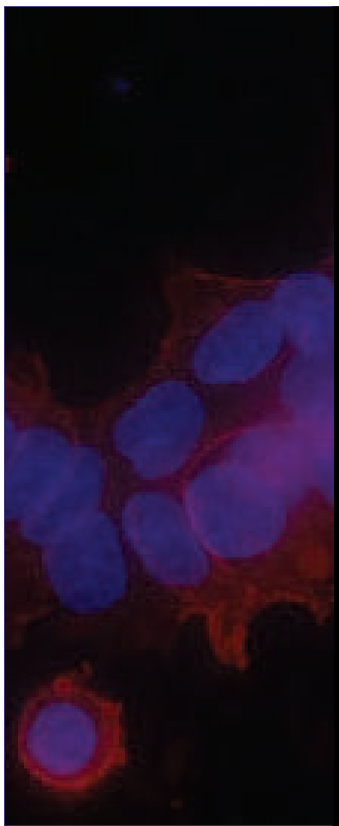
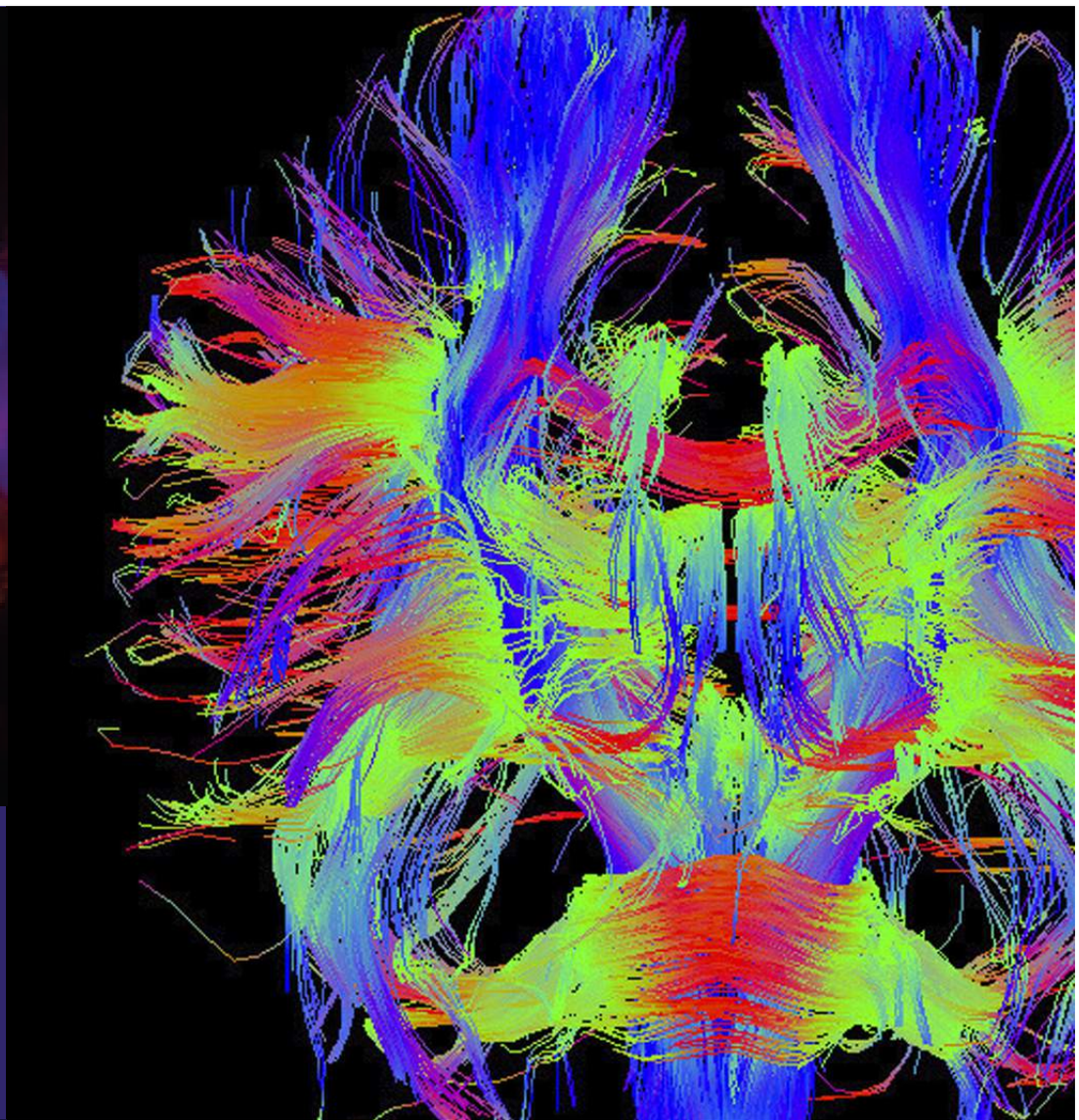
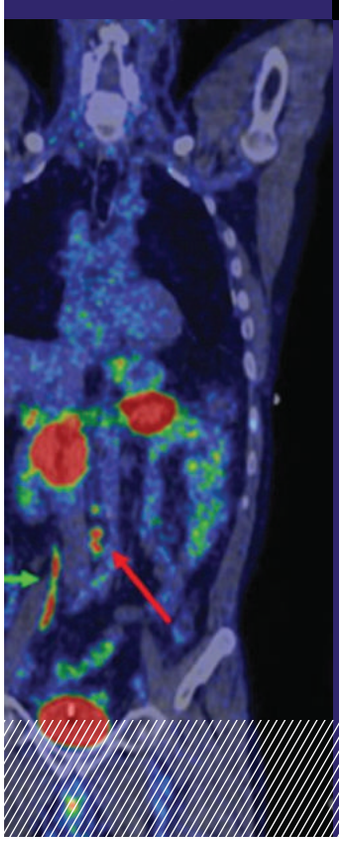




TRAIL

Translational Research and Advanced Imaging Laboratory



2011–2018 Activity Report

LABORATOIRE D'EXCELLENCE — université de Bordeaux

INVESTIR L'AVENIR

université de BORDEAUX

cnrs

Instituts thématiques — Inserm — Institut national de la santé et de la recherche médicale

Bordeaux INP AQUITAINE

Preparing the future

Cluster of Excellence of the University of Bordeaux

Higher education and research are key levers in achieving a new form of growth that is smarter, more sustainable and more inclusive, with the goal being to prepare for a knowledge society in which future generations can achieve fulfilment. The University of Bordeaux and its partners intend to address this challenge by shaping a campus of excellence with an international reputation, uniting its research forces around high-level scientific pillars.

These are neuroscience, medical imaging, cardiology, public health, materials of the future, environment, archaeology, laser optics and digital technologies.

These priorities reflect the research strengths of the Bordeaux site whose excellence is clearly recognised in terms of the standards applicable to the discipline and its high international profile.

Certifications by the French national "Investments for the Future" scheme in 2011 have strengthened this dynamic of ambitious multidisciplinary projects. Today, these centers of excellence backed by innovative training offer great prospects for development, French research and the socioeconomic world. The pursuit of excellence is thus at the heart of the development policy of the University of Bordeaux. Through this tremendous momentum, the University of Bordeaux is seeking to answer the challenges of our environment to prepare for tomorrow's society.

TRAIL: Translational Research and Advanced Imaging Laboratory

Medical imaging plays a central role in meeting public health challenges.

From a medical point of view, imaging provides an earlier, faster and more accurate diagnosis, as well as optimal therapeutic management adapted to the biology and genome of the patient. It also allows a more targeted drug delivery, better monitoring of the effectiveness of treatment and less invasive surgery because of the guidance it provides.

From an economic point of view, imaging optimizes care costs thanks to early diagnosis, optimal treatment and a shorter recovery time. It is also a source of industrial competitiveness.

The Translational Research and Advanced Imaging Laboratory (TRAIL) was accredited in July 2011 to exploit the multidisciplinarity and the translational forces of the Bordeaux imaging community.

→ 4 MAJOR HEALTH THEMES

Neurology | Oncology | Cardiology | Pneumology | Nephrology

→ 7 SCIENTIFIC PILLARS

> Interventional imaging and Magnetic Resonance Imaging (MRI) guided High Intensity Focused Ultrasound (HIFU):

to further develop MRI HIFU towards treatment of tumors in particular for the liver and the kidney, as well as breast and prostate from large animals to clinical trials.

> New imaging sequences:

to increase spatial and temporal resolutions, sensitivity, specificity to become more quantitative and to adapt NMR/MRI to biological systems.

> Dynamic Nuclear Polarization (DNP):

to develop new Targeted DNP-Contrast Enhanced MRI for diagnosis through protease spotting.

> Tracers and contrast agents:

to create responsive agents for molecular imaging, using different imaging modalities towards functional imaging (MR, PET and Optical).

> Biological bioimaging markers:

to detect imaging biomarkers used for prediction and diagnosis of patients at risk, for evaluation of disease progression and evaluation of therapeutic interventions.

> Mathematic simulation and modeling:

to compute patient-specific digital models from multimodal imaging data in order to reproduce diseases and treatments *in silico*.

> Cohort imaging methodology:

to implement structural/functional MRI (3T/7T) neuroimaging platform fields dedicated to translational research in the field of age-related disorders and neurodegenerative diseases.

→ 4 MAIN MISSIONS

- To federate the entire scientific community through multidisciplinary projects in the field of medical imaging translational research and raise the international profile of Bordeaux research;
- To develop an area for collaborations with industrialists, laboratories and international partner;
- To accelerate the process of technology transfer;
- To provide students with a range of internationally recognized training courses in medical imaging.

« TRAIL strongly impacts the Bordeaux imaging community by structuring 7 scientific pillars and by organizing the multidisciplinarity between 10 teams from 7 core laboratories. »

Professor Vincent Dousset, TRAIL Director

Preparing the future

2011-2018 Key figures

(see annex A.1 for details)

Research

283
scientists

10
top level research teams

47
funded research projects (6.4 M€)

155
publications quoting TRAIL

12
patents

Training

45
lectures by international speakers

4
community scientific days

20
supported international symposiums

54
Master internships in TRAIL projects

54
Ph.D students in TRAIL projects

Attractiveness

48
international academic collaborations

40
industrial collaborations

13
European projects

14.9 M€
of cofunding (2.1 M€ private)

13
visiting scholars

178
international communications

54
recruitments (PhD, post-doc, engineers, tech.)

Governance

67
steering committees

7
general assemblies

3
board of trustees meetings

2
scientific advisory board meetings

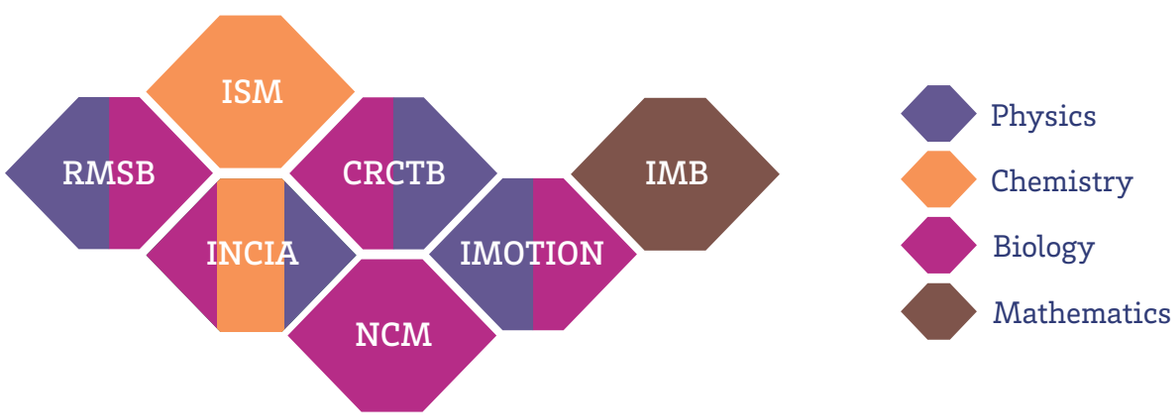
1
mid-period audit from the french research agency

Governance

1.1 CorePartners

TRAIL is a consortium of 7 multidisciplinary units (10 teams) on the same site: imaging clinicians, physicists, biologists, chemists, mathematicians and computer scientists are all assets for developing competitive research.

The Community is composed of 283 persons: researchers, clinicians, post-docs, Ph.D students, engineers and technicians working on complementary themes (see annex A.2 for details).



RMSB:
Center of Magnetic Resonance of Biological Systems

ISM:
Molecular Sciences Institute

Catalysis, Synthesis and Health team
Molecular imaging and photonic team

INCIA:
Aquitaine Institute for Cognitive and Integrative Neuroscience

Neuroimaging and Human Cognition team
Brain Molecular Imaging team

CRCTB:
Cardio-Thoracic Research Center of Bordeaux

Bronchial Remodeling team
Cardiac Electrophysiology team

NCM:
Neurocentre Magendie

Neuro-Glia Interactions team

IMOTION:
Molecular Imaging and Innovative Therapeutics in Oncology

IMB:
Mathematical Institute of Bordeaux

Mathematical Simulation and modelisation team

1.2 Governance boards

The governance of the LabEx TRAIL is formalized by a Consortium Agreement signed by all four institutional trustees (University of Bordeaux, CNRS, INSERM, INP).

BOARD OF TRUSTEES

- 4 members: University of Bordeaux, CNRS, INSERM, INP;
- Role: the Board of Trustees oversees the development of the LabEx, checks the adequacy between objectives and strategy.

DIRECTOR/ANR COORDINATOR

- TRAIL Director is Pr Vincent Dousset; he is the Coordinator of the TRAIL program for the ANR;
- Role: the Director is in charge of the development of the LabEx, the coordination of 7 CorePartners, and the collaboration with all partners; he liaises with the Board of Trustees and IdEx Bordeaux and does a reporting to the ANR, to IdEx Bordeaux and to the Board of Trustees when necessary.

STEERING COMMITTEE

- 7 members: 10 laboratory representatives, 5 thematic axis representatives, 1 international representative and the Director, chairing the Committee (see annex A.3 for details);
- Role: members of the Steering Committee meet monthly to define development strategy, collaborative actions, guidelines of calls for proposals, and to discuss the budget.

WORKPACKAGE COORDINATORS

- 8 Coordinators (see annex A.3 for details);
- Role: Coordinators define scientific themes for calls guidelines, are part of the research project selection process, and are involved in scientific animation.

SCIENTIFIC ADVISORY BOARD

- 4 Members: international medical imaging researchers;
- Role: Members evaluate TRAIL achievements and help the Steering Committee in defining strategy and development actions.

EVALUATION COMMITTEE

- 2 Members: 2 regional scientists independent from TRAIL;
- Role: the Evaluation Committee evaluates scientific projects that were submitted to TRAIL calls and recommends projects to be granted on the basis of external scientific reviews.

1.3 Administrative staff

- The administrative team is composed by the General Manager, Jean-François Bauger, and the Science Communication Manager, Hélène Katz. They are affiliated to the Direction des Grands Projets (DGP-RIPI);
- Role: the administrative team sets up procedures, implements actions, promotes the LabEx, and manages the budget in strong collaboration with the financial teams of the University of Bordeaux.
- The administrative team is accompagnied by RIPI teams in regards to financial monitoring, event organization, creation of graphical charters for communication documents, website redesigning, and benchmarking.

1.4 Monitoring and financial plan

MONITORING

- Developments are monitored by the Steering Committee and the Director, in link with Workpackages Coordinators, the IdEx Bordeaux, and the Trustees.
- The Steering Committee Members met 67 times over the 2011-2018 period. Scientific Advisory Board Members help for global scientific strategy (meetings in 2015 and 2017) and Workpackage Coordinators for calls and scientific animation.
- The Director of TRAIL reports yearly to the National Research Agency, to the Board of Trustees (meetings in 2012, 2016 and 2017), and to the IdEx Bordeaux. Main governance actions are presented to the TRAIL Community during annual General Assemblies.
- The financial team of the IdEx Bordeaux is in charge since 2014 of the management of TRAIL expenses, in deep integration with the TRAIL administrative team.

FINANCIAL PLAN

The financial plan was defined as follows for the 2011-2018 period:

TRAIL OBJECTIVES	STRATEGY	PROGRAM	2011	2012	2013	2014	2015	2016	2017	2018	2011-2018
WORKING ON MAJOR PUBLIC HEALTH ISSUES	Showing importance of TRAIL research to society and scientific community										
DEVELOPING COMPETITIVE RESEARCH	Boosting existing research projects	Doctoral fellowship program	195K€				300K€	400K€			895K€
		Post-doctoral fellowship program			200K€	200K€	100K€	200K€	200K€		900K€
		Research projects consolidation program				220K€	180K€	111K€	50K€	100K€	661K€
	Supporting new research projects	Federative and emerging research program	299K€	1 151K€	694K€	105K€	400K€	688K€	343K€	295K€	3 975K€
	Strategical collective action	MRI time purchase program		57K€			421K€				477K€
FEDERATING THE COMMUNITY AND REINFORCING ATTRACTIVENESS	Governance, scientific animation, attractiveness	Governance (admin. and communication actions, meetings, call reviews, publication costs cofunding), scientific animation, training (scientific event support, summerschools, lectures, mobilities)	41K€	94K€	107K€	122K€	172K€	262K€	161K€	187K€	1 146K€
			535K€	1 302K€	1 001K€	647K€	1 572K€	1 661K€	754K€	582K€	8 054K€

1.5 Support from IdEx Bordeaux

LabEx are scientific pillars of IdEx and the objective of IdEx is to dedicate 80% of its funding to the LabEx perimeter. IdEx accelerates the development of LabEx by helping them to monitor programs, to reinforce attractiveness, and to deploy of cross-disciplinarity research projects.

Reinforcing attractiveness:

- The 2 summerschools supported by TRAIL were also supported by IdEx (2014 Connectomics and 2015 Neurepiomics summerschool);
- TRAIL was granted by IdEx to welcome 9 international scholars;
- TRAIL was granted by IdEx program with fundings for outgoing mobilities to Sherbrooke University (Canada), Aarhus University (Denmark), and Monash University (Australia);
- A doctoral fellow was granted by IdEx in collaboration with Monash University (Australia, 2013-2015, M. Lariviere).

IdEx Bordeaux supports cross-disciplinary research through 'Inter-LabEx Program':

- TRAIL and CPU (Numerical certification and reliability) were granted in 2013 with 134K€ for a neuroimaging data analysis project;
- TRAIL and LabEx BRAIN (Bordeaux Region Aquitaine Initiative for Neurosciences) were granted 146K€ by IdEx Bordeaux in 2014 to develop a new MRI method to assess hippocampal layer (Memo-ms project). CPU co-financed postdoctoral fellow and engineer positions (150K€) for a TRAIL project and BRAIN co-financed the Memos-ms project (120K€).

IdEx Bordeaux and TRAIL have supported the purchase of 3T MRI time for TRAIL research projects developments.

Also, TRAIL built links with other PIA programs (I-Share cohort, OFSEP cohort) and with the IHU LIRYC.

1.6 Mid-period audit by the ANR

TRAIL was audited by the international jury of the National Research Agency in June 2015: "Overall the panel was very impressed by the scientific progress reported by the consortium: it has successful built an impressive collaborative network, potentially positioned to deliver in the future [...]" (see annex A.4 for full evaluation).

Research achievements

2.1 Internal call procedure

The TRAIL strategy is to set up a portfolio of research projects in order to achieve the main objective of translational and multidisciplinary research. Projects are selected through for calls for proposals with international peer-review:

- Emerging calls support new projects looking to fund a proof of concept, to encourage the emergence of scientific breakthroughs. Selected projects are risky but have a high return on investment potential (18 months of funding, up to 50K€);
- Federative calls concern advanced projects seeking to accelerate cross-sectional research, by selecting projects involving teams from several laboratories on transdisciplinary topics (36 months of funding, up to 250K€);
- Doctoral Fellowship and Postdoc calls enable the recruitment of a Doc/Postdoc to extend the development of an already awarded project (24 to 36 months of funding, up to 100K€);
- Open calls concern previously granted projects proposing to broaden and consolidate their research topics (up to 70K€).

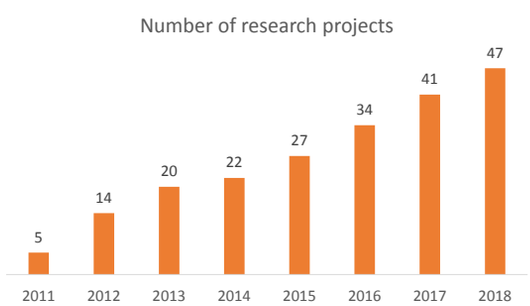
The funding from TRAIL aims at financing human resources costs and running costs. Financial support for equipment is limited to 15 000€ per project. Each submission to a call is analyzed by 2 international scientific reviewers who assess the scientific originality of the project, the quality of the team and of the development plan. Their reviews are given to the Evaluation Committee which recommends projects to be granted, under supervision of the Director of TRAIL.

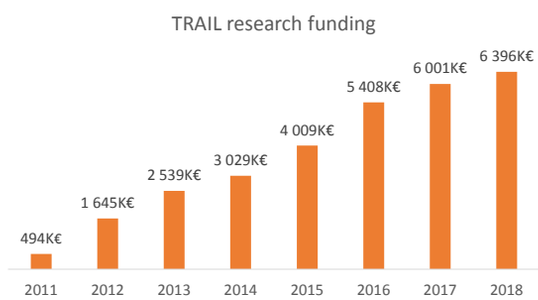
Project leaders report the achievements of research as follows:

- An annual written report describing the scientific developments, recruitments, academic and industrial collaborations, publications, distinctions and awards, dissemination of knowledge, co-funding, expenses;
- An oral scientific presentation during the annual General Assembly to present the project;
- An oral scientific presentation during the annual TRAIL Scientific Day to present research achievements.

From 2011 to 2018, 47 research projects were funded, for a total budget of 6.4M€:

- 2011: 5 federative projects, total budget: 494K€;
- 2012: 4 federative and 5 emerging projects, total budget: 1 151K€;
- 2013: 4 federative projects, 2 emerging projects and 2 Ph.D funding, total budget: 894K€;
- 2014: 2 emerging projects, 4 consolidated projects and 3 PhD funding, total budget: 490K€;
- 2015: 2 federative projects, 3 emerging projects, 3 consolidated projects, 3 Ph.D and 1 Post-Doc funding, total budget: 980K€;
- 2016: 3 federative projects, 4 emerging projects, 2 consolidated projects, 4 Ph.D funding and 2 Post-Doc funding, total budget: 1 399K€,
- 2017: 7 emerging projects, 1 consolidated project and 2 Post-Doc funding, total budget: 592K€,
- 2018: 6 emerging and 2 consolidated projects, total budget: 395K€.





	Interventional imaging and MRI guided HIFU	New imaging sequences	DNP	Tracers & contrast agents	Biological Bio-imaging markers	Mathema-tic simu-lation and modeling	Cohort imaging methodology		
Neurology		179 600 €		98 800 €	1 506 231 €	96 724 €	572 330 €	2 453 685 €	38%
Oncology	80 000 €	45 850 €	532 500 €	932 500 €	185 000 €	530 000 €		2 305 850 €	36%
Cardiology	400 000 €	250 000 €		235 000 €	345 000 €			1 230 000 €	19%
Pneumology					40 000 €	35 000 €	234 448 €	309 448 €	5%
Nephrology					47 000 €	50 000 €		97 000 €	2%
	480 000 €	475 450 €	532 500 €	1 266 300 €	2 123 231 €	711 724 €	806 778 €	6 395 983 €	100%
	8%	7%	8%	20%	33%	11%	13%	100%	

2.2 Research portfolio

The input of the 47 TRAIL granted projects made the cement to build translational research, and gave the capability to achieve research from the most basic to clinical application and cohort imaging in link with hospitals.

MOD
Mathematical modeling of the response to antiangiogenic drugs via medical imaging,
2013, 380 000 € (onco)

NEKOMRI
MRI sequence for bronchial wall segmentation and analysis,
2014, 35 000 € (pneumo)

ARM
Automatic assessment of Radiofrequency ablation Margins,
2016, 150 000 € (onco)

HETEROMRMAP
MR mapping of renal function heterogeneity to characterize parenchymal nephropathies,
2016, 50 000 € (nephro)

DEEP STROKE
DEEP Learning for prediction of long-term motor impairment after STROKE,
2017, 49 924 € (neuro)

BIGDATABRAIN
To develop a new generation of quantitative MRI analysis method to cope with the rise of BigData in neuroimaging,
2018, 46 800 € (neuro)

TRAIL&TRACKS
Atlasing white matter tracts,
2011, 97 500 € (neuro)

ABACI
Automated Brain anatomy softwares for cohort imaging,
2012, 314 830 € (neuro)

ACTE
Cognitive training and brain functional connectivity,
2012, 130 000 € (neuro)

COBRASCAN
Quantitative computed tomography for phenotyping COPD within COBRA cohort,
2013, 234 448 € (pneumo)

ADPP
Brain Topology of AD presymptomatic phase,
2015, 30 000 € (neuro)

HIFU
Alteration of the blood brain barrier induced by HIFU,
2012, 30 000 € (onco)

MRGHIFU
Methodological developments for applications of HIFU in cardiology and oncology,
2013, 400 000 € (cardio-onco)

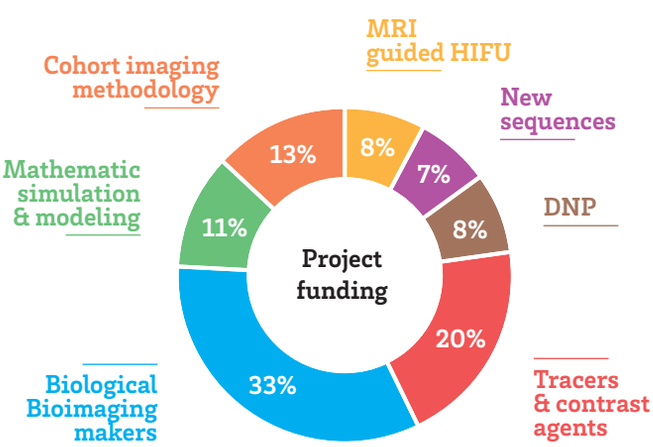
NEMHO
NanoEmulsion for Magnetic Hyperthermia in Oncology,
2017, 50 000 € (onco)

HR-DTI
Developping High-Resolution DTI method,
2012, 130 000 € (neuro)

NEWFISP
Improving MRI resolution to correctly MRI-diagnose cardiac pathologies and metastases,
2012, 250 000 € (cardio-onco)

MDMRI
Methodological Developments in High Spatial/Angular-resolution DTI for *ex-vivo* validation of tractography,
2016, 49 600 € (neuro)

WHOBO-MP2RAGE
Whole body ultra-fast 3D T1 mapping with non-cartesian MP2RAGE sequences,
2017, 45 850 € (onco)



TRAILDNP
To improve *in vivo* DNP in mice at 0.2T,
2011, 242 500 € (neuro)

ONCOFLUX
Metabolic flux MR imaging in tumors,
2013, 240 000 € (onco)

INSIGHT
Implanted NMR microprobes for metabolic insights,
2018, 50 000 € (onco)

INNES
Lactate and neuronal metabolism,
2011, 300 579 € (neuro)

SCICOG&REACTIV
Imaging biomarker in MS,
2011, 130 000 € (neuro)

IBIO-NI
New Imaging Biomarkers of neuroinflammation such as MS,
2012, 310 654 € (neuro)

MIMATHUMAB
Molecular Imaging of Atheroma with Human Antibody,
2012, 295 000 € (cardio)

TRANSFEAR
Cerebral structure changes involved in pathological fear recovery,
2012, 130 000 € (neuro)

BIOPSYPROSTAPROBE
Antibody-based fluorescence probe for biopsy guidance of prostate cancer,
2014, 185 000 € (onco)

IPALICA
Inflammatory pathways leading to intracranial aneurysm growth,
2015, 35 000 € (neuro)

TBI
Longterm neurovascular unit changes after mild traumatic brain injury: potential biomarker & Vasc-TBI,
2015, 250 000 € (neuro)

GMCOG
Grey matters! Toward a better understanding of grey matter alteration and cognitive deficit associated with multiple sclerosis,
2016, 200 000 € (neuro)

STEAMRI
Whole lung oxygen-enhanced imaging in humains using MRI,
2016, 40 000 € (pneumo)

DIFFIR
Ex vivo DIFFusion-weighted MRI of renal Ischemia Reperfusion injury,
2017, 47 000 € (nephro)

BRAIN-RESV
Neuroprotective effect of resveratrol in hypoxic ischemic rat pups: how supplementation of the pregnant female could impact brain lesion of the pups ?,
2017, 50 000 € (neuro)

MEMIM
Multiphoton endomicroscopy for metabolic imaging of macrophages in atherosclerosis,
2017, 50 000 € (cardio)

IMAGANIV
Imaging activity of neurons *in vivo*,
2018, 50 000 € (neuro)

REMOD
Role of AQP4 in extracellular space and tissue remodeling after juvenile Traumatic Brain Injury: From the meso to the nanoscale,
2018, 50 000 € (neuro)

PIAF
18F for PET-imaging angiogenesis,
2011, 164 000 € (onco)

IMMELAPT
Detecting tumors using SPECT molecular imaging and optimized aptamers,
2012, 250 000 € (onco)

PRITOR
NeuroPeptide Receptors Imaging for TumOR Targeting,
2013, 90 000 € (onco)

SUPSIFLU
Supported Silyl Fluorination,
2013, 130 000 € (onco)

NEPMIP
NanoEmulsion Platform for Magnetic Particle Imaging,
2015, 85 000 € (cardio)

TARGLIN
Imaging siRNA targeting of glioblastoma using peptide-based nanoparticules,
2015, 150 000 € (onco)

FITTING
18F-Bioorthogonal probe for imaging traumatic brain injury glyco-biomarkers,
2016, 98 800 € (neuro)

NANOMULTIMAG
Smart multimodal nanoprobes for MRI/MPI/NIRF imaging with magneto/optical contrast agents for atheroma plaque targeting,
2016, 150 000 € (cardio)

INNOVATHER
Innovative ways to enhance radiopharmaceutical therapy,
2017, 50 000€ (onco)

BIMOP
Bimodal Imaging fluorescent/PET Probes for *in vivo* imaging, ***2018, 50 000€ (onco)***

PREXPULSE
Comparison of conventional X-Ray images with laser generated X-Ray images using new multimodal contrast agents
2018, 50 000€ (onco)

MRGHIFU

Methodological developments for preclinical and clinical applications of MR guided HIFU

Bruno Quesson | Oncology-cardiology | 2013 | TRAIL funding: 400 000 €

CorePartner Bordeaux Cardio-Thoracic Research Center (CRCTB, U1045)

The project aims at developing MRI guided HIFU in several preclinical and clinical applications. This requires the development of innovative MRI monitoring methods (WP1), new sonication strategies (WP2), preclinical applications (WP3) and clinical translation for the treatment of breast cancer (WP4).

- WP1: new acquisition methods have been developed to further accelerate image acquisition through the use of Simultaneous MultiSlice acquisition combined with EPI and parallel imaging. Such technique was applied for both thermometry and imaging of the displacement in brain and liver (Bour, ISMRM 2018 and Ozenne, IMSMR 2018, manuscripts in preparation). Shear wave MRI images were also developed (Vappou, Phys Med Boil 2018).

- WP2: MR-ARFI methods: A 3D ultrasound-based target tracking was developed allowing to follow respiration and steer the focal point accordingly. This was validated *in vivo* in large animal model during multi-slice rapid thermometry (Bour, Int J Hyperthermia 2018).

- WP3: MRgHIFU experiments using the preclinical IGT system installed in the 9.4T Bruker MRI at IHU Liryc started July 2018. Focal Heating has been successfully achieved on excised muscle. First experiment using mouse has been performed September 2018 and several technical issues have been identified and fixed. Final steps of the chemical synthesis of thermos-sensitive nanoparticules is ongoing.

- WP4: MR guided HIFU for the clinical treatment of breast cancer has been initiated. The 2 first patients have been treated mid-June with progressive increase in energy deposition and a third one in November with successive energy deposition in several locations covering the tumour. The system is functional and shows hypoperfused region after the treatment in the third patient.

The project shows significant advances on each WP, including clinical application. These results show promising opportunities for the develomment of several clinical applications in neurology, cardiology and oncology.

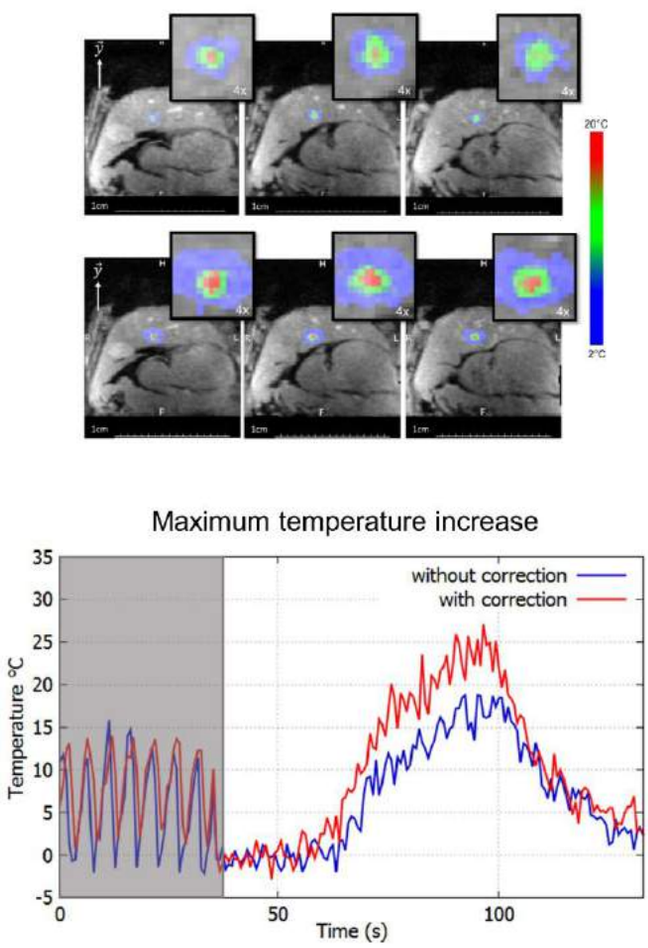


Figure 1. 3D ultrasound motion tracking for HIFU ablation in the liver of pig under real-time MRI thermometry. Left: MRI tempertaure images without (top) and with (bottom) target tracking. Right: temperature evolution at the focus without and with target tracking. (adapted from Bour, Int J hyperthermia 2018).

list of publications p.74

NEMHO

NanoEmulsion for Magnetic Hyperthermia in Oncology

Sylvie Crauste-Manciet Oncology 2017 TRAIL funding: 50 000 €

CorePartner Molecular IMaging and Innovative Therapeutics In Oncology (IMOTION, EA7435)

Hyperthermia cancer therapy appears as a promising alternative and complementary treatment to chemotherapies or radiotherapy, suffering sometimes from a lack of performance. Magnetic nanoparticles constitute a valuable tool to generate local heating inside tumours to kill malignant cells under an appropriate magnetic field. Our objective is to design improved biocompatible nanoformulations able to be administered by IV route for destroying cancer tumors by focused heating using magnetic field.

The first step was the successful formulation of the system developed which was a water-in-oil nanoemulsions bearing iron nanoparticles (superparamagnetic iron oxide nanoparticles: SPION) inside the oil-core and able to be heated when stimulated by a magnetic field [Magnetoactivable Thermogenic Nanoparticles (MTN)]. To obtain the best heating properties, the oil-phase ratio was optimized to load a larger number of magnetic particles and to benefit from the better thermic properties of oil compared to water. Formulation including FDA approved excipients containing 30 % of oil and 3.8 % of surfactants presented proper physicochemical properties with a mean droplets diameter of 184.1 nm, a polydispersity index (PdI) of 0.085 and a zeta potential of -47.7 mV. *In vitro* heating properties of the best formulation showed encouraging results of the nanoemulsion containing 30 % of oil and were increased compared to the one containing 20 % of oil, with a temperature raise of 9.4°C after application of magnetic field at 473.5 kHz for 5 minutes. The impact of the size of the iron oxide nanoparticles was also shown on the heating properties and encourages to use larger particles.

Perspectives are to improve the size of the nanoparticle and to assess efficiency of the system on the tumor mice model.

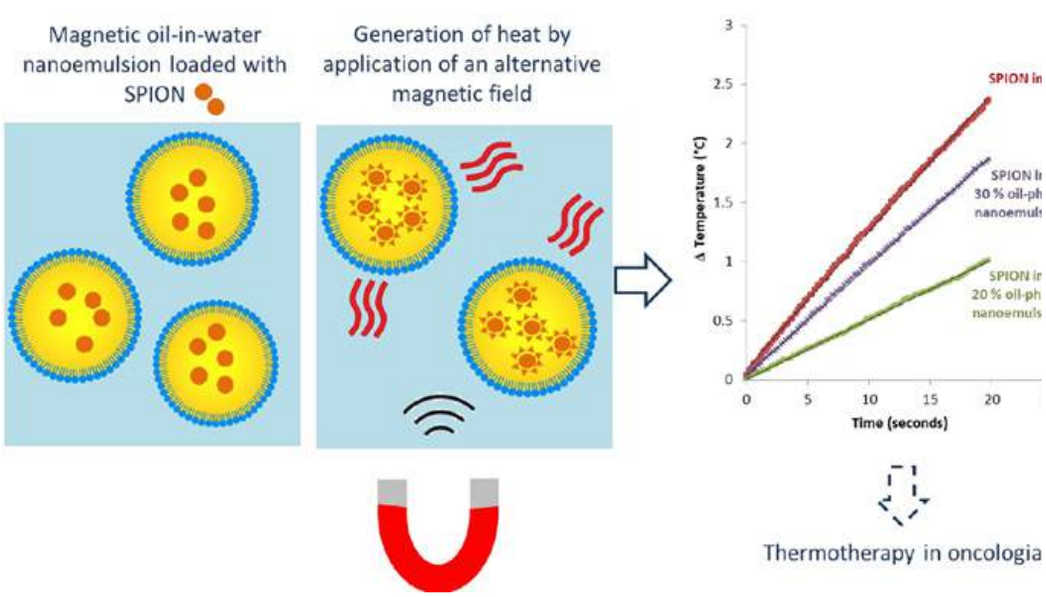


Figure 1. Scheme of Magnetoactivable nanoemulsion and first results on the heating properties.

HIFU

High-Intensity Focused Ultrasound

Klaus Petry | Oncology | 2012 | TRAIL funding: 30 000 €

CorePartner Neuroinflammation, imaging and therapy of multiple sclerosis (U1049)

Passage of the blood brain barrier (BBB) is essential for effective drug delivery into the central nervous system. High-Intensity Focused Ultrasound (HIFU) has shown promising for non-invasive and focal opening of the BBB. Very limited, however, is the understanding of the underlying cellular and molecular mechanisms at the BBB, in particular of the endothelial cells being involved in such HIFU induced opening and eventually induced unwanted side effects. By *in vitro* studies of the BBB model (hCMEC/D3 cell line) under HIFU we will investigate the cellular and molecular dependent transports (clathrin, caveolin, tight junctions) and their specific inhibitions. *In vivo* studies of focally HIFU induced BBB alteration and histopathological evaluation and molecular expression studies of endothelial cells will validate the defined activated cellular and molecular transports. Histopathological studies will evaluate eventual non desired side effects of BBB opening and in adjacent CNS parenchyma due to the focal HIFU application. A portable HIFU system in application to small cell cultures and *in vivo* studies has been locally developed in partnership with Image Guided Therapy SA (Pessac, France) and in collaboration with TRAIL.

HRDTI

High Resolution DTI method

Bassem Hiba | Neurology | 2012 | TRAIL funding: 130 000 €

CorePartner Center of Magnetic Resonance of Biological Systems (CRMSB, UMR5536)

Diffusion MRI (dMRI) is the unique method allowing to investigate non-invasively the cerebral microstructure and connectivity in normal and abnormal brains. A major limitation of this technique is the poor quality of dMRI data that restricts its use in some crucial applications such as neurosurgery. This poor data quality is due to the dMRI inherently low signal-to-noise ratio and to a high sensitivity to different artefacts. We hypothesize that the development of a robust acquisition method, providing high-resolution/artefact-free data could largely increase the diagnostic and prognostic capacities of dMRI and then increase its use and effectiveness for medical and neuroscientific applications.

In this project, we have developed a super-resolution algorithm expected to enhance the dMRI data quality (A). More recently, we have developed in collaboration with SIEMENS HEALTHCARE a dMRI acquisition based on the 3D multi-shot echo planar imaging (3D-msEPI). This method allowed us to acquire in an immobilized brain of macaque, for the first time at 3T, dMRI data with an isotropic resolution of 0.5 mm (B).

In 2018, we have developed a robust strategy to compensate the elastic deformations of brain tissues inside the skull. This strategy enhanced significantly the quality of the dMRI data and provide diffusion weighted images of anesthetized macaque brain with an isotropic spatial resolution up to 300 µm.

The aim of the next step of this work is to transfer the developed technology for human applications. To reach this objective, we need to compensate the random rigid body motion of the head during the MRI scan. Achille Teillac, a post-doctorant funded by TRAIL, will be involved for this step in 2019. This development is planned until 2020.

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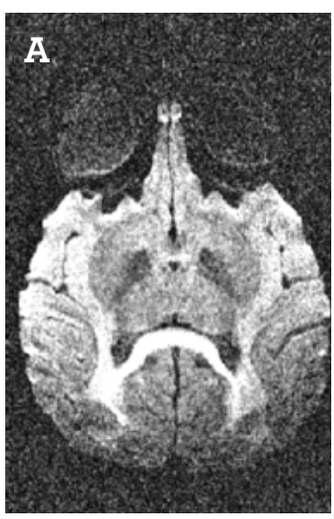

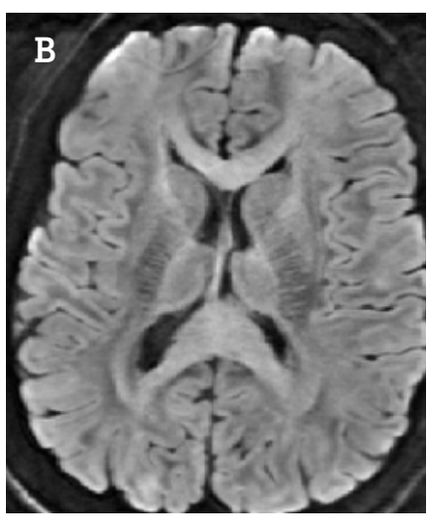

MDMRI

Methodological Developments in High Spatial/Angular-resolution DTI for *ex-vivo* validation of tractography

Bassem Hiba Neurology 2016 TRAIL funding: 49 600 €

CorePartner Aquitaine Institute of Cognitive and Integrative Neurosciences (INCIA, UMR5287)

Tractography based on diffusion-MRI is a unique technique to analyze non-invasively the anatomical connectivity of brain white matter. This technique is widely used in neuroscience and has a high potential for neurosurgery, but still needs to be optimized and validated.

To date the main study that has investigated the capacity of tractography to capture the connectivity revealed by tract tracing showed very poor correlation over medium to long distances. That study looked at the correlation of tract tracing data with tractography data from different brains. Because there is a difference in order of magnitude in connectivity weights for a given connection between individual brains, we hypothesize that the correlation can be improved by carrying out tractography measures and tracing experiments in the same brain as in this proposal.

For the first time, this project aims to compare the white matter connectivity revealed by tractography and by tract tracing in the same brain. This project will provide unique data allowing not only to validate tractography results but also to optimize tractography methods.

5 fixed brains with 12 tract tracing injections were scanned using a home-built very high resolution dMRI pulse sequence (spatial resolution up to 200 µm). Brain connectivity was assessed using tract tracing for all the brains and all the injections (12 injections and 120 volumes of interst). dMRI data have been pre-processed and in 2018 a specific algorithm has been developed in order to perform a very high quality tissue classification and automatic delineation of 120 volumes of interest all over the brain.

We have recently set-up the state-of-art methods of tractography and started to assess the tractography-based connectivity of the 12 white-matter networks injected for track-tracing. In the following 18 months, we will analyze brain connectivity revealed by 3 different tractography methods and two seeding strategies. These results will be compared to the ground truth of the connectivity obtained using track-tracing In order to produce two scientific rapports.

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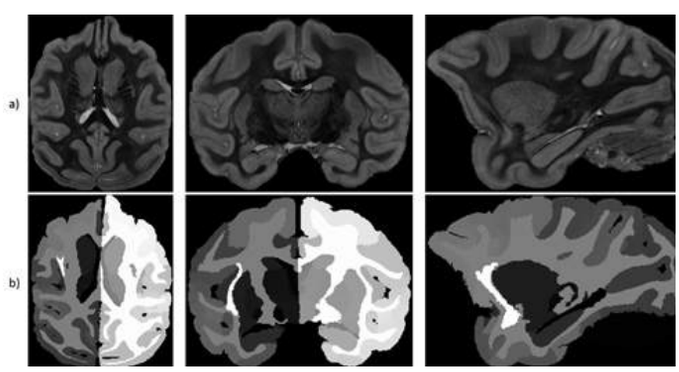

Figure 1. a) Axial, coronal and sagittal views of Diffusion Tensor Imaging (DTI) λ_3 anatomical volume used for segmentation and cortical parcellation. b) Corresponding manually corrected cortical segmentation used for the tractography and tract-tracing comparison.

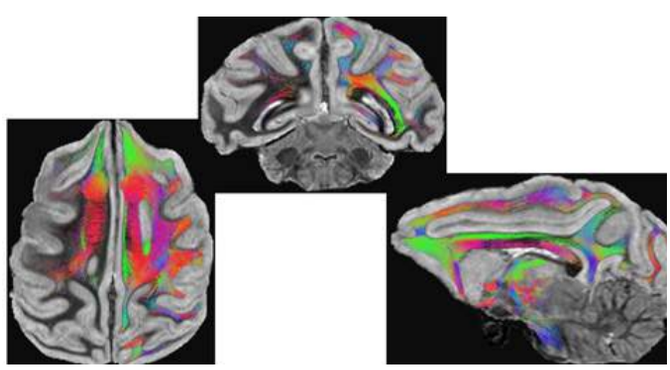

Figure 2. Axial, coronal and sagittal views of a tractogram generated to study the left hemisphere claustrum connectivity merged with the λ_3 anatomical volume.

NEWFISP

Improving MRI resolution to correctly MRI-diagnose cardiac pathologies and metastases

Sylvain Miraux | Cardiology | 2012 | TRAIL funding: 250 000 €

CorePartner Center of Magnetic Resonance of Biological Systems (CRMSB, UMR5536)

The goal of the NewFISP project is to develop original MRI sequences in order to improve the spatial and temporal resolutions of images, to acquire data faster and to obtain quantitative information.

These sequences are intended to be applied in the field of cardiovascular physiology and oncology, in small animals and humans.

During this last year, we continued the methodological developments in radial imaging, especially the ultra-short echo time approach (UTE). A sequence was developed for self-gated 4D Flow MR imaging of small animals. In collaboration with IMB and Baudouin Denis de Senneville, phase unwrapping algorithms were tested on these data. They enabled to obtain better spatial or temporal informations of the flow velocity in the aortic arch.

In parallel, a detailed study of the respiratory movement, coupled with a new algorithm of extrapolation of cardiac signal, made it possible to obtain the first 5 Dimensions cardiac images in mice. These results are part of the Ph.D work of Colleen Cardiet (TRAIL funding). These methods are also in the process of being implemented on a Siemens clinical MRI system.

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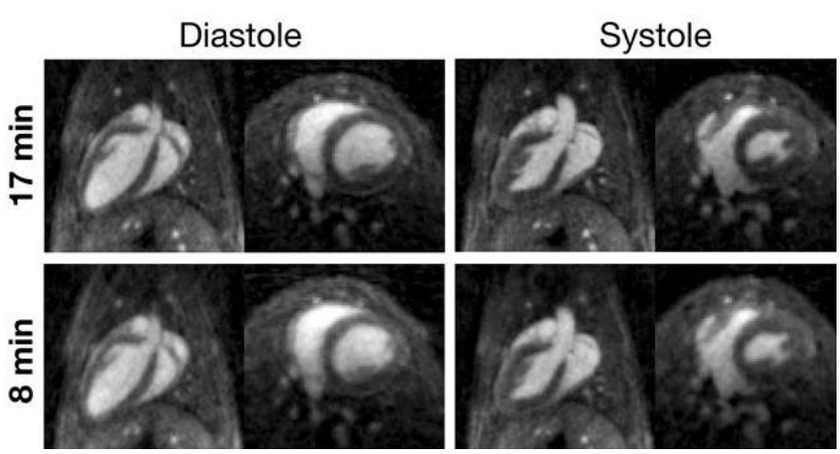

Figure 1. Extracted mouse cardiac images from a 3D-cine data set obtained in 17 minutes or in 8 minutes with an algorithm to optimize the use of all the k-space data, even the ones acquired during respiration motion.

WHOBO-MP2RAGE

Whole body ultra-fast 3D T1 mapping with non-cartesian MP2RAGE sequences

E. Ribot & A. Trotier

Oncology

2017

TRAIL funding: 45 850 €

CorePartner Center of Magnetic Resonance of Biological Systems (CRMSB, UMR5536)

The "Magnetization-Prepared 2 Rapid Gradient Echo" (MP2RAGE) sequence is of great clinical interest because of the high contrasts it generates at high magnetic fields. It is indeed used in neuro-imaging for the segmentation of white and gray matters. It also enables to obtain longitudinal relaxation time (T1) maps in 3 dimensions (3D) relatively quickly (10 min) compared to other standard sequences. This quantitative information is necessary for the monitoring of pathologies. Our goal is to extend its application to pre-clinic and clinic routine and to whole-body imaging. The major difficulties lie in the acquisition time, still very long, and the sensitivity of the sequence to motion artifacts. The corresponding methodological developments were first made on a preclinical scanner to image mice.

First, we modified the Cartesian encoding of the sequence using a variable density Poisson distribution. This enabled to drastically accelerate acquisition time through the combination with the Compressed Sensing technique (collab. with S. Rappachi at the CRMBM UMR7339 CNRS - Univ. Aix-Marseille). 3D T1 maps of mouse brains were thus obtained in <1 min. This development also enabled to measure T1 of mouse-bearing brain metastases, at an early growth stage, when their volumes were still <0.05 mm^3. These improvements are now published in the "Magnetic Resonance in Medicine" journal. Siemens Healthcare has shown its interest in transferring this methodology to a clinical scanner.

In parallel, a radial encoding has been developed to replace the standard Cartesian encoding of the sequence. 3D T1 maps of the mouse abdomen were obtained with high spatial resolutions (195 µm isotropic), without motion artifact, and without synchronizing the acquisition with animal's breathing. Hepatic metastases were detected and characterized over time. Differences in T1 between metastases developing within the same animal and within metastases were measured. These results are under review in the "European Radiology" journal.

In conclusion, we developed new versions of the MP2RAGE sequence allowing its application on the whole body of the mouse. The end of the project will focus on the transfer of these two sequences to a 3T scanner.

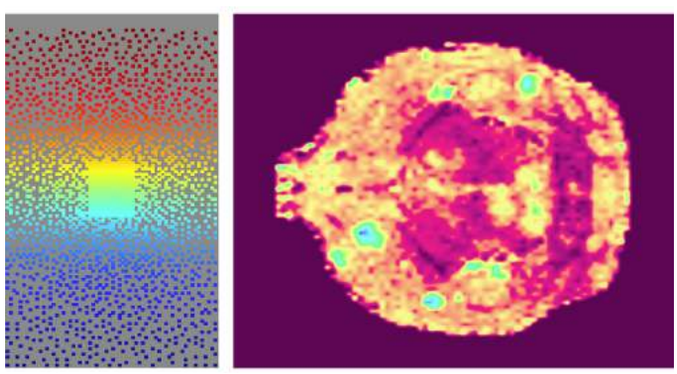

Figure 1. Representation of the encoding using a variable density Poisson distribution of the echoes (left). This encoding was used for the two GRE block of the MP2RAGE sequence, enabling to obtain a 3D T1 map (right) of the mouse brain in less than 1 minute. Breast cancer-derived brain metastases have longer T1 (green areas) than the surrounding healthy brain tissue.

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INSIGHT

Implanted NMR microprobes for metabolic insights

Yannick Crémillieux | Oncology-neurology | 2018 | TRAIL funding: 50 000 €

CorePartner Institute of Molecular Sciences (ISM, UMR5255)

In a general way, the preclinical and clinical applications of implantable microsensors have been increasing rapidly in the last decades in numerous biological and clinical domains. The applications include microsensors (pressure, glucose...), drug delivery or monitoring (insulin, anti-tumoral agents...), stimulators (cardiac, deep brain stimulation, optogenetics...). Despite the variety and wealth of biological information that can be obtained through NMR (nuclear magnetic resonance), the use of implanted NMR microsensors (i.e. microcoils) still remains a relatively unexplored field of research, without emerging or significant biomedical applications.

The main objective of the INSIGHT project is to develop and implement technological solutions to address the challenging and unresolved issues of *in vivo* implantation of efficient and minimally invasive NMR microprobes. Highly sensitive implanted NMR microprobes can contribute and benefit to many scientific and medical aspects of biomedical MRI and MRS (magnetic resonance imaging and spectroscopy). The very high sensitivity increase when using microcoil can be exploited for the profiling (detection, quantification) of biological chemical species. Hence, brain metabolism can be studied at submillimeter level, opening new perspectives for the investigation of brain in physio-pathological conditions, occurring in numerous neurodegenerative pathologies (Alzheimer's disease, Huntington's disease, Parkinson's disease) or following stroke. Similarly, tumor cells exhibit abnormal metabolism. Of note, such pathologies are not restricted to the brain but can concern any tissues or organs accessible to NMR microprobes such as liver, breast, lungs. During the INSIGHT project, some of these applications will be explored in animal models with the aim to establish a cornerstone of *in vivo* NMR with implanted microsensors. Beyond these preliminary *in vitro* and *in vivo* preclinical studies, the objective is to collect data and technically prepare the applicability of the approach for human applications for pathologies justifying minimally invasive implantation of NMR microsensors.

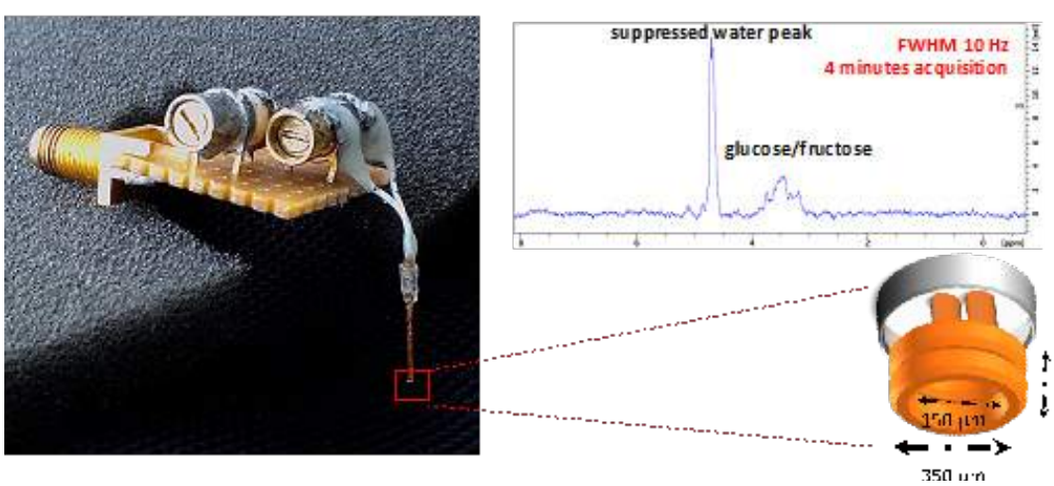

Figure 1. Implantable NMR microprobe (350 microns diameter). The NMR spectrum, obtained in grape berry, displays signal from glucose and fructose.

ONCOFLUX

Metabolic flux MR imaging in tumors

Yannick Crémillieux Oncology 2013 TRAIL funding: 240 000 €

CorePartner Center of Magnetic Resonance of Biological Systems (CRMSB, UMR5536)

Microdialysis is a valuable sampling tool for the monitoring of extracellular small molecules and metabolite concentration in brain. The technique has been widely applied for the investigation of brain energy metabolism in health and disease. The metabolite profiling of the dialysate fluid using NMR is performed remotely from the subjects, rendering lengthy analytical protocols (tens of minutes to hours) and preventing from investigating real-time metabolic changes in dialysate composition. Recently, we reported the feasibility of using an NMR microprobe for enhancing the NMR detection sensitivity on a small (2 µL) dialysate volume and for performing online NMR quantitative assay of extracellular brain metabolites. To completely eliminate the sample preparation and minimize the dialysate transit time, the microcoil is immediately placed at the outlet of the microdialysis probe, enabling for an immediate analysis of the dialysate. The LOD (limit of detection) per unit time of the proton-tuned NMR microcoil is equal to 0.37 nmol.√min, corresponding to metabolite concentration of 200 µM in the dialysate. The variations of lactate concentration in the brain dialysate have been monitored in healthy and glioma-bearing rats. NMR acquisitions were performed in a pre-clinical MRI scanner and the MR spectra were continuously and in real-time updated while the brain perfusate was flowing. Physiological variations in lactate concentration were measured during neuronal activation (whisker barrel cortex S1BF) in healthy animals and during the administration of LDH inhibitors in glioma-bearing animals. In the absence of substances (lipids, macromolecules) interfering with the lactate methyl peak and with the high detection sensitivity of the NMR microcoil, the variations of lactate concentration were unambiguous determined, revealing the dynamic changes in extracellular lactate concentration during neuronal activation and during the administration of LDH-inhibiting drugs.

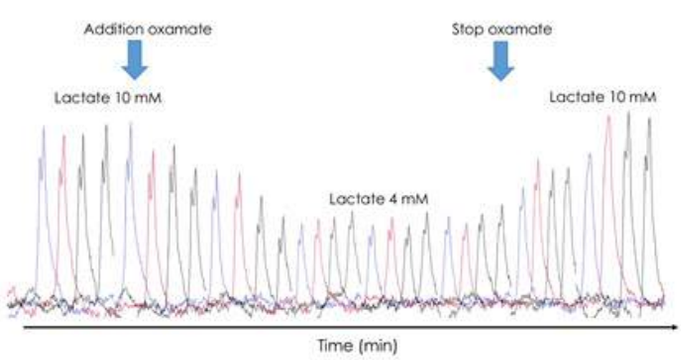

Figure 1. Online MRS monitoring of lactate production in tumor during administration of LDH inhibitor, oxamate.

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TRAILDNP

In vivo DNP in mice at 0.2T

Eric Thiaudière

Neurology

2011

TRAIL funding: 242 500 €

CorePartner Center of Magnetic Resonance of Biological Systems (CRMSB, UMR5536)

Non-invasive early diagnosis of protease-associated diseases is a challenging issue to-date. Both innovative imaging methods and specific probes are to be designed to reach molecular imaging of proteolysis *in vivo*. In this project, it is aimed to develop Overhauser-enhanced Magnetic Resonance imaging (OMRI) in order to overcome MRI low sensitivity and to use novel chemical OMRI-probes to bring specificity to protease detection by OMRI, especially in the case of pulmonary diseases.

It was shown in 2018 that a new radical probe with an Electron Paramagnetic Resonance (EPR) spectrum that can be shifted upon specific proteolysis by neutrophil elastase can be used for efficient elastase detection, either using EPR or OMRI. Moreover, *ex vivo* pulmonary samples of lung-infected mice gave significant OMRI effect with the new radical probe, thus demonstrating the ability of neutrophil elastase detection in biological samples.

The next step is to investigate the ability of OMRI to properly detect and localize lung inflammation in living mice through neutrophil elastase assessment. Such molecular imaging of proteolysis would be of great help in the future for early diagnosis of lung diseases involving inflammation.

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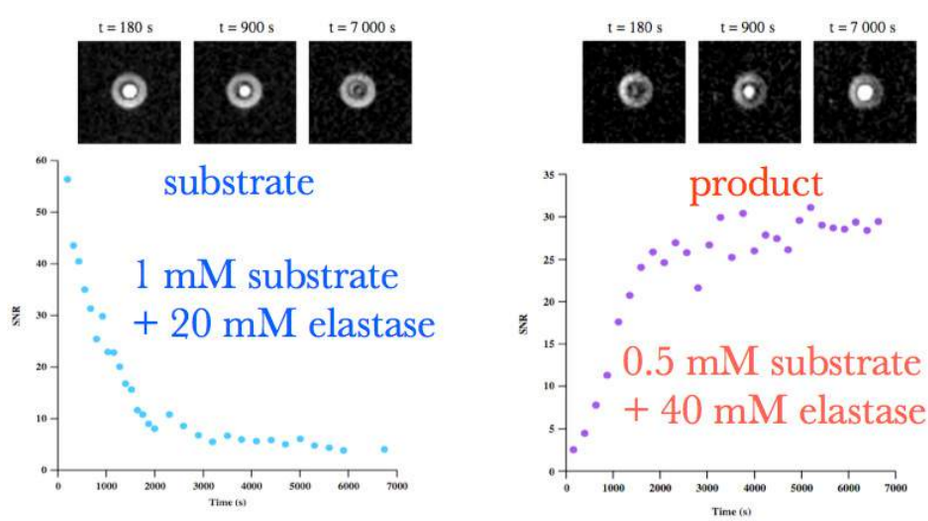

Figure 1. Overhauser-Enhanced imaging (OMRI) of proteolysis of radical substrate of elastase. (LEFT) Substrate hydrolysis by elastase. (RIGHT) Product formation. In images, the central part of the sample is illuminated if Overhauser enhancement occurs. The plots diplay the signal decrease (or increase) upon substrate degradation (or product formation).

BIMOP

Bimodal Imaging fluorescent/PET Probes for *in vivo* imaging

Magali Szlosek

Oncology

2018

TRAIL funding: 48 500 €

CorePartner Institute of Molecular Sciences (ISM, UMR5255)

The development of new radiotracers for PET (Positron Emission Tomography) imaging has experienced an enormous progress due to its specificity and sensitivity in the visualization of target tissues. However, PET alone displays a limited spatial resolution of 1–3 mm in clinical practice and also is not able to allow a morphological correlation of the tracer accumulation which is however especially crucial in case of tumor diagnosis, localization, and staging. Thus, almost all clinical PET systems are combinations of PET and computed tomography (CT) systems, integrating the strengths of both modalities. Despite these favorable properties of PET/CT systems, these modalities exhibit certain limitations: the resection of the tumor mass is difficult due to the intricate intraoperative identification of tumor margins and small metastases. Additionally, the identification of the sentinel lymph node, which is often resected for histology, is not trivial. For this purpose, a combined bimodal imaging consisting of an initial PET scan with a high tissue penetration range to identify and localize tumor lesions throughout the body and a subsequent intraoperative optical imaging (OI) in order to identify tumor margins and infected lymph nodes can result in a significant clinical improvement.

The idea is to design an original bimodal PET(18F)/OI probe for, initially, αvβ3 integrins imaging, as a proof of concept. To do that, we use the CTV core as template, able to wear the two imaging modalities and the molecular specificity by the presence of one or two RGD units. Since the beginning of the Ph.D student work, in October, the synthesis of the first probe is currently underway via a convergent and modular strategy of synthesis based on the preparation of main types of building blocks (CTV+ Fluo / RGD/ aryl-silanes), which are organized, around the CTV based template. Once the first tracer will be obtained, its fluorescence properties and its specificity *in vitro* will be evaluated.

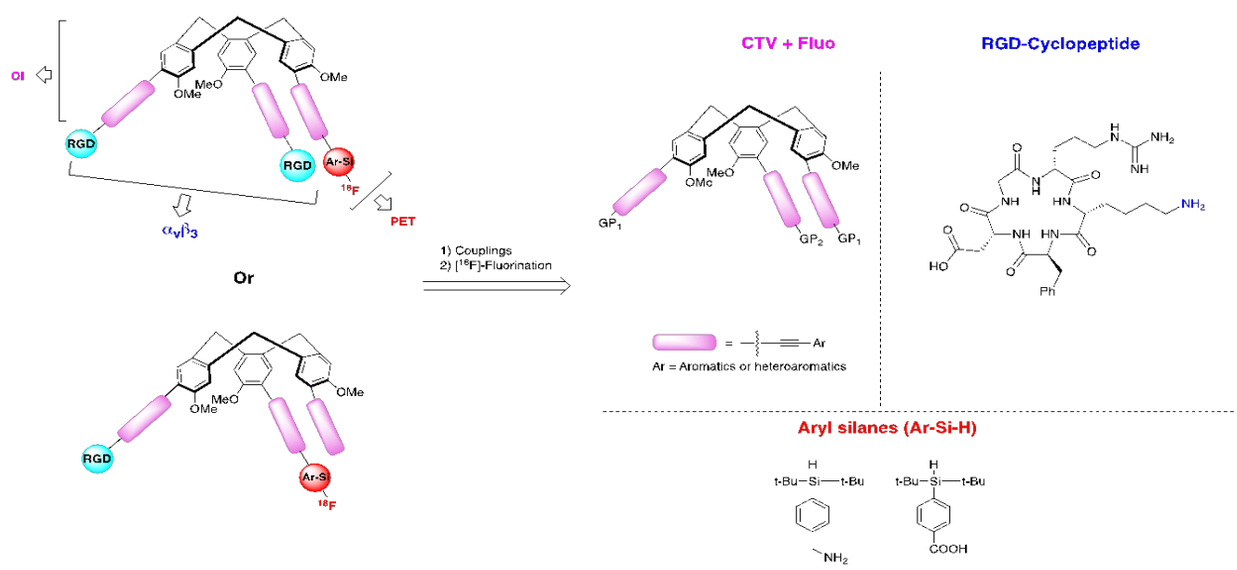

Figure 1. Toward a bimodal PET/OI RGD probe: the pieces of the puzzle.

FITTING

18F-Bioorthogonal probe for imaging traumatic brain injury glyco-biomarkers

Frédéric Friscourt Neurology 2016 TRAIL funding: 98 800 €

CorePartner Aquitaine Institute of Cognitive and Integrative Neurosciences (INCIA, UMR5287)

Traumatic brain injury (TBI) is a major public health issue and represents the leading cause of disability and death in Europe including France among young adults and children. Unfortunately, mild TBI is highly difficult to detect clinically using traditional neuroimaging techniques. Therefore, there is an important societal need to have new biomarkers to follow over the long-term the evolution of the injury after the initial trauma.

In this context, the surfaces of eukaryotic cells are covered with complex glycans that participate in a variety of physiological processes, including cell adhesion and cell-cell interactions. In the brain, polysialic acid (PSA) conjugates have been identified as key players in health of the nervous system. Imaging PSA glycoconjugates would deepen our understanding of cell surface neuroglycans functions and allow us to follow brain remodeling overtime due to traumatic brain injury and lead to potential novel diagnostic tools.

Imaging complex glycans have been historically a challenge due to the lack of specific biochemical tools. Recently, the metabolic oligosaccharide engineering (MOE) technology combined with bioorthogonal chemical ligations has elegantly allowed the visualization of various glycoconjugates in living cells.

The project aims at: 1) validating that PSA can be used as a TBI biomarker using the MOE technology and 2) in order to enable *in vivo* detection of PSA (translational application), a radio-bioorthogonal probe will be developed for PET imaging.

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IMMELAPT

SPECT molecular imaging and optimized aptamers for tumor detection

Jean-Jacques Toulmé | Oncology | 2012 | TRAIL funding: 250 000 €

CorePartner Aquitaine Institute of Cognitive and Integrative Neurosciences (INCIA, UMR5287)

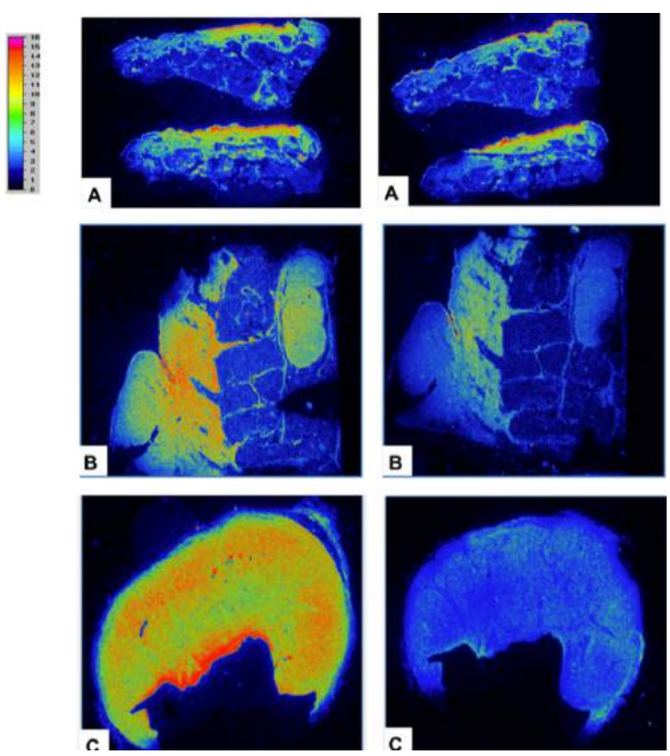

Figure 1. Comparison of the results obtained by radiolabeling of representative tumor tissue sections with ^{111}In-DOTA-F3B aptamer (left image) and ^{111}In-DOTA-control sequence (right image). The difference of activity seems to increase in a tumor grade-dependent manner. (A) Lentigo malignant melanoma, (B) Nodular melanoma, (C) Mostly metastatic node.

The ImMelApt project took advantage of the potential of aptamers for recognizing a target of interest and aims at bringing an innovative answer to the need for imaging tumors *in vivo*. Starting from an aptamer we previously raised against the human MMP-9 -a protein that is overexpressed in tumors and is capable of degrading extra cellular matrix components, thus permitting cancer cell migration. We i) synthesized and characterized several derivatives of this aptamer, ii) converted them into imaging probes, with different modalities, iii) imaged human melanomas *ex vivo*. We were able to evaluate the biodistribution of our probe *ex-vivo* and *in-vivo* on melanoma models (Kryza et al. PLoS One, 2016, 11(2) : e0149387), demonstrating a good specificity of our aptamer probes. Further studies would have required the synthesis of nanoparticle-aptamers in order to increase their blood persistence and tumour uptake.

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INNOVATHER

Innovative ways to enhance radiopharmaceutical therapy

Clément Morgat | Oncology | 2017 | TRAIL funding: 50 000 €

CorePartner Aquitaine Institute of Cognitive and Integrative Neurosciences (INCIA, UMR5287)

Targeting G protein-coupled receptors on the surface of cancer cells with peptide ligands is a promising concept for the selective tumor delivery of therapeutically active cargos. Such an approach is the specific cellular uptake of radiometals for the peptide receptor radionuclide therapy (PRRT). Recently, the radiolanthanide terbium-161 gained significant interest for PRRT application, since it decays with medium-energy β^- radiation, but also emits a significant amount of conversion and Auger electrons with short tissue penetration range. The therapeutic efficiency of a radiometal like terbium-161 can be therefore highly boosted by an additional subcellular delivery into the nucleus, in order to facilitate a maximum dose deposition to the DNA. In this project, we have developped a multifunctional, radiolabeled neuropeptide Y (NPY) conjugate, which is addressing the human Y_1 receptor (hY_1R) in breast cancer for subcellular-targeted PRRT. By using solid-phase peptide synthesis, the hY_1R-preferring [F^7,P^{34}]-NPY was modified with a cathepsin B-cleavable linker, followed by a nuclear localization sequence (NLS) and a DOTA chelator. First, labeling with native terbium-159 was performed. The ^{nat}Tb-peptide conjugate showed a maintained receptor activation and internalization profile and high affinity binding to endogenous hY_1R on MCF-7 cells. Afterwards, the NPY analog was radiolabeled with indium-111 as surrogate for radiolanthanides. Specific internalization of the radiolabeled conjugate into MCF-7 cells was observed and importantly, time-dependent nuclear uptake of indium-111 could be demonstrated. The multifunctional NPY conjugate with a releasable DOTA-NLS unit therefore represents a promising compound for enhanced PRRT with Auger electron-emitting radiolanthanides.

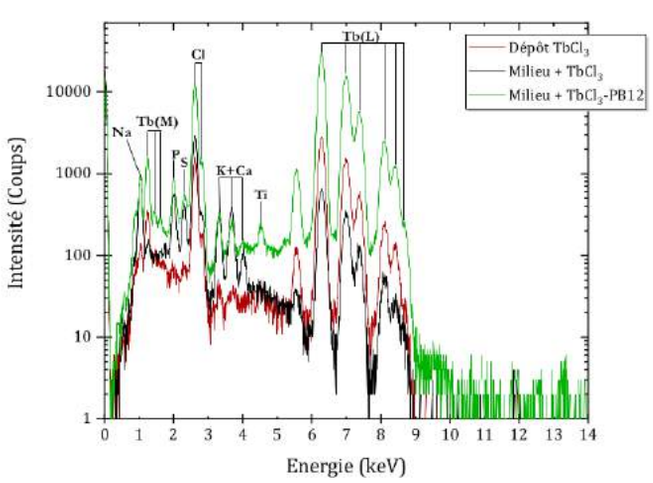

Figure 1. Terbium spectrum as detected using PIXE experiments. M and L rays are easily detectable. Other elements detected (Na, Cl, K...) are from the breast cancer cell line used for the experiment.

NANOMULTIMAG

Smart multimodal nanoprobes for MRI/MPI/NIRF imaging with magneto/optical contrast agents for atheroma plaque targeting

Mireille Blanchard-Desce | Cardiology | 2016 | TRAIL funding: 150 000 €

CorePartner Institute of Molecular Sciences (ISM, UMR5255)

The biological question that NANOMULTIMAG project aims to address is the detection of micrometric atherosclerotic lesions which develop in the intima of medium and large arteries. At this stage, atheroma plaques are at high risk of rupture, thus precipitating acute clinical events such as ischemic stroke and myocardial infarction. NANOMULTIMAG aims at designing innovative nanosystems combining complementary contrast agents for acute and sensitive imaging of the micrometric lesions. Our first approach is based on biocompatible nanoemulsions (NE) incorporating two complementary systems: (1) iron oxide nanoparticles (SPION) which can be imaged by two modalities: MRI and MPI and (2) NIRF-emitting ultra-bright fluorophores dedicated for both one-photon or two-photon (*ex vivo* imaging) fluorescence microscopy. In order to achieve adequate contrast agents, we had to address different issues among which (i) the labelling with biomarkers specific to the pathology, as little immunogenic as possible, (ii) the use of biocompatible carriers able to vehicle the targeted imaging probes to the micrometric lesions, and (iii) the design of dedicated bright far-red to NIR emitting fluorochromes which maintain fluorescence properties in the multicomponent nanosystem and show large two-photon absorption properties in the NIR1 region. The targeting issue has been addressed via the engineering of human antibody fragments specifically obtained by *in vivo* phage display technology to recognize over-expressed molecules in the microenvironment of the lesion. Human antibodies specific to biomarkers of the pathology have been characterized, which were reformatted as ScFv-Fc fragments. Furthermore the "stealth" properties of NE having PEG surface moieties (NE-Peg) have been studied *in vivo* by real time MRI. As a result, stealth and versatile NE (NE Peg-Mal) having maleimide functional groups for further bioconjugation with selected antibody are now available. In addition, biocompatible nanoemulsions loaded with a new ultra-bright far-red emitting (λ_{em}^{max}= 747 nm) fluorophore as well as magnetic contrast agents (SPION) were designed. They retain both magnetic and fluorescent properties and could be used in *in vivo* imaging in mice (Fig. 1).

In addition, novel fluorescent organic nanoparticles (FONDs) that combine high brightness, excellent water solubility and biocompatibility, high capacity for drug immobilization as well as surface grafting of antibody fragments have been designed. Their internalization into cells as well as their ability as nanocarriers has been demonstrated (patent pending).

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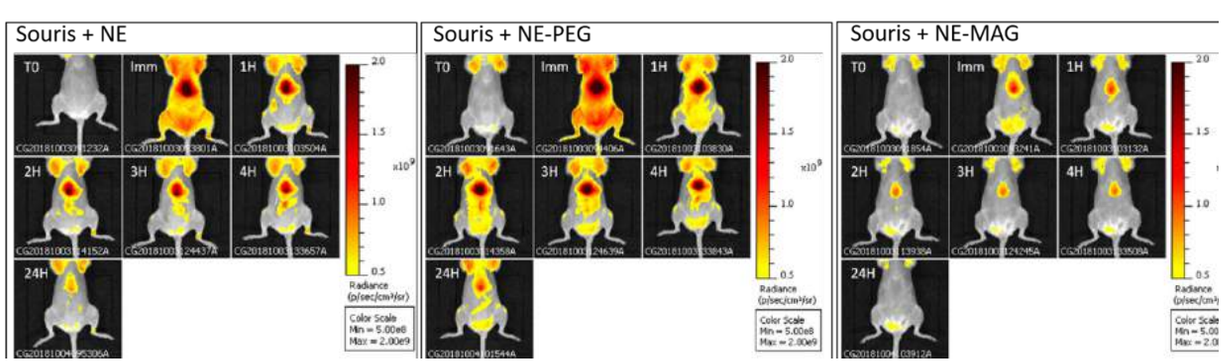

Figure 1. In vivo FRI imaging of mice (Black-6 albinos) after injection of NE tagged with NIRF fluorescent Dye and with/without PEG surface groups or with/without SPION.

NEPMIP

NanoEmulsion Platform for Magnetic Particle Imaging

Sylvie Crauste-Manciet Oncology 2015 TRAIL funding: 85 000 €

CorePartner Center of Magnetic Resonance of Biological Systems (CRMSB, UMR5536)

Atheroschlerosis is a vascular disease characterized by the development of lipid-rich atheroma-plaque located in the arthery wall, some of them when they are vulnerable cause cardiovascular diseases as stroke and heart attack. Detection of vulnable plaque suffers of lack of predictive diagnosis method. The objective of the present work was to design a new bio-imaging contrast agent combining iron oxide nanoparticles and nanovesicular systems (nanoemulsions) grafted with specific antibodies targeting atherosclerotic plaques, using Magnetic Resonance Imaging (MRI) and an emerging method for imaging: Magnetic Particle Imaging (MPI).

The multiples challenges of the project were i) to design stable nanoemulsions (NE) able to load high quantities of superparamagnetic nanoparticles (SPIO NPs) ii) to confirm that the nanosystem was able to give satisfactory signals for both MPI and MRI imaging iii) to graft monoclonal antibodies on the surface of the nanovesicules iv) to show that the nanosystem was able to target the atheroma plaque.

Magnetic NE showed MRI contrast properties and a MPS signal comparable to Resovist® (gold standard). Moreover, functionalization of NE human monoclonal antibodies targeting the αIIbβ3 integrin of platelets (TEG4) allowed for a significant labeling of the atheroma plaque both *in vitro*, *ex vivo* (Fig. 1). For improving time of circulation of the formulation in the blood stream *in vivo*, the surface of the nanovesicules was decorated by stealth agent (PEG derivatives). *In vivo* MRI dynamic study on mice allowed to select for further experiments the best PEG derivative (PEG-3400) giving the longer blood half-life (~100 min) in comparison to the control (1min).

The ongoing consolidation project aims to confirm the imaging capacity of the nanoformulation *in vivo* on mice living model of atheroma (ApoE -/- mice). To improve the plaque targeting, nanovesicles will be decorated with new P3 antibodies recognizing proteins (galectin-3 expressed on macrophage) specifically involved in the vulnerable plaque. Finally, to assess the potentiality of this new nanosystem for combining imaging and therapeutic of the vulnerable plaque, formulation will be designed to include a therapeutic agent i.e. vitamin E recognized as an antioxidant, anti-inflammatory and cardioprotective vitamin able to induce a regression of the vulnerable plaque.

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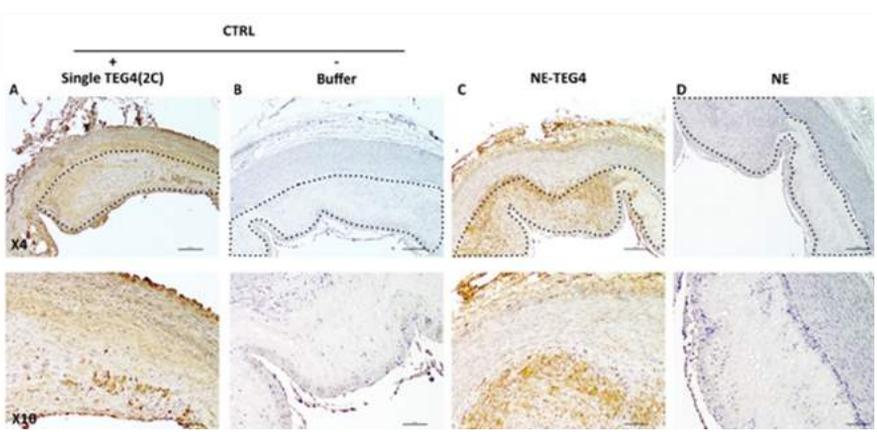

Figure 1. Immunohistochemistery labelling of aorta section from atheroma rabbit model (A) TEG4 antibody as positive control, (B) Buffer as negative control, (C) NE grafted with TEG4, (D) NE. Atheroma plaque highlighted by dashed lines. Darker staining in figures A (TEG4 antibody) and C (NE grafted with TEG4) indicated a positive labelling of the plaque.

PIAF

18F for PET-imaging angiogenesis

Eric Fouquet | Oncology | 2011 | TRAIL funding: 164 000 €

CorePartner Institute of Molecular Sciences (ISM, UMR5255)

The project will firstly establish the interest of the αvβ3 integrin imaging by PET imaging, by conceiving and achieving the synthesis of an original 18F-RGD radiotracer, then experimenting it on a murine tumoral model of melanoma. Secondly, in a perspective of "proof of concept", our molecular imaging project will consist in the validation of the 18F-RGD as a marker of the biological effect induced by therapies, inhibiting neoangiogenesis such as Dendrogenin A (a new and promising anti-tumoral recently discovered). A further objective will be to complete the pre-clinical evaluation of the molecule to bring it up to the clinical state and assess in situ its impact on the tumoral neovascularisation in order to select.

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WORKPACKAGE 'TRACERS & CONTRAST AGENTS'

WP4

PREXPULSE

Comparison of conventional X-Ray images with laser generated X-Ray images using new multimodal contrast agents

Jean Palussière | Oncology | 2018 | TRAIL funding: 50 000 €

CorePartner Molecular IMaging and Innovative Therapeutics In Oncology (IMOTION, EA7435)

This project aims to evaluate X-pulse laser generated absorption images and to compare them with conventional X ray images obtained with a phototube in mouse models of tumors. The project also aims to test 2 innovative multimodal contrast agents to be compared for both conventional imaging techniques such as optic, MR and conventional X-Ray and laser-generated X-ray images.

By testing different contrast agents the aim is to provide different types of images to assay the X-pulse potential.

PRITOR

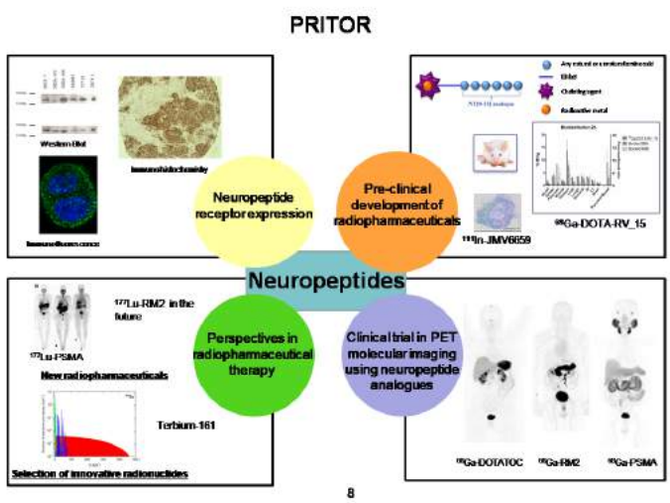
NeuroPeptide Receptors Imaging for TumOR Targeting

Elif Hindié | Oncology | 2013 | TRAIL funding: 90 000 €

CorePartner Aquitaine Institute of Cognitive and Integrative Neurosciences (INCIA, UMR5287)

PRITOR projects (new and consolidation grants) were dedicated to the targeting of neuropeptide receptors for imaging and therapy of cancer. Neuropeptide receptors can be highly expressed on the cell surface of tumor cells, paving the way to their visualization with Positron Emission Tomography (PET) using analogues radiolabeled with ^{68}Ga, ^{64}Cu or $^{43/44}$Sc, but also to select patients who can benefit from radiopharmaceutical therapy using similar analogues radiolabeled with ^{177}Lu (Morgat et al, J Nucl Med 2014). An example has been the development of somatostatin radio-analogues for imaging (^{68}Ga-DOTATOC) and therapy (^{177}Lu-DOTATATE) of neuroendocrine tumors. This concept has gained insight since the discovery of other neuropeptide and their receptors (over)expressed on diverse tumors. PRITOR projects' have been conducted according to several axis, the first being the characterization of the Gastrin-Releasing Peptide receptor (GRP-R belonging to the bombesin receptor family) in estrogen receptor positive breast cancer (Morgat et al, J Nucl Med 2017). The characterization of neurotensin-1 receptor (NTR1) is also almost completed (an article will be obviously written). Then, we developed and characterized a new radiopharmaceutical aiming at targeting the bombesin receptor family (Morgat et al, MedChemComm 2016). Using our facilities in the PET research center we conducted an innovative clinical trial using the somatostatin analog ^{68}Ga-DOTATOC in MEN1 patients suffering from neuroendocrine tumors (Morgat et al, Eur J Nucl Med Mol Imaging 2016). Finally, we pursued perspectives in radiopharmaceutical therapy by having identified terbium-161 (^{161}Tb) as a potential therapeutic radionuclide complimentary to ^{177}Lu (Hindié et al, J Nucl Med 2016, Champion et al, Theranostics 2016).

PRITORS projects have been the ground of a new research area in our team focused on neuropeptide receptors. We now benefit from several local, regional and national grants to further develop this innovative imaging and therapeutic modality.



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SUPSIFLU

Supported Silyl Fluorination

Philippe Hermange

Oncology

2013

TRAIL funding: 130 000 €

CorePartner Institute of Molecular Sciences (ISM, UMR5255)

Positron Emission Tomography (PET) has become a powerful tool for medical diagnostic over the last decades, and incorporation of ^{18}F ($t_{1/2}$ = 109.8 min) into molecules of biological interest has been extremely investigated by organic chemists. However, regarding their extremely short half-lives, the time to prepare the injected sample (i.e. synthesis and purification) has to be reduced to the minimum to achieve an efficient procedure, and the overall operating mode should be manageable by non-chemists technicians. Such constraints can explain the difficulty to transfer new synthetic methods to clinical applications, when standard strategies often imply complex chemical preparations and/or need a time-consuming HPLC purification at the end of the synthesis to remove the large excess of starting material (usually 10^3 to 10^5 fold). Aiming a unique and user-friendly automatized system for the production of multiple tracers, solid-phase supported tracer precursors with a selective labelling-triggered would definitively improve the production process. Indeed, it would enable the pre-packing of the precursor in a convenient cartridge format, thus allowing both easier handling and more simple purifications desired for a wide medical use. In this context, the SUPSIFLU project proposed the synthesis of new structures to prepare resin-supported bioconjugates suitable for the last-step labelling of biomolecule-based structures by $[^{18}F]$fluoride. Firstly, a new silylated precursor was developed, and its fluorination with $[^{19}F]F^-$ and with $[^{18}F]F^-$ was validated on various bioconjugates. Then, its grafting was explored following different strategies, and one of the synthetic pathway showed that the fluorination of resin-supported bioconjugates was possible with $[^{19}F]F^-$. Finally, the $[^{18}F]$ radiolabeled product was observed during preliminary $[^{18}F]F^-$ fluorination experiments, thus validating the chosen strategy.

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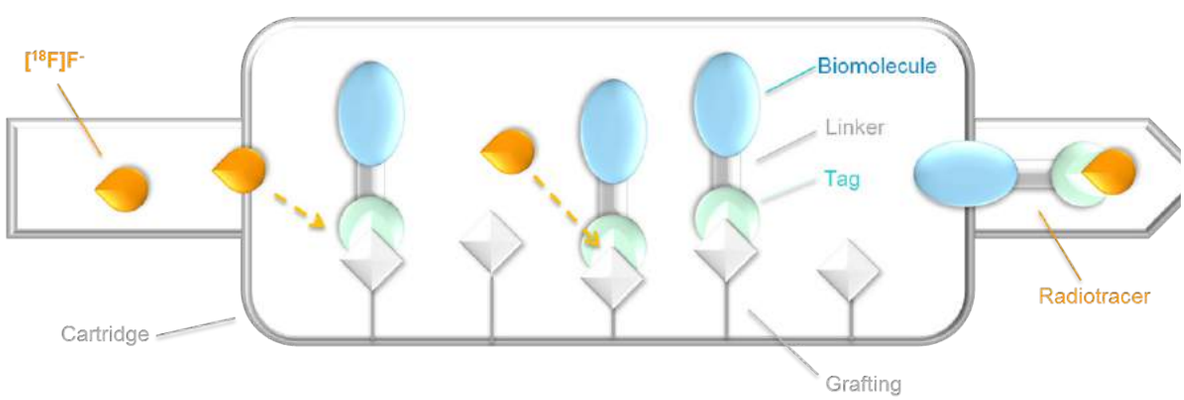

TARGLIN

Imaging siRNA targeting of glioblastoma using peptide-based nanoparticules

Franck Couillaud | Oncology | 2015 | TRAIL funding: 150 000 €

CorePartner Molecular IMaging and Innovative Therapeutics In Oncology (IMOTION, EA7435)

The TARGLIN projet is co-founded by LabEx TRAIL (to IMOTION, University of Bordeaux) and Fondation pour la Recherche médicale (FRM) (Développement d'outils thérapeutiques à base de nanoparticules peptidiques ciblant les gliomes 2016-2018, to Sébastien Deshayes, CNRS, Montpellier). The objective of this project is the development of therapeutic tools based on peptide nanoparticules (PBN) for specific targeting of siRNA to brain tumors. The experimental goal for IMOTION is to establish the proof of concept *in vivo* by imaging that peptide-siRNA nanoparticules are able to inhibit a specific gene in gliomas.

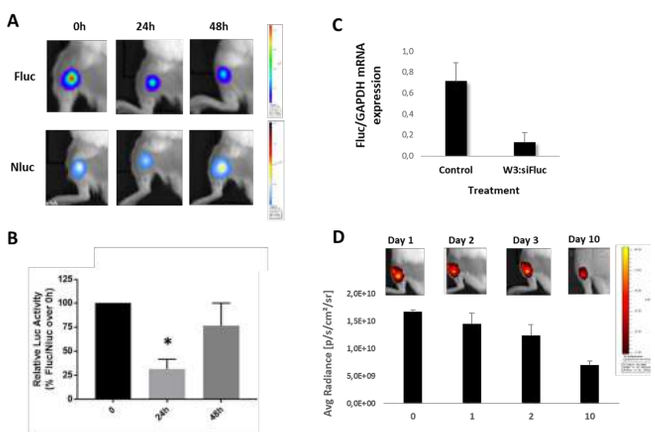

*Figure 1. Silencing in vivo of lucF activity by PBN on sub-cutaneous tumors in vivo. Time course of BLI signal of Fluc et Nluc 0, 24 and 48 hrs after PBNs injection (WRAP5 : siRNA Fluc, 20 µg) in U87 sub-cutaneous tumors. B. Quantitative analysis of Fluc/ Nluc ration at 0 hrs, 24 et 48 hrs after PBN WRAP5 : siRNA Fluc injection. *** P value < 0,0003, * P value < 0,0268, n=11. C. Fluc-mRNA quantification in tumors, 48 hrs after PBNs injection (WRAP5:siRNA Fluc concentration 20 µg), n=4. (Ratio Fluc mRNA by GAPDH mRNA). D. Quantification of in vivo fluorescence signal of PBNs in tumors following intratumoral injection (n=4).*

The project include the development and the characterization of new PBNs for siRNA delivery in glioma cells and glioma tumors. The design of these nanoparticles also incorporates brain-specific targeting motifs as well as stabilization motifs such as PEGs. We have developed a new family of short (15mer or 16mer) tryptophan-(W) and arginine-(R) rich Amphipathic Peptides (WRAP) able to form stable nanoparticles and to enroll siRNA molecules into cells. The lead peptides, WRAP1 and WRAP5, form defined nanoparticles smaller than 100 nm as characterized by biophysical methods. Furthermore, they have several benefits as oligonucleotide delivery tools such as the rapid encapsulation of the siRNA, the efficient siRNA delivery in several cell types and the high gene silencing activity, even in the presence of serum. These nanoparticules were first assayed on cultured cells and target imaging reporter genes. WRAP5 were later-on used to establish the proof of concept *in vivo* by targeting the optical imaging reporter gene firefly luciferase (Fig. 1).

WRAP1 and WRAP 5 was used to target physio-pathological relevant targets such as CDK4 / cyclin D, CDK6 / cyclin D or CDK1. Both PBNs were efficient to reduce CDKs expression but only CDK1 inhibition affect cell growth *in vitro*. *In vivo* injection of WRAP1:siRNA CDK1 in tumors was not able to reduce tumor growth *in vivo*. We are currently trying to find more efficient CDK1-siRNA in order to improve *in vivo* effect.

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BIOPSYPROSTAPROBE

Antibody-based fluorescence probe for biopsy guidance of prostate cancer

Franck Couillaud | Oncology | 2014 | TRAIL funding: 185 000 €

CorePartner Center of Magnetic Resonance of Biological Systems (CRMSB, UMR5536)

The BIOPSYPROSTAPROBE project was dedicated to the development of both (1) a dual modalities imaging setup combining echography and fluorescence tomography and (2) a specific imaging probe for imaging prostate cancer.

1. The development of a hybrid imaging system combining echography and fluorescent tomography is currently ongoing. Supported by the Region Aquitaine, two endorectal hybrid imaging probes have been ordered to VERMON for translational studies on human samples and later on patients. The TRAIL post-doc has improved both hardware and software of the imaging system. He also built a US/fluo probe prototype to perform preclinical experiment in mouse. Both Human and home-made probe were characterized with phantoms containing fluorescent inclusion and provided consistent data. Mice with orthotopic prostate tumor were injected with a fluorescent probe and were successfully imaged by both ultrasound and fluorescent imaging (Fig. 1).

2. The design, synthesis and characterization of a functionalized nanovector specific to prostate cancer has been performed and the proof of concept of its effectiveness for diagnosis has been establish *in vivo* on mice orthotopic model. First evaluation of antibody fragment (scFv) as specific imaging probe for prostate tumor in mice has been successfully performed (Mazzocco et al, 2016). Then, immunocompetent mice models of subcutaneous, orthotopic and metastasis of RM1-protate cancer has been validated (Genevois et al, 2017). Pegylation of dual-labelled silica nanoparticles (NP) has been performed, characterized and evaluated on RM1 subcutaneous model (Adumeau et al, 2017) and The PEGylated NP has been further decorated using the anti PSMA scFv for specific targeting of prostate cancer. Data revealed that scFv decorated PEGylated NP specifically target the prostate cancer and could be monitored *in vivo* by optical imaging and the bimodal setup.

Short term perspectives include (1) test of the US/Fluo human probe on excised prostate samples (2) test in mouse of a clinical relevant labelled scFv currently in a phase 1 clinical TRAIL and (3) organization of a clinical trial using this labelled scFv for testing the bimodal setup for prostate cancer imaging in human.

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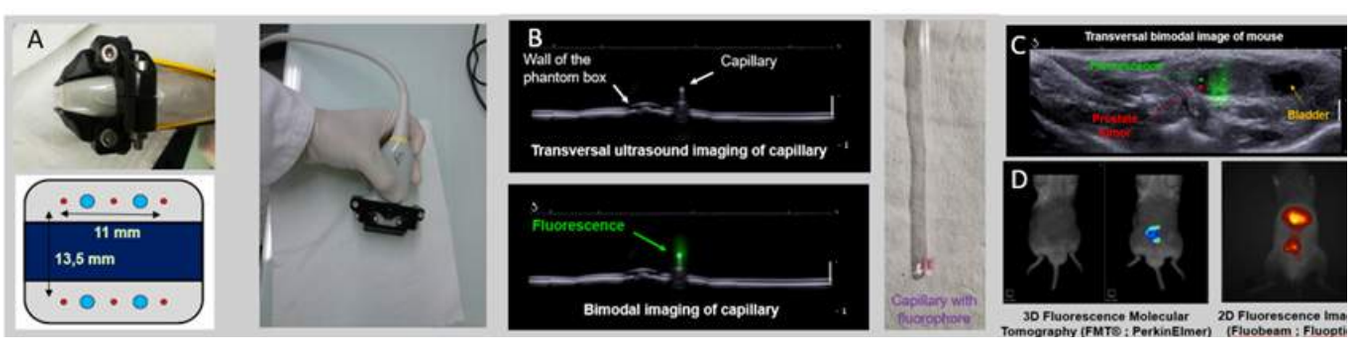

Figure 1. Bimodal experiments on phantoms and mouse model. (A) Picture and Illustrative diagram of the head of acoustic probe SL22 equipped with optical fibers (B) Imaging of a 1.7 mm diameter glass capillary inclusion inside the intralipid phantom (C) In-vivo bimodal imaging of a orthotopic prostate cancer tumor in mice after intravenous injection of fluorescent PEGylated NPs (D) Control of fluorescence signal of the prostate with fluorescent molecular tomography (FMT) and Fluorescence reflectance imaging.

BRAIN-RESV

Neuroprotective effect of resveratrol in hypoxic ischemic rat pups: how supplementation of the pregnant female could impact brain lesion of the pups?

Anne-Karine Bouzier-Sore Neurology 2017 TRAIL funding: 50 000 €

CorePartner Center of Magnetic Resonance of Biological Systems (CRMSB, UMR5536)

Perinatal hypoxia leads to 1,600 cases of death or strong handicap (50/50%) out of 800,000 births per year in France (like babies with the umbilical cord around the neck). Finding ways to prevent or cure such brain diseases is a primary goal of neuroscience research. Resveratrol (RSV) is a polyphenol present in some plants and diet and has been recently shown to have a neuroprotective effect. In our lab, we also demonstrated that RSV increases significantly glycolysis in the liver. We know that brain metabolism and more particularly glycolysis, which leads to lactate production, are of paramount importance in the brain: not only for brain activity but also for neuroprotection. Indeed, in our group we have shown that lactate, an important neuronal substrate, is neuroprotective for hypoxic-ischemic neonates (rat model). Here, we propose to study the potential therapeutic role of RSV on hypoxic-ischemic (HI) rat pup brains, which may occurs by increasing lactate content in the brain in addition to its more classical effects.

The originality of this project mainly rests on our nutritional and transgenerational approach. RSV was administered to the pregnant female, near to a nutritional dose, and brain lesions of the 7-day rat pups were followed *in vivo* by MRI. Results have shown that the RSV treatment of pregnant female is neuroprotective for the hypoxic-ischemic pups.

In addition, to decipher the mechanisms by which RSV could be neuroprotective, *in vitro* experiments will be carried out next year on astrocyte cultures to determine the impact on glial energy metabolism, while rt-qPCR, Western-Blot and immunohistochemistry will be performed rat pup brain samples at specific times post-insult to follow modifications of gene and protein expression.

The second part of this project will be performed in Lausanne, Switzerland. The aim will be to understand the molecular cascades that come into play to explain the neuroprotection role of RSV in hypoixia-ischemia.

The next goal will be to define is RSV treatment is more efficient when given to the pregnant female during gestation, gestation + lactation or lactation alone.

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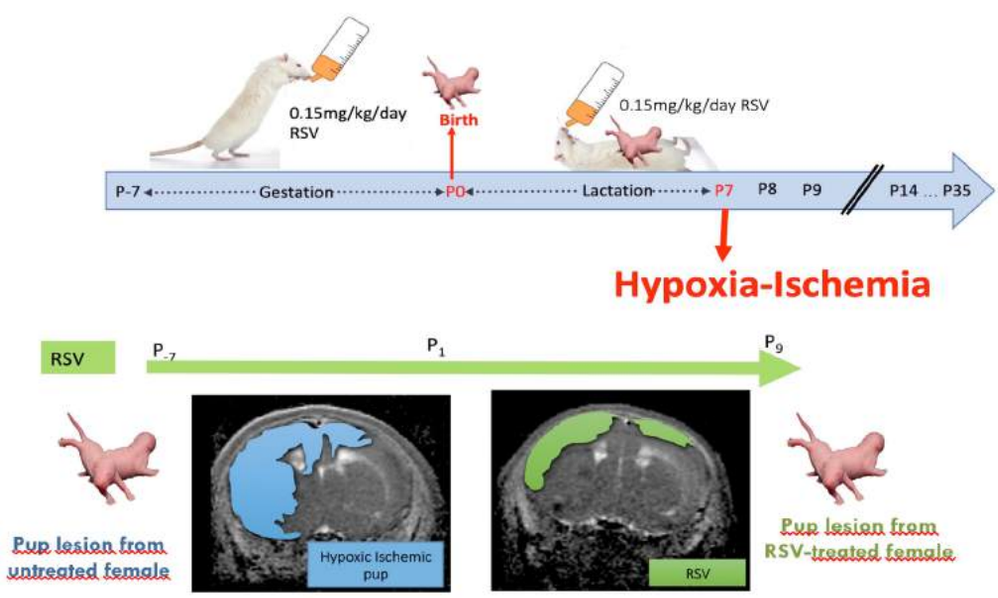

DIFFIR

Ex vivo DIFFusion-weighted MRI of renal Ischemia Reperfusion injury

Souleymane Maïga | Nephrology | 2017 | TRAIL funding: 47 000 €

CorePartner Molecular IMaging and Innovative Therapeutics In Oncology (IMOTION, EA7435)

Ischemia-reperfusion injury (IRI) is a sequence that includes organ harvesting, conservation and implantation in the recipient. It plays a key role in the development of early and chronic graft dysfunction. Understanding the effect and mechanisms of physiological adaptation to stress generated by the IRI is one of the most promising research for improving conservation and preservation of grafts. Functional MRI allow assessment of multiparametric imaging looking at several pathological changes at once, such as renal vasculature, edema formation, and cellular infiltration. MR diffusion tensor imaging (DTI), with calculation of cortical and medullary fractional anisotropy (FA) provides qualitative and quantitative information about the microstructure of renal tissues.

The purposes of this experimental study are to investigate renal microstructural characteristics of normal mouse kidney using DTI parameters obtained with a high resolution *ex-vivo* DTI technique, to evaluate the consequences of IR on these parameters, in terms of injury and remodeling, in a mouse model of renal IRI and to correlate these changes with histopathological changes and with functional outcome.

The project has been impeded by two problems, that are being solved by the development of a new sequences by the CRMSB and the reactivation of the project with Sylvain Miraux and Coralie Genevoix. Coralie will be responsible for the animal model which will be changed from surgical IRI to toxic IRI. The "saisine" is on-going and the first kidney controls should be imaged soon.

GMCOG

Grey matters! Toward a better understanding of grey matter alteration and cognitive deficit associated with multiple sclerosis

A. Ruet & T. Tourdias Neurology 2016 TRAIL funding: 200 000 €

CorePartner Neurocentre Magendie (U1215)

Multiple sclerosis (MS) is an autoimmune inflammatory disorder of the central nervous system that typically affects white matter. However, it is now recognized that grey matter (GM) is also involved which might trigger some specific symptoms such as cognitive impairment. In this multidisciplinary translational project, we aimed to highlight mechanisms responsible for GM alterations in MS and to identify the most vulnerable GM regions in the patients and their impact in terms of cognitive performances.

So far, we have been able to identify specific mechanisms of neuronal damages within GM thanks to the rodent model of MS. Especially we could show that glial cells, which become activated in the context of MS, area responsible for neuronal dysfunctions and we are currently investigating specific cellular pathways. We also pursued an immunological task to understand the role of gut-derived lymphocytes in GM alterations of MS. We focused on the pathogenic role of the CD4 T cells specialized in providing help to B cells: the T follicular helper (TFh) cells. We observed that the increased capacity of gut-derived B cells to express inflammatory cytokines in the early phase of MS is associated to a skewing of the TFh toward a potent B helper phenotype.

In a translational approach, we have initiated different prospective clinical studies in which the MS patients are scanned with advanced MRI techniques and then tested with batteries of neuropsychological tests. So far, we have been able to show that all the GM regions are not similarly affected at the early stage of MS. Our results suggest that the hippocampus is affected at the early stage of MS and that the GM damage spread from hippocampus to the cortex. We could also show that some specific subfields of the hippocampus (Fig. 1) or some specific nuclei of the thalamus are more vulnerable than the others. We found early brain functional reorganization that could mitigate cognitive deficits due to compensatory mechanisms.

Such understanding of GM damages and the development of better imaging tools for their visualization should help to identify new therapeutic strategies.

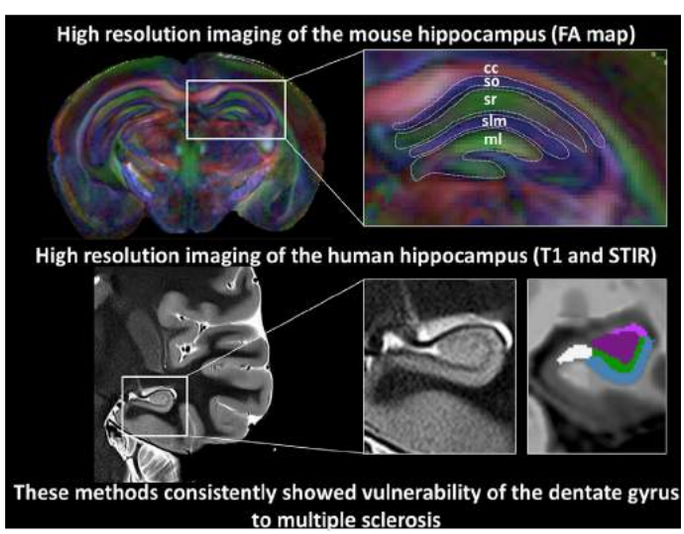

Figure 1. Illustration of one of the results of the project: By using high resolution imaging we showed that the dentate gyrus is more vulnerable than the other layers of the hippocampus at the early stage of multiple sclerosis.

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IBIONI

New Imaging Biomarkers of neuroinflammation such as MS

Bruno Brochet | Neurology | 2012 | TRAIL funding: 310 654 €

CorePartner Neurocentre Magendie (U1215)

This translational scientific project associates different neuroimaging, neuroepidemiological and neuroscience teams to study mechanisms and consequences of neuroinflammation using new imaging biomarkers in experimental models and human diseases, such as multiple sclerosis (MS). We will study (1) lateral diffusion along the astrocyte membrane of AQP4 in live cells using quantum dot imaging; (2) Validation of new biomarkers for tissue integrity characterisation in experimental models of MS using new high-sensitivity Diffusion Tenser Imaging (DTI), MR Diffusion kurtosis Imaging (DKI) and Diffusion Spectrum Imaging (DSI); (3) application of DTI, fMRI and Voxel based morphometry (VBM) to study the mechanisms of cognitive impairment in MS; (4) application of MRI markers in large cohorts of MS patients (OFSEP) and controls (I-Share).

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IMAGANIV

Imaging activity of neurons *in vivo*

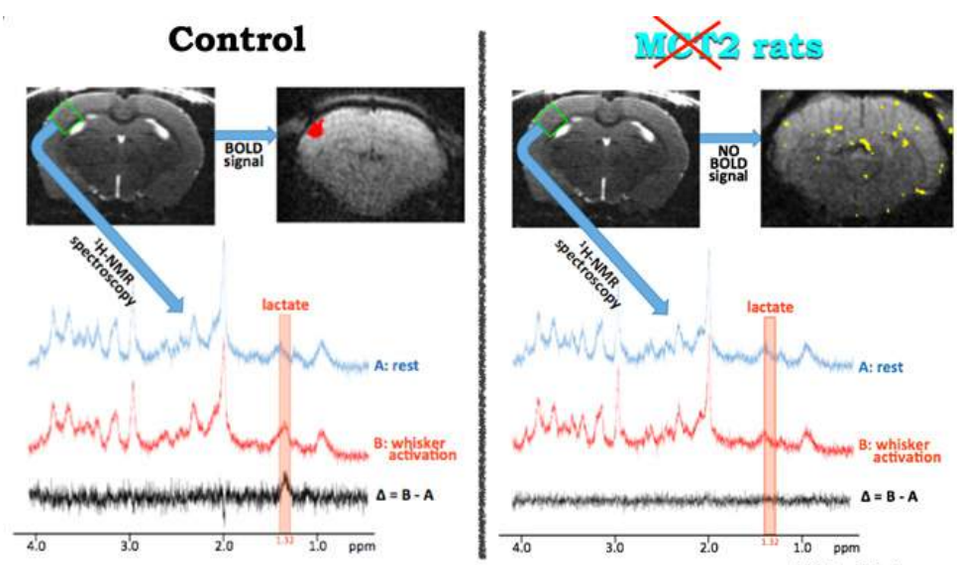
Anne-Karine Bouzier-Sore Neurology 2018 TRAIL funding: 50 000 €

CorePartner Center of Magnetic Resonance of Biological Systems (CRMSB, UMR5536)

Decline of energetics has been suggested to contribute to both cognitive impairment linked to aging and to the etiology of neurodegenerative diseases. In order to understand the reasons for this demise and eventually propose new therapeutic strategies, it is important to unravel the precise mechanisms that so critically depend on efficient energy supply and how it relates to cognition. Few years ago it has been proposed that energy delivery to the neurons may be a lactate shuttle. In this hypothesis, it was suggested that glucose, the main energy substrate of the brain, enters the brain but goes preferentially to the astrocytes, where it is converted into lactate, which is then further transferred to the neurons. The goal of InNES project was to demonstrate that such a shuttle exits *in vivo*.

Using functional MRI, *in vivo* NMR spectroscopy, PET and genetically-modified rats in which transporters for lactate (called MCT) were suppressed, we were able to demonstrate that if the entry of lactate into the neuron is blocked, then brain activity is lost (even if glucose and its transporters are still present).

This result is important to understand how the brain is functioning but has also a direct impact on clinical research: if lactate, rather than glucose, is necessary for brain activation, could it be neuroprotective? This other aspect of the role of lactate in the brain is explored in our team (InNES project).



First evidence that neuronal lactate transporter is necessary for brain activity detected by BOLD fMRI

INNES

Lactate and neuronal metabolism

Anne-Karine Bouzier-Sore | Neurology | 2011 | TRAIL funding: 300 579 €

CorePartner Center of Magnetic Resonance of Biological Systems (CRMSB, UMR5536)

Finding ways to prevent brain diseases is a primary goal of neuroscience research. Reaching it requires an ever-improving understanding of the brain's normal functioning: there is no way to avoid or cure brain damages if we do not know how it works.

To work properly, neurons rely on energetic substrates, their "food", which enter the cell through specific "doors", called transporters. In the group, our aim is to answer this question: what does the neuron "eat", especially when it is activated? Glucose, the main sugar present in the blood, is thought to be this energetic substrate for more than a century. Glucose has his own transporter in the brain to enter neurons. However, we are working on another hypothesis, which proposes that glucose does not go directly to the neurons, but is "pre-digested" by surrounding nursing cells, called astrocytes. Astrocytes will then give back energy to the neurons in a different form, a different molecule than glucose, which is lactate. In an another project (Imaganiv), we were able to demonstrate that lactate, and its transporter (called MCT), are essential to support neuronal activity. This result is important to understand how the brain is functioning but has also a direct impact on clinical research: if lactate, rather than glucose, is necessary for brain activation, could it be neuroprotective? It is known that glucose injected after a stroke is not neuroprotective. Lactate was injected in rat neonates that had suffered from a cerebral lack of oxygen and glucose (hypoxia-ischemia event) to determine if it could be neuroprotective.

We were able to demonstrate that lactate is very efficient to reduce brain lesions and to restore cognitive and motor functions, at short and long-term, indicating its promising interest for clinical trials.

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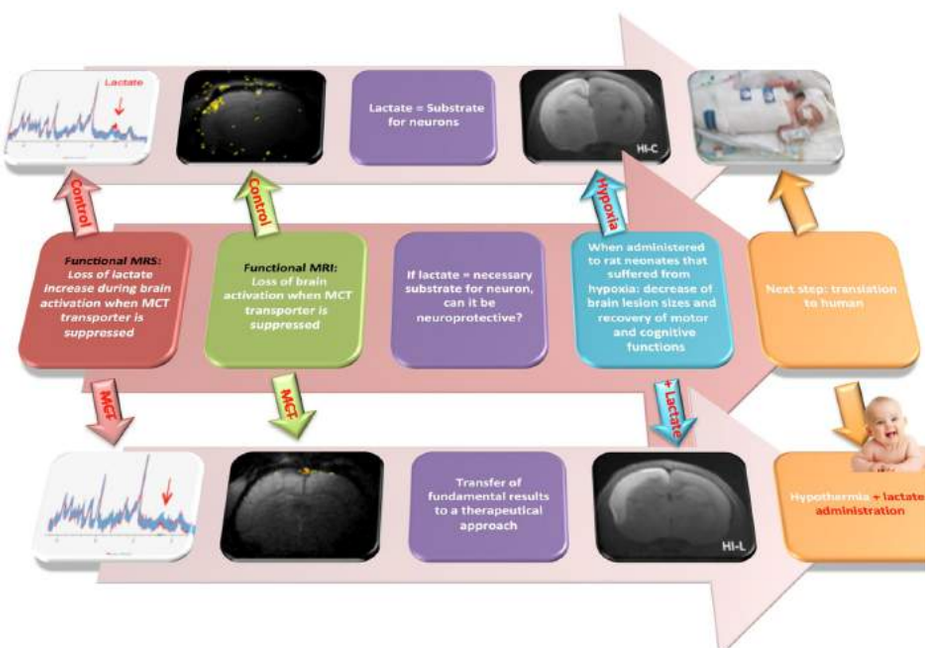

IPALICA

Inflammatory pathways leading to intracranial aneurysm growth

Jérôme Berge | Neurology | 2015 | TRAIL funding: 35 000 €

CorePartner Center of Magnetic Resonance of Biological Systems (CRMSB, UMR5536)

IPALICA project focuses on mechanisms involved in the growth and rupture of intracranial aneurysms. The objective is to better understand the aneurysm physiopathology in order to identify potential biomarkers of aneurysm instability reflecting the rupture risk and to identify potential therapeutic targets. This study is based on the multi-modality analysis: transcriptomics, proteomics, metabolomics and immune-histology of aneurysm walls harvested surgically and intra-aneurysmal blood samples collected during endovascular treatment.

RNA sequencing allowed us to identified different transcriptomic profiles and upregulated interest inflammatory pathways in aneurysm walls compared to normal cortical arteries and in ruptured aneurysm compared to unruptured aneurysm walls. Similary, HR-MAS spectroscopy showed us different metabolomics profiles between ruptured and unruptured aneurysm walls (higher concentration of taurine and lower concentration of choline in ruptured versus unruptured aneurysm walls). Analyses of intra-aneurysmal blood sampling have demonstrated higher concentration of inflammatory proteins compared to peripheral sampling. We have identified different proteomic profiles between intra-aneurysmal sampling of ruptured and unruptured aneurysms.

The correlation between transcriptomic data (gene expression) from the aneurysm wall and proteomic data from intraaneurysmal sampling (cytokines concentration) suggesting that there are intra-aneurysmal blood markers of inflammation of the aneurysm wall.

The prospects following this project are the development of new sequences for non-contrast and contrast-enhanced aneurysm wall imaging, the correlation between *in vivo* pre-operative clinical MRI 3T, *ex vivo* 4,7T MRI, HRMAS spectroscopy profiles and immuno-histological analysis on aneurysm walls and the simultaneous inclusion of patients in UCAN study as part of the collaboration with Dr Bourcier and Pr Desal from Nantes (France).

MEMIM

Multiphoton endomicroscopy for metabolic imaging of macrophages in atherosclerosis

Gisèle Clofent-Sanchez Cardiology 2017 TRAIL funding: 50 000 €

CorePartner Center of Magnetic Resonance of Biological Systems (CRMSB, UMR5536)

Atherosclerosis is an inflammatory disease characterized by lipid depositions called "atheroma plaques" in the arterial wall whose thickening and/or rupture lead to cardiovascular diseases. Blood cell infiltration is characteristic of inflamed areas. Monocytes-derived macrophages (MPs) phagocyte oxidized Low-Density Lipoproteins (oxLDL) and subsequently turn into foam cells presenting impaired cholesterol efflux, sustained inflammation, apoptosis and necrosis conducing to the formation of a pro-thrombotic necrotic core, a key component of vulnerable plaques. More than the number of MPs in the plaques, a local disequilibrium in favor of inflammatory (M1) compared to immunoregulatory (M2) MPs was suggested to induce lesion progression and rupture (Toutouzas, et al. 2015). Recent studies of these *in vitro* functional models of MPs were shown to present different optical properties due to autofluorescent NADH and FAD cofactors of energetic metabolism pathways, M1 being more glycolytic (generating more NADH) and M2 turning preferentially to fatty acids β-oxidation and mitochondrial respiration (leading to FAD accumulation) (Pal & Konkimalla 2016). But to date no experimental model of foamy MPs has been studied regarding their metabolic pathways and functional phenotype. To do so, we developed an original model of foamy MPs based on human primary macrophages incubated with oxLDL and extracts of patient carotid. We reported for the first time a comparative analysis of this model with M1 and M2 states both for functional phenotype (Fig. 1) and metabolism (Fig. 3) (article in preparation). Analyses of this model based on NMR (Nuclear Magnetic Resonance) (Fig.2), but also proteomic analysis were started very recently and will be continued to further the comprehension of foam cells immunometabolism. The final goal of the project is to detect vulnerable plaques *in vivo*, without exogenous labelling, by the visualization of variations of autofluorescent NADH and FAD cofactors in vulnerable areas.

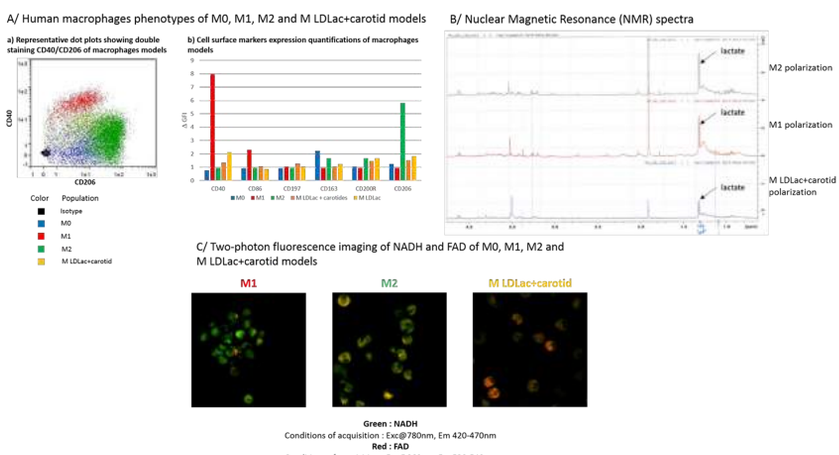

Figure 1.. In vitro differentially treated macrophages were stained with antibodies agaisnt M1 (CD40, CD86, CD197) or M2 cell surface markers (CD163, CD200R, CD206) or isotype control, and analyzed by flow cytometry (MACSQuant Analyzer (Miltenyi)) followed by FlowLogic software analysis. a) Representative dot plots showing double staining CD40/CD206. b) Cell surface markers expression quantifications (ΔGFI = [Geometric mean fluorescence intensity]$_{each\ condition}$/ [Geometric mean fluorescence intensity]$_{M2\ polarized\ condition}$ for M1 markers or [Geometric mean fluorescence intensity]$_{each\ condition}$/ [Geometric mean fluorescence intensity]$_{M1\ polarized\ condition}$ for M2 markers.

Figure 2. ^{1}H NMR spectroscopy measurements performed on an 11.7T spectrometer (DPX 500MHz; Bruker Biospin, Wissenbourg, France) to trace glucose fate within the polarized macrophages (M1, M2, M LDLac+carotid).

Figure 3. Two-photon fluorescence imaging of NADH and FAD in polarized macrophages (M1, M2, M LDLac+carotid).

Here, the preliminary results showed that M LDLac+carotid presented more FAD autofluorescence than M2, themselves more elevated than M1, suggesting that this physiopathologic model use its proper energetic pathway with concomitantly an intermediary phenotypic profile analyzed by flow cytometry. NMR may offer a still unexplored tool to deeply analyse the different metabolic pathways.

MIMATHUMAB

Molecular IMaging of ATHeroma with HUMan Antibody

Gisèle Clofent-Sanchez Cardiology 2012 TRAIL funding: 295 000 €

CorePartner Center of Magnetic Resonance of Biological Systems (CRMSB, UMR5536)

The majority of cardiovascular diseases are due to atherosclerosis, an inflammatory disease resulting in the build-up of atheroma plaques from circulating cholesterol. These plaques evolve under the combined influence of soluble and cellular factors, and their rupture into the blood flow is the cause of lethal ischemic accidents. Because of the wealth of actors involved, molecular imaging based on the targeting of highly specific markers would substantiate the diagnosis of rupture-prone atheroma.

Human antibodies (HuAb) issuing from a combinatorial library were selected by *in vivo* phage display on atheroma lesions in a rabbit model of atherosclerosis. A high-throughput biological assay was implemented to individually test thousands of HuAbs. In parallel, an *in silico* approach was set up. For the first time, third generation PacBio sequencing allows analysing full-length HuAbs (348,659 reads) by IMGT/HighV-QUEST. Clone P3 identified by biological assays to target galectin-3 (Patent PCT/EP2018/077131) was found over-represented (60 P3 reads showing 100% identity plus 25 with point mutations), underlying this *in silico* approach as a powerful tool to identify relevant HuAb candidates. HuAb fragments were further produced in P. pastoris or HEK cells and used to functionalize original nanoparticles, designed for multimodal imaging, in a regio-selective way to preserve their activity. Their targeting efficiency was proven *ex vivo* by IHC on murine, rabbit and human lesion tissues, allowing their use from pre-clinical to clinical assays and *in vivo* by MRI on the ApoE-/- mouse model. Novel site-specific bioconjugation was set up by coupling LPETG tagged HuAbs to poly-G iron-oxide nanoparticles (Samuel Bonnet in collaboration with S. Mornet, UPR9048 CNRS and C. Hagemeyer, Monash University).

The number and diversity of candidates open the way to the discovery of new up-regulated biomarkers of atherosclerosis (such as anti-Galectin-3). Imaging will be complemented by the development of nanoparticles with the ability to convey drugs to regress the plaques in order to fight atherosclerosis (WO2016170010A1).

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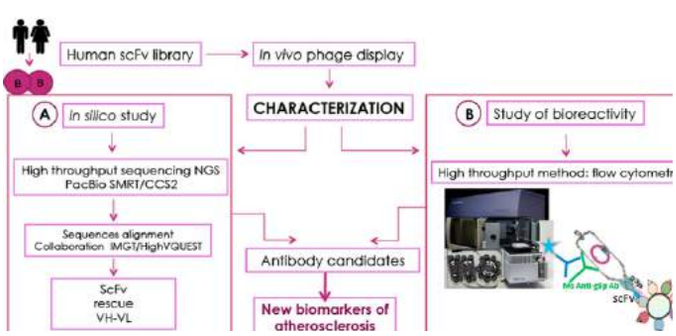
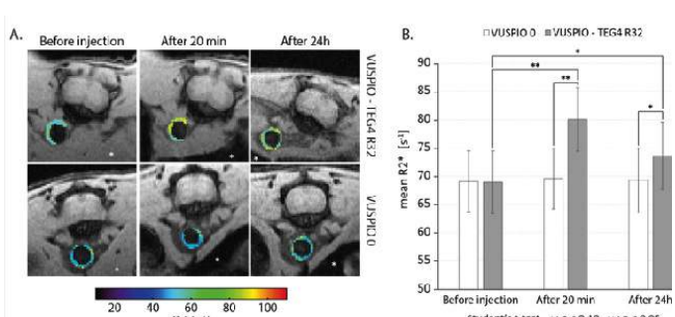
Figure 1. Human antibody selection: ligands for biomarkers of Atherosclerosis



Screening strategy of scFv-phages (single chain Fragment variable (association of VH and VL regions of human antibodies) fused to a coat protein displayed on top of the M13 phage). (A) in silico by NGS analysis of 105 scFv-phages, (B) biological screening of thousands scFv-phages by high-throughput flow cytometry.

Figure 2. Human antibody grafting to multimodal nanoparticles for molecular imaging purposes



In vivo injection of VUSPIO TEG4 R32 compared to the injection of VUSPIO 0. Segmented relaxation rate R2 maps overlayed on their corresponding magnitude images obtained before and after the injections (A). Mean segmented R2* values measured on at least 6 slices of N = 6 mice for VUSPIO TEG4 R32 and N = 3 mice for VUSPIO 0 (B).*

REMOD

Role of AQP4 in extracellular space and tissue after juvenile Traumatic Brain Injury: From the meso to the nanoscale

Jérôme Badaut | Neurology | 2018 | TRAIL funding: 50 000 €

CorePartner Aquitaine Institute of Cognitive and Integrative Neurosciences (INCIA, UMR5287)

Working hypothesis: Traumatic brain injury (TBI) leads to altered AQP4, a water channel, expression in astrocytes, which disrupts peri-neuronal extracellular space (ECS), synapse morphology and behavioral performance.

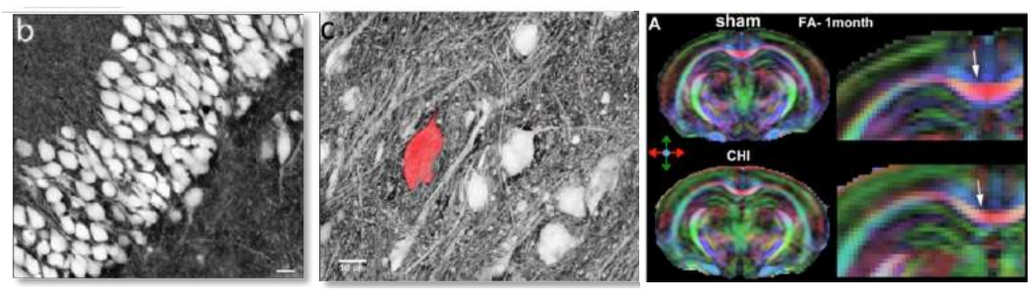
Aim 1: Determine the long-term impact of TBI on brain structure and behavior. Mice will receive TBI at P17 using a new Closed Head Injury with Long-term Disorders (CHILD©) protocol. Mice will repeatedly undergo behavioral tests during the recovery from TBI in parallel with MRI of water diffusion (DTI) and *in vivo* new microscopy methodology, SUSHI, to visualize the ECS and synapse morphology, allowing for detailed correlations between animal behavior and brain anatomy viewed from the nano to the macro scale. Then, *ex-vivo* immune-histological analysis will assess synaptic changes and AQP4 alterations in astrocytes. We expect that TBI leads to pronounced changes in water diffusion directionality that are correlated with increases in ECS, disruption of behavioral performance and a decrease in AQP4 expression.

Aim 2: Determine the role of AQP4 during recovery from TBI. We will assess how AQP4 deletion affects the recovery of brain structure and behavioral performance. We expect that the positive effects of physical therapy on recovery are compromised in AQP4 knock-out animals.

The proposed project brings together complementary expertise in to provide new insights into the biophysical basis of DTI signals and brain remodeling after mild TBI.

The REMOD project has been already initiated in Dr Nägerl lab:

- Trained and gave access to Aleks Ickova to use 2-photon microscope for project-related experiment;
- Cleared administrative hurdles (approval by ethics committee) to carry out *in vivo* animal experiments;
- Started to practice surgery procedure to implant cranial windows for longitudinal *in vivo* STED imaging.



SCICOG&REACTIV

Bio-imaging markers of tissue integrity, predictors of cognitive impairment in inflammatory demyelinating diseases

Bruno Brochet | Neurology | 2011 | TRAIL funding: 130 000 €

CorePartner Neurocentre Magendie (U1215)

Multiple Sclerosis (MS) is the main non-traumatic cause of neurological disability in young adults. There is growing evidence that the clinical disability in MS is not only due to motor deficiencies but also to cognitive deficiencies. Cognitive deficiencies could occur at the early stages of MS (high-risk clinicallyisolated syndromes (CIS) and early MS) and concern mainly information processing speed (IPS) and memory. Recent works suggested that cognitive deficiencies correlate with MRI parameters reflecting diffuse alteration in brain white matter leading to disconnection between cortical areas but also with atrophy of the brain gray matter. The aim of this project is to determine which MRI parameters could be use as a biomarker to predict cognitive deficiencies in CIS and which MRI parameters could predict the responsiveness of MS patients to cognitive rehabilitation. Two parameters will be studied, fractional anisotropy in brain normal-appearing white matter using diffusion-tensor-imaging and volumetric change in brain gray matter using Voxel-Based Morphometry. This project is based on two clinical studies, the SCI-COG, a one-year longitudinal study of CIS patients starting early 2012 and the REACTIV study, an on-going controlled trial of cognitive rehabilitation in MS. This is a 36 months project. Both studies received funding from industrial partners and ARSEP but this application concerns the need for additional human resource (study engineer) to complete image analysis.

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STEAMRI

Whole lung oxygen-enhanced imaging in humans using MRI

Gaël Dournes | Pneumology | 2016 | TRAIL funding: 40 000 €

CorePartner Bordeaux Cardio-Thoracic Research Center (CRCTB, U1045)

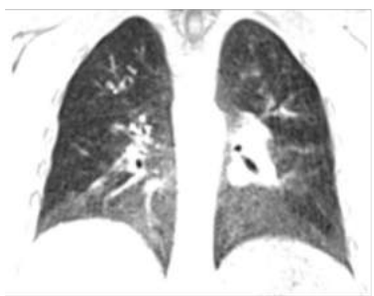
Patients undergoing allogeneic stem cell transplantation may develop non-infectious respiratory complication related to chronic graft versus host disease and called bronchiolitis obliterans syndrome (BOS). The occurrence of BOS is associated with a decreased survival reaching 13% at 5 years (Dudek et al, BBMT 2003). Thus, screening and diagnosis of BOS appear as a priority of post-transplant patients monitoring, in order to begin early therapy if needed. To this end, patients undergo systematic and regular screening using pulmonary function tests (PFTs). In case of abnormal PFTs, tests are completed the screening of respiratory infections and chest computed tomographic scan (CT-scan) is performed. A report from the National Institute of Health described the following criteria required for the diagnosis of BOS : FEV1/vital capacity < 0.7, FEV1 < 75% or a decline >/= 10% from baseline, residual volume > 120%, absence of documented infection, and the presence of CT-scan signs suggestive of BOS: air trapping by expiratory CT or small airway thickening or bronchiectasis.

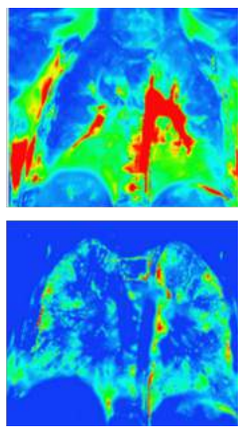
BOS severity depends on the development of fibrotic and fixed damages, poorly responding to therapies. New tools are needed in order to favor early BOS diagnosis.

A recent study from our center showed that repeated CT-scans in stem cell transplant patients is associated with increased risk of neoplasia. In addition, recent studies from our center evaluated the use of pulmonary MRI providing good performance without X-ray exposure (Dournes G et al, Radiology 2015 et Dournes G et al, Eur Radiol 2015).

More recently, Renne et al (Radiology 2015) studied the performance of pulmonary MRI coupled with oxygen transfer analysis for the diagnosis of chronic lung allograft dysfunction. This study showed altered imaging parameters in patients developing BOS, including patients with early BOS stage (0p stage).

As pathogenic mechanisms seem to be shared between post-stem cell transplant and post-lung transplant BOS, we hypothesize that pulmonary MRI with oxygen transfer analysis and ultra short echo time may represent a non-invasive, non-irradiating and sensitive research tool for the detection and quantification of pulmonary lesions in patients screened for post-stem cell transplant BOS.





Thus, we expect to include 20 patients who underwent allogeneic stem cell transplantation and show abnormal respiratory function over a 2 year period study. They will be included according to the following criteria : age > 18 yo, > 3 months post-transplant, absence of documented pulmonary infection, or with a minimum of 6 weeks after a documented pulmonary infection, and the following BOS criteria : abnormal PFTs (FEV1/VC < 0.7, FEV1 < 0.75, residual volume < 120% of expected value) and/or chest CT-scan showing air trapping or small airway thickening. We decided to add, similarly to lung transplant criteria, stage 0p BOS defined according to FEF25-75 values (Estenne et al, JHLT 2002), for which pulmonary MRI with oxygen transfer may guide to early BOS diagnosis.

Patients who give their consent will perform a pulmonary MRI, in the absence of contraindication, using different sequences to evaluate morphologic and functional performances of pulmonary MRI. We will compare CT-scan and MRI performances using blinded analysis from two radiologists.

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TBI

Longterm neurovascular unit changes after mild traumatic brain injury: potential biomarker & Vasc-TBI

Jérôme Badaut | Neurology | 2015 | TRAIL funding: 250 000 €

CorePartner Aquitaine Institute of Cognitive and Integrative Neurosciences (INCIA, UMR5287)

Our working hypothesis is even mild traumatic Brain injury (mTBI) induces long-term phenotypic changes of the neurovascular unit (NVU) associated with the emergence of cognitive dysfunctions and tissue properties changes in diffusion MRI. The project was initiated with the development and characterization of a new model of mTBI using a Closed Head Injury with Longterm Dysfunction (CHILD©). We pursue a unique characterization of the consequences of mTBI at the childhood over the lifespan on behavior and MRI with acquisition of the DTI and PWI changes at 6, 12 and 18 months within a European consortium and collaboration with Dr Obenaus (UC Irvine) with co-supervision of graduate student (Jeong Bin Lee, UCI, USA). The analysis of the changes are still ongoing with development of new tools of analysis for MRI acquisition in our group in particular the tractography analysis from the DTI pictures taken on *ex-vivo* brain tissues at the endpoints (12 and 18 months). In parallel, Mrs Ickova's (Ph.D student) characterizes the changes in the neurovascular coupling after CHILD© with a focus on the astrogliosis. She showed that mild TBI is impairing the cerebral blood vessels reactivity at 1 and 3 days before to normalize by 7 days (paper in preparation). Finally, we are investigating the MRI structural changes after sub-concussive headings with 2 groups of subjects: soccer players with repetitive headings and age/sex matched control group. The scans have already been done for all soccer players with two different soccer teams (Girondins and Bordeaux football club) and the control subjects. Therefore the analysis of the resting has been initiated by Dr Hélène Cassoudale (from Neurorehabilitation department), showing group difference with increase connectivity in motor cortex in Soccer player compared to the control group. From this seeding work we are going to continue to study the cellular and molecular mechanisms of tissue remodeling in mTBI and repeated sub-concussive priming longterm brain functional consequences.

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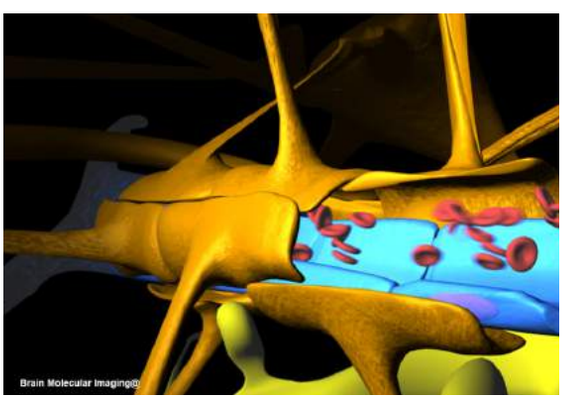

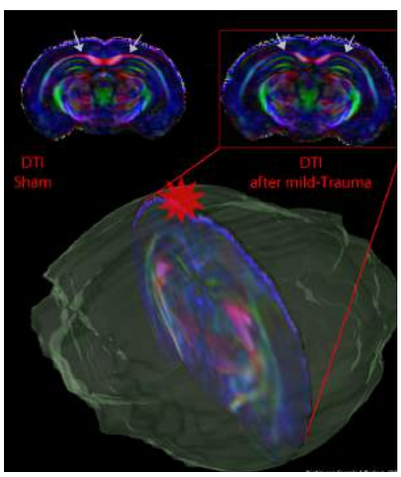

Figure 1. NeuroVascular Unit: Physiological unit & DTI changes at 12 months post-mTBI using CHILD© model.

TRANSFEAR

Translational study of the cerebral substrates involved in pathological fear recovery

Mélissa Bonnet

Neurology

2012

TRAIL funding: 130 000 €

CorePartner Neurocentre Magendie (U1215)

Anxiety Disorders including post-traumatic stress disorders (PTSD) are the most common mental disorders with an estimated lifetime prevalence of 15% -20% in the general population. They occur early in life and are risk factors for other mental disorders later in life such as affective disorders and substance abuse disorders thus presenting a major health problem in industrialized countries (WHO and WONCA 2008). In recent years, it has become evident that associative learning mechanisms and alteration in sleep architecture play a crucial role in relapse of fear behaviors. Indeed, it is known that exposure to stimuli that have been repeatedly associated with traumatic events can precipitate fear behavior during relapse and that the lack of extinction consolidation during post-extinction sleep correlates with high fear recovery. While tremendous progress has been made in identifying the basic mechanisms underlying acquisition of fear and consolidation of extinction, much less is known about the neuronal mechanisms involved in fear relapse after extinction. The present translational proposal aims at identifying the changes in functional connectivity of cerebral structures involved in relapse of fear behavior using innovative technologies in both animal and humans. Firstly, we will develop and validate a fear conditioning and extinction protocol in healthy humans, which shares similarities with that currently used in rodents, in order to provide a strong physiological background on fear extinction mechanisms in healthy context. Secondly, we will study the changes in functional interactions between neuronal structures involved in fear and extinction learning during fear behavior using electrophysiological recordings in rodents and functional Magnetic Resonance Imaging (fMRI) technique in humans. Finally we will assess sleep modifications in rodents and healthy humans by using neuronal recordings and electroencephalography (EEG), respectively. The proposed studies will reveal how the functional organization of specific neural structures directly modulates relapse of fear behavior using relevant animal and human models. Elucidating the neural mechanisms mediating pathological fear recovery should further suggest novel therapeutic strategies for psychiatric conditions characterized by a high propensity to relapse such as PTSD.

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ARM

Automatic assessment of Radiofrequency ablation Margins

Baudoin Denis de Senneville | Oncology | 2016 | TRAIL funding: 150 000 €

CorePartner Bordeaux Institute of Mathematics (IMB, UMR5251)

The aim of this project is to propose a fully automatic pipeline to a fast assessment of 3D-treatment margins that could allow performing additional heating cycle in order to achieve a complete treatment with satisfying margins.

For the successful completion of such medical interventional procedures, several concepts, such as daily positioning compensation, delineation propagation, rely on establishing a spatial coherence between planning images and images acquired at different time instants over the course of the therapy. To meet this need, image-based motion estimation and compensation relies on fast, automatic, accurate and precise registration algorithms. However, image registration quickly becomes a challenging and computationally intensive task, especially when multiple imaging modalities are involved. During the first 24 months of the project, we developed a complete 3D image registration tool designed to compensate for the liver deformation and inherent positioning errors arising between the two imaging sessions. In particular, a keystone of our tool is the capability to estimate organ deformation between images acquired with different imaging sensors (for example, the tool is able to co-register MRI and CT-scans of the abdomen). In particular, the proposed framework selects representative voxels of the registration process, based on a supervoxel algorithm. Costly calculations are hereby restrained to a subset of voxels, leading to a less expensive spatial regularized interpolation process. This results in an algorithm requiring a low number of input parameters, is easily parallelizable and provides an elastic voxel-wise deformation with a subvoxel accuracy.

At this point we have a mock-up for multi-modal deformable registration. Practically, we are now able to register the on the fly CT/CBCT, CT/MRI, MRI-T1/MRI-T2 images. We are also able to compute 3D voxelwise exposure maps, which allows to localize unsufficient treated area of a tumor (see Fig. 1).

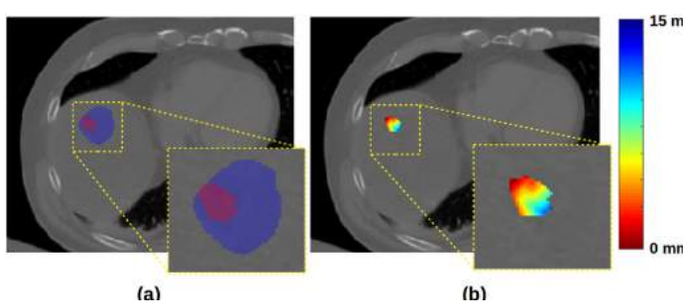

Figure 1. Typical exemple of a 3D exposure map obtained on a liver tumor during a RF-ablation. (a) : binary masks of the tumor (in red) and the ablation zone (in blue) super-imposed on CT-images. (b) : 3D distance map calculated using the two binary masks reported in (a). Insufficient treated areas corresponds to voxels having an exposed distance below a pre-defined margin threshold of 5mm.

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BIGDATABRAIN

To develop a new generation of quantitative MRI analysis method to cope with the rise of BigData in neuroimaging

Pierrick Coupé | Neurology | 2018 | TRAIL funding: 46 800 €

CorePartner Aquitaine Institute of Cognitive and Integrative Neurosciences (INCIA, UMR5287)

Magnetic resonance (MR) imaging plays a crucial role in the detection of pathologies, the study of brain organization and the clinical research. Every day, a vast amount of data is produced in clinical settings and this number is increasing rapidly, which prevents the use of manual approaches for data analysis. As a result, the development of reliable segmentation techniques for the automatic extraction of anatomical structures is becoming an important field of quantitative MR analysis. With the BigDataBrain project, our final goal is to develop a new generation of quantitative MRI analysis methods to cope with the rise of BigData in neuroimaging and, ultimately, to generate new knowledge. Moreover, the proposed methods will be implemented in full open access to the entire community through a web platform.

During this first year of BigDataBrain project we already proposed several pipelines to automatically process massive datasets. First, we proposed 2 pipelines for the segmentation of hyperintense lesions of white matter [1,5]. The presence of white matter lesions (WML) is associated with different brain diseases such as multiple sclerosis (MS), small vessel disease or head injury among others, but it also occurs in normal aging. The reliable and robust quantification of these lesions is of great importance for the diagnosis these pathologies. In addition, we proposed several new methods for the early diagnosis and the prognosis of Alzheimer's disease (AD) [2, 6, 7]. These methods propose competitive results compared to state-of-the-art methods. Moreover, we applied our previous pipelines available on our web platform volBrain to multiple sclerosis [3]. In this study, we showed differential gray matter vulnerability in the one year following a clinically isolated syndrome. Finally, we developed new method based on deep learning for denoising [4] and AD detection.

In the next years, we will improve the architecture of our web platform. Moreover, we will deploy a second site for this platform at the LaBRI UMR CNRS 5800. Finally, we will integrate our new pipelines within the deployed platform.

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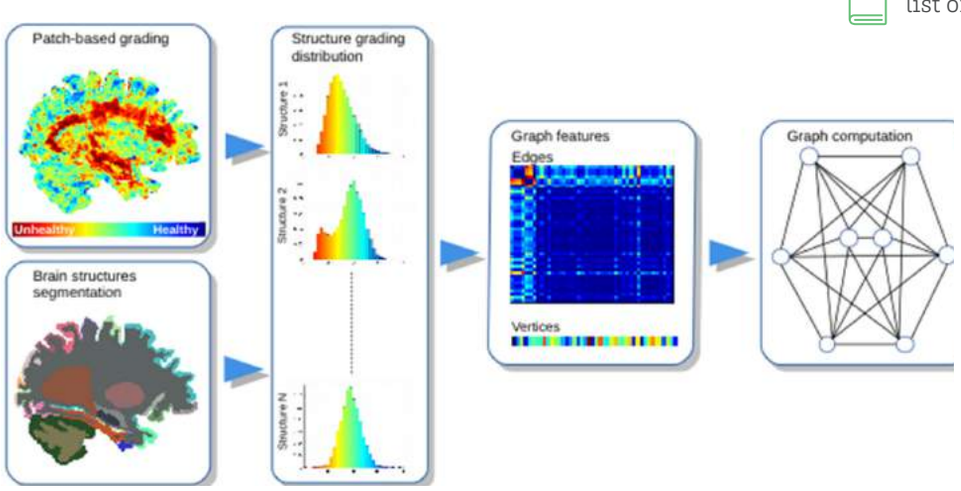

Figure 1. Illustration of the graph construction of our AD prediction method. From left to right, for each segmented structure an estimation of the density probability of pathology grading is computed. Then, histograms are used to build our graph of brain structure grading. Thus, 134 histograms representing each segmented brain structures are estimated. This method enables to better model the AD signature and thus to improve diagnosis accuracy (see text for more details).

DEEP STROKE

DEEP Learning for prediction of long-term motor impairment after stroke

Thomas Tourdias

Neurology

2017

TRAIL funding: 49 924 €

CorePartner Neurocentre Magendie (U1215)

The objective of the partnership between the Neuro-imaging department, the Neuro-vascular unit of Bordeaux University Hospital and DESKi is to create two tools to help medical care of patients suffering from stroke via artificial intelligence approaches.

The first tool aims to automatically segment cerebral acute infarcts on diffusion weighted imaging (DWI) to provide directly the volume and location of the lesion. The second tool aims to predict patients' motor recovery capacity from initial MRI. In order to develop these tools, deep learning algorithms were trained on a large MRI and clinical database of patients suffering from stroke. In this database, acute infarcts lesions were segmented manually by experienced readers (gold standard, n = 929), and patients were followed prospectively with quantification of motor recovery at 3 months and 1 year.

For the segmentation tool, DESKi has developed a 3D hybrid strategy in which learning is based both on the complete image and on patches selected in the regions of the image where the algorithm deviates from the gold standard. It has been shown that this hybrid strategy significantly improves the quality of the segmentations (improvement of the Dice metric) mainly by reducing the number of false positives lesions (Fig. 1) compared to current methods. The manuscript of this work is submitted for publication.

The development of the second tool encountered difficulties inherent to the database. In particular, the patients who are more severely impaired in the early phase (24h-72h) are the patients for whom the prediction of the recovery is the most relevant because they can either remain severe or they can recover substantially. In our cohort only a small number of these severe patients have been included. Our hypothesis was that information within the initial MRI (infarct size, localization, depth of abnormalities...), extracted with deep learning could help anticipate patients' recovery. Many strategies and network architectures have been tested but for the moment without success, which we believe, is related to the small number of severe patients in the learning base. We identified ways to increase the learning base by initiating new collaborations with vascular neurologists and epidemiologists to access clinical and imaging data from regional registry (OBA[2] study).

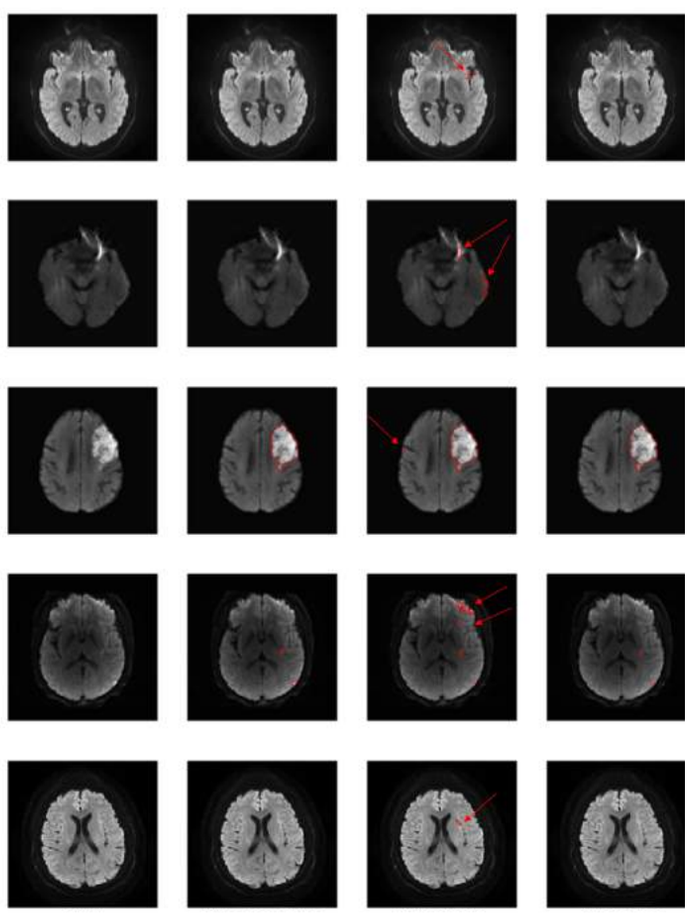

Figure 1. Axial view of MRIs from our stroke database (a) with expert segmentation outlined in red in panel (b). Panel (c) shows automatic segmentation based on regular training where red arrows point to false positives. Panel (d) shows automatic segmentation based on the new hybrid active training which reduces the number of false positive..

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HETEROMRMAP

MR mapping of renal function heterogeneity to characterize parenchymal nephropathies

Benjamin Taton

Nephrology

2016

TRAIL funding: 50 000 €

CorePartner Bordeaux Institute of Mathematics (IMB, UMR5251)

The diagnosis of glomerular nephropathy relies mainly on histologic findings that require kidney biopsy. This is an invasive procedure that comes with high risks of bleeding. Sometimes, depending on the condition of the patient, it cannot even be performed, and when performed the obtained samples only represent a very small fraction of the investigated organ. Previous studies have shown that some inflammatory kidney diseases harm the kidney with a heterogeneous pattern: some regions lose their function while others remain normal. In contrast other diseases such as diabetic nephropathy are assumed to have a diffuse and homogeneous lesion pattern.

Functional magnetic resonance imaging (fMRI) is a non-invasive, non-irradiant, non-nephrotoxic procedure that has the unique potential to build functional maps of the kidneys. Evaluating the heterogeneity of kidney function within the organ could help clinician in determining the nephropathy of their patients, and in making decisions concerning the requirement for a kidney biopsy or even the treatment to be proposed.

The purpose of this pilot study is to compare the heterogeneity of functional MAP of the kidneys in healthy subjects, patients with diabetes mellitus, and patients with inflammatory glomerulopathies (a class of severe kidney diseases with an allegedly patchy pattern of injury): ten healthy subjects, ten patients with a heavy proteinuria attributed to a diabetic nephropathy and ten patients with a biopsy-proven inflammatory glomerulopathy will have a fMRI examination to build the aforementioned functional maps. Using these maps, the heterogeneity of the distribution of kidney function within the parenchyma will be assessed according to various indicators and compared between the 3 groups of subjects: a significant difference would mean that fMRI could a valuable tool to orient the diagnosis of nephropathy.

MOD

Mathematical modeling of the response to antiangiogenic drugs via medical imaging

Thierry Colin | Oncology | 2013 | TRAIL funding: 380 000 €

CorePartner Bordeaux Institute of Mathematics (IMB, UMR5251)

The MOD project aims at developing novel numerical tools for helping clinicians in their decision on diagnosis, prognosis or evaluation of therapies for cancer. For that matter, mathematical models and artificial intelligence approaches are used.

The Ph.D of Cynthia Perier (funded by TRAIL) took a new direction: radiomics approaches for soft-tissue sarcoma. The objective is – by correlating imaging, clinical and omics features to clinical outcome through machine learning – to have a better estimate of the efficacy of the neoadjuvant chemotherapy after two cycles. This is a collaboration with Amandine Crombé at Institut Bergonié. The first results are very promising and an article was just submitted.

Thibault Kritter (in the project but not funded by TRAIL) defended his Ph.D in early October. Two papers were submitted. One on the evaluation of the risk of relapse of patients with low grade gliomas (using radiomics) and one other on a novel approach to personalize mathematical models of brain metastases growth.

Irène Kaltenmark just started her post-doc funded by TRAIL. Her objective is to extend shape analysis method to the context of cancer evolution to have a better descriptor for the shape changes that would ultimately be included in delta radiomics approaches (to improve their accuracy).

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NEKOMRI

MRI sequence for bronchial wall segmentation and analysis

Fabien Baldacci | Pneumology | 2014 | TRAIL funding: 35 000 €

CorePartner Bordeaux Cardio-Thoracic Research Center (CRCTB, U1045)

The aim of this project is to develop bronchial wall segmentation and analysis methods on a new MRI sequence for lung acquisition, allowing both a diagnosis by using a MRI instead of CT scan, and the assessment of bronchial remodeling.

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ABACI

Automated Brain Anatomy softwares for Cohort Imaging

Bernard Mazoyer | Neurology | 2012 | TRAIL funding: 314 830 €

CorePartner Neurofunctional Imaging Group (GIN, UMR5296)

The ABACI project consists in developing, testing and applying a software toolbox dedicated to the automated processing of structural MRI, acquired in the framework of cohort studies. The project closely fits with the TRAIL laboratory of excellence strategic plan that includes population neuroimaging as one of its key topic. The project federates three neuroimaging teams of TRAIL with two non-TRAIL teams specialized in neuroepidemiology. Unsupervised pipelines for registration, normalization, segmentation and morphometric analysis of structural brain MRI acquired in large longitudinal cohorts will be implemented. These pipelines will deliver global and regional brain anatomy phenotypes for grey matter, white matter and CSF. Whenever possible, widely used and validated public domain neuroimage processing algorithms will be integrated. The project will be linked to and run in parallel with i-Share, a large size MRI cohort of students that will serve as a test cohort for the toolbox. In addition, all participating teams will have the opportunity to test and adapt the tools to their own cohorts and settings, with opening applications in the fields of multiple sclerosis, stroke and brain aging. Commercial use of the toolbox by non-academic users will be proposed.

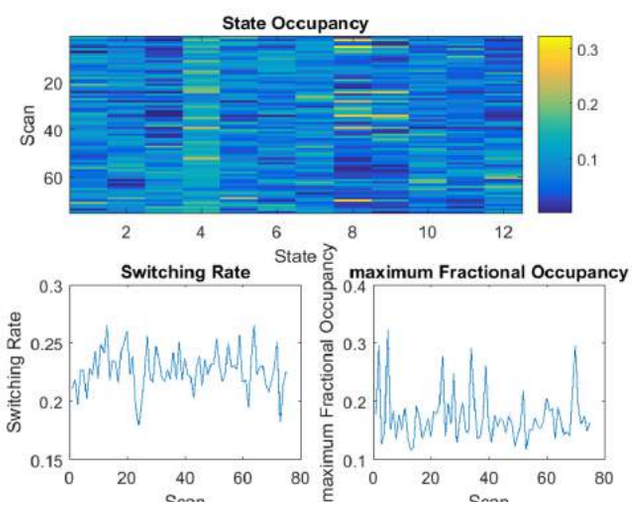
ACTE

Ambulative cognitive training in elderly: Relation with intrinsic brain functional connectivity

Sandra Chanraud | Neurology | 2012 | TRAIL funding: 130 000 €

CorePartner Aquitaine Institute of Cognitive and Integrative Neurosciences (INCIA, UMR5287)

The functioning of the human cerebellum is now widely recognized to cover not only motor control and modulation but also cognitive and emotional processing. In this context, one of the ongoing trends in recent years is to address the manner through which the cerebellum communicates functionally with other brain areas in order to discern its role in cognition and behavior. Accordingly, we aim at expanding the functional repertoire of the cerebellum by delineating its functional dynamics with cortical and subcortical regions through the use of various state-of-the-art techniques and methods from resting-state fMRI connectivity analysis. Two main datasets are included in the scope of our study. First, Max Planck Institute - Leipzig Mind-Brain-Body Open Dataset consisting of 181 healthy controls (1 hour of resting state each) with numerous cognitive variables of interest. Second, Addiction dataset part of the MOBICOGIM protocol which includes 55 addiction patients and 45 healthy controls. In addition, this dataset incorporates ecological momentary assessment data which can provide real-time prediction of symptoms in substance use disorders. The data were preprocessed to remove noise and the connectivity variables are extracted using sliding window with K-means clustering, Hidden Markov Models (HMM), and dynamic graph analysis. These methods can capture and describe several time-resolved brain connectivity states that occur in a timely probabilistic manner in each subject/group and include cerebellar regions. Exemplar results from HMM applied to the MPI-Leipzig dataset is shown in the figure below. It includes the different variables such Fractional occupancy in each brain connectivity state (12 states), and switching rate from one state to another for each subject. Correlations with cognitive variables will be assessed shortly after the imaging variables of interest are fully collected.



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ADPP

Brain topology of AD presymptomatic phase

Gwenaëlle Catheline Neurology 2015 TRAIL funding: 30 000 €

CorePartner Aquitaine Institute of Cognitive and Integrative Neurosciences (INCIA, UMR5287)

The better understanding of Alzheimer's disease (AD) lies in the precise description of the grounds on which is developing the disease, which is the Aging Brain. This is the main aim of our imaging project which concerns the description of the different modifications of brain networks in a large sample of elderly subjects. More precisely, whereas AD patients present both structural and functional changes, the relationship between these different physiopathological events is still poorly understood. In a first series of analyses, we described the association between functional connectivity state of the brain and the age-related episodic decline in a healthy elderly sample of 120 subjects. We observed that the decline is associated with an increase of interhemispheric connections. The second series of analyses is based on the set up of a tractography pipeline to take into account white matter hyperintensities, so frequently observed in subjects under 65 years old. Based on this pipeline, a corrected-cingulum bundle and an uncorrected one were tracked, and we have extracted the diffusion parameters from these two situations. Parameters extracted from the corrected-cingulum are correlated with the verbal fluency task of the elderly whereas the ones extracted from the uncorrected-cingulum are not. The third series of analyses are focused on the posteromedial and parietal cortex. We have observed in this network that low structural connectivity is associated to high functional connectivity and that both parameters explained a part of the episodic memory performance of the elderly subject. This project has provided a better understanding of the set up and the relationship between the different cerebral network changes observed in an aging brain and their association with age-related cognitive modifications.

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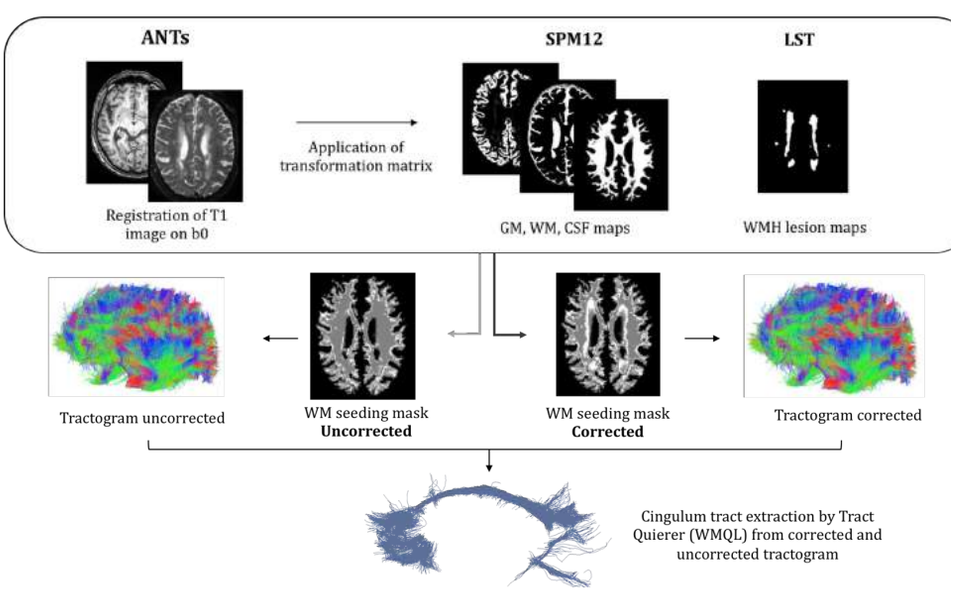

Figure 1. Pipeline for tractography of the cingulum bundle corrected for the presence of White Matter Hyperintensities.

COBRASCAN

Quantitative CT and COBRA cohort for study of chronic obstructive pulmonary disease

François Laurent | Pneumology | 2013 | TRAIL funding: 234 448 €

CorePartner Bordeaux Cardio-Thoracic Research Center (CRCTB, U1045)

Chronic obstructive pulmonary disease (COPD) is expected to be the 3rd leading cause of mortality and the 5th cause of morbidity in the world by 2020. The pulmonary component of COPD is characterized by airflow limitation that is not fully reversible. Airflow limitation is defined by pulmonary function tests (PFT) results and is caused by narrowing of small airways which is a consequence of the combination of airways wall thickening due to airway wall remodeling and loss of tethering force due to emphysematous lung destruction. However patients with the same airflow limitation will present with different clinical subtypes, in term of severity and outcome. The effect of certain treatments can be only proved in term of primary outcomes if there is a mean other than pulmonary function tests for classifying patients into phenotypes in longitudinal studies. The prognostic impact of these phenotypes is still poorly known.

Advance in CT technology and CT image analysis programs, i.e. CT algorithms herein referred to as quantitative CT (QCT) can be used to analyse in details the morphological changes involved in COPD, i.e. the severity of emphysema, airways dimensions, small airways obstruction and small pulmonary vessels on CT images. Our group has developed software needed for combined quantitative analysis of structural changes of proximal and distal airways and can use software dedicated to quantification of emphysema and pulmonary vessels. However, there is still no consensus in term of the best appropriate algorithms for quantification.

The COBRA project directed by INSERM relies on a national cohort of 500 patients. The main objective of the COBRA cohort is to determine clinical, biological and genetical determinants of the outcome of COPD patients. The recruitment started in 2008 and inclusion of 500 patients is finally expected, 211 of them being included so far. Clinical, functional and biological variables will be followed up over 10 years. COBRASCAN will consist in a QCT acquisition performed in each patient included into the COBRA cohort during the 5th year after inclusion. The hypothesis is that a CT quantitative morphological analysis reflecting lung parenchymal destruction (emphysema), bronchial wall remodeling of large and small airways and changes in pulmonary vessels has a significant prognostic impact. The originality of COBRASCAN will be its ability to identify phenotypes of COPD patients based on multiple morphological criteria and to specify their prognostic value. The innovative aspect of the project is the development of a single new software able to combine the acquisition of objective data of emphysema, bronchial wall thickening of proximal and distal airways, large vessels size, reflecting changes of the whole respiratory system. The software will be built based on the most robust and reproducible algorithms available and the most relevant variables for each type of morphological changes will be determined. The study will specify the role of quantitative CT as a biomarker of COPD, and its position in on-going clinical trials. Phenotyping COPD into appropriate subgroups using imaging in addition to PFT is likely to play a role in pharmacological research.

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TRAIL&TRACKS

Atlasing whole brain white matter tractsin 300 healthy humans

Laurent Petit | Neurology | 2011 | TRAIL funding: 97 500 €

CorePartner Neurofunctional Imaging Group (GIN, UMR5296)

The present project proposes, using diffusion tensor imaging (DTI) tractography, to create a normative population-based probabilistic atlas of white matter tracts in healthy humans (TRAIL&TRACKS) for research, clinical and educational purposes. It is based on the BIL&GIN cohort, which includes 300 healthy volunteers aged between 18 and 50 years, balanced between men and women, right-handers and left-handers. The doctoral fellowship application deals with the work to be performed on DTI data, the validation of a method for probabilistic tractography of a set of white matter tracts, the anatomical description of every tracts and how they differ among the 300 subjects in terms of hemispheric asymmetries, gender and handedness. Specific metrics of white matter integrity will be extracted for tracts in the brainstem and projection, association, and commissural tracts. This is not to propose another atlas of the white matter of the human brain, but a tool where inter-hemispheric asymmetry and inter-individual variability will be taken into account into the description of each tract. Once patented, we will deliver an automated tract-labeling tool interfaced with usual neuroimaging analysis software. Several publications are envisaged for the construction of this atlas, including the edition of a textbook and numerical tools such as web-based application for teaching material and training.

2.3 Imaging facilities

Researchers have access to state-of-the-art imaging facilities in Bordeaux:

IBIO

- The Institute of Bio-Imaging (IBIO) dedicates 2 409 m^2 to translational research in imaging. The building is located on the Carreire-Pellegrin campus of the University of Bordeaux, and is connected to the buildings of the University Hospital Pellegrin and of the University. The Institute was built in two phases with the financial support of the Regional Council and the two CPER fundings of 2007-2013 and 2013-2019.
- A technical platform of 1 273 m^2 hosts medical imaging equipment such as MRIs and an Xpulse device. Starting September 2019, several teams will have moved into the IBIO building: research teams of CRMSB, INCIA and ISM, teams of the industrials Canon Medical Systems and Olea Medical, an ALPhANOV team, and an international academic team of the SPINE project.

PTIB

- The Biomedical Innovation Technological Platform (PTIB) is a platform of the University of Bordeaux, in association with the South University Hospital. Its objective is to ensure the technological transfer between a sector of clinical and experimental skills, and the industrial sector, in order to develop or validate diagnostic or therapeutic tools.
- The PTIB hosts start-ups and offers spaces and equipment for partner companies.
- Research teams can also benefit from top-notch equipment from IHU LIRYC cardiology imaging platform.

2.4 Scientific communication

TRAIL PUBLICATIONS

- The TRAIL publications from the 2011-2018 period (see annex B.1.1 for details) feature in journals such as Nature Neurosciences, Angewandte Chemie, Biological Psychiatry, Trends in Molecular Medicine, Brain, Current Biology, Theranostics, Cell Reports, Nature Reviews Nephrology, Thorax, Radiology, Journal of Controlled Release, JNNP Journal, Stroke, Frontiers in Immunology, Chem Communication, NeuroImage, and Organic Letters.
- Publications costs of TRAIL quoted publications are co-funded by the LabEx.

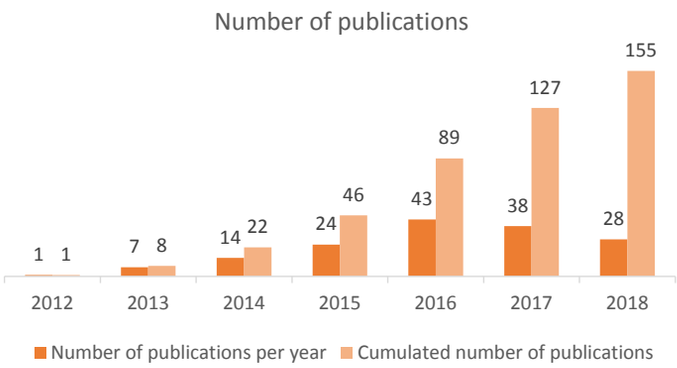
[1] The Field-Weighted Citation Impact metric indicates how the number of citations received by a publications compares with the average number of citations received by all other similar publications; a Field-Weighted Citation Impact of greater than 1.00 indicates that the publications have been cited more than would be expected based on the world average for similar publications.

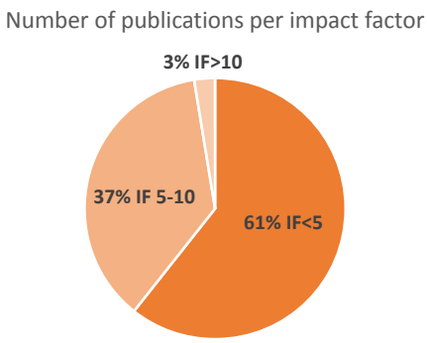
155
TRAIL quoting publications over the 2011-2018 period

46
TRAIL publications amongst the 10% most quoted worldwide (2011-2018 period)

28
TRAIL quoting publications in 2018

1.49
average Field-Weighted Citation Impact[1]





SCIENTIFIC COMMUNICATIONS

› Researchers from the Community have given 178 scientific communications in international events (see annex B.1.2 for details) such as RSNA, European Congress of Radiology, ISMRM, ECTRIMS, IMSCOGS, Human Brain Mapping, ESMRMB, Interventional MRI Symposium, Congress of the European Association of Nuclear Medicine, and FENS. In 2018, 41 scientific communications were given by TRAIL researchers.

2.5 Patents and Software Protection Agency recordings

By the end of 2018, 12 patents and 4 Software Protection Agency recordings issued from TRAIL have been registered. Out of the 12 patents, one new patent was registered in 2018 (see annex B.2 for details): "New vectors of pharmacologically active and hydrophobic molecules and their preparation process", FR 17/61647, Mireille Blanchard-Desce, Diane Braguer, Michel Vaultier, Marie-Anne Estève, Jonathan Daniel, Florian Correard, Maëva Montaleytang.

6
patents on cardiology topics

1
patents on neurology topics

4
patents (and 4 Software Protection Agency recordings) on oncology topics

1
patents on pneumology topics

Regarding patents, Aquitaine Science Transfer (AST) - the technology transfer agency - represents the trustees for intellectual property negotiations with industrials.

Scientific animation & training

3.1 TRAIL scientific events in Bordeaux

CONFERENCES

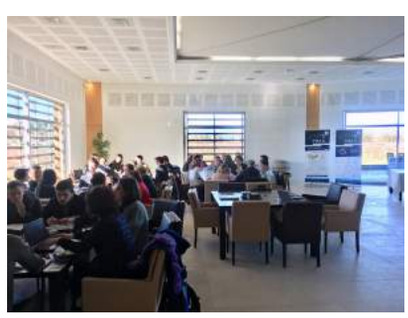
- TRAIL teams invited 45 international speakers to give presentations in Bordeaux (see annex C.1 for details). In 2018, 4 lectures were given:
- "Lost in translation : histoire et définition(s) de la recherche translationnelle" by V Grimaud (Centre Emile Durkheim);
- "Avantages et challenges de l'imagerie de la moelle épinière à 7T" by V Callot (CRMBM, Aix-Marseille Université);
- "Changing the Field, an introduction to Magnetic Particle Imaging" by J Gaudet (Magnetic Insight);
- "Quantitative imaging biomarkers in brain tumors: How we do it" by Y S Choi (Yonsei University, Korea).

ANNUAL GENERAL ASSEMBLIES

- An annual General Assembly is organized every year to present the achievements, research projets, and the development strategy for the upcoming years to the Community.

ASSISES

- The members of the Community met at the first TRAIL Assises in June 2017 to discuss the future of the LabEx after 2020.
- The second Assises took place in January 2018 and the members of the Community produced recommendations regarding the development of the LabEx. They also chose the members of a working group, whom are in charge of defining the scientific roadmap of the future TRAIL program.



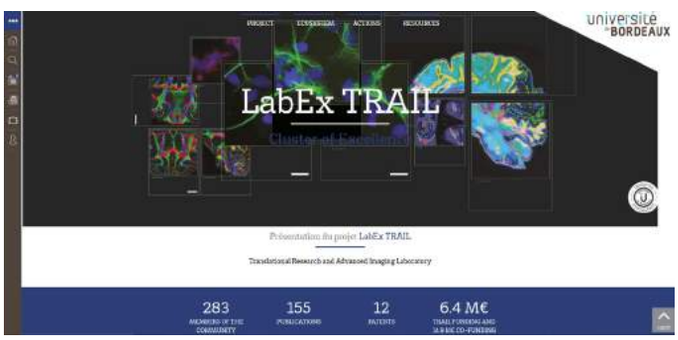
SCIENTIFIC DAYS

- TRAIL research projects are presented by project leaders to the Community during annual "intra-community scientific days", and during "Workpackage scientific meetings".

SUMMERSCHOOLS & THEMATIC SCHOOLS

- 2 international summerschools were organized by the Community: "Connectomics, the wiring diagram of the human brain" in 2014, "Neuroepiomics" in 2015.
- A thematic school "Modulamag, contrast modulation in MRI" was organized in 2012 with the University of Mons, Belgium.

3.2 Informing the Community



The TRAIL website (trail.labex.u-bordeaux.fr) is dedicated to inform about the LabEx, events, and internal calls; in addition, a newsletter is sent to each Member of the Community to highlight specific event/information. The website and the newsletter are both in English; the graphical chart is common to all communication media of the LabEx.

The website was entirely redesigned in October 2017 to offer an easier navigation as well as a faster access to information.

3.3 Partnerships with international scientific events

Specific partnerships were built with international scientific events:

YEAR	SCIENTIFIC EVENT	TOPICS
2012	NGI	Neuron-glia interactions
2015	Euroanalysis (Bordeaux, Sept 2015)	Analytical chemistry
	KidMRI (Bordeaux, Oct 2015)	Functional MRI for renal parenchymal disease: ready for clinical practice
2016	Cosine 6 (May 2016)	Medicine and digital
	Aptamers in Bordeaux (Bordeaux, June 2016)	Aptamers biology, chemistry & technologie
	Congrès de la Section 28 du CNRS (Bordeaux, June 2016)	Pharmacology, bio-ingineering, imaging
	GECO57 (Ascain, Aug 2016)	Organic chemistry
	ESUR (Bordeaux, Sept 2016)	European Symposium on Urogenital Radiology
2017	SFRMBM (Bordeaux, March 2017)	MRI, MR spectroscopy
	NeuroFrance 2017 (Bordeaux, May 2017)	Neurosciences
	5e Ecole d'imagerie du Petit animal appliquée au Cancer (Bordeaux, June 2017)	Oncology preclinical imaging
	ERANET (Bordeaux, June 2017)	Neuroimaging changes after acute brain injuries to evaluate the remote plasticity
	Aptamers in Bordeaux (Bordeaux, Sept 2017)	Aptamers biology, chemistry & technology
	SFNano 2017 (Bordeaux, December 2017)	Nanomedicine
2018	Ecole d'été Biomatériaux et Médecine Régénérative (Jun 2018)	Biomaterials and regenerative medicine
	5th Neurocampus Conference (Bordeaux, Sept 2018)	Neurosciences: aging of memory functions, where are we now?
	Euskampus 2018 (Bilbao, Nov 2018)	Translational Biophysics workshop

3.4 Links with the international Master of Bio-Imaging

- In collaboration with the University of Laval in Quebec and the University of Mons in Belgium, the Master of Bio-Imaging was launched in 2012. The objective is to master theoretical concepts and practical know-how of the main bioimaging techniques with all courses given in English.
- The international Master of Bio-Imaging has been replaced by the Master of Health Engineering in 2017. This course is composed of three pathways (bio-medical imaging, cellular bio-imaging, and biomaterials). In 2018, 33 students enrolled in this program (13 first-year and 20 second-year students).

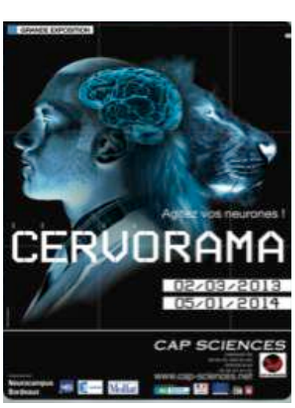
3.5 Links with the FLI network

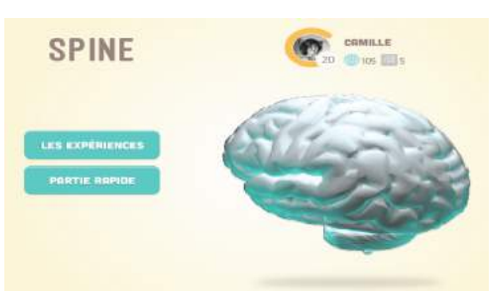
The French Life Imaging (FLI) national infrastructure (Bordeaux, Grenoble, Lyon, Marseille, Paris,...) is reorganizing the educational programs for students and young researchers to make a national and international offer. TRAIL, as a member of FLI, participates to this program and its events.

3.6 Knowledge dissemination to the general public

Several events have been set up to ensure knowledge dissemination to a large audience:

- TRAIL collaborated in 2013 on an exhibition called CERVORAMA which was organized by Cap Sciences Museum in Bordeaux. The exhibition showcased the uniqueness of the brain: brains of animals and humans, cognitive functions, memory, plasticity, 3D interactive presentation of brain anatomy, playing tricks on the brain. 62,000 people visited the exhibition in one year;
- TRAIL is working with Harvard Medical School on a citizen science game project called SPINE with crowd sourcing for large scale medical imaging postprocessing;
- In 2018, TRAIL researchers participated to the Fête de la Science, to a patients congress of the ARSEP fundation, to a radio broadcast, and published an article in a journal dedicated to technology topics.



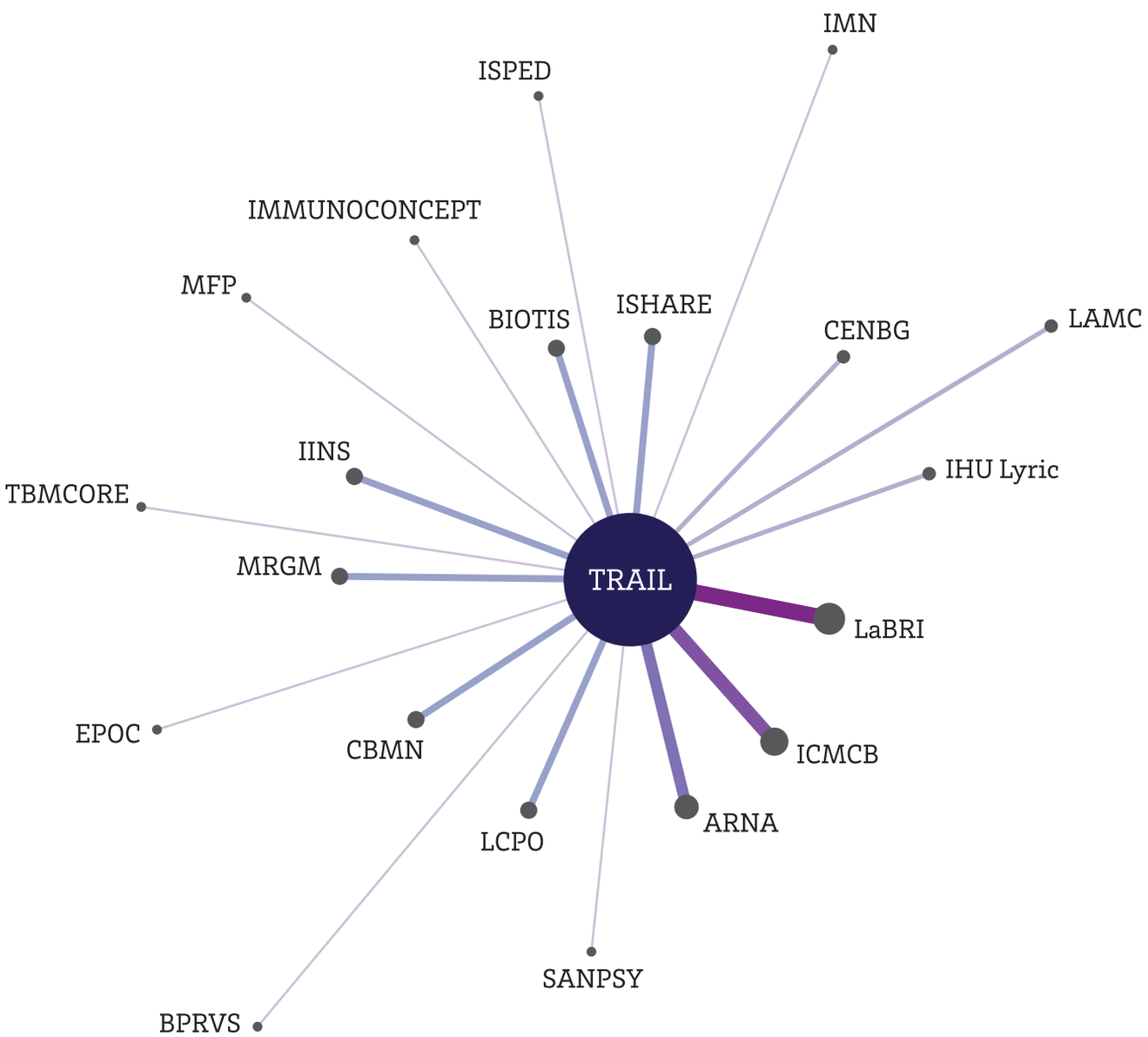


Attractiveness

4.1 TRAIL ecosystem in Bordeaux

Research in TRAIL is based on multidisciplinary teams:

- 83% of TRAIL funded federative projects rely on TRAIL CorePartners collaborations;
- 70% of TRAIL funded projects involve clinicians from the beginning of the project;
- 64% of TRAIL funded projects involve partners of the academic ecosystem of Bordeaux (see below).



4.2 International academic partnerships

› Due to the multidisciplinarity of the TRAIL research portfolio, the TRAIL teams collaborate with numerous international academic partners throughout the world (see annex D.1 for details).

› A total of 69 publications quoting TRAIL (47% of the total number of publications) has been produced with international partners.

4.3 European projects

Since 2012, TRAIL teams have been involved in 13 european projects, increasing its international visibility:

- 2012: ITN Marie Curie-Pi-Net (Spain, France, UK, Germany, Sweden);
- 2013: ERC Advanced SYMPHONY; ITN Marie Curie EDU-GLIA (Germany, UK, France, Sweden, Slovenia, Czech Republic, Israel);
- 2015: ERA-net NEURON-CnsAflame (Germany, France, Sweden, Israel);FLAG-ERA JTC Multilateral (The Netherlands, France, Spain); ANR PRCI;
- 2016: ERA-net NEURON-Trains ; COST Action ; IMI Beat-DKD; ERC Starting grant;
- 2017: ERA-net TRANSCAN ; COST Action;
- 2018: ERA-net NEURON-Misst.

In 2016, one Member of the TRAIL Community was granted an ERC Starting for the ECSTATIC project ("Electrostructural Tomography, Towards Multiparametric Imaging of Cardiac Electrical Disorders", Hubert Cochet).

Also, the LabEx TRAIL is member of the The European Institute for Biomedical Imaging Research (EIBIR, www.eibir.org) since January 2016, that "aims to coordinate and support the development of biomedical imaging technologies and the dissemination of knowledge with the ultimate goal of improving the diagnosis, treatment and prevention of diseases".

4.4 Visiting scholars and mobilities

TRAIL and IdEx Bordeaux welcomed 13 international visiting scholars since 2014:

- Pr Troels Skrydstrupi (Aarhus University, Copenhagen, Denmark);
- Pr Charles Guttmann (University of Harvard, Boston, USA);
- Pr Denis Parker (University of Utah, Salt Lake City, USA);
- Pr Juan P. Bolanos (The Institute of Functional Biology and Genomics, Salamanca, Spain);
- Pr Anil Kumar Mishra (Institute of Nuclear Medicine and Allied Sciences, New Dehli, India);
- Pr Jing-Huei Lee (University of Cincinnati, Cincinnati, USA);
- Pr André Obenaus (Loma Linda University, USA);
- Nicolas Farrugia, Ph.D (University of Brest);
- Pr Luc Pellerin (Unil-CHUV, Lausanne, Switzerland);
- Dr Hassan M Fathallah-Shaykh (University of Alabama, Birmingham, USA)
- Dr Tomohiro Aoki (National Cerebral and Cardiovascular Center, Kyoto-Osaka, Japan);
- José Manjón, Ph.D (Polytechnic University of Valencia, Spain);
- Pr Danielle Skropeta (University of Wollongong, Australia).

Outgoing mobility is supported through partnership between TRAIL teams and international universities:

- Clément Morgat: mobility to INMAS, India;
- Julien Jouganous: mobility to McGill University, Canada;
- Gisèle Clofent-Sanchez: mobility to Monash University, Australia;
- Thomas Tourdias: mobility to Stanford University, USA;
- Thomas Cornilleau: mobility to Aarhus University, Denmark;
- Sébastien Benzekry: mobility to Roswell Park Cancer Institute, USA;
- Samuel Bonnet: mobility to Monash University, Australia;
- Pauline Jeanjean: mobility to Athens University, Greece;
- Sylvain Miraux: mobility to Mons University, Belgium;
- Eric Thiaudière: mobility to State University of Novosibirsk, Russia;
- Gaël Dournes: mobility to Cincinnatti, USA.

4.5 Recruitments

54 persons have been recruited by TRAIL research projects (see annex D.2 for details):

23
post-doctoral fellows

10
engineers

16
doctorals fellows

5
technicians

4.6 Collaboration with industrials

Medical imaging is a highly competitive sector: it has daily clinical applications, it represents the most important health expense in the world, and this huge market attracts many researchers and industrials.

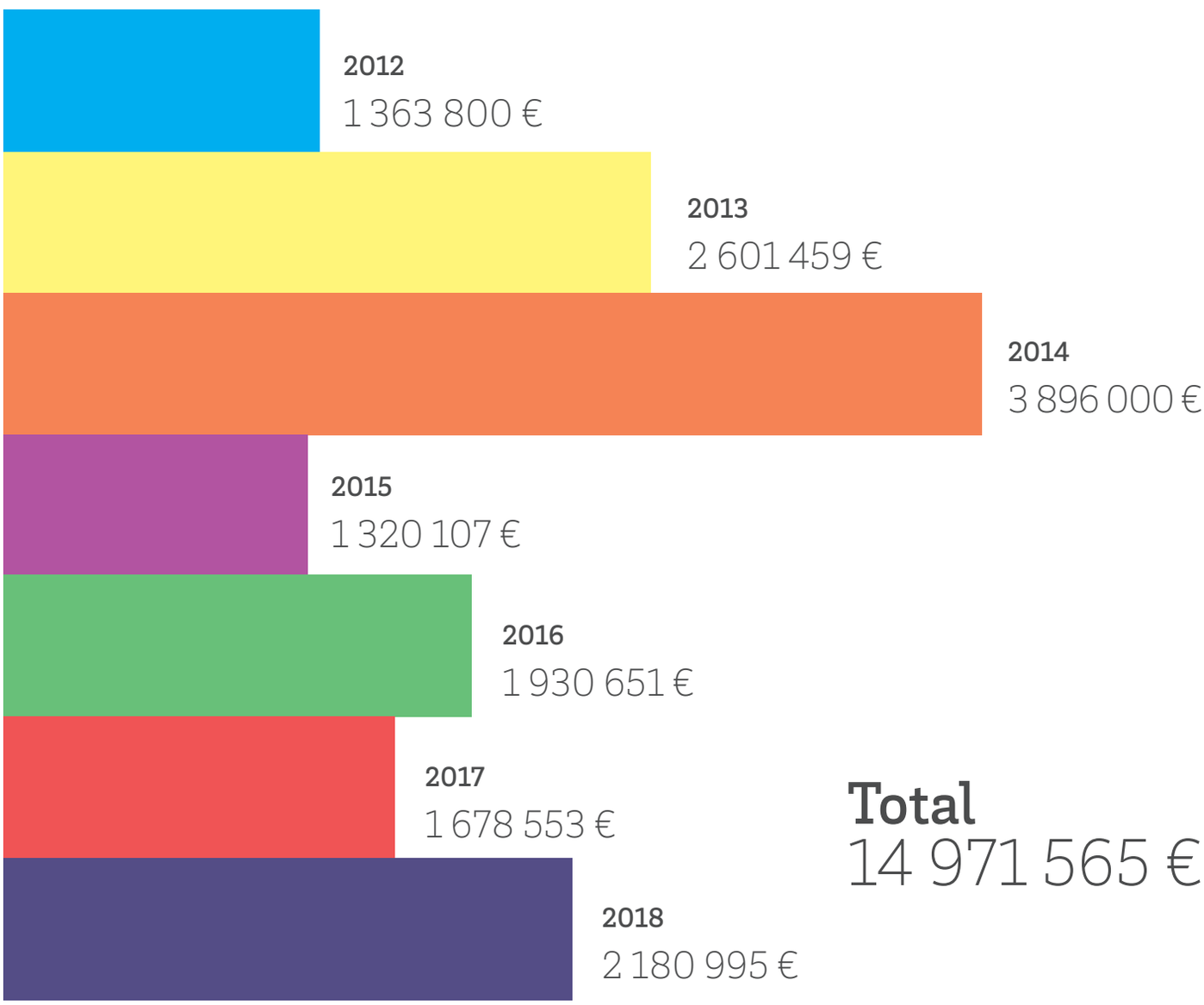
TRAIL Workpackages and research projects show the excellence of Bordeaux research in medical imaging but they are competing with major international research centers as well as industrial research. It is among the TRAIL objectives to define the right moment/Technology Readiness Level to transfer the result of research to industry, either through a proof of concept, or through animal experiment, or through clinical experiment, or through a publication (5 TRAIL quoting publications are in collaboration with industrials).

27 companies have been involved in TRAIL research projects since 2011 through direct cofunding, human resources and free use of their products/equipments:

- ALPhANOV: compact laser source development;
- AFFICHEM: drug design for oncology;
- BALT: endovascular treatment of intracranial aneurysms;
- BRUKER: imaging sequence development and magnetic particle imaging;
- CADESIS: database management for cohort imaging;
- CANON MEDICAL SYSTEMS: MS exploration;
- DESKI: deep learning models;
- GLAXOSMITHKLINE: preclinical oncology imaging and drug efficiency testing;
- IBA MOLECULAR: radiotracers development;
- IGT SA: HIFU development for oncology and cardiology;
- INTRASENSE: post processing for pulmonary imaging;
- LFB BIOTECHNOLOGIES: antibodies engineering;
- MERK SERONO: neuroinflammation clinical studies;
- MICROVENTION: endovascular treatment of intracranial aneurysms;
- NOVAPTECH: aptamer-based tools;
- OLEA MEDICAL: post-processing;
- PACIFIC BIOSCIENCES: human immunoglobulin sequencing;
- PENUMBRA: endovascular treatment of intracranial aneurysms;
- PHILIPS: sequence development;
- ROCHE: immunotherapy modeling;
- SANOFI: MRI/PET bioimaging markers for Alzheimer disease;
- SIEMENS: oncology imaging, HIFU development;
- SOPHIA GENETICS: radiomics and genetics;
- SUPERSONIC IMAGING: imaging equipment prototyping;
- TEVA: support for neuroinflammation clinical studies;
- UNITHER: drug efficiency study;
- VERMON: bimodal endorectal probe.

4.7 Cofunding

TRAIL research projects leaders have reinforced their projects budgets with a total of 14.9 M€ of cofunding, including 2.1 M€ from the private sector (see annex D.3 for details):



Annex

A/ Governance

A.1 TRAIL main figures per year

			TOTAL	2011	2012	2013	2014	2015	2016	2017	2018
RESEARCH	RESEARCH PROJECTS	Number of new projects	47	5	9	6	2	5	7	7	6
		Number of new 'emerging' projects	29	0	5	2	2	3	4	7	6
		Number of new 'federative' projects	18	5	4	4	0	2	3	0	0
		Research budget	6 395 985 €	493 971 €	1 150 866 €	894 448 €	490 000 €	979 618 €	1 399 008 €	592 774 €	395 300 €
		Research budget for 'emerging' projects	2 181 474 €		150 000 €	160 000 €	335 000 €	260 000 €	388 400 €	342 774 €	395 300 €
		Research budget for 'federative' projects	4 214 511 €	493 971 €	1 000 866 €	734 448 €	155 000 €	719 618 €	1 010 608 €	100 000 €	- €
		Number of medical thematics of TRAIL matrix covered by granted research projects	5 (100%)	2	3	4	4	4	5	5	5
		Number of WP of TRAIL matrix covered by granted research projects	7 (100%)	4	6	7	7	7	7	7	7
		WP1 budget	480 000 €		30 000 €	140 000 €		100 000 €	160 000 €	50 000€	
		WP2 budget	475 450 €		280 000 €	100 000 €			49 600 €	45 850 €	
		WP3 budget	532 500 €	97 500 €		180 000 €	45 000 €	160 000 €			50 000 €
		WP4 budget	1 266 300 €	119 000 €	250 000 €	60 000 €	45 000 €	345 000 €	198 800 €	50 000€	198 500 €
		WP5 budget	2 123 233 €	179 971 €	311 036 €	100 000 €	300 000 €	344 618 €	390 608 €	397 000€	100 000 €
		WP6 budget	711 724 €			180 000 €	35 000 €		400 000 €	49 924 €	46 800 €
		WP7 budget	806 778 €	97 500 €	279 830 €	134 448 €	65 000 €	30 000 €	200 000 €		
		EA 7435 (IMOTION) budget	147 000 €							97 000 €	50 000 €
		IMB budget	580 000 €			180 000 €			400 000 €		
		INSERM U1049 budget	30 000 €		30 000 €						
		INSERM U1215 (MAGENDIE) budget	820 578 €	130 000 €	281 036 €		100 000 €	59 618 €	200 000 €	49 924 €	
		U1045 (CRCTB) budget	709 448 €			274 448 €	35 000 €	100 000 €	300 000 €		
		UMR 5287 CNRS (INCIA) budget	1 045 200 €		280 000 €	30 000 €		240 000 €	198 400 €	150 000€	146 800 €
		UMR 5296 (GIN) budget	412 330 €	97 500 €	249 830 €		65 000 €				
		UMR 5536 (RMSB) budget	2 108 929 €	147 471 €	310 000 €	380 000 €	245 000 €	480 000 €	150 608 €	295 850 €	100 000 €
		UMR5255 (ISM) budget	542 500 €	119 000 €		30 000 €	45 000 €	100 000 €	150 000 €		98 500 €
	SCIENTIFIC COMMUNICATION	Publications quoting TRAIL	155		1	7	14	24	43	38	28
		Publications showing an impact factor <5	94		1	5	10	17	24	25	12
		Publications showing an impact factor between 5 and 10	57			2	4	5	18	12	16
		Publications showing an impact factor >10	4					2	1	1	
		Publications of WP1 projects	10					1	2	4	3
		Publications of WP2 projects	30			2	4	10	6	5	3
		Publications of WP3 projects	9			1	2	1	2	2	1
		Publications of WP4 projects	26		1	1	2	1	10	8	3
		Publications of WP5 projects	59			3	5	8	16	11	16
		Publications of WP6 projects	12					2	2	6	2
		Publications of WP7 projects	9				1	1	5	2	0
		Publications of EA IMOTION projects	5						2	3	0
		Publications of IMB projects	7					2	2	2	1
		Publications of INSERM U1215 (MAGENDIE) projects	27			1	4	5	9	6	2
		Publications of U1045 (CRCTB) projects	16					1	5	6	4
		Publications of UMR 5287 (INCIA) projects	26				3	1	9	5	8
		Publications of UMR 5536 (RMSB) projects	58			5	7	14	10	10	12
		Publications of UMR 5255 (ISM) projects	16		1	1		1	6	6	1
		Scientific communications during international events	178	0	0	8	18	26	40	45	41

A/ Governance

			TOTAL	2011	2012	2013	2014	2015	2016	2017	2018
TRAINING	SCIENTIFIC EVENTS	Supported scientific events	20	0	2	0	1	3	5	6	3
		TRAIL cofunding	91 400 €	- €	14 400 €	- €	15 000 €	19 000 €	8 500 €	30 000 €	4 500 €
	TRAIL EVENTS IN BORDEAUX	'Scientific Days'	4	0	0	1	1	1	1	0	0
		Lectures by international speakers	45	0	1	10	5	12	9	4	4
	MASTER BIO-IM.	Number of students	140	nd	14	15	10	11	12	45	33
ATTRACTIVENESS	SCIENTIFIC COLLABORA-TIONS	New academic international collaborations	48	5	14	4	2	2	7	6	8
		New academic national collaborations	45	7	7	8	3	1	5	6	8
		New european project (includ. ERC)	13	0	1	2	0	3	4	2	1
		Visiting scholars (IdEx program)	13	0	0	0	3	2	3	3	2
		Outgoing mobilities	13	0	0	3	0	4	1	1	4
	COFUNDING	Budget	14 971 565 €	- €	1 363 800 €	2 601 459 €	3 896 000 €	1 320 107 €	1 930 651 €	1 678 553 €	2 180 995 €
		Cofunding budget/TRAIL research budget	234%	0%	119%	291%	795%	135%	138%	283%	552 %
	INDUSTRIAL VALORIZATION	Patents	12	0	0	0	7	2	1	1	1
		Software Protection Agency recordings	4	0	0	0	0	0	4	0	0
		Private cofunding	2 153 559 €	- €	40 000 €	511 459 €	520 000 €	62 100 €	145 000 €	138 000 €	737 000 €
		Industrials in link with TRAIL	27	5	9	3	1	3	0	5	1
		New collaborations with industrials	40	6	17	5	2	4	0	6	1
	RECRUITMENTS (FUNDED BY TRAIL)	Post-doctoral fellowships	23	0	0	1	5	4	7	2	4
		Doctoral fellowships	16	0	3	0	2	4	6	1	0
		Engineers	10	0	0	1	3	2	4	0	0
		Technicians	5	0	0	0	1	1	2	1	0
		Administrative staff	3	1	1	0	0	0	0	1	0
		Total number of recruitments (except adm.)	54	0	3	2	11	11	19	4	4
		% of research budget for human resources	67%	76%	47%	64%	75%	83%	78%	55%	56 %
GOVERNANCE	BUDGETS AND GOVERNANCE MEETINGS	Number of Steering Committees	67	4	9	10	8	9	9	9	9
		Number of Scientific Advisory Boards	2	0	0	0	0	1	0	1	0
		Number of Boards of Trustees	3	0	1	0	0	0	1	1	0
		Number of Annual General Assemblies	8	1	1	1	1	1	1	1	1
		Number of Assises	2	-	-	-	-	-	-	1	1
		Audits by the national research agency	1	0	0	0	0	1	0	0	0
		Number of CorePartners - Number of teams	7-10	8-8	8-8	8-8	8-8	8-8	7-10	7-10	7 - 10
		Persons in the Community	285	240	240	240	240	240	260	285	283
		Global TRAIL budget	8 054 331 €	534 671 €	1 301 511 €	1 001 185 €	646 879 €	1 572 489 €	1 661 465 €	753 755 €	582 376 €
		Research budget	6 395 983 €	493 971 €	1 150 866 €	894 448 €	490 000 €	979 618 €	1 399 006 €	592 774 €	395 300 €
		Budget dedicated to governance, training, MRI time for the Community	1 533 291 €	40 700 €	150 645 €	106 737 €	156 879 €	592 871 €	262 459 €	223 000 €	187 076 €

A.2 The Community

The Community is composed of 283 persons: researchers, clinicians, post-docs, PhDs, engineers working on complementary themes.

POSITION	NUMBER OF PERSONS
Researchers/clinicians	139
Postdoctoral fellows	44
Doctoral fellows	46
Engineers & technicians	54
TOTAL	283

A.3 Steering Committee and Workpackage Coordinators

STEERING COMMITTEE					
Function	Unit	Director	Thematics	Team (N=10)	Representative (N=17)
LabEx Director					V Dousset
CorePartner representatives	CRCTB	R Marthan	Bronchial remodeling	P Berger	P Berger
			Cardiac electrophysiology	M Haïssaguerre	H Cochet
	IMOTION	F Couillaud	Molecular imaging and innovative therapies in oncology	F Couillaud	F Couillaud
	IMB	M Arnaudon	Scientific calculation and modeling	R Turpault	O Saut
	INCIA	JR Cazalet	Neuroimaging and human cognition	I Sibon & J Swendsen	I Sibon
			Brain molecular imaging	J Badaut	J Badaut
	ISM	E Fouquet	Molecular imaging and photonic	M Blanchard-Desce	Y Crémillieux
			Catalysis, Synthesis and Health	E Fouquet	E Fouquet
	RMSB	S Miraux	Center for magnetic resonance of biological systems	S Miraux	AK Bouzier-Sore
	MAGENDIE	S Oliet	Glia-neuron interactions	S Oliet	A Ruet
Thematics representatives	Neurology				G Catheline
	Oncology				J Palussiere
	Cardiology				M Montaudon
	Pneumology				G Dournes
	Nephrology				N Grenier
International representative					L Pellerin

WORKPACKAGE COORDINATORS (N=8)	
WP1 - Interventional imaging and MRI guided HIFU	B Quesson
WP2 - New sequences	S Miraux
WP3 - DNP	E Thiaudiere
WP4 - Tracers & contrast agents	M Blanchard-Desce and P Fernandez
WP5 - Biological bio-imaging markers	G Clofent-Sanchez
WP6 - Mathematic simulation and modeling	P Coupé
WP7 - Cohort imaging methodology	F Laurent

A/ Governance

A.4 Mid-period audit by the ANR (2015)

1. Noteworthy productions

1.1. Outstanding progress regarding research

The TRAIL (Translational Research and Advanced Imaging Laboratory project) is an initiative based on internationally competitive research teams located in the Bordeaux area. TRAIL is articulated around seven Workpackages addressing, originally, five major themes (note: nephrology will probably be canceled). The launch of 23 projects has a strong effect on the 6 partners networking and build a very promising multidisciplinary research environment. Indeed, the Panel was most impressed by the capability of the leaders to forge a large, functioning collaborative network. By the end of 2014, achievements were 8 patents, 17 publications acknowledging TRAIL and 190 peer-reviewed publications, but the latter gave no credit to TRAIL funding. The Panel was disappointed in the scientific output from the collaborations, which tended to be published in specialist, low impact journals.

1.2 Striking progress in other "LabEx" fields

a. Formation
In 2012 a international bio-imaging master was started. The master is a joint venture of LabEx TRAIL and BRAIN and take benefit of international support from University of Laval (Quebec) and University of Mons (Belgium). TRAIL also successfully supports mobility for international collaboration. TRAIL set up a summer school on neuro-imaging and attracted 26 international renown speakers. 11 international speakers were invited by the TRAIL community. TRAIL belongs to the French Life Imaging (FLI).

b. Valorization
8 patents were filled and 15 industrial are involved in TRAIL projects.

c. International (outreach, attraction, networking...)
TRAIL does have international collaboration running. However this aspect needs to be further reinforced to raised TRAIL profile outside Bordeaux.

2. Added-value resulting from labeling and funding as a "Laboratoire d'Excellence"

The TRAIL labeling helped to raise 2.5 more co-funding (public as well as private). TRAIL initiative results in the building of an efficient and high level multidisciplinary research between the existing laboratories.

3. Main weaknesses

3.1. Main weaknesses that might require corrective actions regarding the research performed in the "LabEx"

The TRAIL initiative is too much a Bordeaux initiative. International as well as national collaboration should be enhanced. Co-supervision of PhD as well as reinforcing mobility (in both directions) should be considered. There is a great danger in lack of focus with the current strategy of supporting such a wide range of projects. At some point, hard decisions must be made to prioritise funding to achieve high level scientific outputs.

3.2 Main weaknesses that might require corrective actions regarding other fields of the "LabEx"

a. Formation
The TRAIL initiative should increase the academic exchange (both direction) with focus on PhD activity.

b. Valorization
Valorization is developing well but could still be improved. It is essential that exploitation of filed patents is actively pursued.

c. International (outreach, attraction, networking...)
The international networking is good but need to be further developed especially at EU level.

4. "LabEx" contribution to structuring the gathered scientific strengths (governance, synergy, common scientific programming, visibility...)

TRAIL successfully built up a multidisciplinary Bordeaux research network in advanced medical imaging. The governance is well organized. However, the newly hired general manager must solve the issues raised by the scientific advisory board regarding over complex administrative processes and project governance. Streamlining of these processes is important to keep the partners fully engaged with TRAIL.

5. Beyond scientific results specifically obtained by the "LabEx", give an assessment on its contribution to the development, outreach and overall visibility of the concerned institutions and of the corresponding site.

The panel consider that the LabEx support lead to the creation of a strong consortium in advanced imaging in the Bordeaux area. In the mid-term TRAIL initiative, thanks to an adequate selection of projects and partnerships (academic and industrial, nationally and internationally) may reach an international visibility and recognition. With such a profile, the TRAIL project the panel expect a step change in increased academic output.

6. Overall opinion and recommendations

Overall the panel was very impressed by the scientific progress reported by the consortium: it has successful built an impressive collaborative network, potentially positioned to deliver in the future. The panel recommends TRAIL to balance the continuation of existing project with the start of new ones. The panel recommend to further prioritize risky projects focusing on unmet medical needs, at the expense of existing projects that may not come to fruition. Such 'risk projects' need not be peer-reviewed but they should be selected by the Steering Committee and have a clear interdisciplinary vision. It is important that TRAIL select projects that can have high international impact, as currently their output is unsatisfactory. There is clearly a difficult job to be done in balancing the portfolio of diverse research themes so that in the next period a step change of increased publication quality is achieved. On the valorization perspective, the panel recommends to further improve the industrial collaboration and to evaluate how some of the ongoing/foreseen developments may lead to creation of start-up(s). The goal to have a strong local industry active in the field of advanced imaging should be one of TRAIL long term goal. The panel also recommends TRAIL to develop national, outside the Bordeaux area, as well as international collaborations. PhD exchange (both directions) and/or shared PhD could be a way to start such collaborations. The panel recommends to further develop the summer school programs and, if possible, to collaborate with other LabEx similar activities (e.g. CAMI).

International jury from the French National Research Agency, June 2015.

B/ Research achievements

B.1 Scientific communication

B.1.1 Publications quoting TRAIL

155 publications have been published over the 2011-2018 period:

WP	TRAIL PROJECT	YEAR	TRAIL QUOTED PUBLICATION	JOURNAL
WP1 - MR Guided HIFU and interventional imaging	MRGHIFU	2015	Detection of Brain Tumors and Systemic Metastases Using NanoLuc and Fluc for Dual Reporter Imaging. C. Germain-Genevois, O. Garandeau, F. Couillaud. Mol Imaging Biol (2015)	Mol Imaging Biol
		2016	Improved Cardiac Magnetic Resonance Thermometry and Dosimetry for Monitoring Lesion Formation During Catheter Ablation, Valery Ozenne, Solenn Toupin, Pierre Bour, Baudouin Denis de Senneville, Matthieu Lepetit-Coiffe, Manuel Boissenin, Jenny Benois-Pineau, Michael S. Hansen, Souheil J. Inati, Assaf Govari, Pierre Jais, and Bruno Quesson, Magnetic Resonance in Medicine, Jan 2016	Magnetic Resonance in Medicine
		2016	Non-invasive cardiac pacing with image-guided focused ultrasound, Fabrice Marquet, Pierre Bour, Fanny Vaillant, Sana Amraoui, Rémi Dubois, Philippe Ritter, Michel Haïssaguerre, Mélèze Hocini, Olivier Bernus & Bruno Quesson, Nature Scientific Reports, Oct 16	Nature Scientific Reports
		2017	Combination of principal component analysis and optical-flow motion compensation for improved cardiac MR thermometry, S Toupin , B Denis de Senneville, V Ozenne, P Bour, M Lepetit-Coiffe, M Boissenin, P Jais and B Quesson, Physics in Medicine & Biology, Jan 2017	Physics in Medicine & Biology
		2017	Feasibility of real-time MR thermal dose mapping for predicting radiofrequency ablation outcome in the myocardium *in vivo*, Solenn Toupin , Pierre Bour, Matthieu Lepetit-Coiffé, Valéry Ozenne, Baudouin Denis de Senneville, Rainer Schneider, Alexis Vaussy, Arnaud Chaumeil, Hubert Cochet, Frédéric Sacher, Pierre Jaïs, and Bruno Quesson, Journal of Cardiovascular Magnetic Resonance, Feb 2017	Journal of Cardiovascular Magnetic Resonance
		2017	Impact of surface grafting density of PEG macromolecules on dually fluorescent silica nanoparticles used for the *in vivo* imaging of subcutaneous tumors, Laurent Adumeau, Coralie Genevois, Lydia Roudier, Christophe Schatz, Franck Couillaud, Stephane Mornet, BBA - General Subjects, Feb 2017	BBA general subjects
		2017	Real-Time Monitoring of Tissue Displacement and Temperature Changes during MR-Guided High Intensity Focused Ultrasound, Pierre Bour, Fabrice Marquet, Valery Ozenne, Solenn Toupin, Erik Dumont, Jean-Francois Aubry, Matthieu Lepetit-Coiffe, and Bruno Quesson, Magnetic Resonance in Medicine, Jan 2017	Magnetic Resonance in Medicine
		2018	Imaging of conditional gene silencing *in vivo* using a bioluminescence-based method with thermo-inducible microRNAs, K Pinel, C Genevois, C Debeissat, F Couillaud, Nature Scientific Reports 2018; 8:4694.	Nature Scientific Reports
		2018	MR-ARFI-based method for the quantitative measurement of tissue elasticity: application for monitoring HIFU therapy, J Vappou, P Bour, F Marquet, V Ozenne, B Quesson, Phys. Med. Biol. 63 (2018) 095018.	Physics in Medicine & Biology

WP	TRAIL PROJECT	YEAR	TRAIL QUOTED PUBLICATION	JOURNAL
WP1 - MR Guided HIFU and interventional imaging	MRGHIFU	2018	Real-time 3D ultrasound-based motion tracking for the treatment of mobile organs with MR-guided high-intensity focused ultrasound, P Bour, v Ozenne, F, Marquet, B Denis de Senneville, E Dumont and B Quesson, International Journal of Hyperthermia, 2018, Vol 34, Issue 8.	International Journal of Hyperthermia
WP2 - New sequence and new contrast	HRDTI	2013	Collaborative patch-based super-resolution for diffusion-weighted images. Pierrick Coupé, José V. Manjón, Maxime Chamberland, Maxime Descoteaux, Bassem Hiba. NeuroImage 83 (2013) 245–261	NeuroImage
		2013	Diffusion weighted image denoising using overcomplete local PCA. José V. Manjón, Pierrick Coupé, Luis Concha, Antonio Buades, D. Louis Collins, Montserrat Robles. PLoS ONE Sept 2013, Volume 8, Issue 9	PLoS ONE
		2014	Anatomically Constrained Weak Classier Fusion for Early Detection of Alzheimer's Disease. Mawulawo Komlagan, Vinh-Thong Ta, Xingyu Pan, Jean-Philippe Domenger, D. Louis Collins, Pierrick Coupé, and the Alzheimer's Disease Neuroimaging Initiative. Machine Learning in Medical Imaging, pages 141-148, 2014.	Machine Learning in Medical Imaging
		2014	Optimized PatchMatch for Near Real Time and Accurate Label Fusion. Vinh-Thong Ta, Rémi Giraud, D. Louis Collins, and Pierrick Coupé. MICCAI'14, 105-112, 2014.	MICCAI'14
		2015	An Optimized PatchMatch for Multi-scale and Multi-feature Label Fusion. R. Giraud, V-T. Ta, N. Papadakis, J. V. Manjón, D. L. Collins, P. Coupé and ADNI. NeuroImage 2015	NeuroImage
		2015	Detection of Alzheimer's Disease Signature in MR Images Seven Years Before Conversion to Dementia: Toward an Early Individual Prognosis. P. Coupé, V. S. Fonov, C. Bernard, A. Zandifar, S. F. Eskildsen, C. Helmer, J. V. Manjón, H. Amieva, J-F. Dartigues, M. Allard, G. Catheline, D. L. Collins, and ADNI. Human Brain Mapping, 2015	Human Brain Mapping
		2015	MRI Noise Estimation and Denoising Using Non-local PCA, J. V. Manjón, P. Coupé, A. Buades. Medical image analysis, 22(1): 35-47, 2015.	Medical image analysis
		2015	NABS: Non-local Automatic Brain Hemisphere Segmentation. J. E. Romero, J. V. Manjon, J. Tohka, P. Coupé, M. Robles. Magnetic Resonance Imaging, 33(4): 474-484, 201	Magnetic Resonance Imaging
		2015	Non-local means inpainting of MS lesions in longitudinal image processing, Nicolas Guizard*, Kunio Nakamura, Pierrick Coupé, Vladimir S. Fonov, Douglas L. Arnold, D L. Collins, Frontiers In Neuroscience, Nov 2015	Frontiers in Neuroscience
		2015	Rotation-invariant multi-contrast non-local means for MS lesion segmentation. N. Guizard, P. Coupé, V. Fonov, J. V. Manjon, A Douglas, D. L. Collins. NeuroImage: Clinical, 8: 376-389, 2015.	NeuroImage: Clinical
		2016	Automatic thalamus and hippocampus segmentation from MP2RAGE: comparison of publicly available methods and implications for DTI quantification, Erhard Næss-Schmidt, Anna Tietze, Jakob Udby Blicher, Mikkel Petersen, Irene K. Mikkelsen, Pierrick Coupé, José V. Manjón, Simon Fristed Eskildsen, International Journal of Computer Assisted Radiology and Surgery, June 2016	International Journal of Computer Assisted Radiology and Surgery

B/ Research achievements

publications published over the 2011-2018 period:

WP	TRAIL PROJECT	YEAR	TRAIL QUOTED PUBLICATION	JOURNAL
WP2 - New sequence and new contrast	HRDTI	2016	Fasudil treatment in adult reverses behavioural changes and brain ventricular enlargement in Oligophrenin-1 mouse model of intellectual disability, Hamid Meziane, Malik Khelfaoui, Noemi Morello, Bassem Hiba, Eleonora Calcagno, Sophie Reibel-Foisset, Mohammed Selloum, Jamel Chelly, Yann Humeau, , Fabrice Riet, Ginevra Zanni, Yann Herault, Thierry Bienvenu, Maurizio Giustetto and Pierre Billuart, Human Molecular Genetics, May 2016	Human Molecular genetics
		2016	Non Local Spatial and Angular Matching: Enabling higher spatial resolution diffusion MRI datasets through adaptive denoising, Samuel St-Jean,Pierrick Coupé, Maxime Descoteaux, Medical Image Analysis, Mar 2016	Medical image analysis
		2016	VolBrain: An Online MRI Brain Volumetry System, José V. Manjón and Pierrick Coupé, Frontiers in Neuroinformatics, July 2016	Frontiers in Neuroinformatics
		2017	CERES: A new cerebellum lobule segmentation method, Jose Romero, Pierrick Coupe, Remi Giraud, Vinh-Thong Ta, Vladimir Fonov, Min Tae Park, Mallar Chakravarty, Aristotle Voineskos, Jose Manjon, NeuroImage, Jan 2017	NeuroImage
		2017	HIPS: A new hippocampus subfield segmentation method, Jose E. Romero, Pierrick Coupe, Jose V. Manjon, Neuroimage, Nov 2017	NeuroImage
		2017	Towards a Unified Analysis of Brain Maturation and Aging across the Entire Lifespan: A MRI Analysis, Pierrick Coupé, Gwenaelle Catheline, Enrique Lanuza, and Jose Vicente Manjon, Human Brain Mapping, July 2017	Human Brain Mapping
		2017	SuperPatchMatch: An Algorithm for Robust Correspondences Using Superpixel Patches, Rémi Giraud, Vinh-Thong Ta, Aurélie Bugeau, Pierrick Coupé, and Nicolas Papadakis, IEEE, Jul 2017	IEEE TRANSACTIONS ON IMAGE PROCESSING
		2018	MRI white matter lesion segmentation using an ensemble of neural networks and overcomplete patch-based voting. José Manjón, Pierrick Coupé, Parnesh Raniga, Ying Xia, Patricia Desmond, Jurgen Fripp, Olivier Salvado. Computerized Medical Imaging and Graphics, Volume 69, November 2018, pp 43-51	Computerized Medical Imaging and Graphics
	MDMRI	2018	High-resolution 3D diffusion tensor MRI of anesthetized rhesus macaque brain at 3T, Slimane Tounekti, Thomas Troalen, Yann Bihan-Poudec, Mathilda Froesel, Franck Lamberton, Valéry Ozenne, Justine Cléry, Nathalie Richard, Maxime Descoteaux, Suliann Ben Hamed, Bassem Hiba, NeuroImage, Volume 181, November 2018, pp 149-161	NeuroImage
	NEWFISP	2014	Self-gated bSSFP sequences to detect iron-labeled cancer cells and/or metastases *in vivo* in mouse liver at 7 Tesla. E. J. Ribot, T. J. Duriez, A. J. Trotier, E. Thiaudiere, JM Franconi, and S. Miraux. J Magn Reson Imaging. Jun 2014	J Magn Reson Imaging
		2014	Time-resolved TOF MR angiography in mice using a prospective 3D radial double golden angle approach. A. J. Trotier, W. Lefrançois, E. J. Ribot, E. Thiaudiere, JM Franconi, and S. Miraux. Magn Reson Med. 2014 Mar 10.	Magn Reson Med
		2015	Fast and robust 3D T1 mapping using spiral encoding and steady RF excitation at 7T: application to cardiac manganese enhanced MRI (MEMRI) in mice. C. R. Castets, E. J. Ribot, W. Lefrançois, A. J. Trotier, E. Thiaudière, JM Franconi and S. Miraux. NMR in Biomedicine, Mar 2015	NMR in Biomedicine

WP	TRAIL PROJECT	YEAR	TRAIL QUOTED PUBLICATION	JOURNAL
WP2 - New sequence and new contrast	NEWFISP	2015	Free-breathing 3D diffusion MRI for high-resolution hepatic, metastasis characterization in small animals, Emeline J. Ribot, Aurelien J. Trotier, Charles R. Castets, Benjamin Dallaudiere, Eric Thiaudiere, Jean-Michel Franconi, Sylvain Miraux, Clin Exp Metastasis, Nov 2015	Clin Exp Metastasis
		2015	Positive contrast high-resolution 3D-cine imaging of the cardiovascular system in small animals using a UTE sequence and iron nanoparticles at 4.7, 7 and 9.4 T, A. J. Trotier, W. Lefrançois, K. Van Renterghem, JM Franconi, E. Thiaudière and S. Miraux, Journal of Cardiovascular Magnetic Resonance (2015)	Journal of Cardiovascular Magnetic Resonance
		2015	Water Selective Imaging and bSSFP Banding Artifact Correction in Humans and Small Animals at 3T and 7T, Respectively; E. J. Ribot, D. Wecker, A. J. Trotier, B. Dallaudière, W. Lefrançois, E. Thiaudière, JM Franconi, S. Miraux, PLoS ONE, 2015	PLoS ONE
		2016	Fast 3D Ultrashort Echo-Time Spiral Projection Imaging Using Golden-Angle: A Flexible Protocol for *In Vivo* Mouse Imaging at High Magnetic Field; Charles R Castets, William Lefrançois, Didier Wecker, Emeline J Ribot, Aurelien J Trotier, Eric Thiaudiere, Jean-Michel Franconi, and Sylvain Miraux, Magnetic Resonance in Medicine, May 2016	Magn Reson Med
		2016	USPIO-Enhanced 3D-Cine Self-Gated Cardiac MRI Based on a Stack-of-Stars Golden Angle Short Echo Time Sequence: Application on Mice With Acute Myocardial Infarction, Aurelien J. Trotier, Charles R. Castets, William Lefrancois, Emeline J. Ribot, Jean-Michel Franconi, Eric Thiaudiere, and Sylvain Miraux, Journal of Magnetic Resonance Imaging, Jan 2016	J Magn Reson Imaging
		2017	*In vivo* MEMRI characterization of brain metastases using a 3D LookLocker T1-mapping sequence, Charles R. Castets, Néha Koonjoo, Andreea Hertanu, PierreVoisin, Jean-Michel Franconi, Sylvain Miraux & Emeline J. Ribot, Nature Scientific Reports, Jan 2017	Nature Scientific Reports
	WHOBO-MP2RAGE	2018	Compressed-Sensing MP2RAGE sequence: Application to the detection of brain metastases in mice at 7T, Aurélien J. Trotier, Stanislas Rapacchi, Thibaut L. Faller, Sylvain Miraux, Emeline J. Ribot, Magnetic Resonance in Medicine 2018.	Magnetic Resonance in Medicine
WP3 - Dynamic Nuclear Polarization	ONCOFLUX	2016	MR imaging, targeting and characterization of pulmonary fibrosis using intra-tracheal administration of gadolinium-based nanoparticles, Nawal Tassali, Andrea Bianchi, François Lux, Gérard Raffard, Stéphane Sanchez, Olivier Tillement and Yannick Crémillieux, Contrast Media and Molecular Imaging, May 2016	Contrast Media Mol Imaging
		2016	*In vivo* online magnetic resonance quantification of absolute metabolite concentrations in microdialysate, Stefan Glöggler, Silvia Rizzitelli, Noël Pinaud, Gérard Raffard, Vanessa Zhendre, Véronique Bouchaud, Stéphane Sanchez, Guillaume Radecki, Luisa Ciobanu, Alan Wong, Yannick Crémillieux, Nature Scientific Reports, Nov 2016	Nature Scientific Reports
		2017	Online ^{1}H-MRS measurements of time-varying lactate production in an animal model of glioma during administration of an anti-tumoral drug, Yannick Crémillieux, Roberto Salvati, Ursule Dumont, Noël Pinaud, Véronique Bouchaud, Stéphane Sanchez, Stefan Glöggler, Alan Wong, NMR in Biomedicine, Oct 2017	NMR in Biomedicine

B/ Research achievements

publications published over the 2011-2018 period:

WP	TRAIL PROJECT	YEAR	TRAIL QUOTED PUBLICATION	JOURNAL
WP3 - Dynamic Nuclear Polarization	ONCOFLUX	2017	Orotracheal manganese-enhanced MRI (MEMRI): An effective approach for lung tumor detection Andrea Bianchi, Oliviero L. Gobbo, Sandrine Dufort, Lucie Sancey, François Lux, Olivier Tillement, Jean-Luc Coll, Yannick Crémillieux, NMR in Biomedicine, Sep 2017	NMR in Biomedicine
	TRAILDNP	2013	Overhauser-enhanced MRI of elastase activity from *in vitro* human neutrophil degranulation. E. Parzy, V. Bouchaud, P. Massot, P. Voisin, N. Koonjoo, D. Moncelet, J.M. Franconi, E. Thiaudiere, and P. Mellet, PLoS ONE. 8(2) 2013	PLoS ONE
		2014	Alkoxyamines: toward a new family of theranostic agents against cancer. Moncelet D, Voisin P, Koonjoo N, Bouchaud V, Massot P, Parzy E, Audran G, Franconi JM, Thiaudière E, Marque SR, Brémond P, Mellet P. Mol Pharm. 2014 Jul 7;11(7):2412-9.	Mol Pharm
		2014	*In vivo* Overhauser-enhanced MRI of proteolytic activity. Koonjoo N, Parzy E, Massot P, Lepetit-Coiffé M, Marque SR, Franconi JM, Thiaudiere E, Mellet P. Contrast Media Mol Imaging. 2014 Sep;9(5):363-71.	Contrast Media Mol Imaging
		2015	Enzymatically Shifting Nitroxides for EPR spectroscopy and Overhauser-Enhanced Magnetic Resonance Imaging, G. Audran, L. Bosco, P. Bremond, JM Franconi, N. Koonjoo, S. Marque, P. Massot, P. Mellet, E. Parzy, and E. Thiaudiere, Angew. Chem. 2015, 127, 1–7	Angewandte Chemie
		2018	An elastase activity reporter for Electronic Paramagnetic Resonance (EPR) and Overhauser-enhanced Magnetic Resonance Imaging (OMRI) as a lineshifting nitroxide, N Jugniot, I Duttagupt, A Rivot, P Massot, C Cardiet, A Pizzoccaro, M Jean, N Vanthuyne, JM Franconi, P Voisin, G Devouassoux, E Parzy, E, S Marque, A Bentaher, G Audran, P Mellet, Free Radical Biology and Medicine, Vol 126, Oct 2018, pp 101-112	Free Radical Biology and Medicine
WP4 - Tracers and contrast agents	FITTING	2017	Aquaporins through the brain in health and disease: From water to gas movements, Friscourt F, Badaut J, J Neuro Res. Aug 2017	Journal of Neurosciences Research
		2018	Fluorogenic Sydnone-Modified Coumarins Switched-On by Copper-Free Click Chemistry, Camille Favre and Frédéric Friscourt, Organic Letters, 2018, 20, 14, 4213-4217	Organic Letters
		2018	Sydnone Reporters for Highly Fluorogenic Copper-Free Click Ligations, Camille Favre, Lucie de Cremoux, Jerome Badaut, and Frédéric Friscourt, The Journal of Organic Chemistry 2018 83 (4), 2058-2066	The Journal of Organic Chemistry
	IMMELAPT	2016	*Ex Vivo* and *In Vivo* Imaging and Biodistribution of Aptamers Targeting the Human Matrix MetalloProtease-9 in Melanomas, David Kryza*, Frédéric Debordeaux, Laurent Azéma, Aref Hassan, Olivier Paurelle, Jürgen Schulz, Catherine Savona-Baron, Elsa Charignon, Pauline Bonazza, Jacqueline Taleb, Philippe Fernandez, Marc Janier, Jean-Jacques Toulmé, PloS ONE, Feb 2016	PLoS ONE
	NANOMULTI-MAG	2016	Bright Electrogenerated Chemiluminescence of a Bis-Donor Quadrupolar Spirofluorene Dye and Its Nanoparticles; Haidong Li, Jonathan Daniel, Jean-Baptiste Verlhac, Mireille Blanchard-Desce, and Neso Sojic, Chemistry a European Journal, July 2016	Chemistry a European Journal

WP	TRAIL PROJECT	YEAR	TRAIL QUOTED PUBLICATION	JOURNAL
WP4 - Tracers and contrast agents	NANOMULTI-MAG	2016	*In vitro* imaging of b-cells using fluorescent cubic bicontinuous liquid crystalline nanoparticles; V. Miceli, V. Meli, M. Blanchard-Desce, T. Bsaibess, M. Pampalone, P. G. Conaldi, C. Caltagirone, M. Obiols-Rabasa, J. Schmidt, Y. Talmon, A. Casu, and S. Murgia, RCS Advances, June 2016	RCS Advances
		2016	Z-Shaped Pyrrolo[3,2-b]pyrroles and Their Transformation into p-Expanded Indolo[3,2-b]indoles, Rafał Stezycki,Marek Grzybowski, Guillaume Clermont, Mireille Blanchard-Desce* and Daniel T. Gryko*, Chemistry a European Journal, Feb 2016	Chemistry a European Journal
	NEPMIP	2017	Data on atherosclerosis specific antibody conjugation to nanoemulsions. Prévot G, Duonor-Cérutti M, Larivière M,Laroche-Traineau J, Jacobin-Valat MJ Barthélémy P Clofent-Sanchez G, Crauste-Manciet S. Data in Brief, 2017	Data in brief
		2017	Data on iron oxide core oil-in-water nanoemulsions for atherosclerosis imaging. Prévot G, Mornet S, Lorenzato C, Kauss T, Gaubert A, Baillet J, Adumeau L, Barthélémy P, Clofent-Sanchez G, Crauste-Manciet S. Data in Brief, 2017	Data in brief
		2017	Iron oxide core oil-in-water nanoemulsion as tracer for atherosclerosis MPI and MRI imaging Geoffrey Prévota, Tina Kaussa, Cyril Lorenzato, Alexandra Gauberta, Mélusine Larivière, Julie Bailleta, Jeanny Laroche-Traineau, Marie Josée Jacobin-Valat, Laurent Adumeau, Stéphane Mornet, Philippe Barthélémy, Martine Duonor-Cérutti, Gisèle Clofent-Sanchez, Sylvie Crauste-Manciet, International Journal of Pharmaceutics, oct 2017	International Journal of Pharmaceutics
	PIAF	2012	[^{18}F]Si-RiboRGD : the winning combination. From the design and the synthesis to the imaging of $a_v ß_3$ integrins in melanoma tumors. E Amigues, J Schulz, M Szlosek-Pinaud, P Fernandez, S Silvente-Poirot, S Brillouet, F Courbon and E Fouquet, ChemPlusChem 2012, 77, 345-349.	ChemPlusChem
		2013	Pd°-catalyzed methyl transfer on nucleosides and oligonucleotides envisaged as a PET tracer E. Fouquet et al. Molecules, 2013, 18, 13654-13665.	Molecules
		2015	General Last-Step Labeling of Biomolecule-Based Substrates by [^{12}C], [^{13}C], and [^{11}C] Carbon Monoxide. Thomas Cornilleau, Hélène Audrain, Aude Guillemet, Philippe Hermange and Eric Fouquet. Org. Lett. 2015, 17, 354–357	Org Letters
	PRITOR	2014	A phantom-based method to standardize dose-calibrators for new ß$^+$ emitters: ^{68}Ga as demonstrative working example. Morgat C, Mazère J, Fernandez P, Buj S, Vimont D, Schulz J, Lamare F. Nucl Med Commun. 2014.	Nucl Med Commun
		2014	Targeting neuropeptides receptors for cancer imaging and therapy: Perspectives with bombesin, neurotensin and neuropeptide-Y receptors. Morgat C, Mishra A.K, Varshney R, Allard M, Fernandez P, Hindié E. J Nucl Med. 2014;55(10)	J Nucl Med
		2016	A new class of radiopeptides for PET imaging of neuromedin-ß receptor: ^{68}Ga-ranatensin analogs, C. Morgat, R. Varshney, D. Vimont, C. Savona-Baron, C. Riès, C. Chanseau, S. Bertrand, A. K. Mishra, E. Hindié, P. Fernandez and J. Schulz, Med Chem Commun., Apr 2016	Med Chem Commun.

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WP4 - Tracers and contrast agents	PRITOR	2016	Comparison between Three Promising ß-emitting Radionuclides, (67) Cu, (47)Sc and (161)Tb, with Emphasis on Doses Delivered to Minimal Residual Disease. Champion C, Quinto MA, Morgat C, Zanotti-Fregonara P, Hindié E. Theranostics. 2016 Jun	Theranostics
		2016	Dose Deposits from ^{90}Y, ^{177}Lu, ^{111}In, and ^{161}Tb in Micrometastases of Various Sizes: Implications for Radiopharmaceutical Therapy. Hindié E, Zanotti-Fregonara P, Quinto MA, Morgat C, Champion C., J Nucl Med. 2016 May	Journal of Nuclear Medicine
		2016	Evaluation of ^{68}Ga-DOTA-TOC PET/CT for the detection of duodenopancreatic neuroendocrine tumors in patients with MEN1, Clément Morgat & Fritz-Line Vélayoudom-Céphise & Paul Schwartz & Martine Guyot & Delphine Gay5 & Delphine Vimont & Jürgen Schulz & Joachim Mazère & Marie-Laure Nunes & Denis Smith & Elif Hindié & Philippe Fernandez & Antoine Tabarin, EJNMMI, Jan 2016	European journal of nuclear medicine and molecular imaging
		2017	Expression of Gastrin-Releasing Peptide Receptor in Breast Cancer and Its Association with Pathologic, Biologic, and Clinical Parameters: A Study of 1,432 Primary Tumors, Clément Morgat, Gaétan Mac-Grogan, Véronique Brouste, Valérie Vélasco, Nicolas Sévenet, Hervé Bonnefoi, Philippe Fernandez, Marc Debled, and Elif Hindié, Journal of Nuclear Medicine, Oct 2017	Journal of Nuclear Medicine
	SUPSIFLU	2016	Gold-catalysed cross-coupling between aryldiazonium salts and arylboronic acids: probing the usefulness of photoredox conditions, Thomas Cornilleau, Philippe Hermange and Eric Fouquet, Chem Communication, Jul 2016	Chemical Communications
		2017	Last-Step Pd-Mediated [^{11}C]CO Labeling of a Moxestrol-Conjugated o-Iodobenzyl Alcohol: From Model Experiments to *in Vivo* Positron Emission Tomography Studies, Thomas Cornilleau, Mette Simonsen, Maylou Vang, Nada Taib-Maamar, Jean Dessolin, Hélène Audrain, Philippe Hermange, and Eric Fouquet, Bioconjugate Chemistry, Nov 2017	Bioconjugate Chemistry
		2018	Highly hindered 2-(aryl-di-*tert*-butylsilyl)-*N*-methyl-imidazoles: a new tool for the aqueous ^{19}F- and ^{18}F-fluorination of biomolecule-based structures, Marion Tisseraud, Jurgen Schulz, Delphine Vimont, Murielle Berlande, Philippe Fernandez, Philippe Hermange and Eric Fouquet, Chem.Com, 2018, 54, 5098-51010	Chemical Communications
	TARGLIN	2016	*In Vivo* Follow-up of Brain Tumor Growth via Bioluminescence Imaging and Fluorescence Tomography, Genevois C, Loiseau H and Couillaud F, International Journal of Molecular Sciences, Oct 2016	International Journal of Molecular Sciences
		2017	A retro-inverso cell-penetrating peptide for siRNA delivery. Vaissière A, Aldrian G, Konate K, Lindberg MF, Jourdan C, Telmar A, Seisel Q, Fernandez F, Viguier V, Genevois C, Couillaud F, Boisguerin P & Deshayes S Journal of Nanobiotechnology, May 2017	Journal of Nanobiotechnology
		2017	PEGylation rate influences peptide-based nanoparticles mediated siRNA delivery *in vitro* and *in vivo*. Aldrian G, Vaissière A, Konate K, Seisel Q, Vivès E, Fernandez F, Viguier V, Genevois C, Couillaud F, Démèné H, Aggad D, Covinhes A, Barrère-Lemaire S, Deshayes S & Boisguerin P, Journal of Controlled Release, Apr 2017	Journal of Controlled Release

WP	TRAIL PROJECT	YEAR	TRAIL QUOTED PUBLICATION	JOURNAL
WP5 - Biological bioimaging markers	BIOPSYPROS-TAPROBE	2016	*In vivo* imaging of prostate cancer using an anti-PSMA scFv fragment as a probe, Mazzocco C, Fracasso G, Germain-Genevois C, Dugot-Senant N, Figini M, Colombatti M, Grenier N & Couillaud F, Scientific Reports 6, 23314, Mar 2016	Scientific Reports
		2016	Radiologic imaging of the renal parenchyma structure and function, Nicolas Grenier, Pierre Merville and Christian Combe, Nature Reviews Nephrology, Apr 2016	Nature Reviews Nephrology
		2017	*In Vivo* Imaging of Local Gene Expression Induced by Magnetic Hyperthermia, Olivier Sandre, Coralie Genevois, Eneko Garaio, Laurent Adumeau, Stéphane Mornet, and Franck Couillaud, Genes, Feb 2017	Genes
		2017	*In vivo* imaging of prostate cancer tumors and metastasis using non-specific fluorescent nanoparticles in mice. Coralie Genevois, Arnault Hocquelet, Claire Mazzocco, Emilie Rustique, Franck Couillaud, and Nicolas Grenier. Int. J. Mol. Sci. 2017	Int. J. Mol. Sci
	BRAIN-RESV	2018	Consumption of Alcopops During Brain Maturation Period: Higher Impact of Fructose Than Ethanol on Brain Metabolism. El Hamrani D, Gin H, Gallis J-L, Bouzier-Sore A-K and Beauvieux M-C Frontiers in Nutrition (2018) 5:33	Frontiers in Nutrition
		2018	Insulin treatment partially prevents cognitive and hippocampal alterations as well as glucocorticoid dysregulation in early-onset insulin-deficient diabetic rats, Marissal-Arvy N, Campas M-N, Semont A, Ducroix-Crepy C, Beauvieux M-C, Brossaud J, Corcuff J-B, Helbling J-C, Vancassel S, Bouzier-Sore A-K, Touyarot K, Ferreira G, Barat P, Moisan M-P, Psychoneuroendocrinology 93 (2018) 72–81	Psychoneuroendocrinology
	GMCOG	2016	*In Vivo* 7T MR Quantitative Susceptibility Mapping Reveals Opposite Susceptibility Contrast between Cortical and White Matter Lesions in Multiple Sclerosis. X W. Bian, X E. Tranvinh, X T. Tourdias, X M. Han, X T. Liu, X Y. Wang, X B. Rutt, and X M.M. Zeineh, AJNR, Oct 2016	AJNR Am J Neuroradiol
		2016	Selective dentate gyrus disruption causes memory impairment at the early stage of experimental multiple sclerosis. V. Planche, A. Panatier, B. Hiba, E. Ducourneau, G. Raffard, N. Dubourdieu, M. Maitre, T. Lesté-Lasserre, B. Brochet, V. Dousset, A. Desmedt, S.H. Oliet, T. Tourdias. Brain Behavior and Immunity, Dec 2016	Brain, Behavior, and Immunity
		2017	Hippocampal microstructural damage correlates with memory impairment in clinically isolated syndrome suggestive of multiple sclerosis. Planche V, Ruet A, Coupé P, Lamargue-Hamel D, Deloire M, Pereira B, Manjon JV, Munsch F, Moscufo N, Meier DS, Guttmann CR, Dousset V, Brochet B, Tourdias T. Mult Scler. Nov 2017	MS journal
		2017	Microstructural analyses of the posterior cerebellar lobules in relapsing-onset multiple sclerosis and their implication in cognitive impairment. Moroso A, Ruet A, Lamargue-Hamel D, Munsch F, Deloire M, Coupé P, Charré-Morin J, Saubusse A, Ouallet JC, Planche V, Tourdias T, Dousset V, Brochet B. PLoS ONE. Nov 2017	PLoS ONE
		2017	Pattern separation performance is decreased in patients with early multiple sclerosis. Planche V, Ruet A, Charré-Morin J, Deloire M, Brochet B, Tourdias T. Brain Behav. Jun 2017	Brain Behavior

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WP	TRAIL PROJECT	YEAR	TRAIL QUOTED PUBLICATION	JOURNAL
WP5 - Biological bioimaging markers	GMCOG	2018	Deciphering the microstructure of hippocampal subfields with *in vivo* DTI and NODDI: Applications to experimental multiple sclerosis, A Crombe, V Planche, G Raffard, J Bourel, N Dubourdieu, A Panatier, H Fukutomi, V Dousset, S Oliet, B Hiba, T Tourdias, NeuroImage 172 (2018) 357–368	NeuroImage
		2018	Regional hippocampal vulnerability in early multiple sclerosis: Dynamic pathological spreading from dentate gyrus to CA1., Vincent Planche, Ismail Koubiyr, José E. Romero, José V. Manjon, Pierrick Coupé, Mathilde Deloire, Vincent Dousset, Bruno Brochet, Aurélie Ruet, Thomas Tourdias, Hum Brain Mapp 2018; 00:1–11	Human Brain Mapping
	IBIONI	2013	Neuroinflammatory imaging biomarkers : Relevance to Multiple Sclerosis and its therapy. Thomas Tourdias and Vincent Dousset. Neurotherapeutics. 2013 Jan; 10(1): 111–123.	Neurotherapeutics
		2014	Information processing speed impairment and cerebellar dysfunction in relapsing-remitting multiple sclerosis. . Ruet A, Hamel D, Deloire MS, Charré-Morin J, Saubusse A, Brochet B. J Neurol Sci. 2014 Oct 12;347(1-2):246-250	J Neurol Sci
		2014	Optimization of Magnetization-Prepared 3-Dimensional Fluid Attenuated Inversion Recovery Imaging for Lesion Detection at 7 T. Saranathan M, Tourdias T, Kerr AB, Berstein JD, Kerchner GA, Han MH, Rutt BK. Investigative Radiology 2014 May 49(5):290-8.	Investigative Radiology
		2014	Optimization of white matter nulled magnetization prepared rapid gradient echo (MP-RAGE) imaging. Saranathan M, Tourdias T, Bayram E, Ghanouni P, Rutt BK. Magn Reson Med 2014 May 29.	Magn Reson Med
		2014	Visualization of intra-thalamic nuclei with optimized white-matter-nulled MPRAGE at 7T. Tourdias T, Saranathan M, Levesque IR, Su J, Rutt BK. Neuroimage, 2014 Jan 1;84:534-45.	Neuroimage
		2015	Multiple sclerosis lesions are better detected with 3D T1 gradient echo than with 2D T1 spin echo gadolinium enhanced imaging at 3 Tesla. Crombe A, Saranathan M, Ruet A, Durieux M, Roquefeuil E, Ouallet JC, Brochet B, Dousset V, Tourdias T. AJNR Am J Neuroradiol 2015 Mar;36(3):501-7.	AJNR Am J Neuroradiol
		2015	Stroke location is an independent predictor of cognitive outcome, F. Munsch; S. Sagnier; J. Asselineau; A. Bigourdan C.R. Guttmann; S. Debruxelles; M. Poli; P. Renou; P. Perez; V. Dousset; I Sibon; Thomas Tourdias. Stroke, Nov 2015	Stroke
		2016	Cervical spinal cord DTI is improved by reduced-FOV with specific balance between numbers of diffusion gradient directions and numbers of averages; A Crombé, N Alberti, B Hiba, V Dousset, T Tourdias, AJNR, May 2016	AJNR Am J Neuroradiol
		2016	Early Fiber Number Ratio Is a Surrogate of Corticospinal Tract Integrity and Predicts Motor Recovery After Stroke, Antoine Bigourdan, Fanny Munsch, Pierrick Coupé, Charles R.G. Guttmann, Sharmila Sagnier, Pauline Renou, Sabrina Debruxelles, Mathilde Poli, Vincent Dousset, Igor Sibon, Thomas Tourdias, Stroke, Mar 2016	Stroke
		2016	Hippocampal microstructural damage and memory impairment in clinically isolated syndrome, Planche V at al., MS journal., Oct 2016	MS journal

WP	TRAIL PROJECT	YEAR	TRAIL QUOTED PUBLICATION	JOURNAL
WP5 - Biological bioimaging markers	INNES	2013	13C-NMR spectroscopy applications to brain energy metabolism, Tiago B. Rodrigues, Julien Valette and Anne-Karine Bouzier-Sore. Frontiers in Neuroenergetics, Dec 2013.	Front Neuroenergetics
		2013	Glucose and lactate metabolism in the awake and stimulated rat: a ^{13}C-NMR study. Sampol, D., Ostrofet, E., Jobin, M. L., Raffard, G., Sanchez, S., Bouchaud, V., Franconi, J. M., Bonvento, G., and Bouzier-Sore, A. K. Front Neuroenergetics 5, 5 (2013)	Front Neuroenergetics
		2015	High-resolution NMR-based metabolic detection of microgram biopsies using a 1-mm HRμMAS prototype probe. Analyst, accepted 2015, Yusuke Nishiyama, Yuki Endo, Takahiro Nemoto, Anne-Karine Bouzier-Sore and Alan Wong.	Analyst
		2015	Rapid adaptation of rat brain and liver metabolism to a ketogenic diet: an integrated study using ^{1}H- and ^{13}C-NMR spectroscopy. Maggie Roy, Marie-Christine Beauvieux,Jérôme Naulin, Dounia El Hamrani, Jean-Louis Gallis, Stephen C Cunnane and Anne-Karine Bouzier-Sore, Journal of cerebral blood flow and metabolism: official journal of the International Society of Cerebral Blood Flow and Metabolism, Mar 2015	J Cereb Blood Flow Metab
		2015	Uncertainties in pentose-phosphate pathway flux assessment underestimate its contribution to neuronal glucose consumption: relevance for neurodegeneration and aging, Anne-Karine Bouzier-Sore and Juan P. Bolaños, Front Aging Neurosci. 2015; 7: 89.	Frontiers in Aging Neuroscience
		2016	Evaluation of a high-resolution micro-sized magic angle spinning (HRmMAS) probe for NMR-based metabolomic studies of nanoliter samples, Nghia Tuan Duong, Yuki Endo, Takahiro Nemoto, Hiroshi Kato, Anne-Karine Bouzier-Sore, Yusuke Nishiyamaab and Alan Wong, Analytical Method, Aug 2016	Analytical method
		2017	A neuronal MCT2 knockdown in the rat somatosensory cortex reduces both the NMR lactate signal and the BOLD response during whisker stimulation. Mazuel, L., Blanc, J., LRepond, C., Bouchard, V., Raffard G., Déglon, N., Bonvento, G., Pellerin, L., and Bouzier-Sore A.-K. PloS ONE, Apr 2017	PloS ONE
		2017	Current Technical Approaches to Brain Energy Metabolism, Barros LF, Bolaños JP, Bonvento G, Bouzier-Sore AK, Brown A, Hirrlinger J, Kasparov S, Kirchhoff F, Murphy AN, Pellerin L, Robinson MB, Weber B, Glia, Oct 2017	Glia
		2018	AMPK activation caused by reduced liver lactate metabolism protects against hepatic steatosis in MCT1 haploinsufficient mice, Lionel Carneiro, Mohamed Asrih, Cendrine Repond, Christine Sempoux, Jean-Christophe Stehle, Corinne Leloup, François R. Jornayvaz, Luc Pellerin, Molecular Metabolism 6 (2017) 1625-1633	Molecular Metabolism
		2018	Energy metabolism rewiring precedes UVB-induced primary skin tumor formation, Mohsen Hosseini, Léa Dousset, Walid Mahfouf,... Anne-Karine Bouzier-Sore, Rodrigue Rossignol, Hamid Reza Rezvani, Cell Reports, Vol 23, Issue 12, pp 3621-3634	Cell Reports
		2018	Functional Magnetic Resonance Spectroscopy at 7 T in the Rat Barrel Cortex During Whisker Activation, Jordy Blanc, Hélène Roumes, Leslie Mazuel, Philippe Massot, Gérard Raffard, Marc Biran, Anne-Karine Bouzier-Sore, JOVE	JOVE

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WP5 - Biological bioimaging markers	INNES	2018	Neuroenergetics: Astrocytes Have a Sweet Spot for Glucose, Luc Pellerin, Current Biology, 2018, Vol 28, Issue 21, 1258-1260	Current Biology
		2018	Neuroprotective effect of rLosac on supplement-deprived mouse cultured cortical neurons involves maintainance of monocarboxylate transporter MCT2 protein levels, Miryam P. Alvarez-Flores, Audrey Hébert, Cathy Gouelle, Sarah Geller, Ana M. Chudzinski-Tavassi, Luc Pellerin, Journal of Neurochemistry (2018)	Journal of Neurochemistry
	MIMATHUMAB	2014	Nanoparticles functionalised with an anti-platelet human antibody for *in vivo* detection of atherosclerotic plaque by Magnetic Resonance Imaging. M.J Jacobin-Valat, J. Laroche-Traineau, M. Larivière, S. Mornet, S. Sanchez, M. Biran, C. Lebaron, J. Boudon, S. Lacomme, M. Cérutti, G. Clofent-Sanchez. Nanomedicine: Nanotechnology, Biology, and Medicine, 2014	Nanomedicine
		2016	A Recombinant Human Anti–platelet scFv Antibody Produced in Pichia pastoris for Atheroma Targeting. Amelie Vallet–Courbin, Mélusine Larivière, Agnès Hocquellet, Audrey Hemadou, Sarjapura–Nagaraja Parimala, Jeanny Laroche–Traineau, Xavier Santarelli, Gisèle Clofent–Sanchez, Marie–Josée Jacobin–Valat and Abdelmajid Noubhani. PLoS ONE, Dec 2016	PloS ONE
		2016	Solid Lipid Nanoparticles for Image-Guided Therapy of Atherosclerosis, Khalid Oumzil, Michael A. Ramin, Cyril Lorenzato, Audrey Hémadou, Jeanny Laroche, Marie Josée Jacobin-Valat, Stephane Mornet, Claude-Eric Roy, Tina Kauss, Karen Gaudin, Gisèle Clofent-Sanchez, and Philippe Barthélémy, Bioconjugate Chemistry, Jan 2016	Bioconjugate Chemistry
		2017	PacBio sequencing and IMGT/HighV-QUEST analysis of full-length scFv from an *in vivo* selected phagedisplay combinatorial library, Audrey Hemadou, Véronique Giudicelli, Melissa L. Smith, Marie-Paule Lefranc, Patrice Duroux, Sofia Kossida, Cheryl Heiner, Lance Helper, John Kuijpers, Alexis Groppi, Jonas Korlach, Philippe Mondon, Florence Ottones, Marie-Josée Jacobin-Valat, Jeanny Laroche-Traineau, Gisèle Clofent-Sanchez, Frontiers in Immunology, Dec 2017	Frontiers in Immunology
		2018	An innovative flow cytometry method to screen human scFv-phages selected by *in vivo* phage-display in an animal model of atherosclerosis, A Hemadou, J Laroche-Traineau, S Antoine, P Mondon, A Fontayne, Y Le Priol, S Claverol, S Sanchez, M Cerutti, F Ottones, G Clofent-Sanchez, and M-J Jacobin-Valat, Nature Scientific Reports 2018; 8: 15016.	Nature Scientific Reports
	SCICOG & REACTIV	2015	Cognitive evaluation by tasks in a virtual reality environment in multiple sclerosis; D Lamargue-Hamel D, Deloire M, Saubusse A, Ruet A, Taillard J, Philip P, Brochet B. J Neurol Sci. 2015 Dec 15;359(1-2):94-9	J Neurol Sci
		2015	Deciphering depressive mood in relapsing-remitting and progressive multiple sclerosis and its consequences on quality of life. Delphine Lamargue Hamel, Mathilde Deloire, Aurélie Ruet, Julie Charré-Morin, Aurore Saubusse, Jean-Christophe Ouallet, Bruno Brochet, PLoS ONE 10(11):e0142152	PLoS ONE
		2016	Cerebellar assessment in early MS, Moroso A et al., Cerebellum journal, Oct 2016	Cerebellum journal
		2016	Posterior lobules of the cerebellum and information processing speed at various stages of multiple sclerosis, Moroso A et al., JNNP journal	JNNP journal

WP	TRAIL PROJECT	YEAR	TRAIL QUOTED PUBLICATION	JOURNAL
WP5 - Biological bioimaging markers	SCICOG & REACTIV	2018	Differential Gray Matter Vulnerability in the 1 Year Following a Clinically Isolated Syndrome, Koubiyr I, Deloire M, Coupé P, Dulau C, Besson P, Moroso A, Planche V, Tourdias T, Brochet B and Ruet A (2018) Frontiers in Neurology 9:824.	Frontiers in Neurology
	STEAMRI	2017	Allergic Bronchopulmonary Aspergillosis in Cystic Fibrosis: MR Imaging of Airway Mucus Contrasts as a Tool for Diagnosis, Gaël Dournes, Patrick Berger, John Refait, Julie Macey, Stephanie Bui, Laurence Delhaes, Michel Montaudon, Olivier Corneloup, Jean-François Chateil, Roger Marthan, Michaël Fayon, François Laurent, Thoracic imaging, Apr 2017	Journal of Thoracic Imaging
		2017	MRI of the pulmonary parenchyma: Towards clinical applicability? G. Dournes, J. Maceya, E. Blanchard,P. Bergera, F. Laurent, Pneumologie Clinique, Feb 2017	Pneumologie Clinique
		2018	3D Ultrashort Echo Time MRI of the Lung Using Stack-of-Spirals and Spherical k-Space Coverages: Evaluation in Healthy Volunteers and Parenchymal Diseases, G Dournes, J Yazbek, W Benhassen, I Benlala, E Blanchard, M-E Truchetet, J Macey, P Berger, and F Laurent, J Magn Reson Imaging, 2018, 48:1489–1497	Journal of Magnetic Resonance Imaging
	TBI	2016	Chronic cerebrovascular dysfunction after traumatic brain injury. Jullienne A, Obenaus A, Ichkova A, Savona-Baron C, Pearce WJ, Badaut J. J Neurosci Res. Jul 2016	J Neurosci Research
		2016	Improved long-term outcome after transient cerebral ischemia in aquaporin-4 knockout mice, Lorenz Hirt, Andrew M Fukuda, Kamalakar Ambadipudi, Faisil Rashid, Devin Binder, Alan Verkman, Stephen Ashwal, Andre Obenaus and Jerome Badaut, JCBFM, Jan 2016	Journal of Cerebral Blood Flow & Metabolism
		2017	Vascular impairment as a pathological mechanism underlying long-lasting cognitive dysfunction after pediatric traumatic brain injury. Ichkova A, Rodriguez-Grande B, Bar C, Villega F, Konsman JP, Badaut J. Neurochem Int. Apr 2017	Neurochem Int
		2018	Gliovascular changes precede white matter damage and long-term disorders in juvenile mild closed head injury, Beatriz Rodriguez-Grande, Andre Obenaus, Aleksandra Ichkova, Justine Aussudre, Thomas Bessy, Elodie Barse, Bassem Hiba, Gwenaëlle Catheline, Gregory Barrière, Jerome Badaut, Glia 2018;66:1663–1677	Glia
		2018	Involvement of caveolin-1 in neurovascular unit remodeling after stroke: Effects on neovascularization and astrogliosis, Camille Blochet, Lara Buscemi, Tifenn Clément, Sabrina Gehri, Jerome Badaut and Lorenz Hirt, J Cereb Blood Flow Metab. 2018	Journal of Cerebral Blood Flow & Metabolism
		2018	Modulating the water channel AQP4 alters miRNA expression, astrocyte connectivity and water diffusion in the rodent brain, Amandine Jullienne, Andrew M. Fukuda, Aleksandra Ichkova, Nina Nishiyama, Justine Aussudre, André Obenaus, Jérôme Badaut, Nature Scientific Reports (2018)8:4186	Nature Scientific Reports
		2018	The pericyte–glia interface at the blood–brain barrier, Patrizia Giannoni, Jerome Badaut, Cyril Dargazanli, Alexis Fayd'Herbe De Maudave, Wendy Klement, Vincent Costalat and Nicola Marchi, Clinical Science (2018), 132, 361–374	Clinical Science

B/ Research achievements

publications published over the 2011-2018 period:

WP	TRAIL PROJECT	YEAR	TRAIL QUOTED PUBLICATION	JOURNAL
WP5 - Biological bioimaging markers	TRANSFEAR	2015	Neuronal Circuits for Fear Expression and Recovery: Recent Advances and Potential Therapeutic Strategies. C. Dejean, J. Courtin, R. Rozeske, M. C. Bonnet, V. Dousset, T. Michelet, and C. Herry. Biological Psychiatry Sep, 2015; 78:298–306	Biological Psychiatry
		2016	4-Hz oscillations synchronize prefrontal–amygdala circuits during fear behavior, Nikolaos Karalis, Cyril Dejean, Fabrice Chaudun, Suzana Khoder, Robert R Rozeske, Hélène Wurtz, Sophie Bagur, Karim Benchenane, Anton Sirota, Julien Courtin & Cyril Herry, Nature Neurosciences, Feb 2016	Nature Neurosciences
		2016	Preventing long-lasting fear recovery using bilateral alternating sensory stimulation: a translational study, Wurtz, El-Khoury-Malhame, Wilhelm, Michael, Beetz, Roques, Reynaud, Courtin, Khalfa, Herry, Neuroscience, May 2016	Neurosciences
WP6 - Mathematical simulation and modeling	ARM	2017	Development of a fluid dynamic model for quantitative contrast-enhanced ultrasound imaging, Baudouin Denis de Senneville, Anthony Novell, Chloé Arthuis, Vanda Mendes, Paul-Armand Dujardin, Frederic Patat, Ayache Bouakaz, Jean-Michel Escoffre, and Franck Perrotin, IEEE Transactions on Medical Imaging, Aug 2017	IEEE Transactions on Medical Imaging
	BIGDATABRAIN	2018	Adaptative fusion of texture-based grading for Alzheimer's disease classification, Hett K, Ta V-T, Manjon J, Coupé P, Computerized Medical Imaging and Graphics, Oct 2018	Computerized Medical Imaging and Graphics
	DEEPSTROKE	2017	Admission Brain Cortical Volume: An Independent Determinant of Poststroke Cognitive Vulnerability, Sagnier S, Catheline G, Dilharreguy B, Munsch F, Bigourdan A, Poli M, Debruxelles S, Olindo S, Renou P, Rouanet F, Dousset V, Tourdias T, Sibon I, Stroke. 2017 Aug;48(8):2113-2120	Stroke
		2017	Gait Change Is Associated with Cognitive Outcome after an Acute Ischemic Stroke, S Sagnier, P Renou, S Olindo, S Debruxelles, M Poli, F Rouanet, F Munsch, T Tourdias, and I Sibon, Frontiers in Aging Neuroscience, Nov 2017	Frontiers in Aging Neuroscience
		2017	Thalamic alterations remote to infarct appear as focal iron accumulation and impact clinical outcome, Gregory Kuchcinski, Fanny Munsch, Renaud Lopes, Antoine Bigourdan, Jason Su, Sharmila Sagnier, Pauline Renou, Jean-Pierre Pruvo, Brian K. Rutt, Vincent Dousset, Igor Sibon and Thomas Tourdias, Brain, Nov 2017	Brain
	MOD	2015	Computational Modelling of Metastasis Development in Renal Cell Carcinoma, Etienne Baratchart, Sébastien Benzekry, Andreas Bikfalvi, Thierry Colin, Lindsay S. Cooley, Raphäel Pineau, Emeline Ribot, Olivier Saut, Wilfried Souleyreau, PloS ONE Nov 2015	PLoS ONE
		2015	Patient-specific simulation of tumor growth, response to the treatment, and relapse of a lung metastasis: a clinical case. Thierry Colin, François Cornelis, Julien Jouganous, Jean Palussière and Olivier Saut, Journal of Computational Surgery (2015) 2:1	Journal of Computational Surgery
		2016	Computational Trials: Unraveling Motility Phenotypes, Progression Patterns, and Treatment Options for Glioblastoma Multiforme, F Raman, E Scribner, O Saut, C Wenger, T Colin, H M. Fathallah-Shaykh, PloS ONE, Jan 2016	PLoS ONE
		2016	Spatial Modeling of Tumor Drug Resistance: the case of GIST Liver Metastase, Lefebvre G., Cornelis F., Cumsille P., Colin T., Poignard C., Saut O. Mathematical Medicine & Biology, Mar 2016	Mathematical Medicine & Biology

WP	TRAIL PROJECT	YEAR	TRAIL QUOTED PUBLICATION	JOURNAL
WP6 - Mathematical simulation and modeling	MOD	2017	Precision of manual two-dimensional segmentations of lung and liver metastases and its impact on tumour response assessment using RECIST 1.1, F. H. Cornelis, M. Martin, O. Saut, X. Buy, M. Kind, J. Palussiere and T. Colin, European Radiology Experimental, Nov 2017	European Radiology Experimental
		2018	Pre-treatment magnetic resonance-based texture features as potential imaging biomarkers for predicting event free survival in anal cancer treated by chemoradiotherapy, A Hocquelet, T Auriac, C Perier, Ce Dromain, M Meyer, J-B Pinaquy, A Denys, H Trillaud, B Denis De Senneville, V Vendrely, European Radiology, Vol 28, Issue 7, pp 2801-2811	European Radiology
	NEKOMRI	2017	New methods for the geometrical analysis of tubular organs Grélard, F.; Baldacci, F.; Vialard, A.; and Domenger, J. Medical Image Analysis, Nov 2017	J. Medical Image Analysis
WP7 - Cohort Imaging Methodology	ACTE	2014	Compensatory recruitment of neural resources in chronic alcoholism. Chanraud S. and Sullivan EV. Handbook of Clinical Neurology, Vol. 125, 2014	Handbook of Clinical Neurology
		2015	Neuroimaging and Alcoholism. Chanraud S, Bernard C. Annales Médico-Psychologiques 2015	Annales Médico-Psychologiques
		2017	Brain structural investigation and hippocampal tractography in medication overuse headache: a native space analysis, M. Meyer, G. Di Scala, M. Edde, B. Dilharreguy, F. Radat, M. Allard and S. Chanraud, Behavioral and Brain Functions, Apr 2017	Behavioral aand brain function
	ADPP	2016	Activity/rest cycle and disturbances of structural backbone of cerebral networks in aging, Marion Baillet, Bixente Dilharreguy, Karine Pérès, Jean-François Dartigues, Willy Mayo, Gwenaëlle Catheline, NeuroImage, Sep 2016	NeuroImage
		2016	Age-Related Modifications of Diffusion Tensor Imaging Parameters and White Matter Hyperintensities as Inter-Dependent Processes, Amandine Pelletier*, Olivier Periot, Bixente Dilharreguy, Bassem Hiba, Martine Bordessoules, Sandra Chanraud, Karine Pérès, Hélène Amieva, Jean-François Dartigues, Michèle Allard and Gwénaëlle Catheline, Frontiers in Aging Neurosciences, Jan 2016	Frontiers in Aging Neuroscience
		2017	Patterns of brain atrophy associated with episodic memory and semantic fluency decline in aging, Amandine Pelletier, Charlotte Bernard, Bixente Dilharreguy, Catherine Helmer, Melanie Le Goff, Sandra Chanraud, Jean- François Dartigues, Michèle Allard, Hélène Amieva, Catheline Gwénaëlle, Aging, May 2017	Aging
	COBRASCAN	2015	Quiet Submillimeter MR Imaging of the Lung Is Feasible with a PETRA Sequence at 1.5 T1, Gaël Dournes, David Grodzki, Julie Macey, Pierre-Olivier Girodet, Michaël Fayon, Jean-François Chateil, Michel Montaudon, Patrick Berger, François Laurent, Radiology, Jul 2015	Radiology
		2016	Lung morphology assessment of cystic fibrosis using MRI with ultra-short echo time at submillimeter spatial resolution, G Dournes, F Menut, J Macey, M Fayon, J-F Chateil, M Salel, O Corneloup, M Montaudon, P Berger, F Laurent, Eur Radiol, Feb 2016	European Radiology
		2016	CT evaluation of small pulmonary vessels area in patients with COPD with severe pulmonary hypertension, F Coste, G Dournes, C Dromer, E Blanchard, V Freund-Michel, P-O Girodet, M Montaudon, F Baldacci, F Picard, R Marthan, P Berger, F Laurent, Thorax, Apr 2016	Thorax

B/ Research achievements

B.1.2 Scientific communications during international events

WP	TRAIL PROJECT	EVENT	SCIENTIFIC COMMUNICATION	YEAR	CITY	COUNTRY
1	HIFU	23rd Congress Shanghai	Alteration of the blood brain barrier induced by HIFU	2013	Shanghai	China
		Leloir Institute	Alteration of the blood brain barrier induced by HIFU	2013	Buenos Aires	Argentina
		Oxford University	Alteration of the blood brain barrier induced by HIFU	2013	Oxford	UK
	MRGHIFU	IEEE International Ultrasonics Symposium	Marquet F, Bour P, Amraoui S, Vaillant F, Dubois R, Quesson B. Non-invasive cardiac stimulation by MRI-guided focused ultrasound: a feasibility study on isolated beating pig heart.	2014	Chicago	USA
		Congrès international ESMRMB	Toupin S, Ozenne V, Bour P, Quesson B, De Senneville BD. A robust PCA-based motion estimation approach for MR Thermometry radiofrequency ablation monitoring.	2015	Edinburgh	UK
		Congrès international HRS	Marquet F, Bour P, Vaillant F, Amraoui S, Dubois R, Ritter P, Haïssaguerre M, Hocini M, Bernus O, Quesson B. Contactless cardiac stimulation with MRI guided High Intensity Focused Ultrasound.	2015	Boston	USA
		Congrès international ISMRM	Bour P, Marquet F, Toupin S, Lepetit-Coiffé M, Quesson B. Fast Simultaneous Temperature and Displacement Imaging During HIFU Ablation in Swine Liver.	2015	Toronto	Canada
		11th Interventional MRI Symposium	Ozenne V, Toupin S, Bour P, Denis de Senneville B, Vaussy A, Lepetit-Coiffé M, Jaïs P, Cochet H, Quesson B. First Clinical Evaluation of Real-Time Cardiac MR Thermometry.	2016	Baltimore	USA
		11th Interventional MRI Symposium	Toupin S, Bour P, Ozenne V, Lepetit-Coiffé M, Denis de Senneville B, Schneider R, Chaumeil A, Jais P and Quesson B. *In Vivo* monitoring of cardiac radiofrequency ablation by real-time MR Thermometry.	2016	Baltimore	USA
		11th Interventional MRI Symposium	Toupin S, Ozenne V, Bour P, Lepetit-Coiffé M, Denis de Senneville B, Schneider R, Chaumeil A, Jais P, Quesson B. Online visualization of lesion extent during RF ablation by thermal dose mapping: correlation with post-ablation T1-w imaging and gross-pathology.	2016	Baltimore	USA
		37th Heart rhythm Society (HRS)	Marquet F, Bour P, Vaillant V, Amraoui S, Dubois R, Ritter P, Haissaguerre M, Hocini M, Bernus O, Quesson B. *In vivo* non-invasive ultrasound-based cardiac pacing in pigs.	2016	San Francisco	USA
		37th Heart rhythm Society (HRS)	Toupin S, Lepetit-Coiffé M, Bour P, Ozenne V, Denis de Senneville B, Schneider R, K Jenkins, Chaumeil A, Jais P, Quesson B. Real-time visualization of temperature distribution in the myocardium during adiofrequency ablation by Magnetic Resonance thermometry.	2016	San Francisco	USA
		5th international focused ultrasound symposium	Marquet F, Bour P, Vaillant F, Amraoui S, Dubois R, Ritter P, Haïssaguerre M, Hocini M, Bernus O, Quesson B. *Ex vivo* and *in vivo* non-invasive ultrasound-based cardiac pacing.	2016	Washing-ton	USA
		COST radiomag meeting	Couillaud F. Hyperthermia of tumor microenvironment for therapeutic purposes.	2016	Athens	Greece
		COST radiomag meeting	Couillaud F. Odyssey of nanoparticles from the tube to the tumor cells. How to bring bricks together?	2016	London	UK

WP	TRAIL PROJECT	EVENT	SCIENTIFIC COMMUNICATION	YEAR	CITY	COUNTRY
1	MRGHIFU	ISMRM 2016	Bour P, Marquet F, Vaillant F, Ozenne V, Toupin S, Lepetit-coiffe M, Dumont E, Quesson B. Non-Invasive Cardiac Stimulation with MR Guided HIFU: A Rapid, Cardiac Triggered, MR-ARFI Method for Direct Visualization of Stimulation Site and Assessment of Tissue Stiffness.	2016	Singapore	Singapore
		ISMRM 2016	Ozenne V, Troadec T, Bour Pierre, Toupin S, Dumont E, Quesson B. Automatic Temperature Control During MR Guided Catheter Based Radiofrequency Ablation of the Heart.	2016	Singapore	Singapore
		ISMRM 2016	Ozenne V, Toupin S, Bour P, Denis de Senneville B, Vaussy A, Lepetit-Coiffé M, Jaïs P, Cochet H, Quesson B. First Clinical Evaluation of Real-Time Cardiac MR Thermometry.	2016	Singapore	Singapore
		ISMRM 2016	Toupin S, Lepetit-Coiffe M, Bour P, Ozenne V, Denis de Senneville B, Schneider R, Jenkins K, Chaumeil A, Jais P, Quesson B. In-Vivo Echo-Navigated MR Thermometry for Real-Time Monitoring of Cardiac Radiofrequency Ablation. award	2016	Singapore	Singapore
		ISTU 2016	Bour P, Marquet F, Ozenne V, Toupin S, Dumont E, Quesson B. Simultaneous monitoring of MR-ARFI and MR-thermometry during HIFU ablation.	2016	Tel Aviv	Israel
		ISTU 2016	Marquet F, Bour P, Vaillant F, Amraoui S, Dubois R, Ritter P, Haïssaguerre M, Hocini M, Bernus O, Quesson B. Non-invasive cardiac pacing using images-guided focused ultrasound *ex vivo* and *in vivo* in pigs.	2016	Tel Aviv	Israel
		20th International conference of the Society for Cardiac Magnetic Resonance	B Quesson, ICMR EP Instrumentation or devices (conférence invitée)	2017	Washing-ton	USA
		20th International conference of the Society for Cardiac Magnetic Resonance	B Quesson, real-time MRI cardiac Electrophysiology: Disease targets and device progress.	2017	Washing-ton	USA
		38th Heart rhythm Society (HRS)	Ozenne V, Toupin S, Bour P, de Senneville BD, Vaussy A, Lepetit-Coiffé M, Jaïs P, Cochet H, Quesson B. First clinical evaluation of real-time cardiac MR thermometry.	2017	Chicago	USA
		European COST Radiomag	Sandre O, Genevois C, Garaio E, Adumeau L, Mornet S & Couillaud F. *In Vivo* Imaging of Local Gene Expression Induced by Magnetic Hyperthermia. Réseau	2017	Bilbao	Spain
		European Focused Ultrasound Symposium (EUFUS)	Bour P, Ozenne V, Marquet F, Denis de Senneville B, Dumont E and Quesson B. 3D ultrasound based motion tracking with MR-thermometry.	2017	Leipzig	Germany
		International Society of Magnetic Resonance in Medicine 2017	Ozenne V, Toupin S, Bour P, de Senneville BD, Vaussy A, Lepetit-Coiffé M, Jaïs P, Cochet H, Quesson B. First clinical evaluation of real-time cardiac MR thermometry. (*Summa cum laude* award)	2017	Hawaii	USA

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WP	TRAIL PROJECT	EVENT	SCIENTIFIC COMMUNICATION	YEAR	CITY	COUNTRY
1	MRGHIFU	International Society of Magnetic Resonance in Medicine 2017	Active Catheter Tracking for Cardiac MR Thermometry During Radiofrequency Ablation. Toupin S, Ozenne V, Bour P, Schneider R, Lepetit-Coiffé M de Senneville BD Dumont E, Jaïs P, Quesson B	2017	Hawaii	USA
		12th Interventional MRI Symposium	Combining MR-Acoustic radiation force and temperature imaging with simultaneous multislice imaging during MR guided HIFU procedures. Bour P, Ozenne V, Rapacchi S, Schneider R, Mauconduit F, Ben Hassen W, Quesson B	2018	Boston	USA
		12th Interventional MRI Symposium	Real-time in-vivo tissue temperature and displacement measurements in the brain for MR-guided HIFU treatment. Ozenne V, Constans C, Bour P, Santin M, Ahnine H, Valabrègue R, Lehericy S, Aubry JF, Quesson B.	2018	Boston	USA
		18th International Symposium on Therapeutic Ultrasound	3D ultrasound-based motion tracking with MR-thermometry. Bour P, Ozenne V, Marquet F, Dumont E, Denis de Senneville B, Lepetit-Coiffe M, Quesson B	2018	Nashville	USA
		18th International Symposium on Therapeutic Ultrasound	Transesophageal HIFU for cardiac ablation. Lafon C, Bessière F, Greillier P, Constanciel E, Catheline S, Quesson B, Dillenseger JL, Chevalier P	2018	Nashville	USA
		Virtual meeting from the Interventional MRI study group of ISMRM	Highlights of the iMRI conference in Boston, web conference	2018	Boston	USA
2	HRDTI	20th annual meeting of Human Brain Mapping	Impact of DWI denoising on Track-Density Imaging. Coupé P, Periot O, Manjon J, Hiba B, Allard5 M.	2014	Hamburg	Germany
	NEWFISP	ISMRM 2015	5 oral communications or posters	2015	Toronto	Canada
		ESMI	T1 Longitudinal quantification of iron-oxyde particles using a 3D UTE Spiral Look-Locker sequence at 7T	2016	Utrecht	The Nether-lands
		ISMRM 2016	3D Longitudinal MRI Studies on Novel Tissue-Engineered Bone Constructs in Living Rats: Volume & Perfusion Assessments	2016	Singapore	Singapore
		ISMRM 2016	4D Flow MRI of the Cardiovascular System in Small Animals at 7T with an Ultrashort TE Sequence Combined with an Injection of Iron Nanoparticle	2016	Singapore	Singapore
3	ONCO-FLUX	ISMRM	MR Spectroscopy of very small volumes (< 0.4 µl) of ^{13}C-labelled metabolites using microcoil detection: application to online measurements of cerebral microdialysate	2014	Toronto	Canada
		EUROMAR meeting	Online monitoring of brain metabolites: A microdialysis and microcoil approach, CMR meeting	2015	Prague	Czech Republic

WP	TRAIL PROJECT	EVENT	SCIENTIFIC COMMUNICATION	YEAR	CITY	COUNTRY
3	ONCO-FLUX	ISMRM meeting	MR Spectroscopy of very small volumes (< 0.4 µl) of 13C-labelled metabolites using microcoil detection: application to online measurements of cerebral microdialysate.	2015	Toronto	Canada
		European Molecular Imaging Meeting	Simultaneous MRI and MRS spectrocopy of small volume (1 microlitre) intracerebral metabolites: a combined microdialysis and microcoil application	2016	Utrecht	The Nether-lands
		ISMRM 2016	A combined microcoil and microdialysis approach to measure metabolic response in real-time.	2016	Singapore	Singapore
		ISMRM 2016	Simultaneous imaging and ^{1}H spectroscopy of small volume (1 µl) intracerebral microdialysate in healthy and glioblastoma-bearing rats using highly sensitive micro-coils.	2016	Singapore	Singapore
		ESMRMB	Online MRS measurement of extracellular lactate concentration during administration of anti-tumoral drugs in an animal model of glioma	2017	Barcelona	Spain
		International Symposium on Metabolic and redox interactions between neurons and astrocytes in health and disease	Online NMR profiling of subnanomole quantities of metabolites in brain dialysate.	2017	Salamanca	Spain
		ISMRM	135. Quantification of lactate concentration in micro-dialysate during cerebral activation using 1H-MRS and sensitive NMR microcoil	2017	Hawaii	USA
		European Molecular Imaging Meeting	Online MRS profiling of subnanomole quantities of metabolites in brain dialysate: application to measurements of time-varying lactate production during administration of an antitumoral drug.	2018	San Sebastian	Spain
	TRAILDNP	ENIM	*In vivo* OMRI of proteolysis.	2014	Antwerp	Belgium
		ISMRM	*In vivo* OMRI of proteolysis.	2014	Milan	Italy
		Asia-Pacific EPR Symposium	*In vivo* Mapping of Protease Activity using Overhauser-enhanced MRI: Challenges and Promises. Elodie Parzy (oral communication)	2016	Irkurtsk	Russia
		3rd International Conference Innovative Technologies in Biomedicine	Overhauser-enhanced MRI: principles, challenges and applications to proteolysis imaging	2018	Krakow	Poland
		Current Topic in Organic Chemistry	*In vivo* MRI of Proteolysis: Challenges and Outcomes	2018	Sheregesh	Russia
		International Tomography Center	Overhauser-enhanced imaging: principles, main results and applications	2018	Novosi-birsk	Russia
		Novosibirsk State University	Strategies for MRI acquisition of specific biological processes	2018	Novosi-birsk	Russia
		SPCT	OMRI: a promising approach to proteolysis imaging	2018	Novosi-birsk	Russia

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WP	TRAIL PROJECT	EVENT	SCIENTIFIC COMMUNICATION	YEAR	CITY	COUNTRY
4	BRAIN-RESV	ESMRMB	Maternal supplementation with resveratrol and/or ethanol in hypoxic ischemic injury in rat neonates par Roumes, H. Mazuel, L. Dumont, U. Daher, B. Sanchez, S. Blanc, J. Bouchaud, V. Chateil, J. F. Beauvieux, M.–C. Bouzier–Sore, A.K.	2017	Barcelona	Spain
	FITTING	5th European Chemical Biology Symposium	F. Friscourt – Talk – A turn-on bioorthogonal probe for the visualization of biomolecules in no-wash conditions	2017	Budapest	Hungary
		5th European Chemical Biology Symposium	Z. Chinoy – Poster - Novel Glycan-Reporters for Metabolic Oligosaccharide Engineering – Awarded Best Poster Prize	2017	Budapest	Hungary
		Symposium on Molecular Architectures for Fluorescent imaging of Cells	C. Favre – Poster - Sydnones Reporters for Enhanced Fluorogenic Bioorthogonal Ligations	2017	Karlsruhe	Germany
		Symposium on Molecular Architectures for Fluorescent imaging of Cells	F. Friscourt – Talk - The Sweet Imaging of Living Cells	2017	Karlsruhe	Germany
		7th Annual International Chemical Biology Symposium	F. Friscourt – Talk - Sydnone-Modified Monosaccharides for the Metabolic Oligosaccharide Engineering of Living Cells	2018	Vancouver	Canada
		Hungarian Academy of Sciences	F. Friscourt – Talk - Imaging the Glycome using the Metabolic Oligosaccharide Engineering Strategy at Research Centre for Natural Sciences, Institute of Organic Chemistry, Hungarian Academy of Sciences	2018	Budapest	Hungary
	IMME-LAPT	COST Thematic Workshop "Bio-inspired Nanotechnologies for Biosensing"	Aptamers, clever oligonucleotides for bio-sensing	2013	Sitges	Spain
		NanobioEurope	NanobioEurope	2013	Toulouse	France
		Tohoku University	International Symposium, Tohoku University	2013	Sendai	Japan
	INNES	ESMRMB 2016	Short term effect of lactate neuroprotection in neonate hypoxia–ischemia: a metabolic or signal effect? by Mazuel, L., S. Sanchez, J.–F. Chateil, and A.K. Bouzier–Sore	2016	Vienna	Austria
		ESMRMB 2016	Trans–resveratrol supplementation during gestation and lactation attenuates hypoxia–ischemia brain lesions in rat neonates par Mazuel, L., U. Dumont, S. Sanchez, J. Blanc, V. Bouchaud, J.F. Chateil, M.–C. Beauvieux, and A.K. Bouzier–Sore (poster)	2016	Vienna	Austria
		EWCBR 2016	Lactate: more than a neuronal energetic subtrate. by Bouzier–Sore A. K.	2016	Villars-sur-Ollon	Switzer-land

WP	TRAIL PROJECT	EVENT	SCIENTIFIC COMMUNICATION	YEAR	CITY	COUNTRY
4	INNES	ESMRMB	Study of the variations in lactate levels during *in vivo* whisker stimulation BY Functional MRI and localized 1H MRS: comparative study between control and shMCT2 rats par Blanc, J. Jollé, C. Mazuel, L. Roumes, H. Deglon, N. Bonvento, G. Pellerin, L. Bouzier–Sore, A. K.	2017	Barcelona	Spain
		International Symposium on Metabolic and redox interactions between neurons and astrocytes in health and disease	AAV2/DJ–miR30E–shMCT2: Promising tool to specifically knockdown MCT2 expression in neurons and investigate its role in neuroenergetics. par Jollé, C., C. Pythoud, N. Déglon, A.K. Bouzier–Sore, and L. Pellerin.	2017	Salamanca	Spain
		International Symposium on Metabolic and redox interactions between neurons and astrocytes in health and disease	Lactate: more than a neuronal energetic substrate: an NMR approach. Bouzier–Sore	2017	Salamanca	Spain
		International Symposium on Metabolic and redox interactions between neurons and astrocytes in health and disease	Study of variation in lactate levels during *in vivo* whisker stimulation by functional MRI and localized ^{1}H MRS: comparative study between control and shMCT2 rats par Blanc, J. Jollé, C. Mazuel, L. Roumes, H. Déglon, N. Bonvento, G. Pellerin, L. Bouzier–Sore, A. K.	2017	Salamanca	Spain
		XIII European Meeting on Glial Cells in Health and Disease - Euroglia	Lactate: more than a neuronal energetic substrate: a NMR approach by Bouzier–Sore	2017	Edinburgh	UK
	NANO-MULTI-MAG	Antibody Tech, 2017. Monash University	Enrichment of antibodies issued from *in vivo* phage display assessed by *in silico* and *in vitro* assays: potential ligands for atheroma imaging	2017	Prato	Italy
		5th Symposium on Phospholipids in Pharmaceutical Research	PEGylated phospholipids nanoemulsions for *in vivo* imaging of subcutaneous tumors	2017	Heidelberg	Germany
		12th European Molecular Imaging Meeting – EMIM 2017	PEGylated phospholipids nanoemulsions for *in vivo* imaging of subcutaneous tumors	2017	Cologne	Germany
	NEPMIP	Euskampus	Formulation of nanoobjects for Magnetic Particles Imaging	2015	San Sebastian	Spain
		5th Symposium on Phospholipids in Pharmaceutical Research,	PEGylated phospholipids nanoemulsions for *in vivo* imaging of subcutaneous tumors	2017	Heidelberg	Germany
		12th European Molecular Imaging Meeting	MPI/MRI/fluorescence multimodal imaging nanoemulsion platform	2017	Cologne	Germany

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WP	TRAIL PROJECT	EVENT	SCIENTIFIC COMMUNICATION	YEAR	CITY	COUNTRY
4	PRITOR	Congress of the European Association of Nuclear Medicine	Champion C, Zanotti-Fregonara P, Quinto M. A, Morgat C, Hindié E. Comparative efficacy of ^{90}Y, ^{177}Lu and ^{111}1In for the irradiation of tumor cells and micrometasases: a Monte Carlo study using CELLDOSE.	2014	Gothenburg	Sweden
		Congress of the European Association of Nuclear Medicine	Morgat C, Mazère J, Fernandez P, Buj S, Vimont D, Schulz J, Lamare F. Methodological proposal to standardize dose-calibrators for new ß+ emitters: ^{68}Ga as demonstrative working example (oral).	2014	Gothenburg	Sweden
		Congress of the European Association of Nuclear Medicine	Morgat C, Varshney R, Schulz J, Savona-Baron C, Vimont D, Riès C, Bertrand S, Allard M, Mishra A.K, Fernandez P, Hindié E. Identification of GRPR in ER-positive breast cancer cells as molecular basis to develop a new ^{68}Ga-GRPR-antagonist (^{68}Ga-DOTA-RV_15) for PET molecular imaging.	2014	Gothenburg	Sweden
		Theranostics world congress Ga-68 and PRRT	Development of a ^{68}Ga-ranatensin analog for bombesin receptor PET molecular imaging (oral communication)	2015	Baltimore	USA
		Congress of the European Association of Nuclear Medicine	Terbium-161 a promising radionuclide for the irradiation of tumor cells and micrometastases: Monte Carlo assessment using CELLDOSE (communication orale)	2015	Hamburg	Germany
		Annual Meeting of the European Association of Nuclear Medicine	Champion C, Morgat C, Quinto MA, Zanotti-Fregonara P, Hindié E. Monte-Carlo comparison of four beta-emitting radionuclides of interest for targeted radionuclide therapy of small tumors: ^{177}Lu, ^{67}Cu, ^{47}Sc and ^{161}Tb.	2016	Barcelona	Spain
		Annual Meeting of the Endocrine Society	Velayoudom-Céphise FL, Morgat C, Schwartz P, Nunès ML, Guyot M, Schulz J, Mazère J, Gaye D, Smith D, Hindié E, Fernandez P, Tabarin A. Detection of duodenal and pancreatic neuroendocrine tumors in MEN1 patients: comparison of the performances of ^{68}Ga-DOTA-TOC PET/CT and ^{111}In-pentetreotide	2016	Boston	USA
		Annual Congress of the European Association of Nuclear Medicine	Neurotensin receptor-1 expression in human prostate cancer and lymph nodes metastases	2017	Vienna	Austria
		Society of Nuclear Medicine and Molecular Imaging	Expression of Gastrin-releasing Peptide Receptor in, Breast Cancer and Its Association with Pathologic, Biologic, and Clinical Parameters: A Study of 1432 Primary Tumors	2017	Denver	USA
	TARGLIN	Frontier in Delivery Therapeutics	New peptide-based nanoparticles to Wrap and Roll siRNA into cells, Karidia Konate, Marion Dussot, Gudrun Aldrian, Isabel Ferreiro Neira, Franck Couillaud, Eric Vivès, Prisca Boisguerin, Sébastien Deshayes	2018	Tartu	Estonia
5	BIOPSY-PROSTA-PROBE	28th European Congress of Radiology	*In vivo* imaging of prostate cancer using an anti-PSMA fragment as a probe. Mazzocco C, Grenier N, Fracasso G, Germain-Genevois C, Dugot-Senant N, Couillaud F.	2016	Vienna	Autria

WP	TRAIL PROJECT	EVENT	SCIENTIFIC COMMUNICATION	YEAR	CITY	COUNTRY
5	BIOPSY-PROSTA-PROBE	Réseau European COST Radiomag	Impact of surface grafting density of PEG macromolecules on dually fluorescent silica nanoparticles used for the *in vivo* imaging of subcutaneous tumors. Adumeau L, Genevois C, Roudier L, Schatz C, Couillaud F & Mornet S	2017	Bilbao	Spain
		European Molecular Imaging Meeting	Imaging prostate cancer using bi-modal fluorescent tomography/ultrasound imaging setup. Genevois C, Handschin C, Koenig A Vecco-Garda C, Mornet S, Grenier N. and Couillaud F	2018	San Sebastian	Spain
		European Molecular Imaging Meeting	Bimodal system using ultrasound and fluorescence to localize tumors prostate. Handschin C, Boutet J, Herve, L, Koenig A, Redon O, Perriollat M, Genevois C, Couillaud F, Morales S, Dinten JM, Grenier N	2018	San Sebastian	Spain
	GMCOG	10th annual meeting of the FENS	Membrane dynamics of AQP4: a new key pathway for physiopathological brain cell communication?	2016	Copenha-gen	Denmark
		24th annual meeting of the ISMRM	Thalamus Optimized Multi-Atlas Segmentation at 3T	2016	Singapore	Singapore
		European Committee for Treatment and Research in Multiple Sclerosis	Early cerebellar cognitive profile in multiple sclerosis: From saccadic impairment to grey matter alterations	2016	London	UK
		European Committee for Treatment and Research in Multiple Sclerosis	Efficacy and safety of alemtuzumab in 104 patients with active relapsing-remitting MS: one-year follow-up in France	2016	London	UK
		International meeting on cognition in multiple sclerosis	Cognitive impairment in primary progressive multiple sclerosis	2016	New York	USA
		International meeting on cognition in multiple sclerosis	Hippocampal microstructural damage and memory impairment in multiple sclerosis: A translational study from animal models to CIS and MS patients	2016	New York	USA
		International meeting on cognition in multiple sclerosis	Social cognition and cognitive impairment in multiple sclerosis	2016	New York	USA
		EAN	Pattern separation performance is decreased in patients with early multiple sclerosis	2017	Amsterdam	The Nether-lands
		ESMRMB	High resolution NODDI and DTI to highlight hippocampal alterations induced by experimental multiple sclerosis	2017	Barcelona	Spain
		RSNA	High resolution imaging and beyond	2017	Chicago	USA
		XIII European meeting on glial cells in health and disease	Imaging and pathophysiology of early memory impairment in multiple sclerosis.	2017	Edinburgh	UK

B/ Research achievements

WP	TRAIL PROJECT	EVENT	SCIENTIFIC COMMUNICATION	YEAR	CITY	COUNTRY
5	GMCOG	5th European Congress of Immunology	The properties of integrin α4β7+ CD4 T cells are altered in multiple sclerosis N. Schmitt	2018	Amsterdam	The Nether-lands
		Canon Medical Systems Advanced seminar	Translational research with imaging. T. Tourdias	2018	Tokyo	Japan
		ECF	Longitudinal study of functional brain network reorganization in clinically isolated syndrome	2018	Baveno	Italia
		ECTRIMS	Changes in select resting-state brain functional networks and preservation of social cognitive performances in multiple sclerosis	2018	Berlin	Germany
		ECTRIMS	Microstructural damage in cortico-subcortical white matter tracts in patients with clinically isolated syndrome: prediction of cognitive functioning and follow-up of its change for 1 year	2018	Berlin	Germany
		Organization for Human Brain Mapping	Reorganization of functional brain network topology in clinically isolated syndrome: A 1-year longitudinal study	2018	Singapore	Singapore
	IBIONI	ECTRIMS ACTRIMS	Including ecological assessment in cognitive screening in MS D Hamel	2014	Boston	USA
		IMSCOGS	Ecological assessment in cognitive screening in MS B Brochet	2014	Barcelona	Spain
		ECTRIMS	"Hippocampal microstructural damage and memory impairment in clinically isolated syndrome". V. Planche	2015	Barcelona	Spain
		ECTRIMS	"Vulnerability of dentate gyrus to microglial activation leads to early memory impairment in a model of multiple sclerosis." V. Planche	2015	Barcelona	Spain
		ECTRIMS	Cerebellar sub-structures in cognitive impairment: Volumetric And Microstructural Analyses At Different Stages Of Multiple Sclerosis. A Moroso.	2015	Barcelona	Spain
		ISMRM	"Imaging biomarker and pathophysiology of early memory impairment in multiple Sclerosis: a pre-clinical study with diffusion-tensor imaging of hippocampal layers". T. Tourdias	2015	Toronto	Canada
	INNES	Euroglia	Organisation of a symposium "Astrocyte network contribution in neuroimaging signals" and conference "Functional neuro-energetic and brain imaging: how do astrocytes contribute to the signal?"	2013	Berlin	Germany
		Gordon conférence	Gordon conference, poster	2013	Ventura	USA
		Université Lausanne	NMR spectroscopy "for dummies" and its application to decipher metabolism. Conférence invitée.	2014	Lausanne	Switzer-land
		ISMRM	Towards MRS using High–Resolution Magic–Angle Coil Spinning: application to brain metabolism.	2014	Milan	Italy
		ESMRMB	Early neuroprotective effect of lactate in neonatal hypoxic ischemic brain damages.	2015	Edinburgh	UK
		Euroglia	Neonatal hypoxic ischemic brain damages: early neuroprotective effect of lactate.	2015	Bilbao	Spain
		Gordon Conference	Early neuroprotective effect of lactate in neonatal hypoxic ischemic brain damages.	2015	Ventura	USA

WP	TRAIL PROJECT	EVENT	SCIENTIFIC COMMUNICATION	YEAR	CITY	COUNTRY
5	INNES	ISMRM	MR Spectroscopy of very small volumes of ^{13}C-labelled metabolites using microcoil detection: application to online measurements of cerebral microdialysate.	2015	Toronto	Canada
		European Winter Conference on Brain Research	Importance of the lactate shuttle: from brain imaging during cerebral activation to neuroprotection during hypoxia. A.K. Bouzier-Sore	2018	Villars-sur-Ollon	Switzer-land
	IPALICA	Meeting aneurysm patho-physiopathology	IPALICA	2017	Kyoto	Japan
	MIMA-THUMAB	10th International Conference on the Scientific and Clinical Applications of Magnetic Carrier	Versatile and Multimodal Imaging Tool for Biological Appli-cations;Adumeau L., Laroche-Traineau J., Jacobin Valat M.-J., Nouhbani M., Clofent-Sanchez G., Duguet E., Mornet S.	2014	Dresden	Germany
		Conferences in the Baker Heart and Diabetes Institute	Theranostic of atherosclerosis using human antibody-targeted multi-modal nanoparticles for in situ delivery of drugs	2015	Melbourne	Australia
		Euskampus	Multi-modal nanoparticles for atherosclerosis imaging	2015	San Sebastian	Spain
		PEGS Europe Protein & Antibody Engineering Summit	A high-throughput method based on flow cytometry for the screening of phage-scFvs for the theranostic of atherosclerosis	2015	Lisbon	Portugal
		10th International Conference and Exhibition on Nanomedicine and Nanotechnology in Health Care	Theranostic of atherosclerosis using human antibody–targeted multi–modal nanoparticles for in situ drug delivery (G Clofent-Sanchez)	2016	Bangkok	Thailand
		10th International Conference and Exhibition on Nanomedicine and Nanotechnology in Health Care	Targeted nanoparticles for multimodal molecular imaging in a mouse model of atherosclerosis (M Larivière)	2016	Bangkok	Thailand
		7th PEGS Europe Protein & Antibody Engineering Summit	Theranostic of atherosclerosis: a high throughput method based on flow cytometry for the screening of phage-scFv (A Hémadou)	2016	Lisbon	Portugal
		Antibody Tech, Monash University	Enrichment of antibodies issued from *in vivo* phage display assessed by *in silico* and *in vitro* assays: potential ligands for atheroma imaging	2017	Prato	Italie
		ESMRMB 34th Annual Scientific Meeting	Targeted multimodal nanoparticles for molecular imaging in a mouse model of atherosclerosis	2017	Barcelona	Spain
		Seminar at Monash University	Enzymatic site-specific grafting to iron-oxide based nanoparticles	2018	Melbourne	Australia

B/ Research achievements

WP	TRAIL PROJECT	EVENT	SCIENTIFIC COMMUNICATION	YEAR	CITY	COUNTRY
5	STEAMRI	European Congress of Radiology	MRI of airways	2017	Vienna	Austria
		World Congress of Thoracic Imaging	ABPA in cystic fibrosis	2017	Boston	USA
		European Congress of Radiology	MRI of airways	2018	Vienna	Austria
	TBI	Gordon Research Conference	CNS Barrier Function in Juvenile Traumatic Brain Injury	2016	New London	USA
		Brain 2017	Acute gliovascular phenotype depends on primary injury severity in a new juvenile Closed Head Injury with Longterm Disorders (CHILD) model par B. Rodriguez-Grande, A. Obenaus, A. Ichkova, T. Bessy, J. Aussudre, E.Barse, B. Hibba, G. Catheline, G. Barriere and J. Badaut (oral communication)	2017	Berlin	Germany
		Brain 2017	Vascular reactivity changes of the intracortical blood vessels after juvenile traumatic brain injury par A. Ichkova, B. Rodriguez-Grande and J. Badaut (poster)	2017	Berlin	Germany
		SFN 2017	Intracorical blood-vessel and MRI alterations after juvenile closed head injury par J. Badaut, A. Ichkova, G. Coutrand, S. S. Bertrand, B. Rodriguez-Grande, A. Obenaus	2017	Washington	USA
		National Neurotrauma Symposium 2017	Acute gliovascular phenotype depends on primary injury severity in a new juvenile Closed Head Injury with Long-term Disorders (CHILD) model par B. Rodriguez-Grande, A. Obenaus, A. Ichkova, T. Bessy, J. Aussudre, E.Barse, B. Hibba, G. Catheline, G. Barriere and J. Badaut (poster)	2017	Snowbird, UT	USA
		National Neurotrauma Symposium 2017	"Dawn of a New Day: Brain Edema is 'Back in the Game' with New Discoveries!" Badaut-Obenaus Water Channels and Brain Edema: Success and Failure Badaut	2017	Snowbird. UT, USA	USA
		10th International Symposium on Neuroprotection, Neurorepair	1) Neuroimaging changes at longterm after a single mild TBI in childhood: neurovascular unit dysfunction (Badaut J, Oral), 2) Targeting aquaporin–4 in astrocyte to reduce edema (Badaut J, Oral)	2018	Dresden	Germany
		Hotchkiss Brain Institute: Advances in Glial Biology	Astrogliosis after pediatric mild traumatic brain injury: role in neurovascular unit dysfunction (Badaut J, Oral)	2018	Calgary	Canada
		International Stroke Conference	Targeting Aquaporin-4 in Astrocytes to Reduce Edema, Badaut	2018	Los Angeles	USA

WP	TRAIL PROJECT	EVENT	SCIENTIFIC COMMUNICATION	YEAR	CITY	COUNTRY
5	TBI	National Neurotrauma Symposium	1) Head impacts over a semi–professional soccer season: effect on resting–state functional brain connectivity (H Cassoudesalle, H Petit, I Sibon, J Badaut, P Dehail, Poster) 2) Morpho–functional changes in astrocytes associated with vascular dysfunction after juvenile mild traumatic brain injury (A Ichkova, J Aussudre, U. Valentin, Nagerl, J Badaut, Poster) 3) Morpho–functional changes in neurovascular unit after juvenile mild–traumatic brain injury. (J Badaut, Oral) 4) Role of cxcr3 in neurovascular remodeling after mild traumatic brain injury (M–L Fournier, J Aussudre, F Casse, C Billottet, A Bikfalvi, J Badaut, Oral)	2018	Toronto	Canada
		Society for Neuroscience	1) Caveolin–1 involvement in early tissue remodeling after stroke: Effects on angiogenesis and astrogliosis (Poster) 2) Role of CXCR3 in astrogliosis after mild traumatic brain injury (Poster) 3) Spatiotemporal astroglial evolution following juvenile mild traumatic brain injury (Poster)	2018	San Diego	USA
6	ARM	15th IEEE International Symposium on Biomedical Imaging	Analysis of contrast-enhanced ultrasound using fluid dynamic	2018	Washing-ton	USA
		23rd European Symposium on Ultrasound Contrast Imaging	Quantitative Contrast-Enhanced Ultrasound Imaging using a fluid dynamic model	2018	Rotterdam	The Nether-lands
		IEEE International Ultrasonics Symposium	A fluid dynamic model for quantitative contrast-enhanced ultrasound imaging: validation for the assessment of uteroplacental perfusion	2018	Kobe	Japan
	BIGDATA-BRAIN	International Conference On Medical Image Computing & Computer Assisted Intervention	Graph of brain structures grading for early detection of Alzheimer's disease	2018	Granada	Spain
		International Conference on Machine Learning in Medical Imaging	Graph of hippocampal subfields grading for Alzheimer's disease prediction	2018	Granada	Spain
		Patch-MI	LesionBrain: An Online Tool for White Matter Lesion Segmentation	2018	Granada	Spain
		Patch-MI	MRI Denoising using Deep Learning	2018	Granada	Spain
	DEEP STROKE	RSNA 2018	Enhanced Value of Neuro MR Imaging using Deep Learning Reconstruction Denoising Methods. V. Dousset	2018	Chicago	USA

B/ Research achievements

WP	TRAIL PROJECT	EVENT	SCIENTIFIC COMMUNICATION	YEAR	CITY	COUNTRY
6	MOD	Cancer seminar, UAB	Imaging and cancer (T. Colin)	2017	Birmingham	USA
		Waves 2017	Imaging, modeling and cancer (T. Colin)	2017	Athens	USA
		Virtual Physiological Human	Modeling and inverse problems in tumor growth	2018	Zaragoza	Spain
		Math. Biology Conf, Fields Institute	Evaluating growth and risk of relapse of intracranial tumors	2018	Toronto	Canada
	NEKOMRI	CAIP 2015	Precise cross-section estimation on tubular organs	2015	Valetta	Malta
		ESTI 2015	Lung morphology assessment of cystic fibrosis using MRI with ultrashort echo time at submillimeter spatial resolution	2015	Barcelona	Spain
		RSNA 2015	Lung morphology assessment of cystic fibrosis using non-contrast enhanced proton MRI with submillimeter details at 1.5 Tesla	2015	Chicago	USA
7	ACTE	Donders Discussions.	Motor control in aging: Sensori-motor network connectivity at rest and motor performance -Dupuy M.	2015	Nijmegen	The-Netherlands
		EFIC 8th International Pain in Europe Congress	Brain functional connectivity and morphology changes in medication-overuse headache: evidence for addiction-related processes. Radat F., Di Scala G ., Dilharreguy B., Schoenen J., Allard M., Chanraud S. October 2013	2015	Firenze	Italy
		Cognitive Neuroscience Society Congress	Age-related differences in time course of brain activation and connectivity during feedback-based associative learning.	2016	San Francisco	USA
		Human Brain Mapping	Age-related differences in time course of brain activation and connectivity during associative learning.	2016	Geneva	Switzerland
		Cognitive Neurosciences	Age-related differences in time course of brain connectivity during associative learning.	2017	San Francisco	USA
		Organization for Human Brain Mapping	Linking fMRI to Mobile Technologies in Schizophrenia: Pathophysiology of Executive Deficits. M. Abdallah , M. Dupuy , D.Misdrahi, M.Auriacombe, M.Fatséas,F .Serre, N.Farrugia, J.Swendsen, S. Chanraud	2018	Singapore	Singapore
	COBRA-SCAN	European Society of Thoracic Imaging	G. Dournes, F. Coste, C. Dromer, F. Baldacci, F. Picard, M. Montaudon, R. Marthan, P. Berger, F. Laurent. CT measurement of small vessels as a tool to phenotype COPD subjects with severe pulmonary hypertension.	2014	Amsterdam	The Netherlands

WP	TRAIL PROJECT	EVENT	SCIENTIFIC COMMUNICATION	YEAR	CITY	COUNTRY
7	TRAIL & TRACKS	ISMRM Scientific Workshop	Hau J, Sarubbo S, Petit L, Stem-based tractography of long association fibers of the human brain. In: ISMRM Scientific Workshop - Diffusion as a Probe of Neural Tissue Microstructure.	2013	Podstrana	Croatia
		20th Conference of the Organization for Human Brain Mapping	Poster: Anatomical connectivity of the inferior fronto-occipital fasciculus using stem-based tractography. By Hau J, Perchey G, Sarubbo S, Joliot M, Crivello F, Jobard G, Zago L, Mellet E, Mazoyer B, Tzourio-Mazoyer N, Petit L.	2014	Hamburg	Germany
		20th Conference of the Organization for Human Brain Mapping	Poster: Stem-based tractography to study the anatomical connectivity of human brain white matter pathways. By Hau J, Sarubbo S, Perchey G, Crivello F, Joliot M, Zago L, Jobard G, Mellet E, Mazoyer B, Tzourio-Mazoyer N, Petit L	2014	Hamburg	Germany
		Brain Imaging and Analysis Center (BIAC)	Petit L, Stem-based approach to study the anatomical connectivity of human brain white matter pathways. The inferior fronto-occipital fasciculus.	2014	Durham	USA
		Laboratoire d'Imagerie de la Connectivité de Sherbrooke (SCIL)	Hau J Mapping whole brain white matter tracts in 410 healthy humans.	2014	Sherbrooke	Canada
		ISMRM	Poster : Recognition of bundles in healthy and severely diseased brains" by Garyfallidis E, Côté M-A, Hau J, Perchey G, Petit L, Cunnanne SC, Descoteaux M	2015	Toronto	Canada

B/ Research achievements

B.2 Patents and Software Protection Agency recordings

CARDIOLOGY

"Antibodies for molecular imaging of vulnerable plaques in atherosclerosis."
Number and publication date: WO2013072438 - 23/05/2013.
Inventors: Gisèle Clofent-Sanchez, Kamel Deramchia, Marie-Josée Jacobin,Stéphane Bonetto, Jeanny Traineau.

"Method for fat quantification in a region of the heart."
Number and publication date: WO2015165978 - 05/11/2015.
Inventors: Hubert Cochet, Pierre Jaïs.

"Method to control a target area of the heart, ablation method of target area of the heart, associated system".
Number and publication date: WO2016034594- 10/03/2016.
Inventors: Fabrice Marquet, Pierre Bour, Bruno Quesson, Fanny Vaillant.

"Method to control focused ultrasound calibration for cardiac stimulation, cardiac stimulation method, associated systems and devices."
Number and publication date: WO2016034590- 10/03/2016.
Inventors: Fabrice Marquet, Pierre Bour, Bruno Quesson, Fanny Vaillant, Rémi Dubois.

"Lipid based nanocarrier compositions loaded with metal nanoparticles and therapeutic agent."
Number and publication date: WO2016170010 - 27/10/2016.
Inventors: Jean-Philippe Barthélémy, Khalid Oumzil, Gisèle Clofent-Sanchez, Marie-Josée Jacobin, Jeanny Laroche-Traineau, Stéphane Mornet, Karen Gaudin, Abdelmajid Noubhani, Xavier-François Santarelli.

"A specific binding molecule directed against galectin-3 protein."
Number and publication date: EP17306337.1 - 05/10/2017
Inventors: Gisèle Clofent-Sanchez

NEUROLOGY

"Stroke prediction: methods and tools."
Number of deposit: PCT/FR2015/053480
Date of deposit: 14/12/2015
Inventors: Thomas Tourdias, Vincent Dousset, Igor Sibon, Fanny Munsch, Paul Perez, Julien Asselineau.

ONCOLOGY

"Matrix metalloproteinase 9 (MMP-9) aptamer and uses thereof."
Number and publication date: WO2013153138 - 17/10/2013.
Inventors: Jean-Jacques Toulmé, Sonia Da Rocha, Eric Dausse, Michèle Allard, Laurent Azéma.

"Kits-of-parts comprising Nucleic Acids able to form a kissing complex and their uses thereof."
Number and publication date: WO2015071385 - 21/05/2015.
Inventors: Jean-Jacques Toulmé, Eric Dausse, Guillaume Durand, Eric Peyrin, Corinne Ravelet.

"Method for tumor growth prediction".
Number and publication date: WO2016097050 - 23/06/2016.
Inventors: Thierry Colin, Olivier Saut, Marie Martin, Julie Jouganous, Julie Joie.

"New vectors of pharmacologically active and hydrophobic molecules and their preparation process."
Number of deposit: FR 17/61647.
Inventors: Mireille Blanchard-Desce, Diane Braguer, Michel Vaultier, Marie-Anne Estève, Jonathan Daniel, Florian Correard, Maëva Montaleytang

PNEUMOLOGY

"Method for MRI characterisation of airways lung."
Number of deposit: PJ2015-054/BV2016-007
Date of deposit: 05/2016
Inventors: Gaël Dournes, Fabien Baldacci, François Laurent, Patrick Berger.

SOFTWARE PROTECTION AGENCY RECORDINGS

"Muppet"
IDDN.FR.001.220007.000.S.P.2015.000.31230

"Meta_poumon"
IDDN.FR.001.220006.000.S.P.2015.000.31230

"CADMOS"
IDDN.FR.001.220005.000.S.P.2015.000.10600

"Segmentit: Antepedia Deposit"
215-12-03-10-27-36

C/ Scientific animation & training

C.1 Conferences

TRAIL teams invited 45 international speakers to give lectures in Bordeaux:

DATE	SPEAKER	ORGANIZATION	LECTURE
November 2012	Dr Pr Marco ESSIG	Heidelberg University, Germany	Anticipating medical imaging research evolutions
April 2013	Dr Ernesto SANZ-ARIGITA	CITA Alzheimer, San Sebastian, Spain	Multidimensional biomarkers for early detection of neurodegeneration
July 2013	Professor Jeff W.M. BULTE	The Johns Hopkins University School of Medicine, Baltimore, USA	Seeing Cells with MRI
	Professor Martin MEYER	Department of Psychology, Plasticity and Learning in the healthy aging brain, University of Zurich, Switzerland	Time, speech, and the right hemisphere
November 2013	Professor Yasutaka FUSHIMI	Department of Diagnostic Imaging and Nuclear Medicine, Kyoto University, Japan	Cooperation between Kyoto University and Toshiba Medical
September 2013	Dr Wafaa ZARAOUI	University of Marseille, France	Brain sodium MRI: implications for multiple sclerosis
	Dr Franz SCHMITT	Siemens Research and Developement	Most recent development of High performance gradients and Ultra High Field
	Dr Lori BRIDAL	University Pierre et Marie Curie, Paris, France	Evaluating tumor vascular structure and its response to therapy with pre-clinical contrast-enhanced ultrasound
	Pr Mike MODO	University of Pittsburgh, USA	Image-guided injection and non-invasive monitoring of tissue engineering in stroke
	Pr Constantin COUSSIOS	BUBBL, Oxford University, United Kingdom	Real-time passive acoustic mapping of tissue ablation and drug delivery by ultrasound
	Pr Sébastien LECOMMANDOUX	University of Bordeaux, France	Biomimetic polymersomes, a promising platform towards personalized nanomedicine
January 2014	Pr Dennis PARKER	Utah Center for Advanced Imaging Research, Salt Lake City, USA	MRI Guided Focused Ultrasound of the Breast
May 2014	Pr Brian RUTT	Stanford School of Medicine, USA	Neuroimaging at ultra high field
	Aurobrata GHOSH	Inria Sophia-Antipolis, France	Diffusion MRI: From Diffusion to Brain connectomics
July 2014	Dr Christopher HAGEMEYER	Vascular Biotechnology Laboratory at Baker IDI in Melbourne, Australia	Enzyme-mediated Site-specific Bioconjugation for Molecular Imaging and Drug Delivery
September 2014	Pr David PERRIN	Department of Chemistry, University of British Columbia, Vancouver, Canada	One-step Kit-like Radiofluorination of Peptides and other large molecules

C/ Scientific animation & training

DATE	SPEAKER	ORGANIZATION	LECTURE
January 2015	Dr. Nicoleta BAXAN	Bruker BioSpin MRI GmbH, Ettlingen, Germany	Magnetic Particle Imaging: A Novel Fast 3D *In Vivo* Imaging Modality based on Magnetic Nanoparticle Contrast Agents
February 2015	Pr Juan P. BOLANOS	University of Salamanca, Spain	Molecular bases of the metabolic programs of neurons and astrocytes
April 2015	Pr Juan P. BOLANOS	University of Salamanca, Spain	Astrocytes boost neuronal protection during glutamatergic neurotransmis-sion
May 2015	Pr Yukio MIKI	Osaka City University, Japan	Imaging of the pituary
	Pr Juan P. BOLANOS	University of Salamanca, Spain	Mitochondrial respiratory chain assembly dictates differential ROS production in neurons and astrocytes
July 2015	Dr Stanislas RAPACCHI	University of California, Los Angeles, USA	Accélération de l'Angiographie par IRM par Compressed Sensing
	Dr Karen ALT	Baker Heart and Diabetes Institute, Vascular Biotechnology Laboratory, Melbourne, Australia	Platelets: good or bad guys
September 2015	Prof. Shuh NARUMIYA	Kyoto University, Japan	Aneurysm and inflammation
	Dr Robert INNIS	NIH, USA	Positron emission tomography of human brain can monitor neuroinflammation and camp signaling: applications to alzheimer's disease and depression
October 2015	Pr Dennis PARKER	Utah Center for Advanced Imaging Research, Salt Lake City, USA	MR-guided HIFU of the Brain: potentials and challenges
	Pr Franck SEMAH	CHRU Lille, France	Respective value of PET and MRI in the presurgical evaluation of patients with partial epilepsy
December 2015	Pr Maxime DESCOTEAUX	Sherbrooke connectivity Imaging Lab (SCIL), University Hospital of Sherbrooke, Canada	White matter bundle analytics: buil-ding atlases and tractometry in the space of streamlines
January 2016	Pr Philippe DOUEK	Cermep, centre d'imagerie du vivant, Lyon, France	Le scanner spectral à comptage photonique
February 2016	Dr Anatol KONTUSH	INSERM Research Unit 1166, University Pierre and Marie Curie, Paris, France	Nanoparticules pour le théranostic de l'athérosclérose
June 2016	Pr OBENAUS	Loma Linda University, USA	Long-term Neuroimaging of Human Neural Stem Cells following Neonatal Hypoxic-Ischemic Injury
	Associate Pr Simon ESKILDSEN	Aarhus University, Denmark	Capillary dysfunction in Alzheimer's disease

DATE	SPEAKER	ORGANIZATION	LECTURE
September 2016	Associate Pr Nicolas FARRUGIA	University of Brest, France	Spatio temporal dynamics of functional connectivity extracted using dictionary learning approaches
October 2016	Dr. Florence DELMAS	Bruker	PET/MRI multimodal imaging: unparalleled accuracy
November 2016	Pr Lorenz HIRT	Unil-CHUV, Lausanne, Switzerland	Non invasive biomarkers in the ischemic mouse brain
	Dr Joao DUARTE	Laboratoire d'imagerie du métabolisme, Lausanne, Switzerland	Alterations of brain metabolism in type 2 diabetes: a magnetic resonance study *in vivo*
	Pr Luc PELLERIN	Unil-CHUV, Lausanne, Switzerland	Bolstering neuroenergetics as a neuroprotective strategy
February 2017	Pr Banafshe LARIJANI	Ikerbasque	Oncoprotein activation and dynamics in cancer: a new vision of cancer diagnostics
June 2017	Pr Bertrand TAVITIAN	Charité, Berlin, Germany	Retinal imaging in neurology-current research and clinical applications
	Pr Friedemann PAUL	MR Solutions	New TEP/MRI developments not using cryogenic liquids
July 2017	Fabrice CHAUMARD	INSERM U970 & Hôpital Européen Georges-Pompidou, Paris, France	Exploration du lien entre métabolisme et vascularisation par imagerie
March 2018	Vincent GRIMAUD	Centre Emile Durkheim, Bordeaux	Lost in translation: histoire et définition(s) de la recherche translationnelle
May 2018	Dr Virginie CALLOT	CNRS UMR 7339, Aix-Marseille Université	Avantages et challenges de l'imagerie de la moelle épinière à 7T
June 2018	Dr Jeff GAUDET	Magnetic Insight	Changing the Field: An introduction to Magnetic Particle Imaging
	Dr Yoon Seong CHOI	Yonsei University College of Medicine, Seoul, Korea	Quantitative imaging biomarkers in brain tumors: How we do it

D/ Attractiveness

D.1 International academic partnerships

WP	APPLIED MEDICAL AREA	TRAIL PROJECT	INTERNATIONAL COLLABORATION
1	Cardiology	MRGHIFU	NIH (Mickael Hansen): open source image reconstruction software (2015)
			University of Utah: performing hardware and sequence adaptation for different MRI scanner
2	Cardiology	NEWFISP	University of Mons: contrast agents development for preclinical cardio imaging
			University of Wisconsin: algorithms for 4D angiography
	Neurology	HRDTI	Universidad de Valencia: extending HR-DTI method for q-ball and high b-value WDI
			Université de Sherbrooke: extending HR-DTI method for q-ball and high b-value WDI
		MDMRI	Automatation, Chinese Academy of Sciences: tractography, diffusion MRI data processing
			Université de Sherbrooke, SCIL: image processing, tractography, data analyses (2016)
3	Oncology	ONCOFLUX	Max-Planck Institute, Göttingen, Germany: micro-antenna conception
			University of Pisa, Italy: anti-tumor molecules
4	Neurology	FITTING	Complex Carbohydrate Research Center, University of Georgia, USA: chemical devolpment
	Oncology	INNOVATHER	Leipzig University, Germany: synthesis (DOTA-NLS Y1 analogue)
		PRITOR	INMAS, NewDehli, India: preclinical micro TEP imaging
5	Cardiology	MIMATHUMAB	Australian Center for Blood Disease, Monash University: atheroma plaque PET imaging
			Baker IDI Melbourne: generation and testing of targeted MRI contrast agents and PET tracers
			VIT University, India: apolipoprotein development
	Neurology	BRAIN-RESV	University of Lausanne, Laboratory of Neurotherapies and Neuromodulation: adenovirus production
			University of Lausanne, Department of Physiology: molecular biology
		GMCOG	Harvard, CNI: image post processing
			Stanford University: analyses of thalamic data
		IBIONI	BICAMS group: collaborations as part of consortium in cognitive impairment in MS
			Buffalo University, NY
			Harvard Medical School: post processing
			Magnims Network, Buffalo University NY, Royal Holloway London, MS Center Amsterdam
			MS Center Amsterdam
			Royal Holloway London
			Stanford: use of sequence development by Stanford for human application (2015)
		IMAGANIV	University of Lausanne, Department of Physiology: molecular biology
			University of Lausanne: production of Adenovirus and genetically-modified rats
		INNES	University of Lausanne: providing anti-MCT2 antibodies
			Univeristy of Lausanne, Department of Physiology: molecular biology
		IPALICA	National Cerebral and Cardiovascular Center, Kyoto-Osaka, Japan (Tomohiro Aoki): physiopathology of aneurism
		SCICOG&REACTIV	Magnims Network, Buffalo University NY, Royal Holloway London
		TBI	Loma Linda University, California: vascular biology component
			University of Lausanne: pre-clinical work on Cav-1, a new pathway
			University of California, Irvine: new analysis tool for DTI and PWI. Student exchange

WP	APPLIED MEDICAL AREA	TRAIL PROJECT	INTERNATIONAL COLLABORATION
5	Oncology	BIOPSYPROS-TAPROBE	University of Verona (Fracasso & Colombatti): antibodies engineering (2015)
6	Oncology	MOD	Humanitas Hospital, Milan: glioma
			University of Alabama at Birmingham (Hassan Fathallah): glioblastoma models
			Université de Sherbrooke: PET phamacokinetic modeling
	Neurology	BIGDATABRAIN	Polytechnic University of Valencia: medical imaging analysis (Volbrain platform)
	Pneumology	NEKOMRI	NIH: image reconstruction
7	Neurology	ABACI	Washington University USA (HCP): population neuroimaging studies (multiple reference spaces)
		ACTE	SRI International: acquisition, data analysis
7	Neurology	TRAIL&TRACKS	Dpt of Neurosciences of Santa Chiara Hospital, Trento, Italy: white matter tracts analysis
			Sherbrooke University (SCIL): tractography
			University of Ferrara, Italy: white matter tracts analysis (2013)

D.2 Recruitments (funded by TRAIL)

POSITION	WP	TRAIL PROJECT	RECRUITMENTS
Postdoctoral fellow	1	MRGHIFU	BOUR Pierre
			MARQUET Fabrice
			OZENNE Valéry
	2	HRDTI	BLED Emilie
		NEWFISP	RIBOT Emeline
			TROTIER Aurélien
	3	ONCOFLUX	RIZZITELLI Silvia
	4	TARGLIN	FEREIRO Isabel
	5	BIOPSYPROSTAPROBE	HANDSCHIN Charles
			MASSANTE Cyril
			MAZZOCCO Claire
		BRAIN-RESV	ROUMES Hélène
		GMCOG	TEILLAC Achille
		IBIONI	CIAPPELLONI Silvia
		INNES	MAZUEL Leslie
		MIMATHUMAB	LORENZATO Cyril
		TBI	RODRIGUEZ-GRANDE Beatriz
		TRANSFEAR	ROZESKE Robert
			VALERIO Stéphane
	6	MOD	GROZAT Vladimir
			KALTENMARK Irène
		NEKOMRI	KRAHENBUHL Adrien
	7	COBRASCAN	COSTE Florence

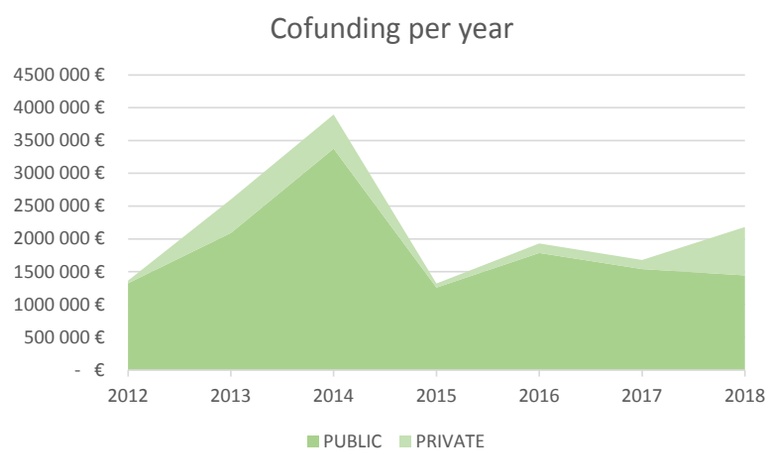
D/ Attractiveness

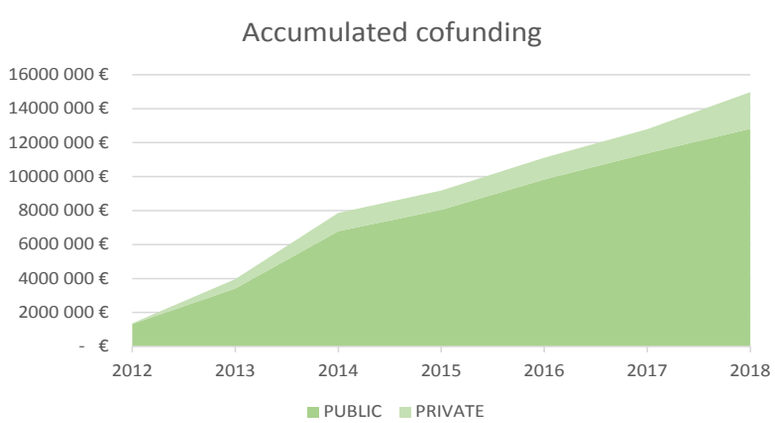
POSITION	WP	TRAIL PROJECT	RECRUITMENTS
Doctoral fellow	1	MRGHIFU	JEANJEAN Pauline
	2	NEWFISP	CARDIET Colleen
	3	TRAILDNP	KOONJOO Neha
			RIVOT Angelique
	4	IMMELAPT	KENNEL Sybille
		SUPSIFLU	TISSERAUD Marion
	5	BRAINRESV	DUMONT Ursule
		GMCOG	KOUBIYR Ismail
		IBIONI	MUNSCH Fanny
		INNES	BLANC Jordy
		MIMATHUMAB	BONNET Samuel
		TBI	ICHKOVA Aleksandra
	6	MOD	PERIER Cynthia
			PERETTI Agathe
	7	ACTE	ABDALLAH Majd
		TRAIL&TRACKS	HAU Janice
Engineer	3	ONCOFLUX	ZHENDRE Vanessa
	4	IMMELAPT	PAURELLE Olivier
		PIAF	MOUGEL Aurélie
	5	TBI	AUSSUDRE Justine
	6	ARM	LAFITTE Luc
		MOD	PIANET Vivien
	7	ABACI	DURIEZ Quentin
			HERVE Pierre-Yves
			LEROUX Gaelle
		ADPP	THEAUD Guillaume
Technician	4	IMMELAPT	BONAZZA Pauline
		NEPMIP	BAILLET Julie
		PRITOR	CHASTEL Adrien
	5	MIMATHUMAB	ANTOINE Ségolène
	7	ADPP	MAYOLINI Maxime

D.3 Cofunding

COFUNDING PER YEAR	2012	2013	2014	2015	2016	2017	2018	TOTAL
PUBLIC	1 323 800 €	2 090 000 €	3 376 000 €	1 258 007 €	1 785 651 €	1 540 553 €	1 443 995 €	12 818 006 €
PRIVATE	40 000 €	511 459 €	520 000 €	62 100 €	145 000 €	138 000 €	737 000 €	2 153 559 €
TOTAL	1 363 800 €	2 601 459 €	3 896 000 €	1 320 107 €	1 930 651 €	1 678 553 €	2 180 995 €	14 971 565 €

ACCUMULATED COFUNDING	2012	2013	2014	2015	2016	2017	2018
PUBLIC	1 323 800 €	3 413 800 €	6 789 800 €	8 047 807 €	9 833 458 €	11 374 011 €	12 818 006 €
PRIVATE	40 000 €	551 459 €	1 071 459 €	1 133 559 €	1 278 559 €	1 416 559 €	2 153 559 €
TOTAL	1 363 800 €	3 965 259 €	7 861 259 €	9 181 366 €	11 112 017 €	12 790 570 €	14 971 565 €





Notes

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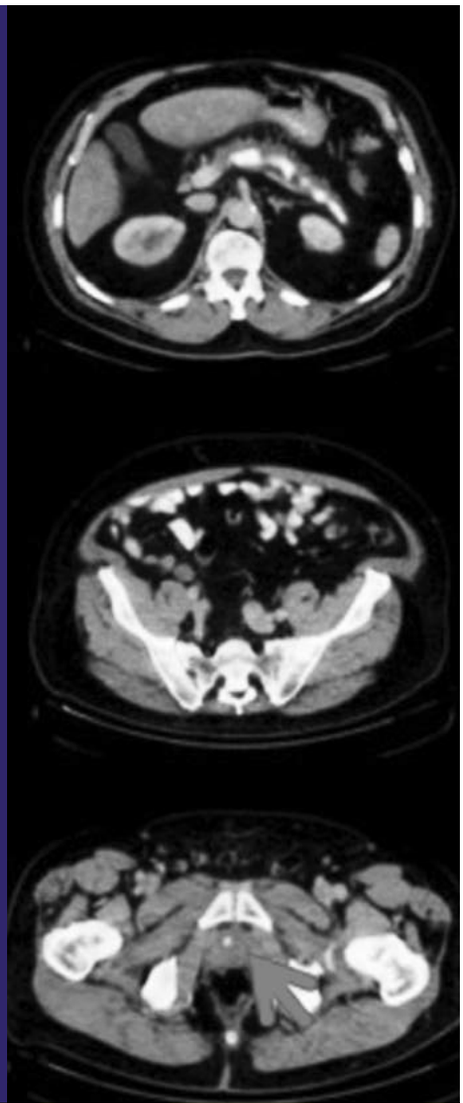

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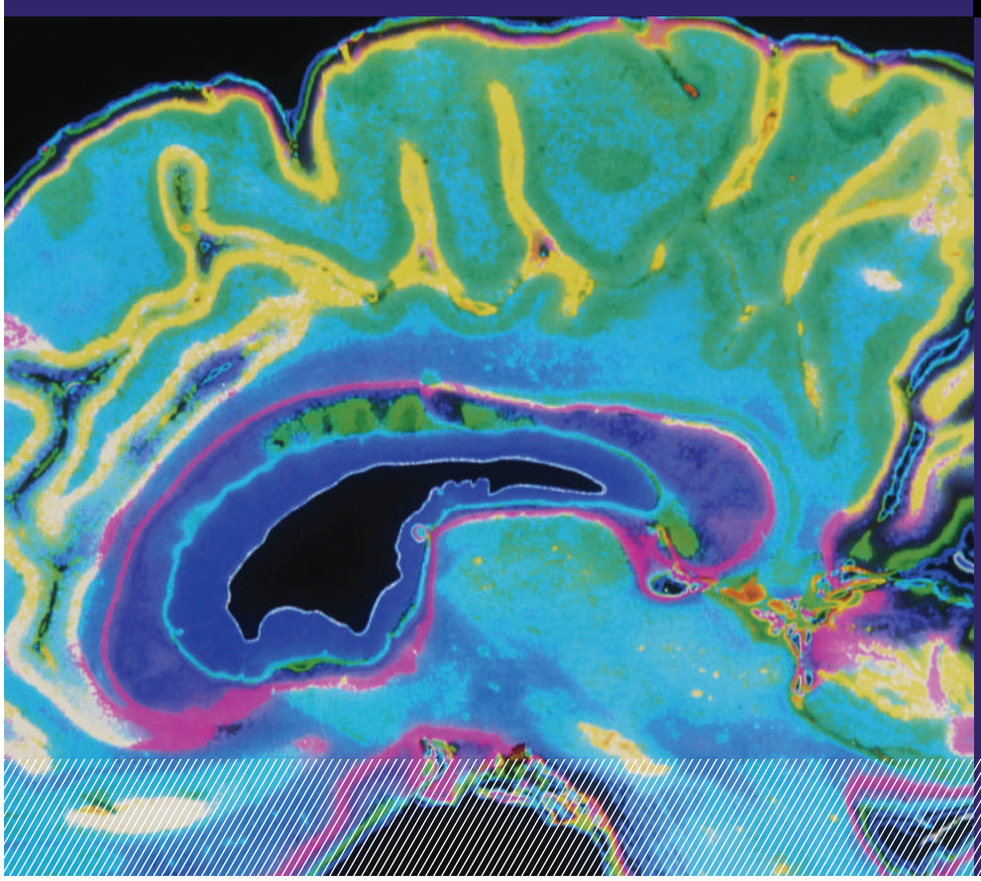

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