PhD at LabTAU (Lyon, France) in collaboration with CarThera (Lyon, France) – CIFRE convention

Ultrasound-induced opening of the Blood Brain Barrier: Optimization of exposure conditions with the SonoCloud® implantable ultrasound system

The laboratory INSERM LabTAU and the company CarThera SAS offer a 3-year PhD position on topics related to the development of an implanted ultrasound device for the opening of the blood brain barrier.

Academic partner: LabTAU, INSERM U1032, Lyon, France

The LabTAU, UMR-S 1032, is fully affiliated to the University Claude Bernard Lyon 1 (UCBL1) and to the French National Institute for Health (INSERM). Research at LabTAU aims at developing and optimizing innovative ultrasound therapies from bench to bedside. The team gathers interdisciplinary research scientists and professors from INSERM, UCBL1, and clinicians from Lyon’s University Hospitals and Regional Cancer Center Léon Bérard. The laboratory has worldwide renowned expertise in (i) ultrasound physics (ultrasound- and shear-wave propagation, bubble dynamics), metrology and bioeffects (thermal, cavitation) (ii) design and manufacturing of image-guided therapeutic transducers for thermal ablation and drug delivery, (iii) clinical transfer, (iv) fundamental modeling of therapeutic ultrasound beam, simulation and optical characterization of bubbles dynamics, (v) ultrasound-based methods of transfection, (vi) ultrasound molecular imaging with targeted contrast agents, (vii) ultrasound-triggered activations liposomes or micro-emulsions. LabTAU with its quality insurance system (certified ISO9001 since 2008) has a long history in collaborating with industrial partners.

http://labtau.univ-lyon1.fr/

Industrial partner: CarThera, Paris, France (R&D located in Lyon, France)

CarThera is a French company, which aims to design and develop innovative medical devices using the therapeutic potential of ultrasound to significantly improve the efficacy, comfort, and cost of treating a range of medical conditions. CarThera has focused on the treatment of brain tumors for the first applications of its innovative medical devices. CarThera's devices are developed by a multidisciplinary team of medical doctors, biologists, and physicists. This multidisciplinary effort takes into account, from the early stages of development, the needs of both patients and physicians, and leads to innovative solutions. The medical devices developed by CarThera originate from the work of Pr. Alexandre Carpentier, a neurosurgeon at the University Hospital Pitié-Salpêtrière in Paris, France. They are designed to respond to unmet clinical needs. The subject of the PhD thesis will focus on the SonoCloud an implantable device designed to reversibly disrupt the blood-brain barrier.

http://carthera.eu/
**Context: Ultrasound and microbubble-mediated opening of the blood-brain barrier**

The treatment of brain tumors using chemotherapy is currently not very effective. One of the major causes is the low penetration of chemotherapeutic agents into the brain due to the Blood-Brain Barrier (BBB) which prevents most substances present in the blood stream from penetrating into the parenchyma. Many articles in the scientific literature have demonstrated that the blood-brain barrier can be opened using ultrasound in combination with systemic injection of an ultrasound contrast agent. This opening allows for an increased concentration of chemotherapeutic agents in the brain tissue. Until now, most of the research in the field have used focused external ultrasound devices and has been limited to small areas in the brain.

Primary brain tumors are often a diffuse disease. The objective of CarThera is to open a larger zone of the BBB to allow for an optimal penetration of chemotherapy drugs into the tumor and its diffusion margins. In addition, as chemotherapy sessions are performed repeatedly, CarThera's ultrasound system is compatible with repeated opening of the BBB in an outpatient setting. Please refer to [http://carthera.eu/sono-cloud/for-a-selective-brain-therapy](http://carthera.eu/sono-cloud/for-a-selective-brain-therapy/).

Early 2015, the BBB was opened in a patient for the first time in the world using the SonoCloud Device. This device is currently being evaluated in a phase I/IIa clinical trial at the Hospital Pitié-Salpêtrière in Paris, France ([https://clinicaltrials.gov/ct2/show/NCT02253212](https://clinicaltrials.gov/ct2/show/NCT02253212)). Preliminary results are extremely promising.

**Research Program:**

The aim of this research is to build up the understanding of BBB-opening with the SonoCloud device in humans, in order to enhance even more the efficacy and safety of the treatment and orient future developments towards personalized treatments.

The data from the ongoing clinical trial will be consolidated with the acquisition of cavitation acoustic emission information. The PhD student will be involved in the development of a cavitation monitoring system (sensor development, signal and image processing). The cavitation monitoring system will first be characterized in vitro. Then, the cavitation monitoring system will be translated to human clinical use.

The data acquired during the clinical trial will be analyzed. The correlation between BBB opening assessed from MRI images and various physiological and acoustic parameters, including cavitation emission information, will be evaluated by the PhD candidate.

Based on the clinical data analysis, and additional in-vitro, in-vivo (small animals), and in-silico modelling, the student will propose and evaluate new treatment methods.
LabTAU - Unité de recherche U1032
Applications des ultrasons à la thérapie
Cyril Lafon, directeur

Application:

Applicants must hold a Master's degree (or equivalent) in electrical, mechanical or biomedical engineering, be skilled in signal processing, and ideally have basic knowledge in acoustics (bubble dynamics, sound wave propagation).

Applications (3 pages max.), including a CV, a cover letter and contact information of referees should be sent to Cyril Lafon (cyril.lafon@inserm.fr) and Guillaume Bouchoux (guillaume.bouchoux@carthera.eu). Candidates will be invited for interviews. The selected candidate will sign a CIFRE convention and become a PhD student at the University of Lyon via the doctoral school EDISS (http://www.ediss-lyon.fr). The thesis is aimed to start in fall 2016, or earlier. The duration will be 3 years. The PhD student will be located in Lyon, half-time in the CarThera R&D offices and half-time in the LabTAU (10-minute walk between the two facilities).