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LUCA

LASER AND ULTRASOUND CO-ANALYZER FOR THYROID NODULES

NEWSLETTER

This Issue's CONTENT:

3rd LUCA Consortium Meeting

Milano, May 18-19, 2017

The **3rd Consortium meeting** gathered all consortium members in **Milano** to provide an overall view of the current situation of the workpackages (WP) short-run objectives and deliverables due this year.

T. Durduran gave a general overview and then each of the WP leaders presented the current situation of their specific WP: **M. Renna** presented the Time Resolved Spectroscopy (TRS) components and sub-systems, **T. Durduran** gave an update on the Diffuse Correlation Spectroscopy (DCS) components and its subsystems, presenting stability test results, which validate the use of the laser for LUCA. Then, **H. Deghani** gave an update on the multi-modal data analysis, demonstrating that NIRFAST (Near Infrared Spectroscopy numerical modelling and image reconstruction) has been achieved, which means a major step forward in real-time processes.

U. Weigel talked about the integration of the TRS and DCS sub-components into the combined probe and ultrasound system that will finally be integrated in a fully functional LUCA demonstrator, while **A. Dalla Mora** reported on the different phantom characterization and validation procedures that are currently being studied and implemented. Finally, **F. Hanzu** did a recap on the clinical protocols that are being designed for further approval of Spanish ethic committees. In fact, she reported that ethical approval was granted for the first mock session, since the images produced by the components and the probe were considered good to be used.

As project managers of the project, **N. Charles-Harris** and **K. Krischak**, facilitated all consortium members with useful management information regarding upcoming deliverable and report deadlines as well as timelines for future tasks and responsibilities. **P. Zolda** presented the dissemination activities carried so far and the future initiatives for this upcoming semester. Finally, **S. Royo** explained the preliminary market analysis and exploitation intentions, emphasizing, among other issues, that not only the commercial but also the academic exploitation should be taken into account.

D. Contini introduced **Dr. Paolo Ravazzani**, a member of the Medical Advisory Board (MAB) and Director of Research at the CNR-IEIIT in Milano, Italy, who was invited to give the main talk of the meeting. He gave an overview of his research interests and projects as well as standardization committees and regulations in the medical/engineering field. Expert in novel diagnostics tools and innovative therapies in neuroengineering and biomedicine for non-invasive brain stimulation, he provided expertise on how international regulations and standards work, and gave advice to the LUCA consortium on how to prepare technical procedures to reduce any sort of delay in risk assessment.

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Interview with Sixte de Fraguier

R&D and Quality Manager at ECM

How did you become involved in this project?

Initially I was contacted by An Nguyen Dinh from VERMON, the French ultrasound probe manufacturer in charge of the LUCA optics-ultrasound combined probe. An Nguyen Dinh asked me if ECM would be interested in collaborating with an EU-funded research project on a new approach combining ultrasound imaging and photonics techniques to improve thyroid screening and diagnosis.

Since the piezoelectric transducer is a key component of the ultrasound imaging system, it is crucial for our company to have a very close collaboration with the probe designer (VERMON). This is why, over the past 10 years, ECM has developed a strategic business relationship with VERMON, who today represents our major ultrasound probe supplier.

VERMON introduced us to Turgut Durduran and after several very interesting technical discussions, it was very clear that this project could perfectly fit both our R&D roadmap and our product market positioning strategy.

What will be your major contribution to the project?

ECM designs, manufactures and sells ultrasound imaging systems for both medical and veterinary applications in more than 100 countries worldwide. Therefore, our company is contributing to the LUCA project with our vast expertise in ultrasound imaging systems, both from a technical and marketing point of view.

Our first task is to develop a specific interface software to integrate our high-end Exapad system together with the optical modalities of the LUCA demonstrator, offering clinicians the ability to drive all functions and retrieve optical measurements results through the ultrasound imaging system user interface.

Integrating the ultrasound imaging functionality within a larger, broader medical system to provide visualization or localization of selected areas of interest, for diagnosis or treatment purposes, is a very interesting market trend for us. Since the conventional medical imaging market is very competitive and controlled by large multinational groups, we believe that we may have a competitive advantage thanks to our small enterprise flexibility to address this B-to-B market. Thus, interfacing our imager into the LUCA demonstrator is in line with several of our R&D goals. This may also lead to very exciting future telemedicine applications.

In addition, due to our expertise in acoustics, we will give support to the multi-modality phantom design and validation and offer our technical support during the LUCA demonstrator clinical evaluation.

As a member of the exploitation committee, together with the other industrial partners, we will develop a strategic plan to address potential innovation protection and to evaluate market acceptance of the LUCA device as a new thyroid diagnostic tool. We will analyse cost constraints and price positioning in order to select the best marketing approach for the future LUCA device.

LUCA is a multidisciplinary project. You have worked in such projects before, thus what kind of learning experiences do you think you can bring to the table for this project and help make it be successful?

I think ECM's knowledge and experience in introducing medical devices to the market will be of great value to the LUCA project, ensuring that development tasks and the future commercial product design can be performed in compliance with current medical device regulations.

Compared to other projects I have been involved with, I have the feeling that the LUCA project will benefit from the very high level of expertise from all partners in their own field. I think it is essential to efficiently gather clinical needs and environment, academic researchers' know-how and industrial processes and promote synergies between partners that ensure the project's success. From this perspective, the LUCA consortium is very efficient and I do appreciate the large spectrum of complementary skills from all partners.

As a developer of mainly of ultrasound devices, how do you foresee the type of impact the project will have for the medical field and thus, society in general?

There is no doubt in my mind that, if the LUCA project can demonstrate better sensitivity and specificity in the field of endocrinology, it will also open the way to new clinical applications of such multi-modal approach, providing us with the opportunity to develop new medical devices and offer better healthcare tools.■

ECM

Based in Angoulême, France, ECM is a French independent company that designs, manufactures and sells ultrasound imaging systems for medical and veterinary applications. Founded in May 2001 to address veterinarians and breeders' need for a pregnancy control tool, ECM has developed a range of small portable battery-operated low-price ultrasound scanners. In 2005, the company decided to enter the medical market and developed a new line of high-end systems, mainly focused on low-price portable systems, while building up a new distribution network specially dedicated to the medical market. Today ECM has 35 medical and 60 veterinary distributors around the world, which sell approximately 700 products per year that represent a total turnover of 5 M€.

Sixte de Fragier obtained an Engineering degree in Physics from the Ecole Supérieure de Physique et Chimie Industrielles (ESPCI) in Paris, France in 1982. After graduating, he worked as a design engineer in the field of X-ray sources for medical applications at Thomson CSF group for 5 years and applied for several patents. He then worked at Thales for 3 years, manufacturing ultrasound probes for sonar and medical applications. He held a position of R&D probe designer and then Product Line manager. From 2001-2005, Sixte joined a Thales start-up company developing an innovative concept of portable medical ultrasound system as an interface to a standard PC. In 2006, he joined ECM, where he currently leads the development of the new ECM line of medical and veterinary products.

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Dr. Lorenzo Cortese

BIOPHOTONICS at ICFO

How did you learn about the project?

I met Turgut Durduran when I was a PhD student. I was attending a summer school in Cargése, Corsica, on "waves in complex system" and Turgut's talk was completely different compared to the rest of the extremely theoretical talks. I believe I can consider that moment as a breaking point for me since I began to show interest and follow new advances in medical optics and realize that diffuse optics could have a very high impact in innovative technological developments for the medical field. When I finished my PhD, I contacted Turgut to see if there was a possibility of working for him as a postdoc. During my interview, Turgut offered me the possibility of working on the LUCA project, an innovative technology project, where the kind of research I would have to carry out would be completely different to what I had done previously. Personally, I like it a lot, most of all, the multidisciplinary aspect of the initiative. It is quite normal to work with medical doctors, engineers, interact with patients and discuss basic physics every day. I'm also learning a lot working in collaboration with companies... It is a completely new world for me!

Based on your previous work experience, what kind of learning experiences do you bring to this project?

Although I have a lot of experience in experimental optics and instrumentation, my research has also been focused on photonics of biological systems, such as structural coloration of plants and animals, which have been an inspiration for the development of new advanced photonic materials (bioinspired photonics). In fact, my PhD thesis studies focused on theory of light diffusion applied to particular optical properties of two species of white beetles of South-East Asia that are characterized by an extremely brilliant white reflectance.

Even though my doctoral studies were focused on fundamental, basic research, I ended up covering different fields of study, ranging from bio- to nanophotonics, from fabrication to modelling, etc., which is something that I believe I can bring to this project. I have always been very interested in applied research and the impact this research could have on technology. That is why I am very enthusiastic about working on LUCA.

What were your major challenges at the beginning of the project?

At first, I encountered several issues and problems when trying to create device interfaces that should be up and running, ready to perform measurements in hospitals, on patients... Luckily, I work together

Dr. Giuseppe Lo Presti

BIOMEDICAL ENGINEERING at ICFO

How did you become involved in the LUCA Project?

Right after I finished my PhD, I had an interview with Turgut Durduran for a postdoc position at ICFO, and during this interview I noticed his interest in my level of expertise with ultrasound systems and the ability to produce phantoms. It was then that I understood he was looking for someone to work on LUCA, someone with skills not only in data analysis and optics, but also with capabilities in communicating and collaborating with industrial partners and clinicians.

What kind of projects did you carry out before joining ICFO and the LUCA project?

Before coming to ICFO, I worked on developing navigators for minimally invasive surgery, such as an ultrasound-guided surgical navigator for holmium laser enucleation of the prostate. I also spent a lot of time writing codes and building hardware prototypes that were used, as collateral aid for diagnostics or innovation in surgery.

I was part of the following national projects: MILoRDS (Minimally Invasive Laser Robotic Assisted Diagnosis and Surgery), OPERA (Advanced Operating Room), STHARS (Surgical Training in identification and isolation of deformable tubular structures with hybrid Augmented Reality Simulation), LASER (Electromagnetic guided in-situ laser fenestration of endovascular endoprosthesis), all related to diagnostics and surgery. All the technical skills and know-how I learned during those projects will definitely be a plus for the LUCA project.

What previous experience do you bring to the project?

In the past, I have often used my knowledge to supply patient-specific 3D models and solid replicas to surgeons and radiologists for surgical planning. I enjoyed replicating anatomical structures by means of 3D printer processes and developing software to segment medical images as well as using applications to elaborate DICOM images loaded in the Picture archiving and communication system (PACS). From this perspective, I believe LUCA is the perfect environment for me: I have the chance of spending one day with industrial partners designing and testing components for the device, and the following day running measurements with radiologists and endocrinologists acquiring data from different subjects. It is exciting to collaborate on this multidisciplinary project.

What will be your main role in the project?

I work together with Lorenzo Cortese, my colleague at ICFO. Both of us will be developing the new diffuse correlation

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with Giuseppe Lo Presti, my colleague from ICFO, who has experience in medical devices and technologies since he is a biomedical engineer, and together we have worked at solving these issues. I also became aware at the beginning that there were many medical concepts concerning thyroid anatomy and physiology that were completely new to me, so I spent part of last summer studying endocrinology to acquire these concepts and terminology. Never during my PhD studies did I imagine I would be doing this. This was definitely a learning experience, which has allowed me to broaden my field of knowledge into other areas of science that I had not considered before.

As far as challenges are concerned, we have dealt with the interpretation of measurements and have had to model the theory in order to get meaningful results. We have also had to search for various alternatives to optimize the design of the ergonomic probe so that the clinicians using the device could handle it in a very easy manner.

Tell us about LUCA and the team you are working with.

The background diversity of all team members is very interesting. When we discuss different topics, everyone contributes in a very productive manner. The environment encourages exciting discussions that range from medicine one day to basic physics or robotics on another.

What is your role in the project?

Both Giuseppe and I have been working together quite a lot in such a way that our work overlaps quite often. We both try to do everything since we believe that we should both have the same capabilities and knowledge to carry out all lab (or all hospital) tasks and assignments. I have more experience in optics and modelling while Giuseppe has experience in robotics and medical instruments. But the fact that we work together, side by side, every day, has made us learn from one another. And even though we have different backgrounds and, at the beginning, I did more data analysis and managed the optical element tasks while Giuseppe dealt with instrument programming and design custom components, such as the combined ultrasound-optical probe, now we very much assist one another in everything. ■

spectroscopy system that will be part of the LUCA system and helping with the project management. It is very nice to be aware of what partners are doing, to collaborate with them and have continuous exchange of know-how, ideas and experiences.

One of my main tasks will be to develop the software and the hardware components of our devices: now, running a device based on light transport theory and correlation diffusion equations is pretty difficult if it is the first time you have to deal with it. Even more, handling optical elements that you did not use previously is also challenging. I am lucky to work in collaboration with Lorenzo, who loves to engage in discussions about theory, which has been extremely helpful for me, especially at the beginning. I think we make a great team since he compensates for my theoretical shortcomings as I devote more of my expertise to code development and probe design.

What challenges have you found so far?

We should never underestimate the tremendous difference between a lab device and a device that is ready to be used in the clinical scenario; sometimes we are not aware about the details of a device when working in the lab, but these need to be taken into account when moving into the hospital environment: encumbrance, the length of cables, the time you need to run an experiment. ■

Lorenzo obtained his Physics degree from Università degli Studi di Firenze, in Italy, and his Master's degree in Physics and Astrophysics, specializing in Matter Physics. He then pursued a PhD degree at the International Doctorate in Atomic and Molecular Photonics in LENS, the European Laboratory for Non-Linear Spectroscopy, in Italy, in the group led by Prof. Diederik Wiersma.

He is interested in photonics, diffuse optics and experimental optics in general. He has experience in experimental optics and instrumentation: laser sources, detectors, optical components, microscopy, imaging techniques, among others. He also specialized in micro/nano fabrication with 3D direct laser writing lithography, acquiring extensive knowledge in photonic structure manufacturing, ranging from photonic crystals, to disordered or amorphous (hyperuniform) structures. He has in-depth knowledge (theoretical and experimental) of diffuse optics, light propagation and transport in complex optical systems. In addition, he has experience working in clean room environment, in particular contributing in assembling one from scratch for the LENS research group.

Giuseppe received his Master's degree in Biomedical Engineering in 2011, which was centered on the development and validation of a vibrating system with sensory feedback for rehabilitation platforms. That same year he was granted a research fellowship for 3D reconstruction of vascular model of the lower limbs and segmentation of medical images (Computed Tomography -CT, Magnetic Resonance Imaging -MRI, angiographic CT, 3D Ultrasound -3D US).

For four years, he conducted his research at EndoCAS University of Pisa, Italy, within the Cisanello Hospital of Pisa, which allowed him to engage with clinicians of many different specialities and foster continuous collaborations with them. At the beginning of 2016, he obtained an international PhD degree in BioRobotics on "Intracorporeal soft tissue navigation for minimally invasive surgery" from the Scuola Superiore S'Anna of Pisa.

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