ANNUAL REPORT 2021

The Electrophysiology and Heart Modeling Institute

_CONTENTS

ABOUT LIRYC

Liryc is a unique institute dedicated to heart rhythm diseases. From a stroke to sudden cardiac death, heart failure or cognitive disorders, heart rhythm diseases affect millions of people worldwide.

Liryc is one of seven university hospital institutes created by the French government as part of the "National Investments Programme," with the aim of spurring research and medical innovation in France.

To meet this major public health challenge, Liryc is committed to four missions: research, innovation, patient care and training. The objectives are to better understand the mechanisms underlying these diseases, to develop therapeutic, diagnostic and preventive tools to treat patients and to share the acquired expertise to the greatest number of centres around the world.

Liryc brings together researchers, doctors and engineers, for the benefit of patients. International multidisciplinary experts strive every day to better understand and treat the electrical dysfunctions of the heart, which are:

- ***Atrial fibrillation***, the most common arrhythmia that affects nearly 33 million people worldwide.
- ***Ventricular fibrillation***, the main cause of 4.25 million sudden cardiac deaths per year worldwide, i.e. 10% of deaths in Western societies.
- ***Heart failure***, which affects 26 million people in the world.

In a unique technological environment and a dynamic ecosystem, Liryc aims to **revolutionize the treatment and prevention of heart rhythm diseases for the direct benefit of the greatest number of people in the world**.

For further information, please visit **www.ihu-liryc.fr/en/**

_EDITORIAL

FOREWORD BY ALAIN ROUSSET, PRESIDENT OF THE NOUVELLE-AQUITAINE REGION

The Liryc Institute is a model in terms of medical research and innovation.

It demonstrates its expertise in the strategic field, for public health, of cardiovascular diseases, which are the cause of nearly one-third of all deaths in the world.

As such, its approach is in perfect synergy with the regional strategy at the crossroads of research, innovation, training and patient care.

Support for scientific and technological progress will enable everyone to benefit from these innovations and will position our region as a leader in the industrial, research and service fields.

This ecosystem of cooperation between research in health, mathematics, digital and human sciences represents real value-added for the Nouvelle-Aquitaine region.

The central expertise of the region, economic development, is also critical in meeting this challenge.

At the beginning of the Covid-19 pandemic the situation was terrible and France lost the game of independence in terms of health. We must take stock of this and now meet the challenge with you to win it back.

This is a fight for jobs, for sovereignty and for public health.

The region is committed to initiating efforts to win back custom and relocate industry, particularly in the fields of drugs and their components, masks and medical devices.

However, it's also a question of placing our region at the forefront of emerging treatments and new prevention approaches.

As such, I can only salute the region's partnership with the Liryc University Hospital Institute, which has been strengthened this year with, in particular, the consolidation of research and innovation projects, such as the launch of three major European projects and a master's course.

Together we contribute to placing research and its promotion at the service of everyone's health.

_ **Alain Rousset**, president of the Nouvelle-Aquitaine Region

Liryc was structured as a foundation for scientific cooperation under the aegis of the Bordeaux University Foundation. Its founding members are the University of Bordeaux, the Bordeaux University Hospital Centre, the French National Institute for Research in Computer Science & Control (INRIA) and the Nouvelle Aquitaine Region. The founding members provide resources to the institute, support its strategic direction and ensure its correct functioning. Liryc also has two major academic partners, the French National Institute for Health and Medical Research (INSERM) and the French National Centre for Scientific Research (CNRS).

Dotation ANR n°ANR-10-IAHU-04

2021 IN FIGURES

159 members

22 nationalities

13,1 € million in expenditure

1,8 € million in private fundraising

_RESEARCH

44 projects funded by grants

111 clinical trials

298 scientific publications

_INNOVATION

17 industrial collaboration contracts

28 patents

4 startup

_PATIENT CARE

7 150 patients remotely monitored

5 764 consultations/ teleconsultations

3 017 operations

_TRAINING

431 professionals trained

36 doctoral students and students welcomed in training

30 training sessions

A MESSAGE FROM THE CEO

INNOVATING TO MEET THE CHALLENGES OF HEART RHYTHM DISEASES

_ **Pr Pierre Jaïs**, CEO of Liryc

The year 2021 was disturbed again by the Covid-19 crisis, calling on the inventiveness of the teams to meet the major challenges of cardiac electrophysiology. In this context, the constant search for innovation, whether in practice or in approaches, has enabled us to continue our activities and even to surpass ourselves, keeping in mind our primary vocation: to give birth to major medical advances that will provide better care for patients.

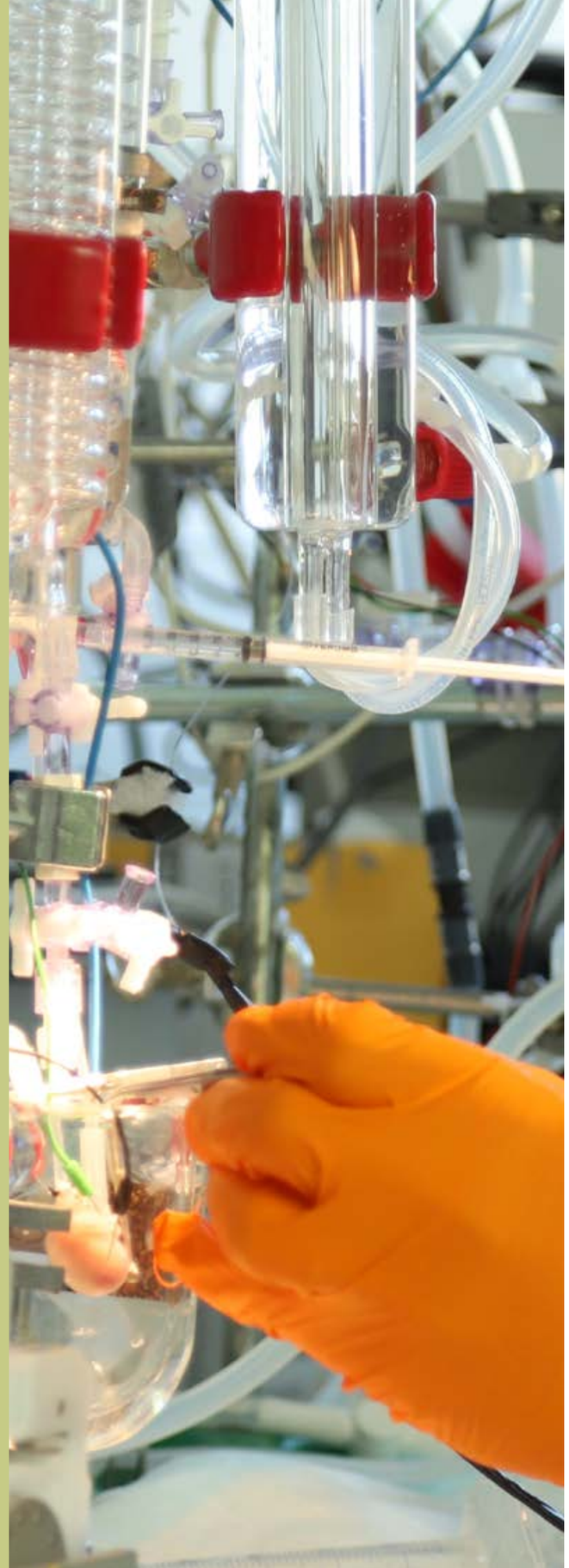
This year once again, joint efforts have been rewarded and acclaimed internationally, in the rankings of universities and research centres in cardiac rhythmology, with a seventh position in the world; and in France, with a first place in the 2021 list by the Le Point magazine for the electrophysiology and cardiac stimulation care teams of Bordeaux University Hospital Centre. I'd like to congratulate all of Liryc's employees, who have enabled us to carry our ambitions high. At the end of my first year as CEO, I'm particularly proud to lead such an institute of excellence.

On the scientific level, the year 2021 was marked by the launch of three European projects, BEAT-AF, MICROCARD and SimCardioTest, which encourage international translational collaborations to respond to the urgency of heart rhythm diseases. These projects are part of the institute's scientific roadmap, which relies in particular on artificial intelligence and modelling tools to draw up sustainable innovations, fast-track research and create real opportunities for diagnosing cardiac anomalies.

This momentum is also found in the training component of Liryc, with the launch of a two-year international master's course, which promotes a resolutely innovative teaching approach; and several initiatives to digitize training, to be more agile and to share our scientific and clinical knowledge better.

We should also note the official launch of the *"Light Up Your Heart"* fundraising campaign in 2021, which supports research, innovation, patient care and training. As such, it carries our collective ambition to prevent and cure heart rhythm diseases.

_RESEARCH



FEATURED IN 2021

- **Regarding atrial fibrillation**

Significant progress has been made in understanding the molecular, cellular and tissue mechanisms and in the implication of metabolism in persistent atrial fibrillation progression.

New personalized mathematical models and a new method to model the fibre directions in the atria have been developed. Computed tomography (CT) image processing and the use of different artificial intelligence approaches have also enable better guided ablation therapies, avoiding damage to surrounding tissues and predicting the outcome of ablation.

Work is continuing on new ablation approaches, with the ethanol infusion of the Marshall vein and the follow-up of 75 patients who have benefited from this approach, as well as pulsed field ablation of the pulmonary veins.

- **Regarding ventricular fibrillation and sudden cardiac death**

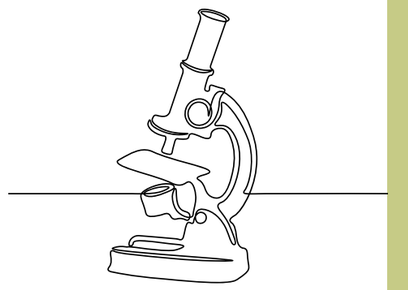
Teams at Liryc have demonstrated that the centres of electrical activity that maintain the initial phase of ventricular fibrillation originate, in the majority of the patients studied, from a defined localized substrate, often undetectable by clinical imaging. This substrate represents an interesting therapeutic target, but also a prospect for screening.

New clinical studies have also highlighted an important role of Purkinje fibres, located in the inner wall of the ventricles, in the maintenance of ventricular arrhythmias and a male-female difference in patients suffering from ventricular fibrillations.

- **Regarding heart failure**

Research teams are studying the mode of action of the OP2113 molecule and its potential to reduce the risk of myocardial infarction.

On the clinical side, a number of studies have been carried out in connection with remote monitoring and the use of connected devices, such as smartwatches, for the diagnosis of cardiac disorders, also with applications in paediatric cardiology.



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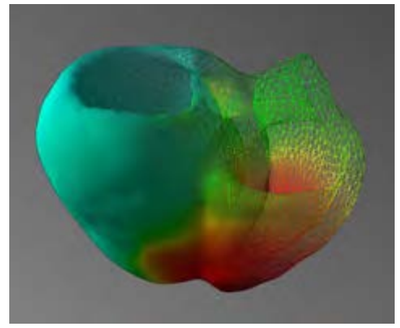
Liryc is ranked seventh in the list of international universities and research centres specializing in heart rhythmology.



FEATURED IN 2021

- **In general**

The year 2021 stood out scientifically for the launch of three European projects, BEAT-AF, MICROCARD and SimCardioTest, aiming to revolutionize the treatment of atrial fibrillation, going further in cardiac modelling and designing new tools to predict heart rhythm diseases.

Several major achievements in terms of innovation should be noted: the development of new mapping methods and ablative therapies; the implementation of new multimodal imaging approaches, coupled with personalized modelling; the discovery of specific tissue substrates involved in various arrhythmias, in particular thanks to a unique research programme on the human heart, made possible by organ donation for research.

This year once again, the bibliometric study carried out by the Software for Analysis and Management of Publications & Research Assessment (SAMPRA) team from the University of Lille positions Liryc in the top 10 of international universities and research centres on cardiac rhythmology. The rise of two places compared with 2020 reflect the scientific movement in which Liryc's multidisciplinary teams are part.

_ **Prof. Olivier Bernus**,
Scientific Director of Liryc

MAJOR PUBLICATIONS IN 2021

- Cluitmans, MJM; Bear, LR; Nguyên, UC; van Rees, B; Stoks, J; Ter Bekke, RMA & al.

  Noninvasive detection of spatiotemporal activation-repolarization interactions that prime idiopathic ventricular fibrillation. Sci Transl Med. 2021. PMID 34788076

- Banus, J; Lorenzi, M; Camara, O; Sermesant,

  M. Biophysics-based statistical learning: Application to heart and brain interactions. Med Image Anal. 2021. PMID 34020082

- Kamakura, T; Derval, N; Duchateau, J; Denis, A; Nakashima, T; Takagi, T & al. Vein of Marshall

  Ethanol Infusion: Feasibility, Pitfalls, and Complications in over 700 Patients Circ Arrhythm Electrophysiol. 2021. PMID 34280029

- Haïssaguerre, M; Nademanee, K; Sacher, F; Cheniti, G; Hocini, M; Surget, E & al.

  Multisite conduction block in the epicardial substrate of Brugada syndrome. Heart Rhythm. 2021. PMID 34737095

- Bustin, A; Toupin, S; Sridi, S; Yerly, J; Bernus, O; Labrousse, L & al.

  Endogenous assessment of myocardial injury with single-shot model-based non-rigid motion-corrected T1 rho mapping. J Cardiovasc Magn Reson. 2021. PMID 34670572

- Haliot, K; Dubes, V; Constantin, M; Pernot, M; Labrousse, L; Busuttil, O & al.

  A 3D high resolution MRI method for the visualization of cardiac fibro-fatty infiltrations. Sci Rep. 2021. PMID 33927217

FAST-TRACKING MEDICAL INNOVATION WITH MODELLING AND SIMULATION

Modelling and digital simulation have the ability to fast-track the development of innovations for the benefit of patients around the world. The SimCardioTest[1] and MICROCARD[2] research projects, funded by the European Commission respectively to the tune of €8 million and €6 million, implement these tools at different scales to improve the management of heart rhythm disorders.

Dramatically increasing R&D costs and regulatory complexity are significantly hampering the commercialization of new drugs and medical devices. SimCardioTest brings disruptive innovation by creating an integrated and secure platform that will standardize simulation models, in silico testing and certification support, fast-tracking the adoption of digital simulation to design cardiac drugs and medical devices.

The project, coordinated by Maxime Sermesant, a researcher at the French National Institute for Research in Computer Science & Control (INRIA) and Head of the Multimodal Data Science team at Liryc, brings together an international consortium of 10 academic and industrial partners to demonstrate the feasibility, effectiveness and advantages of in silico clinical trials for these devices and drugs.

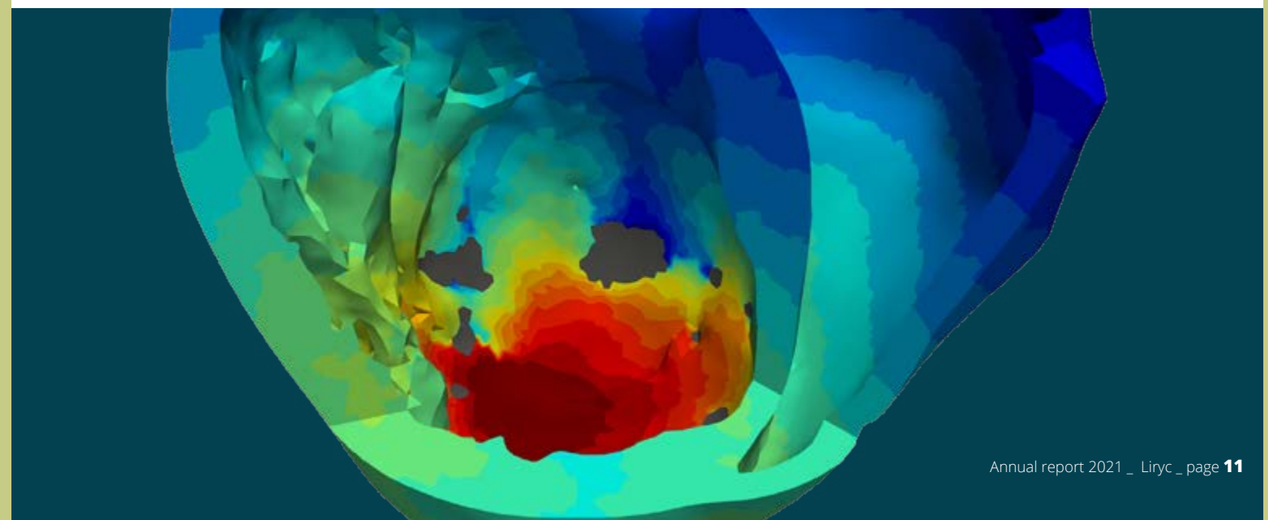
Advanced big data and artificial intelligence tools will make it possible to finely analyse the simulation results. The platform will also have a strong societal impact by contributing to the personalization of healthcare.

Digital modelling is a key element for understanding the mechanisms responsible for arrhythmias. Digital models of this system are very sophisticated and widely used, but they are still not powerful enough to replicate observations in ageing and diseased hearts affected by structural abnormalities at the microscopic level.

The European MICROCARD project aims to build a software capable of simulating the electrical behaviour of an entire heart modelled cell by cell, through the use of future exascale supercomputers. The project, coordinated by researcher Mark Potse from the modelling team at Liryc, brings together experts in high-performance computing, computer scientists, biomedical engineers and scientists from academia and industry in Europe, to develop a platform capable of answering current questions in cardiac rhythmology.

On top of the scientific and medical impact for patients, these two projects contribute to the positioning of a competitive Europe in terms of medical and healthcare innovation.

1- Funding of the European Union's Horizon 2020 research and innovation program under grant agreement no. 101016496
2- EuroHPC JU funding – European High-Performance Computing Joint Undertaking – under grant agreement no. 955495



INNOVATION

FEATURED IN 2021

- **News from Liryc startups**

  Liryc has taken a stake in the business Careline Solutions, which now makes it the institute's fourth startup.

  The Certis Therapeutics startup experienced a strong growth phase in 2021, which included the filing of three patents and a fundraising round of €1.5 million.

  The startup inHEART welcomed a new CEO, Todor Jeliaskov, with more than 20 years of international experience in leadership positions within large businesses and startups in the health sector. *"I'm delighted to be joining the talented team at inHEART, who have developed a unique solution to plan and guide cardiac catheter ablation procedures and I'm excited to be a part of this revolution. I look forward to leading its international deployment and to help more patients to benefit from it."* – Todor Jeliaskov.

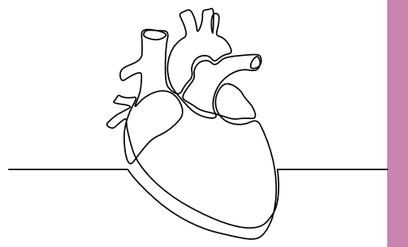
- **Patent filings**

  2021 was a fruitful year, with a total of seven patents filed on different themes:

  - Two patents on the issue of early diagnosis of ventricular arrhythmias.
  - One patent and one utility model for improving patient care with implantable cardiac stimulation devices.
  - One patent on a process for simulating electrophysiology signals to assist the training of doctors.
  - Three patents on magnetic resonance imaging (MRI) thermometry technology, in collaboration with the startup Certis Therapeutics.

- **Continuation of industrial partnerships to fast-track innovation**

  The partnership continues with the company Agile MV for the development of catheters intended to treat atrial fibrillation with the ethanol infusion of the Marshall vein. The teams are preparing a clinical trial aimed at validating the prototype developed within the framework of the partnership.



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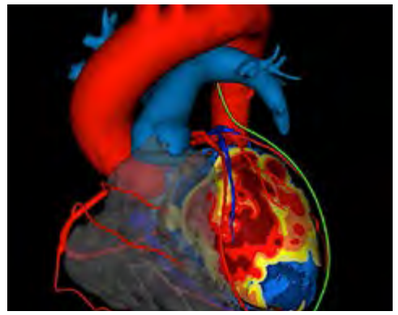
ACTIVE PATENTS
Liryc has a portfolio of 28 active patent families, including eight co-owned with an industrial partner.



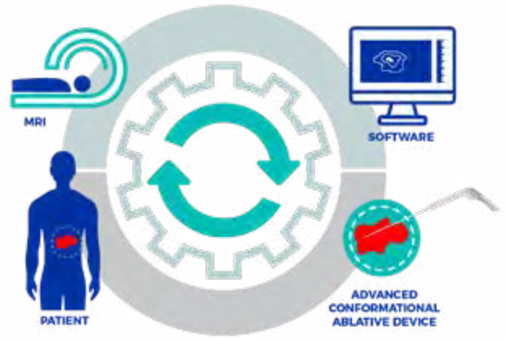
2021, A PROSPEROUS YEAR FOR THE CERTIS THERAPEUTICS STARTUP

With fundraising, software marketing and recruitment, 2021 was synonymous with growth for the startup Certis Therapeutics. Here we look back at the firm's great successes with Stéphane Chemouny, Co-Founder and President of Certis Therapeutics.

At a time when the global economy was recovering from the pandemic, the startup, specializing in minimally invasive therapies guided by magnetic resonance imaging (MRI), raised €1.5 million for the marketing of its first medical devices. As such, Medevice Capital (via Medevice Capital III), as well as regional funds Aquiti Gestion (via NACO), GSO Innovation and Crédit Agricole Aquitaine Expansion joined in 2021 the historical technological and financial partners of the startup, which was created in 2019 from research work by the Liryc team of Dr. Bruno Quesson.

"This fundraising gives us the means to achieve our ambitions. It also enables us to welcome an expert in the medical field into our capital and to continue to develop our anchorage within the regional ecosystem. We are delighted to welcome Medevice Capital, NACO, GSO Innovation and Crédit Agricole Aquitaine Expansion alongside our historical investors, business angels and the Aquitaine Science Transfert technology transfer acceleration company (SATT), "* says Stéphane Chemouny, Co-Founder and President of Certis Therapeutics.

Encouraged by the success of the fundraiser, the startup doubled its workforce to fast-track its development, particularly the commercial deployment of its products. As of the end of 2021, Certis Therapeutics had 12 people, mostly doctors or engineers with research and development missions and computer, physical and biomedical science profiles.



In 2021, the startup launched its first software product, thereby becoming the first industrial player to market a real-time and 3D, multi-organ MRI thermometry solution. With unprecedented precision, the tool is used to control minimally invasive thermo-ablation therapies, which aim to destroy diseased tissues using thermal energy. The real-time 3D approach revolutionizes the treatment workflow and guarantees the quality of movement, with a complete view of the target area to be ablated, which must be completely destroyed to avoid a recurrence, as well as of the surrounding tissues to be preserved.

The business has obtained ISO 13485 medical certification and its software has received its first CE marking. The technology was initially developed based on research work at Liryc on the heart, one of the most complex themes from an imaging point of view.

Today, the firm has chosen to carry out its first clinical developments on liver cancer, which began in autumn 2021, within the MRI interventional radiology team at the University Hospital of Munich, led by Prof. Seidensticker. Certis Therapeutics is the only player on the market to offer a real-time thermometry solution on moving organs. While forthcoming projects will concern the brain, and tumours of the kidney and the prostate, in the medium term, applications in cardiology will be proposed.
"The monitoring of cardiac thermo-ablations is a difficult and strategic subject. It could improve the benefit/risk ratio of the procedures" says Stéphane Chemouny.

* ABOUT SATT AQUITAIN

SATT Aquitaine's mission is to invest in the transformation of academic research results into innovations. It also supports the creation of deep-tech start-up projects based on the work of researchers. In this respect, the SATT has supported the engineering of the Certis Therapeutics project in its early stages, which stems from the research work of the Liryc team. The SATT invested more than €200,000 in the maturation of the technology to establish the proof of concept, set up an intellectual protection strategy (patents & software) and ensure its follow-up. A license has been signed between the start-up and the SATT for the exploitation of the technology.

PATIENT CARE

FEATURED IN 2021

- **First place in the list of hospitals and clinics 2021 of Le Point magazine,** among 348 establishments in France, proving once again the excellence of the electrophysiology and cardiac stimulation teams of the Bordeaux University Hospital Centre in the management of patients with cardiac arrhythmias.

- **Clinical studies to improve patient care**

  The clinical teams continued their work to improve patient care, in particular through 111 observational or therapeutic clinical trials in 2021, including:

  - The ECG-HD project carried out by Prof. Michel Haïssaguerre to evaluate electrocardiographic measurements by high-density electrode, which is part of the programme for the prevention of sudden cardiac death.
  - The REACT multicentre study carried out by Dr. Sylvain Ploux, studying the remote programming of active implantable cardiology medical devices.

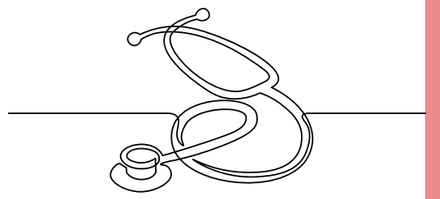
- **Continuous deployment of remote monitoring**

  On the stimulation side, most of the activity was devoted to the continuous deployment of telemonitoring for better prevention and personalized health care, with the validation of new tools, such as connected devices and the use of artificial intelligence.

- **Patient quality of life and extra-medical support**

  Deployment of research programmes to study the quality of life in children or adults with congenital heart disease through the implementation of cardiovascular rehabilitation. The programmes are led by Dr. Pascal Amédro who has recently joined the Complex Congenital Cardiac Malformations (M3C) National Reference Centre.

  The Reference Centre for Hereditary Rhythmic Diseases (Cmary) launched a study in the spring that focuses on post-traumatic stress in patients resuscitated after sudden cardiac death to offer better support to them and their loved ones. The centre also organized a second day of discussions between patients, families, paramedics and doctors to talk about of diagnoses, treatments and daily life.



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The care teams have contributed to the development of five care recommendations[3], developed methodically to help practitioners offer the most appropriate care in a given clinical context.

3- Recommendations in Brugada syndrome – Long QT Syndrome – Arrhythmogenic right ventricular dysplasia – Hypertrophic cardiomyopathies – Rhythm and conduction disorders of complex congenital heart diseases in adults.

BEAT AF PROJECT: REVOLUTIONIZING THE MANAGEMENT OF ATRIAL FIBRILLATION

The BEAT AF study, coordinated by Prof. Pierre Jaïs, brings together nine European clinical centres to help reduce the burden of atrial fibrillation, the most common arrhythmia, which affects more than 10 million people in Europe. The project has received €6 million in funding from the European Union's Horizon 2020 programme.

Atrial fibrillation (AF) is characterized by abnormalities in the formation and conduction of electrical impulses in the heart, resulting in ineffective contraction of the atria. The reference treatment to date is the ablation of AF by isolation of the pulmonary veins. Despite progressive improvements in technologies, energy approaches, radiofrequency or cryo-balloon, still have limitations contributing to the lesser use of ablation, since only two percent of patients with AF have access to this procedure.

The overall objective of the BEAT AF study is to demonstrate, within the framework of a five-year project, that the isolation of pulmonary veins by pulsed field ablation, a newly available energy for cardiac arrhythmias, is more efficient, faster and safer than radiofrequency, the golden standard to date. Pulsed field ablation uses high-voltage electric micro-shocks to open nanoscale pores in cell membranes, without damaging non-cardiac collateral tissue.

Two separate randomized clinical trials are being conducted to provide evidence for the superiority of pulsed field ablation for paroxysmal atrial fibrillation and its potential effectiveness for persistent AF. These first two clinical trials launched in 2021 pave the way for other studies that will then be needed to establish pulsed field ablation as the reference energy in international standards.

In the last 30 years, no new technology has achieved this level of hope in this field.

If we had to imagine the ideal atrial fibrillation ablation procedure, it would be easy to perform, in an hour or less, associated with a success rate greater than 90% at one year of follow-up, without the risk of disabling or fatal complications.
Is this a realistic aim?
We are actually very close to achieving such an ambitious goal.

_ **Prof. Pierre Jaïs**,
Cardiologist and
Principal Investigator

WHAT LESSONS FOR SMARTWATCHES?

Smartwatches create real opportunities to diagnose cardiac abnormalities, such as atrial fibrillation, the most common arrhythmia in clinical practice often remained undiagnosed. With products by Apple, Samsung, Withings, among others, the market for smart watches capable of performing electrocardiograms (ECGs) is expanding. Are there differences in the diagnostic potential of watches? How far can we go? The cardiac stimulation clinical team at the Bordeaux University Hospital Centre, attached to Liryc, looked into the matter.

Apple has marketed the first smartwatch that performs ECGs, but watches from competitors, such as Samsung or the French company Withings can also record ECG traces[4]. The team of Prof. Pierre Bordachar, with Dr. Marc Strik and Dr. Sylvain Ploux, compared the diagnostic potential for detecting atrial fibrillation of the three smartwatches in a prospective clinical study on 100 patients with atrial fibrillation and 100 patients with normal sinus rhythm.

The diagnostic accuracy of their automated interpretations varies from model to model, as does the quality of recorded ECG traces for manual interpretation. The accuracy of Apple and Samsung's automated atrial fibrillation diagnostics was superior to that of Withings. The quality of the plots was more precise for Withings and Apple than it was for Samsung.

The results of the study nevertheless show that the sensitivities and specificities of the three algorithms are high, even if the screening test is imperfect. Artificial intelligence approaches are expected to improve the accuracy of automated smartwatch diagnostics.

Beyond the detection of atrial fibrillation, improving filtering, modifying algorithms and measuring other leads opens many other perspectives, such as the detection of abnormalities and conduction, as well as repolarization disorders, which are responsible sudden cardiac death.

_ **Dr Marc Strik**,
Cardiologist at Bordeaux
University Hospital & Liryc

4- Smartwatches measure the electrical activity of the heart, i.e. the electrical impulse that crosses the heart to allow its contraction, thanks to two electrodes, one placed under the watch in contact with the wrist, and a second at the level of a push button. Unlike the 12-lead ECG used in a clinic, they check a single lead, a single "point of view" of electrical activity, enabling a possible atrial fibrillation to be detected.

TRAINING

FEATURED IN 2021

- **E-training**

  Official launch in 2021 of the digital learning platform www.liryc-education.fr that promotes the sharing and global dissemination of knowledge on the specialty of cardiac electrophysiology.

  Liryc has carried out a digital transformation of its training programmes by offering hybrid formats to reach a wider and more international target.

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- **Diploma courses**

  Liryc organized a new promotion of remote monitoring of implantable heart prostheses, bringing to 55 the number of nurses and clinical research associates trained in this new practice over the last three years.

  Liryc has launched the first promotion of the new ***"master II electromechanical heart disease"*** international course. This two-year master's course is part of the so-called "UB GRAD's" initiative, coordinated and operated by the College of Doctoral Schools of the University of Bordeaux.

- **Continuing professional development and simulation**

  Continuing education sessions designed in partnership with leading electrophysiology industries have contributed to the training of 146 professionals through intensive case studies, practical simulation sessions, workshops and live case broadcasts.

  The experimental platform has also made it possible to a host robotic training centre from the company Intuitive Surgical, which has benefited the entire surgical community in different disciplines (urology, gynaecology, pneumology, digestive surgery, etc.).

- **Congresses and scientific events**

  The "Alliance Bordeaux Programme" conference on new treatment techniques, jointly organized with the industrialist Boston Scientific, brought together more than 300 professionals in a hybrid format.

  Several scientific animation events were held, promoting the sharing of knowledge between peers: international workshop, journal clubs, thematic breakfasts, one-off workshops, etc. The teams also contributed to or jointly organized numerous national and international conferences in 2021.

430+

Health professionals trained In 2021

+32%

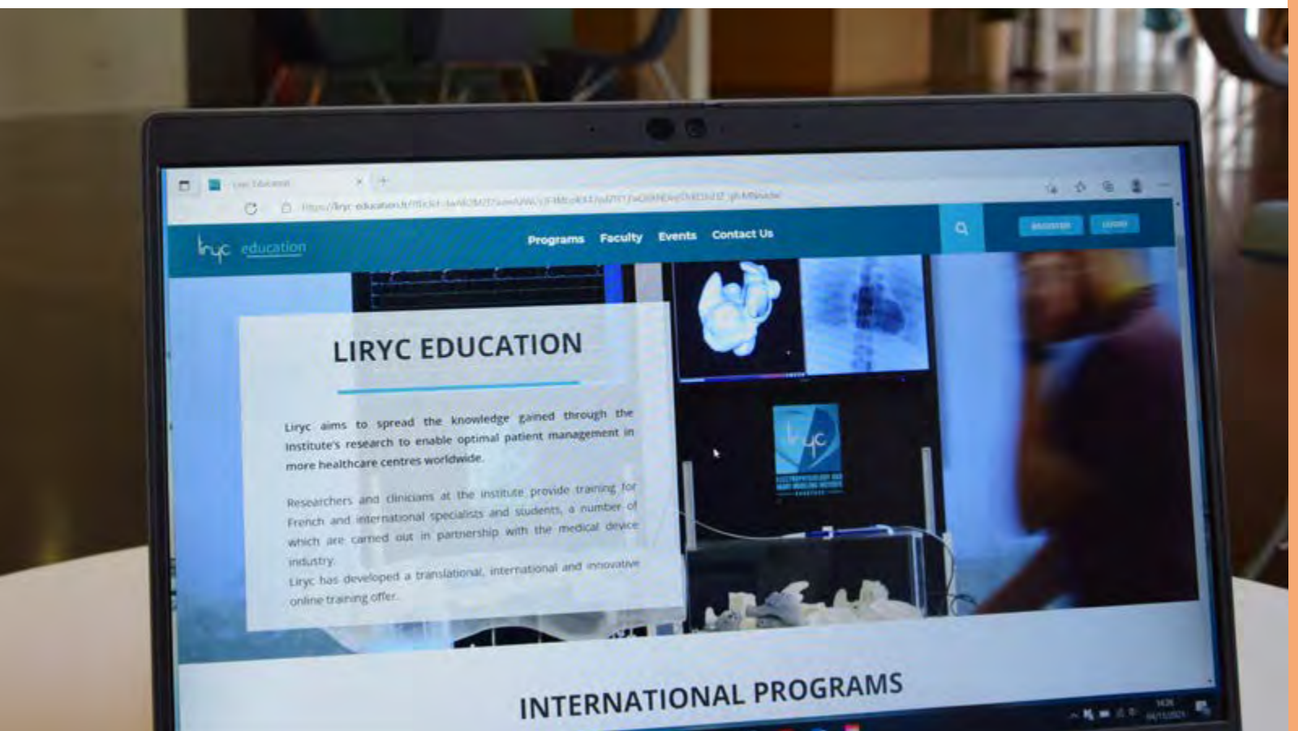
A DIGITAL EDUCATIONAL PLATFORM TO FAST-TRACK KNOWLEDGE TRANSFERS

Launched in 2020 to meet the intensification of local, national and international training needs, the Liryc teaching team launched an e-learning platform in the spring of 2021 at www.liryc-education.fr.

The e-learning platform offers varied and interactive training content in the field of electrophysiology, and more specifically ablation and cardiac stimulation: video content, such as commented interventions, practical cases, broadcasts of conferences or more traditional educational materials, such as courses, bibliographies and scientific articles.

"It's a tool that offers us unlimited possibilities to share content personalized to the heterogeneous needs of our different training audiences, whether they're students or professionals in research, healthcare and industry," says Prof. Pierre Bordachar, Cardiologist at the Bordeaux University Hospital Centre and a member of the institute's teaching team, who piloted the project. The platform makes it possible to offer personalized content accessible by profile, with step-by-step monitoring of the various courses, in particular in support of the training programmes delivered at Liryc.

Liryc-Education is a more flexible, accessible and responsive tool, which allows Liryc to go further in the dissemination of scientific and medical knowledge, resulting from research work and clinical practice, to as many people as possible. It also strengthens Liryc's positioning in new "à la carte" and "on-demand" training trends as it aims to respond to the new constraints related to the expansion of the Covid-19 crisis. As such, it makes it possible to offer healthcare and research professionals a continuum of training that will enable them to train according to their availability, anytime and anywhere.



I never expected that such renowned experts would teach us in such an intimate environment

_ **Mohua Jalali**, student of the cardiac EP master's course promotion 2021

THEY ARE TALKING ABOUT IT – A LOOK BACK AT THE CARDIAC EP MASTER'S COURSE

As part of the Graduate School for Young Researchers at the University of Bordeaux, the "Cardiac EP Electromechanical Heart Diseases" two-year master's course, launched in 2021, offers training focused on research and innovation for high-level specialists in the field of electrophysiology and cardiac bio-engineering.

"The first highlight from a teaching point of view is that we've succeeded in delivering a very broad and varied training course with a multidisciplinary approach, much like the way research activity is structured at Liryc; even though we have chosen to do a master's degree in a very specific and restricted field of research," explains Prof. Pierre Dos Santos, Director of Training and Education at Liryc.

The pedagogical team has consolidated an innovative approach, combining theory and practice with teaching through transversal projects in an international environment, meeting experts in the field.

"Before joining the master's course, I expected to have a brief glimpse of the cardiology world, but in fact, we were all completely immersed into the field! We went from seeing a microscopic view of the heart to understanding cardiac devices and ablations – we even got to see a surgery!" says Mohua Jalali.

Another innovative aspect of this training is that it takes place within a research environment in direct contact with world-renowned experts, university partners and international industrialists, thereby broadening the network of students with a view to their imminent entry into the job market.

MANAGEMENT

FEATURED IN 2021

- **Renewal of the International Scientific Advisory Board**

The International Scientific Advisory Board welcomed two new members: Prof. Srijoy Mahapatra (University of Minnesota, USA) and Prof. Dobromir Dobrev (Duisburg-Essen University, Germany), alongside Prof. Barbara Casadei (United Kingdom) and Prof. Katja Zeppenfeld (Netherlands). They were able to carry out their mission of supporting the main scientific orientations of the Institute during the Scientific Workshop, organized on December 1 and 2, 2021, bringing together the Liryc teams for two days of scientific exchanges.

- **Measuring the ecological impact**

In 2021, Liryc initiated a voluntary process aimed to evaluate the institute's greenhouse gas emissions, supported by the consulting firm NEPSEN. The emissions profile of Liryc corresponds to 1,884 tons of CO2e per year. The three main sources of emissions are the purchase of goods (28% of total emissions), visitor travel (22%) and energy consumption (20%). This approach aims to drive a more global policy of ecological transition for Liryc.

On a European scale, the Liryc Institute and the EHRA (European Heart Rhythm Association) launched a survey in November 2021 to collect data on current practices, perspectives and expectations of cardiac electrophysiology professionals in Europe in terms of sustainability. The aim is to explore sustainability challenges and opportunities in cardiac electrophysiology, where high-tech, invasive and single-use medical devices are required in large quantities in procedures.

RAISING PUBLIC AWARENESS OF HEART RHYTHM DISEASES

Jean Galfione, Ambassador of the Liryc institute, finished 10th in the Class40 category of the Transat Jacques Vabre, with his boat in the colours of Liryc, an opportunity he seized to highlight research to reduce heart rhythm diseases.

The institute also took part in several events to raise awareness of innovation in heart rhythm diseases with educational, virtual reality and workshops, including the European researchers' night and the international awareness day for cardiac arrest alongside the ***"Choquez-Nous"*** ("Shock Us") association and the French Federation of Cardiology.

FINANCIAL REPORT

The Financial Report is presented on the overall scope of the university hospital institute.

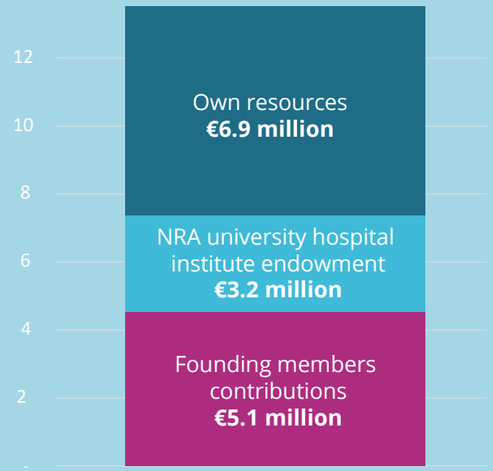
It takes into account:

- The funds managed within the foundation hosted by the Bordeaux University Foundation.
- The funds managed by the founding members on behalf of the university hospital institute, both on the National Research Agency (NRA) agreement and on the other research agreements they hold for the university hospital institute.
- The promotion of the personal contributions of the founding members and partners of Liryc.
- Sources of own funding: training, provision of services, industrial collaborations, fundraising and national and international grants.

The funds related to the management of the patient care activity, managed directly by Bordeaux University Hospital Centre, are exempt.

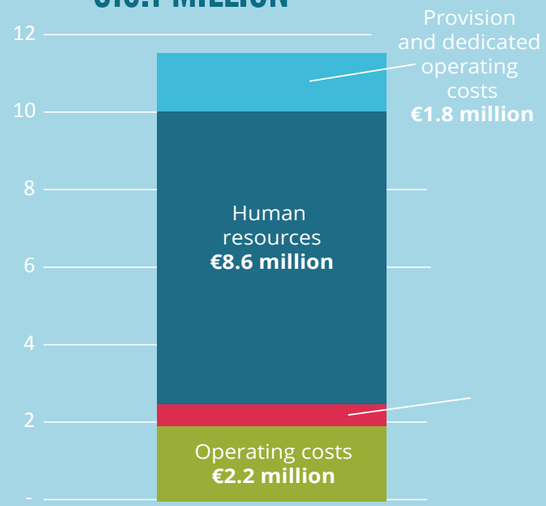
RESOURCES IN 2021

€15.2 MILLION

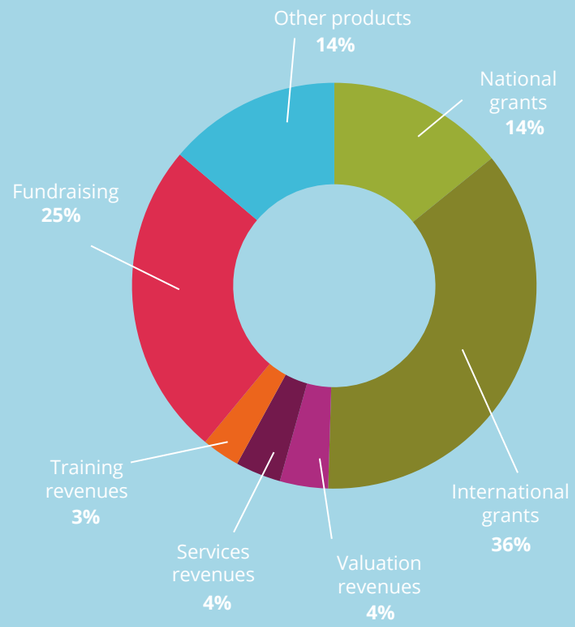


EXPENDITURE IN 2021

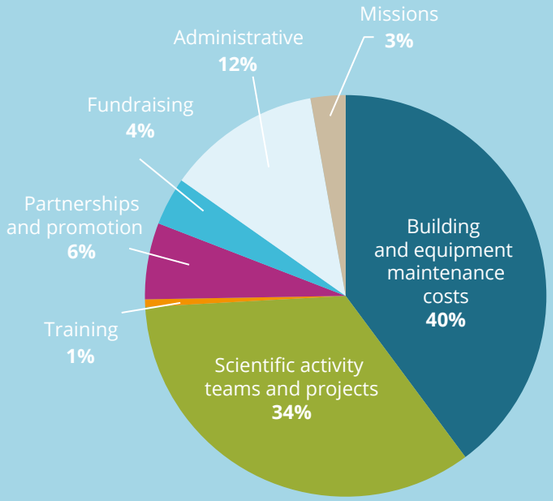
€13.1 MILLION



BREAKDOWN OF OWN RESOURCES



BREAKDOWN OF OPERATING EXPENDITURE

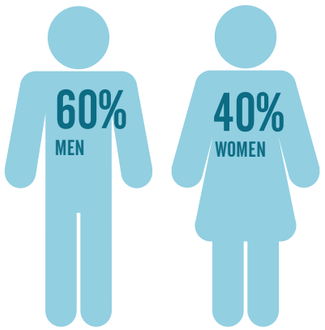


The 2021 financial report shows that 45% of the institute's overall resources are own resources, which reflects the considerable effort made by the Liryc teams to meet the financial targets set by the National Investment Programme towards self-financing. The achievement of these targets has been made possible, on the one hand, thanks to the ability of researchers to obtain large-scale competitive funding (50% via French and international grants) and, on the other hand, to the generosity of our donors, whose private funds make it possible, in addition to public funding, to ensure the achievement of Liryc's ambitious scientific program.

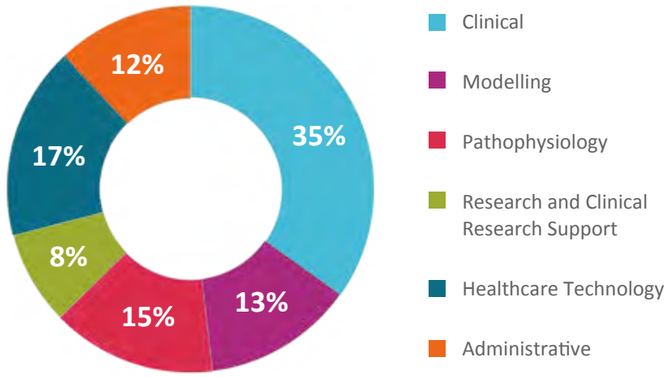
_ **Julie Boussuge-Rozé,**
Executive Director of Liryc

SOCIAL REPORT

159
TOTAL WORKFORCE IN 2021

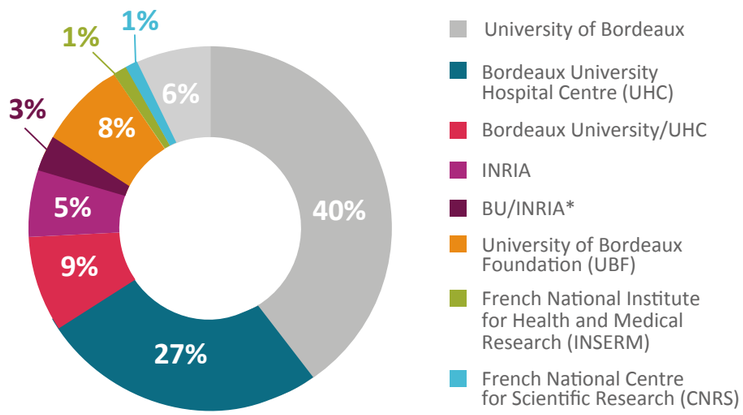


SIX DEPARTMENTS BREAKDOWN OF EMPLOYEES PER DEPARTMENT



37,7 years old
AVERAGE AGE

BREAKDOWN BY EMPLOYER

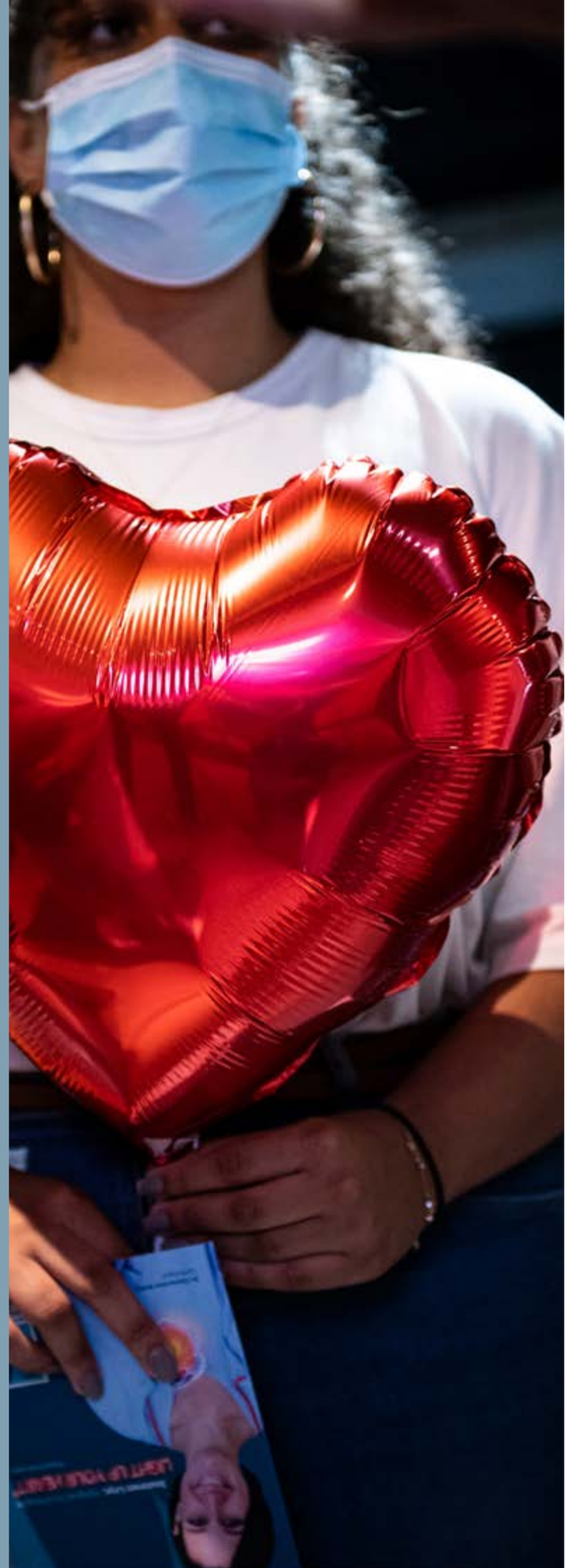


** Personnel with a double assignment*

23 NATIONALITIES

- Belgium
- Brazil
- Cambodia
- Canada
- Chad
- China
- Czech Republic
- France
- India
- Italy
- Japan
- Lebanon
- Mauritius
- Morocco
- Netherlands
- New Zealand
- Palestine
- Spain
- Switzerland
- Tunisia
- United Kingdom
- United States
- Venezuela

FUNDRAISING



FEATURED IN 2021

- ***Light up your heart* campaign launch party**

On September 29, on the occasion of World Heart Day, Liryc officially launched its campaign to collect "Light up your heart" funding during an exceptional evening at the Château Pape Clément, made available by Bernard Magrez, a major donor to the institute. This event brought together the community of donors and partners of Liryc to celebrate and thank the first major supporters of the institute.

- **International dynamics of the fundraising campaign**

Liryc's fundraising campaign is also being built on an international scale.

The world leader in the science of diagnosis and treatment of cardiac arrhythmias, Biosense Webster, of the Johnson & Johnson group, has signed a multi-year fundraising agreement. Liryc and Biosense Webster have been collaborating scientifically for more than 20 years, with the common goal of innovating in the treatment of cardiac arrhythmias. This fundraising agreement will make it possible to support, in particular, the work of the scientific chair of excellence in the prevention of sudden cardiac death.

In March, in a virtual format, the institute took up the challenge of immersing in its laboratories and platforms around fifty American philanthropists gathered around Mark and Laura Bailey, major donors to the institute. The event made the guests aware of the public health issue of heart rhythm disorders and of Liryc's ambition to create new diagnostic and therapeutic solutions.

€1.8 million
in private fundraising in 2021

They support us*:
- Abbott
- Ancre
- Association Paul et Philippe Perrot
- Bailey Mark & Laura
- Bernard Magrez SAS
- Biogen
- Biosense webster
- Boston scientific
- Bureau François Lillet
- Cap Ingelec
- Ceva Santé Animale
- Clavis Foundation
- Crédit Mutuel Arkea
- Fonds de dotation Caisse d'Epargne Aquitaine Poitou-Charentes
- Lemerpax
- Maincare
- Mannion Family Foundation
- Medtronic
- Pny
- Reuben foundation
- Rubis

* *Donation amount greater than 10 000€. Also includes 3 anonymous donors.*

FEATURED IN 2021

- **Donation and opportunities for regional meetings**

On March 10, 2022, Liryc hosted a plenary session of the Nouvelle Aquitaine Mid-Size Businesses Club[6]. It was an opportunity to present the institute and its projects to 90 regional business leaders and to pave the way for opportunities for collaboration and fundraising. Welcoming the Club to Liryc is part of the institute's desire to forge close relationships with businesses in the region and to stimulate a regional trend.

In December 2021, Liryc and Ceva Santé Animale signed a fundraising agreement placing the fifth largest veterinary laboratory in the world among the five largest donors to the institute. This support reinforces all of Liryc's research projects to improve the management of heart rhythm disorders. It also reflects a common desire of the two major health players in Nouvelle Aquitaine to be part of the "One Health" approach to push back the frontiers of scientific knowledge, for the benefit of human, animal and environmental health.

- **A first virtual tour of Liryc**

In April 2022, Liryc organized a first 100% virtual visit to go behind the scenes of research and innovation in cardiology and to keep in touch with the institute's donors. This virtual visit, followed by a question and answer session, was an opportunity to meet all those who work alongside Liryc teams to cure patients suffering from heart rhythm diseases.

6- Mid-size businesses

FUNDRAISING REPORT IN 2021

28 businesses

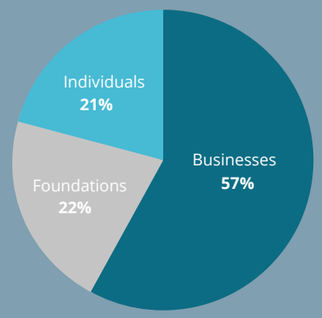
10 foundations, associations, charities

134 individuals

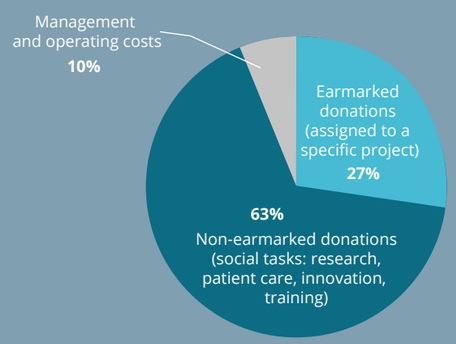
34% of donations come from abroad

			Other
66%	30%	3%	1%

ORIGIN OF DONATIONS



USAGE RATIO OF COLLECTED RESOURCES FROM DONORS



A MESSAGE FROM A DONOR

Meeting with Bernard Magrez, the Bordeaux businessman and owner of some forty châteaux in France and around the world, including four classified Grands Crus, and a major donor to the institute, involved in the *"Light up your heart"* fundraising campaign committee.

_ **Bernard Magrez**, major donor to the institute, involved in the fundraising campaign committee

What first encouraged you to support Liryc?

I was first of all won over by the passion, hard work and pursuit of scientific excellence of Liryc's management team; by this constant desire for improvement and innovation.

Being a donor is the choice of the heart, a story of encounters.

I support music, art, literature, abandoned children, but I first became a donor through medicine. Illness is an injustice. Injustice revolts me.

How do you support Liryc? What does it bring you to be a major donor of Liryc?

First of all, I provide financial support to Liryc and I also participate in the campaign committee, to put my energy more broadly at the service of the cause.

Being a major donor to Liryc is something I'm very proud of. I would even say that it is a real moral commitment for me.

I consider myself to be very lucky in life. As an employer at 21 years old, I started little by little, in Port, then spirits, before investing in wine then castles and Grands Crus, until the success that I know today came about through hard work. Now it's my turn to help others. It is my duty, my personal mission.

What message would you like to send to potential future sponsors of Liryc?

I would say that it is also their duty to support such an initiative, quite simply to save lives.

Being a donor means serving others in their true needs, without them even sometimes expressing them. Everyone feels their duty somewhere.

AWARDS AND HONOURS

They were awarded funding for their research project in 2021:

- ***Maxime Sermesant*** from the European Commission (Horizon 2020) for his artificial intelligence project.
- ***Pascal Amedro*** from the European Commission (European Joint Programme for Rare Diseases – EJPRD) for his research project on quality of life in paediatric and congenital cardiology.
- ***Aurélien Bustin*** and ***Julie Magat*** from the National Research Agency for their imaging research project (Young Researchers and Collaborative Research Project).
- ***Aurélien Bustin, Guido Caluori*** and ***Kanchan Kulkarni*** from the Lefoulon Delalande Foundation.
- ***Marc Strik, Aurelien Bustin, Rokhaya Faye*** and ***Dounia El Hamrani***, as part of Liryc's internal call for projects, which rewards collaborative translational research projects led by researchers at the beginning of their career. This project is supported by the major donors Mark and Laura Bailey

Buntheng Ly and ***Aurélien Maillot*** won the ANCRE prize at the fourth edition of the Liryc International Scientific Workshop.

Congratulations to:

- ***Mélèze Hocini***, who received the rank of Knight of the Academic Palms class of 2020.
- ***Matthias Stuber***, who received a gold medal at the Society for Cardiovascular Magnetic Resonance 2021 conference, the highest honour in the profession.
- ***Aurélien Bustin***, who is the winner of an ISMRM Junior Fellow 2021 prize, rewarding the work of excellence of young researchers.

COMING UP IN 2022

- **Launch of the HELP program**

  Led by Prof. Michel Haïssaguerre, winner at the European Research Council as part of the prestigious ERC Advanced Grant 2021, it aims to solve the major challenge of preventing sudden cardiac death, which is responsible for 350,000 deaths every year in Europe. The aim of this program is to develop an innovative non-invasive heart rhythm mapping system that is capable of identifying subjects at risk of sudden cardiac death.

- **Development of the cardiac imaging platform**

  The arrival of a two-photon counting scanner within the institute's cardiac imaging platform will open up new fields of research. This is a revolutionary instrument that combines a much higher spatial resolution than the existing one, with tissue characterization capabilities comparable to those of magnetic resonance imaging, which will make it possible to visualize cardiac structure abnormalities at the origin of atrial fibrillation or sudden cardiac death.

- **Update of the institute's strategic plan**

  A true multi-year roadmap for the accomplishment of the institute's research, innovative patient care, innovation and training missions, the strategic plan will be updated to take into account the latest scientific and technological developments, as well as the new challenges it faces in its international ecosystem.

- **Development of the Summer Schools programme**

  The Summer School of Cardiac Electrophysiology will once again welcome professionals, students, engineers and international researchers wishing to train in cutting-edge techniques. The programme will be completed with the launch of a new Summer School Percutaneous Therapies in Congenital Cardiopathies as part of the University of Bordeaux's Summer Schools programme.

The year 2022 will be marked by work to update Liryc's strategic roadmap to take into account the new scientific and economic challenges imposed on an international scale in a rapidly changing ecosystem. This work will also make it possible to prepare the forthcoming evaluation of university hospital institutes by the international jury in 2023, with a view to the renewal of public funding for an additional five years. I'm delighted to see the launch in 2022 by the government of a third university hospital institute call for projects, creating a new wave of university hospital institutes and confirming the relevance of the model for transforming research into innovations.

_ **Michel Vounatsos**, Chairman of the Administrative Board

The Electrophysiology and Heart Modeling Institute

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