LUCA

**LASER AND ULTRASOUND CO-ANALYZER FOR THYROID NODULES**

NEWSLETTER

Welcome to the LUCA Newsletter

On behalf of all its members and partners, the European LUCA project welcomes you to this newsletter, intended to give visibility to the project during its creation and development as well as help raise awareness towards the need for a new medical tool that could help provide much better and accurate information on thyroid cancer.

In this newsletter, which will be published every semester, the members of LUCA will show you the advancements, goals and objectives they accomplish as well as their different experiences, bringing to the table their expertise, professional background and the reasons why they have joined this exciting project that will most definitely change the chances of survival and recovery of patients that suffer from this illness.
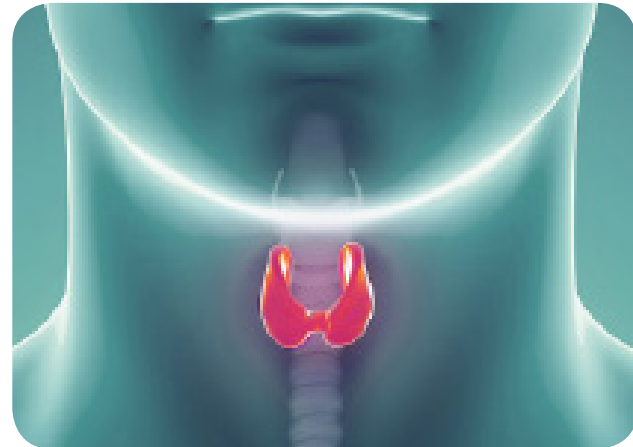
THYROID CANCER

A FASTER AND MORE EFFECTIVE SCANNING PROBE

Thyroid cancer is a major and growing health challenge with around three hundred thousand new cases diagnosed worldwide annually. Current methods do not provide sufficient support to surgeons in their decision on the appropriate course of action, which leads to a significant number of unnecessary surgeries and a reduced quality of life for patients. This calls for an increased sensitivity and specificity of the conventionally applied screening process.

The **EU-funded project Laser and Ultrasound Co-analyzer for Thyroid Nodules (LUCA)** aims to develop a new, low-cost device that will provide doctors with enhanced information required to provide better and more specific results in thyroid nodule screening and enable better diagnosis.

"*The device combines ultrasound and near-infrared diffuse optical technologies in a single device and a probe. By combining information about tissue hemodynamics, chemical constitution as well as anatomy, it will overcome the shortcomings of present techniques while screening for malign thyroid nodules. If successful, this will save millions of euros over the coming decades and improve the lives of millions of Europeans*", says ICREA Professor at ICFO **Turgut Durduran,** Scientific Coordinator of LUCA.

A multidisciplinary team made up of eight partners including clinical endocrinologists, radiologists, physicists, engineers and industry players will carry out this ambitious research project. Phase 1 of the project will be focused on the development and construction of device components, while phase 2 will see the implementation and clinical validation of the LUCA demonstrator.

"*A new tool made concomitantly with thyroid ultrasound may provide additional information to help us distinguish between benign and malignant nodules. This would allow a reduction in the number of surgeries for these reasons and would have an important socio-economic impact, diminishing the number of surgeries and the associated comorbidities, as well as improving the quality of life of the patients affected*", comments **Dr. Mireia Mora** from the August Pi i Sunyer Biomedical Research Institute (IDIBAPS) in Barcelona, Spain, which will be responsible for the clinical application of the tool, under the direction of Prof. Ramon Gomis.

The LUCA device has the potential to represent a very innovative tool for other types of cancer diagnosis, screening and therapy monitoring in areas of the body accessible to both techniques. Therefore, LUCA is expected to have a significant impact not only in the field of thyroid cancer but also in additional areas of cancer screening.

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Interview with Dr. Turgut Durduran
SCIENTIFIC COORDINATOR OF LUCA

The **LUCA project** will develop a device based on a novel technological concept that will combine diagnostic standard **ultrasound** techniques with upcoming modalities based on photonics, that is, two diffuse optical modalities known as **time resolved spectroscopy** (TRS) and **diffuse correlation spectroscopy** (DCS).

Birth of a new collaboration

In 2010, Prof. Durduran was invited to give a talk to the department of endocrinology led by Dr Ramon Gomis at Hospital Clinic Barcelona. As Durduran clearly remembers, *"I knew very little about the topic so I did a bit of research and decided to focus my talk on potential applications in diabetes. However, since most of my work to date has focused on brain monitoring and breast cancer, I had many examples in these areas. After my talk, Dr. Gomis and Dr. Mireia Porta approached me and asked me whether we could measure the thyroid".* Consequently, they started a collaboration with a pilot study, where the preliminary results, published in PLOS ONE, showed that it was feasible to probe the depth of thyroid tissues and it was possible to differentiate types of nodules, thus demonstrating that diffuse optics was a promising clinical tool that could provide outstanding diagnosis improvements. Hence, Prof. Durduran *"put together a consortium that includes specialists in diffuse optics (instrumentation and algorithms), partners from industry (Ultrasound and diffuse optics), and Hospital Clinic Barcelona and other representatives as end-users"* and responded to an ICT-KET call by the European Commission, which was granted. Prof. Durduran is the project's Scientific Coordinator and his research group is contributing to the project with expertise in diffuse correlation spectroscopy modality. Durduran also emphasizes that *"we will also be playing a role in data acquisition and interpretation with our colleagues at the hospital".*

Is this device and technology the first to be developed?

Durduran comments *"So far the team has published the first study on thyroid cancer screening using diffuse optics and this project will actually be the first professional system being developed for research and the markets. The primary goal of this device will concentrate not on the detection of tumor cells but on the characterization of large nodules that are screened with ultrasound. It is a low-cost device, implying minimal additional costs due to the optics and therefore in the price range as of conventional ultrasound systems; it is a point-of-care machine, meaning that it is portable and can be used in the same way clinicians use ultrasound equipment; is it multi-modal because it combines the two diffuse optical modalities with ultrasound; it will definitely be faster because the results will be available in real-time; and it will be non-invasive, meaning that it*

will be able to reach up to two centimeters deep into most tissues".

The device is being built in a modular configuration so that, as other technologies improve, such as different versions of ultrasound or photo-acoustics techniques, the device will be able to adapt and combine its modalities to these newer versions and provide higher quality diagnosis. In addition to the morphological information clinicians obtain using ultrasound in nodule screening, Durduran states that *"they will also obtain information about the constituents (e.g. collagen, lipid, and water content), physiology (blood flow, blood oxygen saturation, oxygen metabolism) and vascularization of the nodule. Together, all this information will provide a more accurate, non-invasive discrimination between benign and malignant nodules".*

What challenges do you expect to face and when do you envision a robust clinically approved device ready to be used on patients?

Durduran remarks that *"the biggest challenge that I believe we will face is to see what true positive and false negative rates we obtain when we begin using the system in the clinics. We do not expect a failure on data quality, system signal-to-noise ratio or its usability, so we believe that this multi-modal approach that brings physiological, morphological and structural information to the early stages of screening will reduce the number of false-positives. Now, as for timings, if I am really optimistic about when it will be ready, I would say five to ten years to complete all the clinical trials, CE and FDA certification. But this is the multi-million Euro question".*

Prof. Turgut Durduran is the head of the 'Medical Optics' research group at ICFO, an inter-disciplinary group that develops and uses advanced optical tools for pre-clinical and clinical applications. The group's main expertise is in diffuse optical monitoring and tomography which uses photon diffusion to probe "deep" (0.1-10cm) into tissues. Their research aims to advance the field in theoretical instrumentation and application oriented approaches in parallel. Of particular interest to the group are bed-side neuro-intensive care monitoring, cancer therapy prediction and translational neuroscience and oncology.

Interview with Dr. Manuel Puig-Domingo
MEMBER OF THE LUCA MEDICAL ADVISORY BOARD (MAB)

Dr. Manuel Puig-Domingo has been working in thyroid cancer research for more than 25 years, at first as a clinical investigator and currently with a team of basic researchers aimed at generating translational research.

Dr. Puig worked as a staff endocrinologist at the Hospital Clínic de Barcelona from 2003 to 2010 and, during this time and in collaboration with the Endocrine Unit staff, they tried to promote research in the area of thyroid cancer, offering different training courses regarding thyroid ultrasonography for primary care physicians. During this time, they introduced the clinical use of ultrasonography by attending endocrinologists and also promoted it at a national level through the Spanish Society of Endocrinology and Nutrition, of which Dr. Puig is the current president. Thereafter, he was contacted by LUCA project researchers, by **Dr. Mireia Mora** and **Dr. Mattia Squarcia**, who invited him to become a member of the Advisory Board.

How will LUCA's technology benefit patients and thyroid cancer screening?

"Currently, the most important issues in the field of thyroid cancer concern the optimization of biomarkers to allow the identification of those cases that will have a negative clinical-biological evolution, and require a more aggressive therapeutic approach after diagnosis. In the last decade we have refined the treatment of those cases with low risk of malignant evolution, through less aggressive treatment modalities, but on the other hand, those cases with poor prognosis are waiting for more effective therapies. In these latter cases, recent new biological therapies have not proved to be as successful as desired and moreover, the safety profile is far from being acceptable. Moreover, the LUCA project will throw a lot more light onto thyroid cancer management by means of incorporating predictive bio-imaging markers that will be able to identify the biological nature of thyroid nodules that are currently ticketed as being of indeterminate nature, namely those cases with grade 3 Bethesda classification".

What will you bring to the project in terms of expertise?

"I am a member of the Medical Advisory Board; thus, in my current professional position as Director of the Germans Trias i Pujol Research Institute and Head of Endocrinology at Germans Trias i Pujol University Hospital, I have been invited to give support to the strategic evaluation of the LUCA Project, its feasibility and its implementation."

How does this technology differ from any other that you are currently using for end-user patients that suffer from this illness?

"This project is developing the use of an innovative optical technology to measure oxygen saturation, volume and blood flow, collagen and lipids at thyroid tissue level. The fact that this technology is combined with ultrasound, the most sensitive tool that we currently have to evaluate thyroid nodules, means that if it is as successful as we expect it will be, it will represent a very remarkable advance in the field of endocrinology. In my opinion, it could give additional, complementary and very relevant information to ultrasound data, thus potentially avoiding unnecessary biopsies, as well as avoiding unnecessary thyroidectomies and associated comorbidities in the cases where the biopsy is inconclusive".

Do you see this device fulfilling the needs of your sector?

"As a physician, I need to be able to use new biomarkers for my patients in order to facilitate the decision-making process for the evaluation of thyroid nodules so we can better identify those of malignant origin. These new biomarkers should be of a bio-imaging nature that would be detectable in real-time at the bed-side, this would clearly accelerate the diagnostic procedure."

LUCA project is constituted by a multidisciplinary group. What advantages does it have?

"A multidisciplinary approach, in every way, is the only way to make good science and thus to go further in order to reach new solutions for the patients and their unresolved needs. The clinicians have the patients' problems and the questions; the scientists, and especially the basic scientists and engineers, have the answers but do not know the questions. Thus putting them together to work in a multidisciplinary team is the way to find solutions."

As a doctor, could you comment on the challenges this project could face, if any?

"The technology being developed by the LUCA Project has to demonstrate its clinical applicability in the fields of radiology and endocrinology, mostly but not only, for the diagnosis of nodular thyroid disease for the differentiation between malignant and benign pathology. The technology to be applied in humans has to be very robust, sensitive and specific in the discrimination of malignant and benign tissue; if this is reached, it would be useful also in other organ tissues. From the scientific point of view, I trust that the results of this project will be very relevant and will have an international impact."

Dr. Manuel Puig-Domingo is currently Head of the Endocrinology Services of the Hospital Germans Trias i Pujol as well as the Scientific Director of the Germans Trias i Pujol Health Sciences Research Institute. He is also Director of the Rossend Carrasco i Formiguera Foundation and President of the Spanish Society of Endocrinology and Nutrition. The research carried out by Dr. Puig and his team focuses on the prevention of type 1 diabetes, the treatment of type 2 diabetes and obesity, endocrinology of aging, thyroid cancer, thyroid physiology and pituitary adenomas.

LUCA Kick-Off MEETING
February 21-22, 2016 - Vienna, Austria

LUCA's Kick-off and **1st Consortium General Assembly** Meeting took place at the beginning of the year in Vienna, Austria. **Prof. Turgut Durduran**, researcher from ICFO and LUCA Scientific Coordinator, welcomed all members of the consortium, and commenced by highlighting the main motivations of the project, focused mainly on reducing the number of unnecessary surgeries, with possibilities of being able to differentiate between malignant and healthy nodules. Then, **Dr. M. Mora**, from IDIBAPS, talked about the clinical overview, briefly summarizing thyroid anatomy and physiology as well as nodular thyroid pathology. She presented the standard tools for its diagnosis and emphasized the limitation of the existing methods, pointing out the economic impact of nodular thyroid pathology. **Dr. P. Zolda**, from EIBIR, was responsible of delivering an outline of the work plan, timeline and tasks and responsibilities for the project and for each established work package. Leaders of the work packages introduced their contribution to the initiative, presented as follows:

- Project Management (WP1): N. Charles-Harris & K. Krischak
- Development of components and sub-systems (WP2): T. Durduran
- Development of a demonstrator (WP3) U. Weigel
- Ex vivo, phantom validation & standardization (WP4) A. Dalla Mora
- Validation in real-settings (WP5): F. Hanzu
- Dissemination (WP6) P. Zolda
- Exploitation (WP7) S. Royo

The Steering Committee, Consortium General Assembly, Medical Advisory Board (led by **Dr. M. Puig** and **Dr. Ravazzani**) and the Innovation and Exploitation Committee were established and introduced to the consortium.

2nd LUCA Consortium Meeting
September 29-30th 2016- Barcelona

The **2nd LUCA Consortium Meeting** took place at **ICFO** - in Barcelona, where LUCA members gathered to discuss on the project's progress. Amongst the different issues discussed, a progress overview was given by each of the work package leaders, including updates on the development of laser components as well as timing systems (**T. Durduran- A. Tosi - D. Contini**), the current state of communications between ultrasound and optical devices (**S. de Fraguier**), the design of the Optical-Ultrasound multi-modal probe (**B. Rosinski**), the real-time multi-modal data analysis (**S. Wojtkiewicz**), the novel LUCA demonstrator and the integration of sub-systems (**U. Weigel**) as well as the characterisation of LUCA technologies in laboratory settings (**A. Dalla Mora**) and clinical protocols elaboration, ethical approvals and demonstrator testing in real-settings for healthy thyroid tissue, benign and malign thyroid nodules in patients (**M. Mora**). Finally a general view of the dissemination and communication actions regarding the project were presented (**P. Zolda**) as well as the development a strategy for exploiting results (**S. Royo**).

Dr. M. Puig, member of the MAB, gave an in-depth talk on the state of thyroid disorders in Europe and the expected pathway research should move into for this particular field, emphasizing the EU's awareness that thyroid research is of uttermost importance for Europe. Finally, strategies for exploiting the results were presented to establish clear procedures on what the market and business models could be once the project ends.

LUCA Consortium

Academic
ICFO - Institute of Photonic Sciences, Barcelona, Spain
Politecnico di Milano, Milano, Italy
University of Birmingham, Birmingham, United Kingdom

Industrial
Vermon, S. A., Tours, France
Hemophotonics, Barcelona, Spain
Echo Control Medical, Angoulême, France

End-Users
EIBIR European Institute for Biomedical Image Research, Vienna, Austria
IDIBAPS: August Pi i Sunyer Biomedical Research Institute, Barcelona, Spain
Hospital CLINIC of Barcelona, Barcelona, Spain

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