Electrophysiology and heart modeling institute

THE LIRYC BEAT

NEWSLETTER N° 14 /// MAY 2022

EDITORIAL

IMPACT AT THE HEART OF LIRYC'S CONCERNS

By **Julie Boussuge-Rozé**, Secretary General of Liryc

The primary purpose of the Liryc Institute is to improve human health to better prevent and cure heart rhythm diseases, from which millions of people suffer throughout the world. At a time when social and environmental responsibility is becoming a real international priority, beyond its impact on public health, Liryc is concerned about optimizing its socio-economic impact, while controlling that of its activity on the environment.

Throughout this newsletter, you will discover flagship research projects with strong clinical and scientific impact, such as the HELP, UNMASC, MAESTRO or MUSIC projects on sudden cardiac death and atrial fibrillation, and as continuation, a strengthened innovation mission to best ensure the transfer of these projects to the market.

The impact of this research and the care delivered is also assessed, as in the InEURHeart project with a medico-economic approach, and maximized, through the implementation of new training programmes aiming to disseminate the knowledge acquired to as many people as possible.

Finally, improving human health cannot be complete without respect for the environment. It is in this "One Health" philosophy that CEVA Santé Animale became a major donor to Liryc and that the institute carried out its first carbon assessment to reduce its environmental footprint.

→ SPOTLIGHT

CONGRATULATIONS TO PROF. MICHEL HAÏSSAGUERRE, WINNER OF AN ADVANCED GRANT FROM THE EUROPEAN RESEARCH COUNCIL (ERC) FOR HIS PROJECT "HELP".

The aim of the programme is to solve the major challenge of preventing sudden cardiac death, responsible for 320,000 to 400,000 deaths each year in Europe, by developing a novel non-invasive rhythm mapping system that can ultimately identify subjects at risk of sudden cardiac death. The project will significantly advance understanding of the mechanisms of sudden cardiac death and define new diagnostic standards that could potentially replace current electrocardiographic methods.

The HELP project was funded by the European Research Council under the European Union's Horizon 2020 research and innovation programme (funding ID 101054717).

UNDERSTANDING THE MECHANISMS OF ATRIAL FIBRILLATION FOR THE DEVELOPMENT OF INNOVATIVE TREATMENTS

The progression of Atrial fibrillation (AF), the most common heart rhythm disorder? is characterized by an increase in episodes frequency and duration. The UNMASC research project, launched in 2018 by Profs. Pierre Jaïs and Pierre Dos Santos, with the coordination of Dr. Philippe Pasdois, is coming to an end. Its aim was to assess whether disturbances in the energy metabolism of the muscle cells in the atria played a role in the stabilization of AF.

The UNMASC project is a translational research project that studied three types of remodeling[1], characterizing AF at three distinct levels:

- Electrophysiological remodeling, studied by invasive mapping but also over the long term by the implementation of a telemetric platform, unique in Europe.
- Structural remodeling.
- Metabolic remodeling[2], which is very little studied at present.

The work demonstrated for the first time that metabolic remodeling actively participates in stabilizing AF.
The research project advance the understanding of the biological mechanisms responsible for this arrhythmia, in particular thanks to the cooperation of many researchers, engineers and technicians from Liryc developing new, original and promising projects.
These advances offer prospects for identifying patients at risk, as well as in identifying innovative therapeutic strategies. In April 2022, the last phase of the project will use a preclinical study to assess the impact of a metabolic therapy approach in the progression of AF. Obtaining a positive result would pave the way for a future clinical research project to assess whether metabolic therapy is a viable option to combat AF.

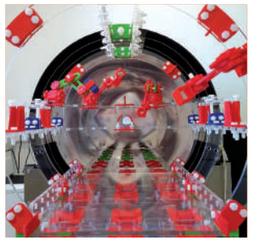
The UNMASC project is funded by the National Research Agency (ANR).

1- Remodeling is a complex process that results in significant changes to the physiology of the heart muscle and in the adaptation of the system to its new working conditions

2- Set of chemical reactions that enable cardiac cells to perform their primary function: to contract.

EXAMINING THE MAGNETIC FIELD OF THE HEART

The MAESTRO project led by Pr Haïssaguerre with Pr Rémi Dubois and researcher Dr Laura Bear is part of the scientific challenge of identifying subjects at high risk of sudden cardiac death.



The original hypothesis of the MAESTRO project is that new, highly sensitive magnetic sensors can detect arrhythmogenic substrates in the heart that are responsible for ventricular fibrillation.

These sensors focus on the magnetic signal associated with of electrical conduction abnormalities in the heart, promising a greater sensitivity and specificity than the techniques used at present. To develop and approve a magnetic system for identifying signals associated with a considerable risk of sudden death, the team relies on the expertise of researchers at CEA Grenoble who have already made considerable progress with this technique on the brain.

A first shielding system was installed at Liryc at the end of 2021. The first ex-vivo experiments in February provided promising results; the follow-up started at the end of April.

The MAESTRO project is funded by the National Research Agency (ANR).

NEW INNOVATION DIRECTOR AT LIRYC

With a background combining research and enterprise, Marc Chevalier joined Liryc as Director of Innovation in February 2022.

Marc Chevalier will contribute, in close collaboration with the institute's researchers, engineers and doctors, to developing and implementing Liryc's innovation strategy. He will coordinate Liryc's new cardiac bio-engineering translational platform, aiming to accelerate and promote technological innovation in the service of care.

→ ZOOM ON

LIRYC ACQUIRES STAKE IN ITS FOURTH STARTUP, CARELINE SOLUTIONS

CareLine SOLUTIONS

As part of its innovation program, the university-hospital institute Liryc has acquired a stake in its partner startup Careline Solutions, thereby reaffirming its support for the digital multi-parameter remote monitoring platform.

Developed in 2018 by cardiologists from the private and public sectors, in partnership with Liryc, Careline Solutions aspire to improve patient prognosis and optimize patient care by using remote monitoring data in an ambitious artificial intelligence research programme.

FACILITATING ACCESS TO INNOVATIVE THERAPIES TO TREAT PERSISTENT ATRIAL FIBRILLATION

The vein of Marshall is an embryological remnant, consisting of a drainage vein and complex musculature. Several studies have established that this structure has a singular role in the onset and persistence of atrial fibrillation. It is an essential therapeutic target, yet its particular anatomical configuration makes current methods ineffective, requiring a different approach to ensure its ablation via the infusion of a 96% alcohol solution.

This particular gesture requires expertise and, in spite of this, remains impossible in nearly 5% of cases. **The challenge is therefore twofold: to offer a dedicated catheter to simplify the approach and to increase the success rate.**

The Liryc team, in particular with Drs. Nicolas Derval, Thomas Pambrun and Josselin Duchateau, was a pioneer in proposing a new therapeutic strategy, combining the ethanol infusion in the vein of Marshall with the isolation of the pulmonary veins and linear lesions. This innovative technique has proven to be both effective and risk-free.

However, this strategy remains complex. The purpose of the Marshall Innovation clinical study is to ensure the feasibility of the intervention with a prototype catheter designed, patented and developed specifically for the procedure in collaboration with the Quebec company Agile.

After having tested and ensured the reliability of this catheter in a pre-clinical study, it will now be used from May 2022 in the context of a clinical trial in humans. This catheter would shorten the duration of ablation procedures, thereby improving patient safety. It would also make the procedure simpler – and therefore more easily accessible to specialized but non-expert centres – significantly impacting the management of persistent atrial fibrillation.

The design and marketing of a catheter made in French is also a rare and significant event from an economic point of view.

IMAGING TO BETTER DIAGNOSE AND TREAT CARDIAC ARRHYTHMIA

The EQUIPEX MUSIC[3] project has enabled the development of a unique multimodal platform, combining the various existing technologies in the study of cardiac structure and functions for an optimized therapy of cardiac arrhythmias.

Fully operational since 2014, the MUSIC platform was developed by a multidisciplinary team, including doctors, researchers, computer engineers and radio operators, under the leadership of Prof. Pierre Jaïs, Prof. Hubert Cochet and Dr. Bruno Quesson. MUSIC is both a unique hybrid electrophysiology laboratory and a cutting-edge software, combining electrophysiology and imaging data into a 3D model of the heart customized to each patient. The platform allow to precisely map the anatomy of the heart, as well as the structural and electrical substrate, to better diagnose and treat patients suffering from different cardiac arrhythmias.

This research programme led to the development of image-guided ablation. It has also led to the modification of international care recommendations on catheter ablation for ventricular tachycardia, generalizing the use of imaging to plan procedures and to reduce the recurrence of arrhythmia. This technology was made available since 2015 to a network of clinical sites in the United States, Europe and Australia, to disseminate these cutting-edge tools.

Over 4,000 patients worldwide have since benefited from MUSIC technology. In addition to the major contribution to care, the MUSIC project has helped to improve imaging methods, particularly the sensitivity of magnetic resonance imaging (MRI). This unique technological platform attracts multiple partners, from industry or academic research, wishing to jointly develop or approve methods.

3- Multi-modality platform for Specific Imaging in Cardiology – This work has benefited from funding from the National Research Agency (ANR) under the programme title "Investments of the Future," carrying the reference "ANR-11-EQPX-0030".

→ ZOOM ON

The Reference Centre for Hereditary Rhythmic Diseases - Cmary - has received accreditation from the European Reference Network (ERN) in recognition of the excellence of the organization of care and research.

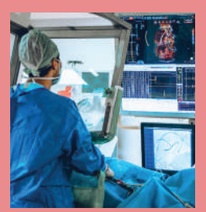
The ERNs are European network linking healthcare professionals specializing in rare diseases across Europe. Cmary has joined the one specific to cardiology, ERN Guard Heart, which brings together 44 expert centres. Accreditation encourage research collaboration, by pooling databases and multiplying ambitious international research projects with the help of patient associations.

"This is really good news for the centre and patients, as it confirms the international recognition of our centre and enables us to better understand these rare diseases, by collaborating with our European colleagues and pooling our databases."

Maider Piquet,
Rare Diseases Officer

EVALUATING THE MEDICO-ECONOMIC PERFORMANCE OF IMAGE-GUIDED ABLATION

Over the last 20 years, cardiac imaging and modeling have made enormous progress, revolutionizing catheter interventions. The challenge today is to continue to improve the efficiency of the treatment of complex cardiac arrhythmias.



In this context, Liryc is coordinating a medico-economic project, InEurHeart, led by researcher Maxime Sermesant, and Profs. Frédéric Sacher and Hubert Cochet on the clinical side. Inclusions will begin in June 2022 and will involve 15 centres in Europe.
The aim is to compare the effectiveness and the average intervention time between the ablation of ventricular tachycardias guided by imagery and the conventional ablation strategy. Shorter procedures would result in fewer complications and greater cost-effectiveness. Furthermore, a simplified approach, with less material, would become feasible outside expert centres, which promotes access to ablation for more patients around the world.
The project is funded by the European institute of Innovation and Technology (EIT).

TRAINING MEDICAL INTERNS IN RHYTHMOLOGY

As part of the specialization and professionalization of medical interns, Liryc launched a unique rhythmology training programme in 2021. Prof. Pierre Bordachar, who initiated the programme, answers a few practical questions to present the training.

What is the educational content of the programme?
The training programme enables medical students to acquire the basics in cardiac rhythmology.
Every week, a course programme is delivered by the stimulation and electrophysiology teams of the Bordeaux University Hospital. The programme covers both the different implantation techniques (implantable Holter, pacemakers, leadless pacemakers, subcutaneous defibrillators) and ablation, with the handling of ablation catheters on the SIMRIC simulator developed by Liryc teams.
Dr. Rémi Chauvel offers a complete course in this context on the ablation of cardiac arrhythmias, with a weekly zoom course and in-depth video modules available on the online training platform.

Who is the training programme for?
This training programme is intended for interns in cardiology at the Bordeaux University Hospital and is also accessible to other University Hospitals in France (Toulouse, Clermont, Poitiers, Tours, Brest, Marseille, Dijon, Besançon, Limoges, Paris) who have chosen the rhythmology option.

In practice, how is this programme innovative?
The strength of the programme is that it offers an innovative pedagogical approach, with hybrid learning that combines face-to-face lessons, remote courses, e-learning modules and practical workshops on simulators.
All materials, including videos of live lessons, are available on the Liryc online education platform liryc-education.fr and are also open to all the institute's clinical and research teams.

TWO *SUMMER SCHOOLS* AT THE FOREFRONT OF INNOVATION IN CARDIOLOGY

Liryc is organizing two editions of its *Summer School* in 2022 as part of the University of Bordeaux's Summer University programme.

After the success of the first edition in 2019, the Cardiac Electrophysiology Summer School will welcome, from 27th June to 1st July, 2022, medical students, engineers and experienced researchers wishing to improve their knowledge on all aspects of cardiac electrophysiology, from the molecular level to pre-clinical investigations and patient care.

From 22nd to 24th June, 2022, the Percutaneous Therapies in Congenital Cardiopathies Summer School will bring together international professionals who wish to share and improve their knowledge around successive stages, ranging from the design of a device to its implantation.

Thanks to an intensive course programme, combining theoretical and practical sessions, these two Summer Schools are a unique opportunity for participants to meet world-class experts and to learn about cutting-edge techniques.

For further information and to register, visit www.ihu-liryc.fr.

CEVA SANTÉ ANIMALE BECOMES MAJOR DONOR TO LIRYC, PROMOTING A "ONE HEALTH" PLATFORM OF EXCELLENCE IN CARDIOLOGY

In December 2021, Liryc and Ceva Santé Animale signed a fundraising agreement placing the fifth largest veterinary laboratory in the world among the largest donors of the institute.

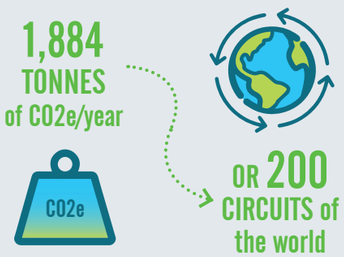
This support strengthens all of Liryc's research projects to improve the management of heart rhythm disorders. It also reflects a common desire to be part of the "One Health" approach to push back the frontiers of scientific knowledge, for the benefit of human, animal and environmental public health.

" This partnership marks the beginning of a remarkable relationship between Ceva Santé Animale and Liryc, two major health players in Nouvelle Aquitaine. We are delighted to be able to contribute to improving the interactions between animal and human health to serve the notion of "One Health" that we have been defending for more than 10 years. "

Dr Marc Prikazsky,
CEO of Ceva Santé Animale

THE INSTITUTE'S CARBON FOOTPRINT

In 2021, Liryc initiated a voluntary process aimed at evaluating the institute's greenhouse gas emissions, supported by the consulting firm NEPSEN.
This approach aims to drive a more global policy of ecological transition for Liryc.



The carbon footprint was assessed thanks to the involvement of a project team within the institute for data collection, under the coordination of the Quality, Health and Safety manager, Fanny Bourrée.

The emissions profile of the institute corresponds to 1,884 tonnes of CO2e per year, given that Liryc already has a LEED[4] building that meets high environmental quality criteria. The three main sources of emissions are the purchase of goods (28% of total emissions), visitor travel (22%) and energy consumption (20%).

Liryc will involve the institute stakeholders concerned by emitting activities to define its strategy for the short- and medium-term reduction of the institute's emissions.

4- Leadership in energy and environmental design

REDUCING THE ENVIRONMENTAL IMPACT OF CATHETERS IN PARTNERSHIP WITH THE INDUSTRY

A partnership has been set up with the industrial company Boston Scientific, to consider the reduction of the environmental impact of single-use cardiac electrophysiology catheters used for procedures to treat cardiac arrhythmias.

This partnership was led by Julie Boussuge-Rozé, General Secretary of the IHU Liryc, as part of the 2021-2022 Postgraduate Programme in Sustainable Business at the University of Cambridge.

A multidisciplinary team has been mobilized to conduct a recyclability study of the innovative OrionTM diagnostic catheter.

A large European survey was also launched in partnership with the European Heart Rhythm Association (EHRA) to assess current practices and expectations of cardiologists to reduce the environmental impact of their practices.

A step forward in favor of more sustainable medical practices!

Boston Scientific

CONGRATULATIONS

Michel Haïssaguerre won an advanced grant from the European Research Council as part of ERCADG-2021 for his project on sudden death.

Aurélien Bustin and **Julie Magat** are winners of a call for projects from the National Research Agency (ANR) for their imaging research project (Young Researchers (JCJC) and Collaborative Research Project (PRC)).

Pascal Amedro is a winner of the European Joint Programme for Rare Diseases (EJPRD) call for projects for his research project on quality of life in paediatric and congenital cardiology.

Aurélien Bustin, Guido Caluori, Kanchan Kulkarni and **Vladimir Sobota** are recipients of a grant from the Lefoulon Delalande Foundation for their research project.

Olivier Bernus is the recipient of funding from the French Federation of Cardiology for his project on sudden death.

Josselin Duchateau received the "technology and innovation" communication prize at the European Heart Rhythm Association (EHRA) congress.

Congratulations to **Sébastien Chaigne, Estelle Renard, Yingjing Feng, Néstor Pallarés Lupón, Lisa Gottlieb, Matthieu Douard** and **Oumayma Bouhamama** for obtaining their thesis.

PORTRAIT OF FANNY BOURRÉE

Meeting with Fanny Bourrée, Quality, Health and Safety Manager at Liryc.

What does your job entail at Liryc?
My position comprises implementing the orientations and objectives defined by management in terms of Quality, Health and Safety to establish an optimized and functional working environment for all the teams.
In terms of quality, I establish an approach according to the standards and regulations in force in our activities and ensure the continuous improvement of our processes.
On the health and safety side, the main theme is the protection of Liryc workers and property.
It is a very cross-functional occupation, involving dialogue at the interface between management, control and supervisory bodies, external service providers and all the people working at Liryc to find solutions on a daily basis and meet the different requirements. Initial training in research, a doctorate in epidemiology and public health, supplemented by training in quality management, enable me to adapt to the different situations that I may encounter on a daily basis.

What are you most proud about?
I am very proud to contribute through teamwork, with all my colleagues, to the fact that the institute complies with many standards, directly linked to its environment, which is a very evolving field, and to the requirements of all interested parties.
I also hope that we will be part of an accreditation process in the future to promote this collaborative work.

And can you tell us a fun fact about your job?
My record is 8,000 steps at work: between meetings, encounters with the various teams in the laboratories, the platforms and the Technological Platform for Biomedical Innovation of the University of Bordeaux, to which I am also attached... or 7.5 km in one day! Real fieldwork!

A LOOK BACK AT THE KEY EVENTS

→ 16TH NOVEMBER 2021

An internal ecological transition workshop was held, inviting all teams to jointly construct an action plan to reduce the institute's environmental impact.

→ 1ST DECEMBER 2021

A fourth international workshop took place, bringing together the Liryc teams to present and discuss the latest advances in terms of basic/clinical research and innovative technologies, joined by members of the International Scientific Council.

→ 27TH DECEMBER 2021

The European Beat AF clinical trial was launched, with the inclusion of a first patient. The study should demonstrate that the isolation of pulmonary veins by pulsed field ablation is more effective than radiofrequency, the standard treatment to date, thereby helping to reduce the enormous burden of atrial fibrillation.

→ 5TH MARCH 2022

Awareness day on life-saving gestures alongside the French Cardiology Federation and the Choquez-Nous association. It was an opportunity for Liryc members to come together to raise public awareness of heart rhythm disorders and to learn how to react better to cardiac arrest.

→ 5TH APRIL 2022

First implantation in France of a biodegradable cardiac prosthesis by the team of the paediatric and congenital cardiology department of the Bordeaux University Hospital.

→ 9TH APRIL 2022

Third patient day at the Reference Centre for Hereditary Rhythmic Diseases (Cmary), a day to discuss and share between patients, families, paramedics, doctors and Liryc researchers.

WE CAN SUPPORT LIRYC TOGETHER
TO PREVENT AND CURE HEART RYTHM DISEASES

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"THE LIRYC BEAT"

NEWSLETTER N° 14 /// MAY 2022
Publication Directors: the Executive Committee, comprising: P. Jaïs, M. Hocini, O. Bernus, J. Boussuge-Rozé, M. Chevalier, P. Dos Santos, R. Marthan, H. Normand, M. Haïssaguerre. • **Editors:** E. Gaillacq • **Graphic design:** F. Garcia • **Photo Credits:** Maitetxu Etcheveria, Grilled Cheese, Production du désert, Gautier Dufau, Marie-Astrid Jamois, Liryc.

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