN-13] F. Lin, C. Cachard, R. Mori, F. Varray, F. Guidi, and O. Basset, "Ultrasound Contrast Imaging: Influence of Scatterer Motion in Multi-pulse Techniques", *IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control*, In Press.
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8. [VARR-13c] F. Varray, O. Basset, P. Tortoli, and C. Cachard, "CREANUIS: A Nonlinear Radio Frequency Ultrasound Image Simulator", *Ultrasound in Medicine and Biology*, pp. 1915-1924, 2013 .
9. [ZAHN-13a] G. Zahnd, M. Orkisz, A. Sérusclat, P. Moulin, and D. Vray, "Evaluation of a Kalman-based block matching method to assess the bi-dimensional motion of the carotid artery wall in B-mode ultrasound sequences", *Medical Image Analysis*, vol. 17, no. 5, pp. 573-585, 2013 .
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11. [VARR-13d] F. Varray, and H. Liebgott, "Multi-Resolution Transverse Oscillation in Ultrasound Imaging for Motion Estimation", *IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control*, vol. 60, no. 7, pp. 1333-1342, 2013 .
12. [ALES-13b] M. Alessandrini, O. Bernard, A. Basarab, and H. Liebgott, "Multiscale optical flow computation from the monogenic signal", *IRBM*, vol. 34, pp. 33-37, 02/2013 .
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25. [DEPR-11] J. F. Deprez, E. Brusseau, J. Fromageau, G. Cloutier, and O. Basset, "On the potential of ultrasound elastography for pressure ulcer early detection", *Medical Physics*, vol. 38, no. 4, pp. 1943-1950, 2011.
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38. [LIEB-10a] H. Liebgott, A. Basarab, P. Gueth, D. Friboulet, and P. Delachartre, "Transverse oscillations for tissue motion estimation", *Ultrasonics*, vol. 50, no. 6, pp. 548-555, 2010 .

Team 4: Tomographic Imaging and Radiotherapy

Key words: tomography; image reconstruction; image registration; image guided radiation therapy; Monte-Carlo simulations

1. People: 12 permanent staff

Team leader	Peyrin Françoise	DR INSERM (HDR)	
Vice leader	Sarrut David	DR CNRS (HDR)	
Létang Jean Michel	MCU INSA (HDR)	Maxim Voichita	MCU INSA
Freud Nicolas	MCU INSA (HDR)	Sixou Bruno	MCU INSA (HDR)
Rit Simon	CR CNRS	Robini Marc	MCU INSA
Langer Max	CR CNRS	Carrie Christian	MD CLB (HDR)
Olivier Cécile	IE INSERM	Gouttenoire PierreJean	IE CNRS

and 15 PhD students, 8 post-docs

2. Research activity

The goal of the team is the development of new methods for tomography and therapy by radiation. There are two principal driving applications: the development of 3D cellular imaging of bone tissue, and image and simulation guided radiation therapy for cancer treatments. These objectives motivate research in inverse problems, tomographic reconstruction, dedicated three-dimensional image analysis, image registration and computer-based physics simulations mainly focused on particle beam therapy. Specifically, we address the three following axis:

i) theoretical questions and inverse problems raised by emerging modalities such as synchrotron phase CT, Compton camera CT and optical tomography,

ii) multi-scale assessment of bone structure, from the micro structure level to the cellular level,

iii) image and simulation guided radiation therapy, both for photon and particles beams

3. International and national context

Advanced methods for tomographic image reconstruction are still a major field of research with the attendance of new usages and modalities: X-ray phase CT, motion compensated reconstruction, multi-energy CT, optical tomography, etc. Such research is addressed by teams like (M. Brady, Oxford, J. Fessler, USA, M. Unser, EPFL, S Arridge, UCL).

Imaging bone microstructure has pushed the development of X-ray micro-CT that is now used in routine in bone biology. Nevertheless, new interest has shifted toward a better understanding of bone at the cellular network that begins to be addressed by means of Synchrotron radiation imaging by teams such as (R Muller, ETH Zürich, D Thomas, Melbourne, Australia).

Ion beam therapy is a rapidly expanding field in Europe and worldwide, with the construction of several new facilities every year, mainly protontherapy centers, but also few with carbon beams (CNAO in Italy and MedAustron in Austria). Guidance by image is recognized as one of the major current challenges in radiation therapy treatments (D. Verellen Be, M. VanHerk Nl, G. Baroni It, G. Sharp US, and others). Monte-Carlos simulations for radiation therapy also show important activities, with several teams (H. Paganetti USA, Jiang USA etc) and a strong French group around the international opengate collaboration (I. Buvat fr, D. Visvikis fr etc).

4. Imaging platform / experimental platform / computing infrastructure

Team 4 has the strong relationships with two main technical facilities: the European Synchrotron Radiation Facility (ESRF), Grenoble, and the radiation therapy department of the Léon Bérard cancer center in Lyon (CLB). Parts of the team are located in these two facilities. Moreover, there is also a strong and continuous collaboration with the physicians and the medical physicists of both institutes.

5. Scientific Coordination and Outreach

(Grants, technology transfer, industrial collaborations, conference organisation, research, academic and administrative responsibilities)

Scientific coordination

F. Peyrin : Leader LabEx PRIMES, "Physique Radiobiology medical Imaging and Simulation", Lyon University, 2012-2019, JM Létang : Leader of WP1 and D Sarrut : Leader of WP5 in LabEx PRIMES

F. Peyrin : Leader GdR Stic Santé, 2011-2014

D. Sarrut : Leader of the WP4 of the LYRIC project (Lyon Cancer Integrated Research, INCA, 10 M€)

F. Peyrin : IEEE BISP committee of the IEE SP section

F. Peyrin : scientific committee IEEE ISBI 2014

F. Peyrin : CSS8 INSERM committee 2012-2015

European Projects

2012-2015: European Spatial Agency (ESA), ERISTO IV (90 k€)

2009 –2013 : Long Term Proposal ESRF, coordinator, 11 partners, beam time allocation (eq. 288 k€)

2009-2012: ULICE FP7 100k€, 2010-2014 : ENVISION FP7 150k€

National projects

2009-2012 : FRM project, MICROTOMOS, 200 k€, PI : F Peyrin

2013-2015 : ANR TECSAN project « SPEPIX », (PI : M Arques, CEA LETI), 72 k€

2009-2012 : ANR project Cosinus hGate, 110k€ and PROUESSE (100k€)

2011-2012 : ANR project Physicancer ProTom, 60k€

2012-2014 : ANR project MC-Smart, 105k€

2013-2017 : ANR project DROITE, 16k€

2014-2017: ANR project MULTIPS (4 partners, PI : P Laugier, LIP Paris), 118 k€

Industrial projects

2011-2014 : Elekta (2xCIFRE, clinical study 250k€)

2011-2014 : Philips (research study, 78 k€)

2011-2013: IBA (MCIR, 150 k€)

6. Scientific production 2011-2013

- Publications in peer reviewed journals : 67
- Books and chapters : 7
- Publications in International conferences : 50
- Invited conferences : 15
- Number of defended PhD : 8

7. Five most significant journal publications

- 1st image of the Lacunar-Canalicular Network by 3D SRμCT at 300nm [PACU-12], Med Phys.
- 3D Magnified X-ray SR Phase nano CT at the cellular scale (50 nm) [LANG-12], Plos One
- Non-linear phase retrieval, [DAVI-12], IEEE Signal Proc Letter
- FBP algorithm for proton CT, [RIT-13], Med Phys
- Pencil beam scanning proton simulation, [GREV-12], Phys Med Biol

8. Perspectives

Our perspectives are the following

1) Reconstruction/inverse problems for emerging modalities

Propagation-based synchrotron phase CT, Compton camera CT, proton-CT, region of Interest reconstruction in X-Ray CT, binary reconstruction in X-ray CT, super-resolution methods for in vivo HR pQCT, spectral CT, scatter compensed cone-beam reconstruction, ROI Cone-Beam reconstruction

2) Multi-scale assessment of bone structure

New developments in 3D X-ray cell nano-CT, application of synchrotron CT in bone tissue engineering, cancer research and bone biomechanical modelling

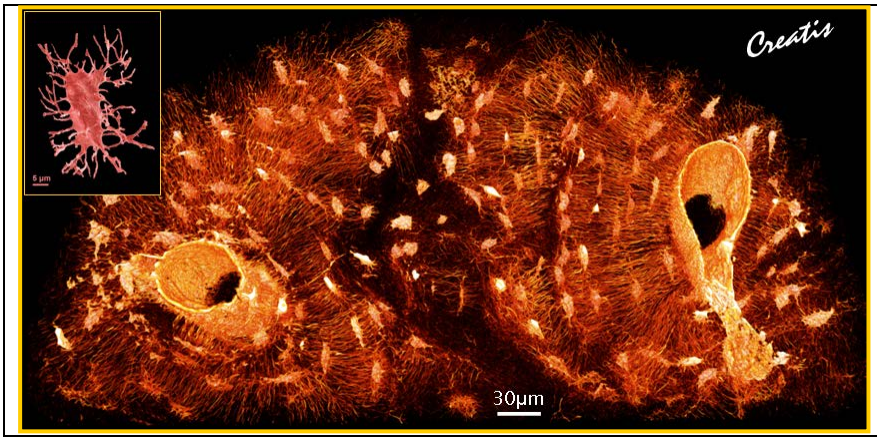
3) Image Guided Radiation Therapy and simulation

Fast hybrid Monte-Carlo simulation (low E X-ray, prompt-gamma, small-animal irradiation). Simulation-based optimisation of prompt-gamma devices for dose monitoring in protontherapy (with IPNL). Simulation of radioimmunotherapy for new monoclonal antibody OTSA101 against Frizzled Homolog 10 (FZD10), toward patient specific dose prescription. Intra-fraction US guided prostate treatment. Lung cancer treatment with midposition strategy (1st clinical study in progress, 2nd to start within 3 years). Direction dependent regularisation for deformable image registration

9. Highlights

3D bone ultrastructure resolved by synchrotron nano-CT
A Pacureanu prix thèse 2012 SFGBM, Chap IEEE EMBS, AGBM, GdR Stic Santé

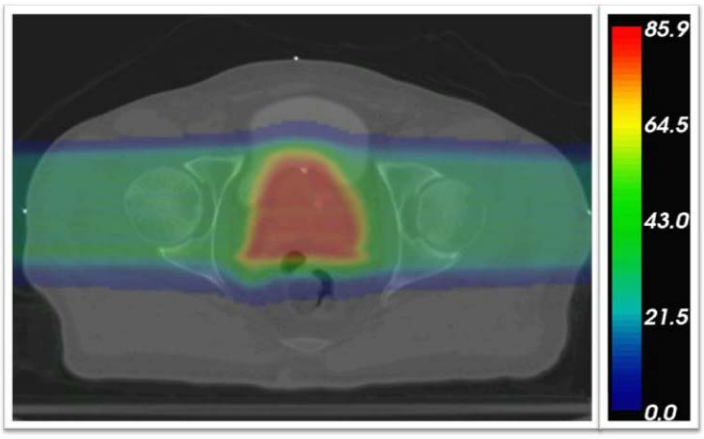
The crucial role of the bone osteocyte network in mechano-sensing and mechano-transduction has been recently highlighted. However, a clear picture of the 3D organization of bone has not been established yet due to lack of adapted imaging techniques. We proposed the first 3D images of the osteocyte network using synchrotron CT imaging. SR micro-CT allowed to get 3D images of the network osteocyte network at300nm on entire osteons. Furthermore, Magnified X-ray Phase nano-CT at 60nm provided a detailed rendering of osteocyte lacunae as well as a 3D map of the mass density within the sample. [PACU-12, LANG-12, PACU-13, VARG-13]



3D rendering of the osteocyte network in two osteons imaged with SR micro-CT (voxel size: 300 nm): osteocytes lacunae are linked through the small canaliculi channels. Top left insert: detailed rendering of an isolated osteocyte lacunae imaged by Magnified X-ray Phase nano-CT (voxel size : 60nm)

Simulation of proton pencil beam scanning treatment plan
Loic Grevillot, prix du jeune chercheur de la ville de Lyon

In the framework of the European project PARTNER and in collaboration between CREATIS and the IBA company (worlwide leader in protontherapy), we developed an original method allowing to simulate a complete patient proton treatment plan with pencil-beam scanning modality. We first proposed a generic method for modelling scanned ion beam delivery systems without the time consuming simulation of the treatment nozzle and based exclusively on beam data library (BDL) measurements required for treatment planning systems (TPS). We upgraded the GATE/GEANT4 Monte Carlo platform in order to recalculate the patient 3D dose distributions from clinical plans. Comparisons with measurements and commercial TPS were made. [GREV-11; GREV-12; GREV13]



3D dose distribution overlaid on a CT slice for a two beams prostate proton plan computed with the GATE platform.

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Team 5 : NMR and Optics : Methods and Systems

Key words: MR signal coding theory, RF and optoelectronic devices design, NMR signal quantification, functional optical imaging, NMR and optics coupling, pre-clinical and clinical applications, cartilage morphology and structure, digestive wall and liver dysfunction.

1. Peoples : 10 permanent staff members

Team leader	BEUF Olivier	DR CNRS	
Vice leader	RATINEY Hélène	CR CNRS	
CAVASSILA Sophie	PU UCBL	MONTCEL Bruno	MCU UCBL
GRENIER Denis	IR CNRS	PERRIN Emmanuel	PU UCBL
PERRIER Anne-Laure	MCU UCBL	SABLONG Raphaël	MCU UCBL
PILLEUL Frank	PR CLB	TSE VE KOON	MCU UCBL

with 6 PhD students, 5 master students.

2. Scientific objectives and research activity

The objectives of the team are to increase the quantity and quality of acquired in vivo information in animal models and human subjects so as to improve the understanding of 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. The underlying challenge is the weak interaction with the media under investigation, whether it be in MR or optics, and thus yielding a low signal to noise ratio. The addressed modalities are operated in synergy to provide, in vivo, relevant metabolic and functional information in addition to anatomy. Methods used pertain to MR signal coding theory, electromagnetic simulations, radio frequency and optoelectronic devices design, and also NMR and optical signal processing for reliable quantification of relevant parameters. Research focuses on new instruments and methodology for biomedical imaging applications. More specifically, we develop morphological, functional and interventional imaging for liver, gastro-intestinal wall exploration, musculosqueletal characterization as well as brain functional imaging. The main domains of expertise are: MR and Optical instrumentation, MRI and MRS sequence development, in vivo MR protocol design, multi-parametric MR analysis, functional optical imaging.

3. International and national context

The research projects of the team, though each one has its own dynamics and community, are sought to interact with mutual enrichment would it be to combine MR and optical techniques or to develop new acquisition or signal processing techniques. Indeed, recently, there has been a great deal of interest in further improving the in vivo characterization of tumors by interrogating tissues with multiple simultaneous measurement techniques (in particular optical spectroscopy/diffuse imaging, and MRI/MRS) that provide complementary information about the state of the sample under investigation. In this respect, our team profile is close to the French Team IMIS (Imagerie multimodale integrative en Santé, Laboratoire ICube, Strasbourg) except that our applications do not concern brain or breast but brain, cartilage and abdomen.

Fields	Team 5 Specificity	Competing Teams
Bimodal MRI/Optic	Endoluminal exploration Neuro-vascular coupling in cerebral activity	Gulsen G, UC Irvine, US and Lin YH, Nziachristos V, Germany ; Sonmez AE
Optical Functional Imaging	Intra-operative optical and fluorescence spectroscopy	Torricelli A.; Politechnico di Milano; Hillmann E.; Columbia University; Boas D.; Harvard Boston; Durduran T., ICFO, Barcelona.
MRI	Multiparametric MR for diffuse liver diseases: perfusion, diffusion, spectroscopy and quantitative analysis MR Elastography	van beers B., Paris; Reeder S., University of Wisconsin Ehman R., mayo clinic USA; Sinkus R., Paris
In vivo MR Spectroscopy	Quantitative 2D MRS: Sequence development associated to quantification algorithms	Boesiger P., Zürich; Kreis R., Bern Van Huffel S., Leuven, Maudsley A., University of Miami
MR instrumentation	Small animal multi-channel coils	Webb A., Leiden University
MR signal coding theory	MR virtual MAS acquisition: acquisition during excitation	Garwood M., University of Minnesota

National collaborations are established with **methodologists in NMR and/or Optics** (H. Saint-Jalmes LTSI, Rennes; Y Le Fur CRMBM, Marseille; S. Mottin Hubert Curien, St Etienne; E. Wolf, Institut Néel, CNRS, Grenoble, D. Sugny, ICB), **with physicians** from Hospices Civils de Lyon (J. Guyotat, Service de Neurochirurgie; D. Moussata, service d'hépato-gastro-entérologie (HEH); J-B. Pialat, service d'imagerie ostéoarticulaire; PJ. Valette, service d'imagerie digestive; M. Laville, maladies de la nutrition), with **chemists** (ENS Lyon), with **biologists** (IGFL, ENS Lyon; CRNL, Lyon; LPPA, Nancy; U855, Lyon) and with small business companies (Kapteos, Chambery; Voxcan, Marcy l'Etoile; CIRMA, Marcy l'Etoile; Bone therapeutics, Brussels) or major companies (Siemens, Erlangen; GEHC, Buc). Our international collaborations are with D. Merhej, Liban; D. Pelletier, Yale; SJ Nelson, UC San Francisco; A. Van Der Linden, Bio-Imaging Lab, Antwerp; R. Ehman, Mayo clinic; S. Conolly, UC Berkeley; Teoh Swee Hin, NU of Singapore; Marek Kretowski, Bialystok University of Technology, Poland.

4. Imaging platform / experimental platform / computing infrastructure

- Probe based confocal Laser Endomicroscope, Cell-Vizio Lab (MKT®)
- Optical bench for fibered spectroscopy: endoscopic and intraoperative characterization of tissues
- Multi-channel spectrometer for hyper-spectral optical imaging
- RF measurement bench with network analyzer, 500 MHz oscilloscope, mechanical etching…
- ^{1}H dual channel imaging modulus on the laboratory 4.7T system

Access to pre-clinical Animage platform (7T MRI; µPET) and MRI department (1.5T) of CERMEP, 3T clinical MRI systems from Centre Hospitalier Lyon Sud and Hôpital Edouard Herriot.

5. Scientific Coordination and Outreach

In the last five years: Coordinators of Project CIBLE "Région Rhône Alpes" in collaboration with 1 industrial, of workpackages in 3 ANRs, stepping projects (5 PEPS-CNRS, 1 defi Instrumentation-MI-CNRS, 1 Réseau Optique et Photonique-MRCT-CNRS); Partner of an FP7 ITN project, an INCA project, a CLARA project, a DGA project and one European project Eurostar in collaboration with 3 industrial partners. Coordinators of Work package 2 « Emerging Imaging Techniques » of the labex PRIMES. Organizer of national conference 'inter GDR' in Dec 2012 entitled "Nouvelles méthodologies en imagerie du vivant"; Distinguished reviewer of JMRI, member of the editorial board of Journal of Medical Engineering, board member of the French society of MR in Biology and Medicine (SFRMBM).

6. Five most significant journal publications

B. Leporq, H. Ratiney, F. Pilleul, and O. Beuf, "Liver fat volume fraction quantification with fat and water T1 and T2* estimation and accounting for NMR multiple components in patients with chronic liver disease at 1.5 and 3.0 T", *European Radiology*, **23**(8):2175-86, 2013.

R. Ayde, G. Gaborit, P. Jarrige, L. Duvillaret, R. Sablong, A. L. Perrier, and O. Beuf, "Potentialities of an Electro-Optic Crystal Fed by Nuclear Magnetic Resonant Resonant Coil for Remote and Low-Invasive Magnetic Field Characterization", *IEEE Sensors Journal*, **13**(4):1274-1280, 2013.

N. Ramamonjisoa, H. Ratiney, E. Mutel, H. Guillou, G. Mithieux, F. Pilleul, F. Rajas, O. Beuf, and S. Cavassila, "In vivo hepatic lipid quantification using MRS at 7T in a mouse model of glycogen storage disease type 1a", *J Lipid Res*, **54**(7):2010-22 (2013).

B. Montcel, L. Mahieu-Williame, X. Armoiry, D. Meyronet, and J. Guyotat, "Two-peaked 5-ALA-induced PpIX fluorescence emission spectrum distinguishes glioblastomas from low grade gliomas and infiltrative component of glioblastomas", *Biomedical Optics Express*, **4**(4):548-558, 2013.

A. Ramgolam, R. Sablong, L. Lafarge, H. Saint-Jalmes and O. Beuf, "Optical spectroscopy combined with high-resolution MRI for digestive wall assessment: endoluminal bimodal probe conception and characterization in vitro, on organic sample and in vivo on a rabbit", *J Biomed Opt*, **16**(11):117005, 2011.

Published manuscript of the team can be find at: http://www.creatis.insa-lyon.fr/site/fr/biblio/keyword/79.

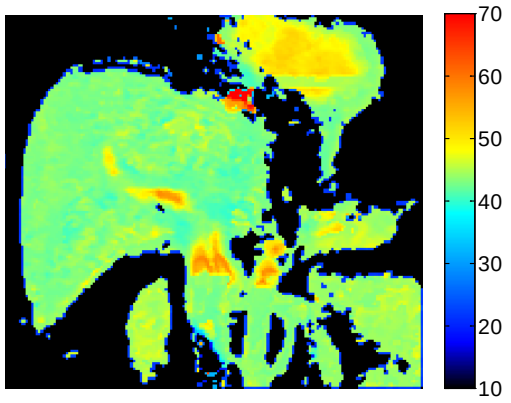
7. Perspectives

The pluri- and trans-disciplinary characteristics of our team are enticing medicine, physics in MR and optics as well as signal processing. This strength enables a systemic approach of identified biomedical issues going from the detection device, acquisition methods, and signal processing to medical outcomes. The main research directions are: (1) "Tissue and metabolic characterization using MR"; (2) "Bimodal optics/MRI" either associated to endoluminal probe or imaging of cerebral activity; (3) "NMR RF coils" mainly designed to small animal imaging.

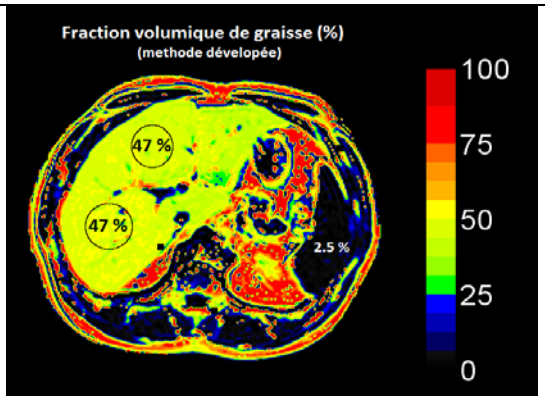
8. Highlights

Tissue and metabolic characterization for liver diagnosis

Multiparametric analysis by combining the methods of perfusion, diffusion (intravoxel incoherent motion) and estimation of tissue viscoelastic properties (MR Elastography) associated in the same time to both imaging and proton spectroscopy (MRS) techniques for the quantification of fatty components provides extremely valuable informations non-invasively. This protocol, based on magnetic resonance, and performed within a single examination allows a non-invasive longitudinal monitoring for liver diagnosis.



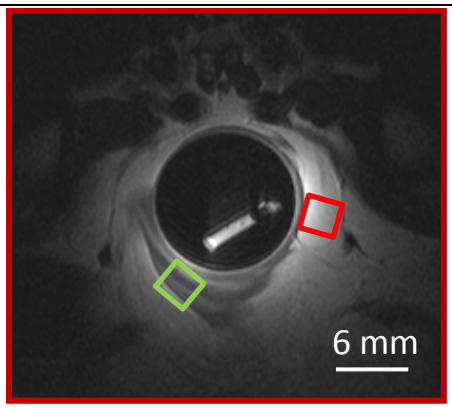
Hepatic perfusion index(%) maps obtained using the European Grid Infrastructure (3 hours of computing against 16 days on a laptop PC): gain x126 (**HEPATOMAP project**)



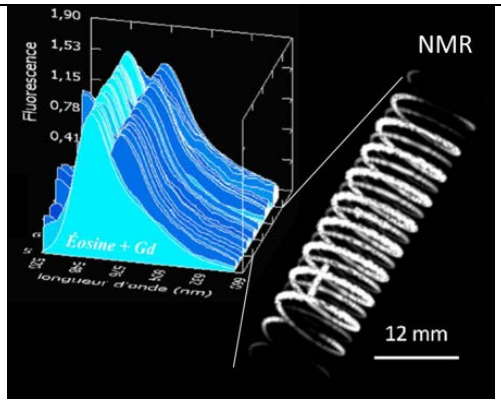
Fat Volume Fraction (%) based on a multi peak resonance approach and correcting for T1, T2* and RF B1 non uniformity and solving the dominant component ambiguity.

Endoluminal bimodal probe conception

Imaging and spectroscopic advantages of NMR and optics are combined to improve non-invasive early detection and diagnosis of lesions in the gastro-intestinal tract. The development of endoluminal radiofrequency (RF) coils removes the obstacles inherent to the investigation of deep organs. The high spatial resolution achievable with endoluminal coil provides detailed information on the local anatomy and pathology. Optoelectronic components have to be used to address safety issues using MR endoluminal RF probes. Our approach is to combine optical spectroscopy in the form of autofluorescence and reflectance spectroscopy with High spatial Resolution Magnetic Resonance Imaging (HR-MRI) within an endoluminal bimodal probe to provide a tool capable of extracting both biochemical data and morphological data simultaneously. In parallel, safety aspects due to RF inducing local heating are investigated and electro-optic conversions of NMR signal of endoluminal coils are studied.



MR images of the colon wall in the rabbit. The contours of the mucosal and sub mucosal complex are clearly distinguishable on the high spatial resolution MR images obtained with the endoluminal coil.



Comparison of the left and right ROI fluorescence spectra obtained on the cylindrical phantom (MIP image of the cylindrical phantom obtained with a T1 Flash 3D sequence at 3T). Eosin fluorescence was observed at 555 nm and rhodamine B at 575 nm.

Publications in International Journals 2010-2013
Team 5: NMR and Optics: Methods and Systems

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Team 6: Cerebral Imaging

Key words: Stroke, Multiple sclerosis, Inflammation, Neuroprotection, Magnetic Resonance Imaging, Molecular imaging.

1. **People**: 10 permanent staff and 7 PhD students, 4 master students

Team leader	NIGHOGHOSSIAN Norbert (PU-PH)		
Vice leader	SAPPEY-MAINIER Dominique (MCU-PH)		
ROUSSEAU David	PU	COTTON François	PU-PH
FRINDEL Carole	MCU	FAKRI-BOUCHET	Latifa MCU
CHO Tae-Hee	PHU	HANNOUN. Salem	Post-doc
WIART Marlène	CR CNRS	DURAND-DUBIEF.	Françoise PH
BERTHEZENE Yves	PU-PH	GUTTMANN R.G.	Charles ..Prof. Invité

2. Scientific objectives:

The team aims at investigating brain pathologies through two different diseases: stroke and multiple sclerosis, using both pre-clinical and clinical imaging in a translational perspective. Stroke is one of the most common causes of death in the world. Ischemic stroke, which results from the occlusion of a cerebral artery, accounts for 88% of all stroke cases. To date, the only treatment approved for ischemic stroke is reperfusion therapy; however only a small percentage of stroke patients are eligible for this therapy, due in part to the narrow therapeutic window (4.5h post-onset). To better understand and exploit the mechanisms at work in focal cerebral ischemia, and propose new therapeutic strategies, molecular events need to be examined in detail in animal models. The aim of our team is the development and validation of molecular imaging techniques in order to investigate the pathophysiology of cerebral ischemia and to evaluate new neuroprotective strategies. Multiple Sclerosis (MS) is a chronic, inflammatory and demyelinating disease affecting both white (WM) and grey matter (GM). While WM lesions are easily visualized by conventional MRI, the detection of alterations in normal appearing WM (NAWM) and GM remains challenging. For this purpose, MRI acquisitions and post-processing techniques are developed to better characterize the pathological mechanisms. T1, T2, and T2*-weighted MRI and FLAIR sequences are used to measure the lesion load and provide volumetric assessment of GM and WM atrophy. Further, more advanced techniques such as MR spectroscopic imaging (MRSI) and diffusion tensor MRI (DTI) aimed to detect and characterize diffuse metabolic and micro-architectural alterations in lesions, NAWM, and deep GM structures. Therefore, the goal of the team is to better characterize the MS alterations in several brain structures (GM nuclei, cerebellum,…) and tissue (WM, GM) of different clinical forms of the disease such as relapsing remitting (RR), secondary progressive (SP) and primary progressive (PP). The relationship between morphometric, metabolic and diffusivity markers, as well as brain lesion load and clinical status of the patients, were longitudinally analyzed and correlated, in order to better understand the evolution of each clinical form. The main domains of expertise of the team are the following: Animal models of cerebral ischemia, Imaging of stroke, Contrast agents/molecular imaging, Data post-processing and quantification, Design of NMR coils and Implantable micro-coils.

3. Collaborations:

Sabine Van Huffel, Leuven University, Leuven; Leif Oestergaard; Aarhus University, Aarhus; Thomas Vorup-Jensen Interdisciplinary Nanoscience Center; Aarhus; Götz Thomalla, UKE, Hamburg ; Charles R.G. Guttmann, Boston; Michel Lagarde, Laboratoire de Recherche en Cardiovasculaire, Métabolisme, Diabétologie et Nutrition (CarMeN, U1060 Inserm), Lyon; Serge Nataf, Centre de Recherche en Neurosciences de Lyon (CRNL, UMR CNRS 5292, UMR_S 1028 Inserm), Lyon; Christiane Charriaut-Marlangue, Physiopathologie, conséquences fonctionnelles et neuroprotection des atteintes au cerveau en développement (U676 Inserm), Paris; Stéphane Parola, Laboratoire de Chimie de l'ENS Lyon (UMR CNRS 5182), Lyon; Emmanuelle Canet-Soulas, Laboratoire de Recherche en Cardiovasculaire, Métabolisme, Diabétologie et Nutrition (CarMeN, U1060 Inserm), Lyon; Patrick Poulichet, Laboratoire ESYCOM, ESIEE Paris; Cherif Dridi, Monastir University of sciences, Pham Huy Hoang and Phan Dinh HUAN, Ho Chi Minh University of Technology, Ho Chi Minh Polytechnic Institute; Youssef Zaim Wadghiri, NYU School of Medicine Center for Biomedical Imaging.

4. Imaging platforms / experimental platforms / computing infrastructures

Plateforme d'imagerie du petit animal Animage & département IRM, CERMEP-Imagerie du vivant. http://www.cermep.fr and European Synchrotron Research Facility (ESRF). http://www.esrf.eu

5. Research, academic and administrative responsibilities

Member of CREATIS Council (Conseil d'unité, membre élue, Marlène Wiart, 2006-2010).
D. Sappey-Marinier, President of SFRMBM (2011-2013)

Conferences organization

12ème Congrès du GRAMM (Lyon, 2008) and 13ème Congrès du GRAMM (Rennes, 2011)
Workshop of French Imaging Platform FLI (Lyon, 2012) and Journée « Etat de l'art en imagerie » JFR-FLI (Lyon , 2013)
Journée SFRMBM aux Congrès des Journées de Radiologie Françaises (JFR) (Paris, 2009-2013)
Journée SFRMBM au 30ème Congrès de l'ESMRMB (Toulouse, 2013).

National projects

Partner in transverse program of CREATIS including : ANR National Infrastructure FLI – France Life Imaging (Partner), ANR Equipex LILI– Lyon Integrated Life Imaging (Partner), ANR Labex PRIMES – Physique, Radiobiologie, Imagerie Médicale et Simulation (WP2)
ANR INFLAM – *INFLAMmation in brain and vessels with iron nanoparticles and cell trafficking: a multi-scale approach of tissue microenvironment, iron nanostructure and iron biotransformations*, 2007-2010, total amount: 849 kEuros for 8 academic partners and 2 industrial partners (PI: Pr Yves Berthezène and co-PI: Marlène Wiart).
ANR NEUROPROTECT – 2007-2011, total amount: 550 kEuros for 5 partners, PI: Pr Michel Lagarde. (Work Package leader: Norbert Nighoghossian)
ANR AVC in silico – 2006-2010, 4 partners, PI: Emmanuel Grenier (Partner: Marlène Wiart)
PHRC CsA Stroke – 2010-2013, 7 partners (PI: Norbert Nighoghossian)
ANR-10-COHO-002, Programme des Investissements d'Avenir Cohorte nationale OFSEP – 2010_2020, (PI: Christian Confavreux)

European projects

FP6/IKNOW – *Integrating Information from Molecule to Man: Knowledge Discovery Accelerates Drug Development and Personalized Treatment in Acute Stroke,* 2006-2011, PI: Leif Oestergaard (National PI: Norbert Nighoghossian)
FP6/ FAST – 2006-2011, 13 partners (10 academic, 3 industrial), PI: Danielle Graveron-Demilly (CREATIS, Lyon)
FP7/WAKEUP – 2012-2016, 5 partners, PI: Götz Thomalla (National PI: Norbert Nighoghossian).
FP7/ TRANSACT - 2013-2017, 13 partners (10 academic, 3 industries) PI: Sabine Van Huffel (Leuven), (National PI: Dominique Sappey-Marinier).

Industrial collaborations

Guerbet – Contrast agents evaluation in the brain; SANOFI – New neuroprotective treatment evaluation

6. Five most significant journal publications

1. MRI prediction of stroke outcome: Hermitte L, Cho TH, Ozenne B, Nighoghossian N, Mikkelsen IK, Ribe L, Baron JC, Ostergaard L, Derex L, Hjort N, Fiehler J, Pedraza S, Hermier M, Maucort-Boulch D, Berthezène Y. Very Low Cerebral Blood Volume Predicts Parenchymal Hematoma in Acute Ischemic Stroke. *Stroke*;44(8):2318-2320, 2013.
2. Investigation of USPIO-enhanced MRI to study neuroinflammation: Desestret V, Brisset JC, Devillard E, Moucharrafie S, Nataf S, Honnorat J, Nighoghossian N, Berthezène Y, and Wiart M. Early stage investigations of USPIO-induced signal changes after focal cerebral ischemia in mice**.** *Stroke*, 40:1834-1841, 2009
3. Inverse problem in perfusion weighted imaging : C. Frindel, M. Robini, D. Rousseau. A 3-D Spatio-Temporal Deconvolution Approach for MR Perfusion in the Brain. *Medical Image Analysis (MEDIA)*, 2013 (accepted).
4. MR Spectroscopy characterization of Multiple sclerosis patients : M. Bagory, F. Durand-Dubief, D. Ibarrola, J-C. Comte, F. Cotton, C. Confavreux and D. Sappey-Marinier: Implementation of an absolute brain 1H-MRS quantification method to assess different tissue alterations in multiple sclerosis. IEEE Trans Biomed Eng. 2012 Oct;59(10):2687-94.
5. *Evaluation of Coils for Imaging Histological Slides: Signal-to-Noise Ratio and Filling Factor:* Dung Minh Hoang, Evelyn B. Voura, Chao Zhang, Latifa Fakri-Bouchet, and Youssef Zaim Wadghiri, Magn Reson Med. 2013 Jul 15. doi: 10.1002/mrm.24841.

7. Perspectives: Concerning the "stroke" program, new developments will be oriented towards new kind of hybrid nanoparticles (NP) that tricks the brain blood barrier (BBB) into guiding the probe into the brain and combines: 1) optical probes for intravital microscopy, 2) magnetic properties for magnetic resonance imaging (MRI) and 3) radio opacity phase-contrast X-ray computed tomography. Specifically, Stéphane Parola with the LC ENS (UMR 5182, Lyon) propose to build a NP targeted at the integrin Mac-1 (CD11b/CD18 or alpha M/beta 2) to assess neuroinflammation non-invasively, based on luminescent conjugated polythiophenes (LCP), an agent that has been shown to have capacity to cross the BBB. LCPs will be attached to magnetic NP consisting of a mineral core (gadolinium-based compound) and an organic shell (PEG chains). These NPs can also be coated with gold nanoshells to enhance opacifying properties. Targeting of Mac-1 will be achieved by grafting a fibrinopeptide at the surface of the NP. The biological and imaging properties of the obtained NPs will be fully characterized in collaboration with the Grenoble intravital microscopy platform (France Life Imaging, located at the Grenoble Institute of Neuroscience (GIN) INSERM U836 and Clinatec). Proof-of-concept of molecular imaging of Mac-1 expression will then be established in a model of transient middle cerebral artery occlusion in wild type and Mac-1 null mice. Concerning the MS program, these methodological developments, particularly in DTI, will be applied to better characterize the alterations along the WM fibers to better explain the retro/anterograde effects of lesions on different WM or GM tissue (corpus callosum, cerebellum…). For this purpose, DTI at high angular resolution will be developed at 3T. This research will continue in the frame of the national cohort program "OFSEP" (Observatoire National de la Sclérose en Plaques). With the recent (2011) venue of 2 permanent staff member experts in image processing in the team, new image processing approaches will be developed in synchronization with clinical and preclinical studies. This includes new inverse problem approach for the deconvolution problem of MR perfusion imaging, the quantification of nanoparticules in phase contrast X-ray imaging with detection-based phase retrieval in synchrotron imaging to go beyond the sole visualization of inflammatory. Also, as another illustration, we will undertake the quantification of the shape of lesions in stroke and MS and their relation to the evolution of the lesions. New instrumentation methods will be developed in collaboration with team 5 of CREATIS to perform continuous acquisition of cerebral blood flow together with ECG for patients monitoring after stroke.

8. Highlights

Dual mapping of iron oxides in the mouse brain (MRI and SR-PCT): Marinescu M, Chabrol A, Langer M, Durand A, Olivier C, et al. Synchrotron Radiation Micro-Computed Tomography as a new method to detect iron oxide nanoparticles in the brain. Molecular Imaging & Biology, 2013 (in press). We have pioneered the development of an innovative Magnetic Resonance Imaging (MRI) method devoted to the analysis of neuroinflammation following cerebral ischemia, based on the in vivo magnetic labelling of phagocytic cells with ultrasmall superparamagnetic particles of iron oxide (USPIO-enhanced MRI) in mice. We have shown that monitoring of the effect of minocycline, an anti-inflammatory treatment, can be achieved using this approach. Limitations of USPIO-enhanced MRI, however, lie in the difficulty of interpreting MR signal changes. For example, determining the precise topography of labeled cells on MR images is hampered by the low spatial resolution (100x100-µm in plane with 1000-µm slice thickness) compared to phagocytic cells size (40-µm) and by the "blooming" effect (the local magnetic field created by labeled cells extending well beyond the actual cell radius). We therefore used in-line Synchrotron Radiation X-ray Phase Computed Tomography (SR-PCT) as a new method of visualizing USPIO distribution into the whole brain of mice with cerebral ischemia (Figure 1). SR-PCT images displayed brain anatomy as clearly as histology as well as the marked cells at an isotropic spatial resolution of 8-µm.

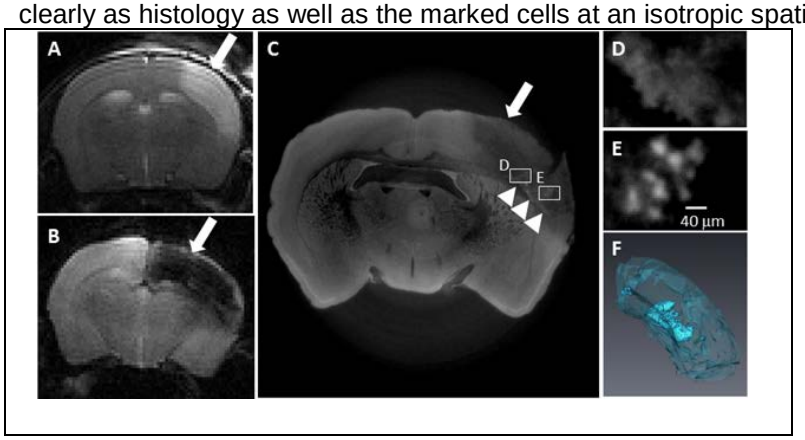

Figure 1- USPIO distribution in the brain of a mouse with focal cerebral ischemia A) Pre- and B) post-contrast T2-weighted MRI. The lesion can be seen as a hyperintense region before USPIO injection (arrow). The hypointense signal that appears in the lesion 48h post-injection is caused by USPIO presence in the brain. C) SR-PCT image of the same mouse with hyperintense areas (arrowheads) appearing either as: D) a diffuse signal or E) bright spots. These hyperintense areas reflect USPIO distribution in the lesion. The difference in appearance arises from the difference in compartmentalization (interstitial vs. intracellular). F) 3D reconstruction of hyperintense area distribution (light blue)

Characterization of subcortical gray matter using DTI in MS: S. Hannoun, F. Durand-Dubief, C. Confavreux, D. Ibarrola, N. Streichenberger, F. Cotton, C. Guttmann, D. Sappey-Marinier: DT-MRI Evidence for Extra-Axonal Neuronal Degeneration in Caudate and Thalamic Nuclei of MS Patients. American Journal of Neuro-Radiology 2012 Aug;33(7):1363-8. First, we have developed of an absolute ^{1}H MR spectroscopy quantification method showing increases of choline, creatine, and myo-inositol concentrations in PP and SP patients compared to controls, whereas the concentration of N-acetyl compounds remained constant. These findings suggest choline concentrations and Cho/tNA ratio as putative markers of progressive onset to monitor neurodegenerative processes (Bagory et al., 2012). Second, significant correlations were observed between metabolic contents and DTI metrics in WM. A comparison analysis of these methods demonstrated a better sensitivity/specificity of DTI over MRSI (Hannoun et al 2012). Nevertheless, NAA/Cho ratio could better differentiated PP patients from controls. If diffusivity changes related to microstructural alterations were correlated with metabolic changes, DTI provided a better sensitivity to detect early changes, particularly in RR patients, subject to inflammatory processes. In contrast, the better specificity of metabolic ratios to detect axonal damage and demyelination may provide a better index for identification of PP patients. Third, the DTI analysis of subcortical GM nuclei showed a significant FA increase in the caudate and the thalamus of MS patients. This result was associated with volume decreases of both nuclei, suggesting that FA may constitute a sensitive marker of neurodegenerative processes, such as dendrites loss and/or swelling of neuronal cell bodies in GM.

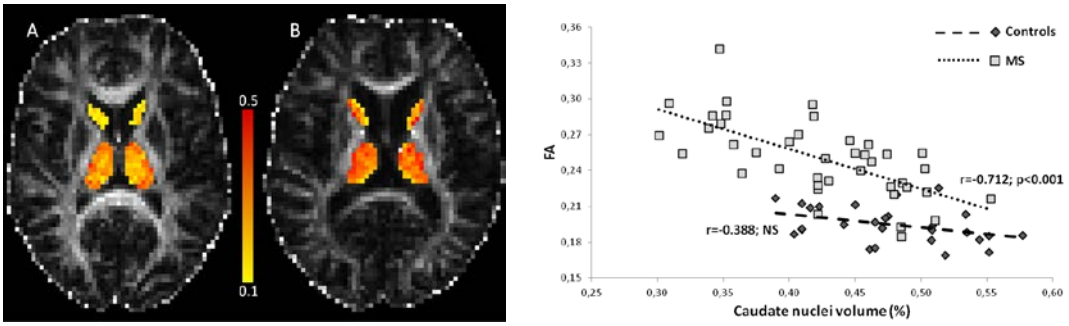

Figure 2: On left, colored FA maps showing increased FA values : 1) in thalamus compared to caudate in Control (A) and 2) in MS patient (B) compared to Control (A). On right, the increased FA is significantly correlated with the atrophy of the caudate nuclei in MS patients but not in Controls.

Publications in International Journals 2010-2013
Team 6 : Cerebral Imaging

1. Hermitte L, Cho TH, Ozenne B, Nighoghossian N, Mikkelsen IK, Ribe L, Baron JC, Ostergaard L, Derex L, Hjort N, Fiehler J, Pedraza S, Hermier M, Maucort-Boulch D, Berthezène Y. Very Low Cerebral Blood Volume Predicts Parenchymal Hematoma in Acute Ischemic Stroke. *Stroke;*44(8):2318-2320, 2013.
2. Panouillères M, Alahyane N, Urquizar C, Salemme R, Nighoghossian N, Gaymard B, Tilikete C, Pélisson D. Effects of structural and functional cerebral lesions on sensorimotor adaptation of saccades. *Exp Brain Res*, 2013 (in press)
3. Haesebaert J, Termoz A, Polazzi S, Mouchoux C, Mechtouff L, Derex L, Nighoghossian N, Schott AM. Can hospital discharge databases be used to follow ischemic stroke incidence? *Stroke;*44(7):1770-4, 2013
4. Ritzenthaler T, Lhommeau I, Douillard S, Cho TH, Brun J, Patrice T, Nighoghossian N, Claustrat B. Dynamics of oxidative stress and urinary excretion of melatonin and its metabolites during acute ischemic stroke. *Neurosci Lett*. 7;544:1-4, 2013
5. Apetse K, Mechtouff L, Cho TH, Derex L, Nighoghossian N, Turjman F. Mechanical thrombectomy with the solitaire stent at Lyon, France. *Eur Neurol*;69(6):325-30, 2013
6. Thomalla G, Fiebach JB, Ostergaard L, Pedraza S, Thijs V, Nighoghossian N, Roy P, Muir KW, Ebinger M, Cheng B, Galinovic I, Cho TH, Puig J, Boutitie F, Simonsen CZ, Endres M, Fiehler J, Gerloff C; WAKE-UP investigators. A multicenter, randomized, double-blind, placebo-controlled trial to test efficacy and safety of magnetic resonance imaging-based thrombolysis in wake-up stroke (WAKE-UP). *Int J Stroke*. 2013
7. Østergaard L, Jespersen SN, Mouridsen K, Mikkelsen IK, Jonsdottír KÝ, Tietze A, Blicher JU, Aamand R, Hjort N, Iversen NK, Cai C, Hougaard KD, Simonsen CZ, Von Weitzel-Mudersbach P, Modrau B, Nagenthiraja K, Riisgaard Ribe L, Hansen MB, Bekke SL, Dahlman MG, Puig J, Pedraza S, Serena J, Cho TH, Siemonsen S, Thomalla G, Fiehler J, Nighoghossian N, Andersen G. The role of the cerebral capillaries in acute ischemic stroke: the extended penumbra model *J Cereb Blood Flow Metab.;*33(5):635-48, 2013
8. Svahn J, Cho TH, Derex L, Mechtouff L, Nighoghossian N. [Subarachnoidal hemorrhage and multiple vascular cerebral abnormalities in β-thalassemia major]. *Rev Neurol* (Paris).;169(3):266-8, 2013
9. Ong E, Mechtouff L, Bernard E, Cho TH, Diallo LL, Nighoghossian N, Derex L.Thrombolysis for stroke caused by infective endocarditis: an illustrative case and review of the literature. *J Neurol*.;260(5):1339-42, 2013
10. Matrat A, De Mazancourt P, Derex L, Nighoghossian N, Ffrench P, Rousson R, Hanss M. Characterization of a severe hypofibrinogenemia induced by alteplase in two patients thrombolysed for stroke.*Thromb Res*. 131(1):e45-8, 2013
11. Porthault-Chatard S, Termoz A, Derex L, Polazzi S, Cakmak S, Nighoghossian N, David JS, Schott AM. Effectiveness of thrombolysis in the Rhône region, France: a prospective population-based study. *Int J Stroke*. 2012 Oct;7(7):E13. 2013
12. Marinescu M, Chabrol A, Langer M, Durand A, Olivier C, et al. Synchrotron Radiation Micro-Computed Tomography as a new method to detect iron oxide nanoparticles in the brain. *Molecular Imaging & Biology*, 2013 (in press)
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17. Marinescu M, Chauveau F, Durand A, Riou A, Cho TH, Dencausse A, Ballet S, Nighoghossian N, Berthezène Y, Wiart M. Monitoring therapeutic effects in experimental stroke by serial USPIO-enhanced MRI, *European Radiology*, 23(1):37-47, 2012.
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21. Ritzenthaler T, Cho TH, Wiart M, Berthiller J, Østergaard L, Hermier M, Derex L, Berthezène Y, Nighoghossian N. Assessment of baseline hemodynamic parameters within infarct progression areas in acute stroke patients using perfusion-weighted MRI. *Neuroradiology*. 53(8):571-576, 2011.
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23. Chauveau F, Cho TH, Berthezène Y, Nighoghossian N, Wiart M. Imaging inflammation in stroke using magnetic resonance imaging. *Int J Clin Pharmacol Ther*, 48(11):718-728, 2010.
24. Chauveau F, Moucharrafie S, Wiart M., Brisset JC, Berthezène Y, Nighoghossian N, and Cho TH. In vivo MRI assessment of permanent middle cerebral artery occlusion by electrocoagulation: pitfalls of procedure**.** *Experimental & Translational Stroke Medicine*, 2:4, 2010.
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30. Evaluation of Coils for Imaging Histological Slides: Signal-to-Noise Ratio and Filling Factor Dung Minh Hoang, Evelyn B. Voura, Chao Zhang, Latifa Fakri-Bouchet, and Youssef Zaim Wadghiri, Magn Reson Med. 2013 Jul 15.
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