Doctoral Project Proposal:

Development and Clinical Translation of Cold Atmospheric Plasma (CAP) Technology for Treating Biliary Tract and Pancreatic Cancers

Abstract

Biliary tract cancer (BTC) and Pancreatic cancer (PC) represent significant clinical challenges due to their poor prognosis and high mortality rates, particularly among elderly and female populations. Despite the availability of surgical and chemotherapeutic interventions, the therapeutic outcomes remain unsatisfactory. This project aims to develop, characterize, and standardize an innovative cold atmospheric plasma (CAP) technology for the treatment of BTC and PC, leveraging its potential to selectively target cancerous tissues while minimizing damage to healthy cells.

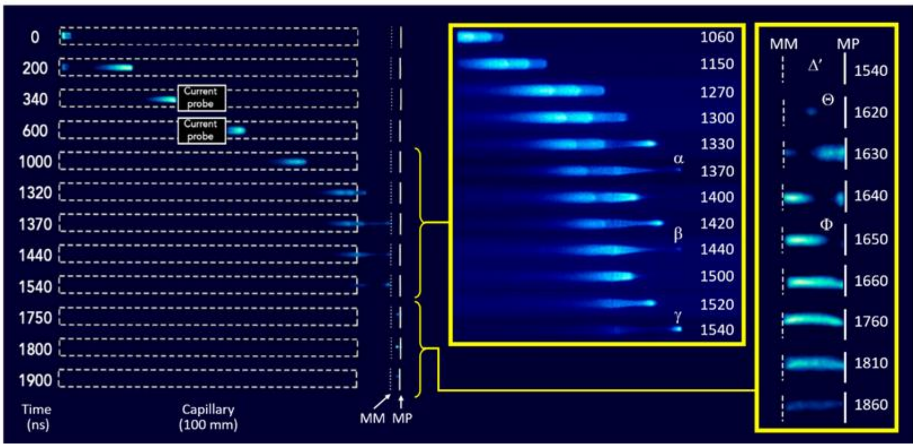
Objectives

- To engineer a state-of-the-art CAP device tailored for BTC and PC treatment, incorporating a plasma/sensor module, plasma delivery system, and versatile power supply units. The device will generate CAP with tunable reactive oxygen and nitrogen species (RONS), UV radiation, and electric fields, suitable for medical applications.
- To conduct comprehensive in vitro and in vivo experiments with the guidance of a post-doctoral biologist researcher, to assess the efficacy and safety of CAP treatment on PC and BTC, using established cell lines and animal models. This phase will also define the optimal operational parameters for CAP application.
- To establish the foundation for future clinical trials, focusing on the safety, efficacy, and standardization of CAP treatment, ensuring compliance with relevant EU regulations and standards.

Work packages

WP1: CAP Device Development and Characterization

The PhD student will design and construct a CAP prototype, integrating diagnostic sensors and a flexible delivery system to facilitate targeted plasma application. She/he will then evaluate different power supply configurations, including kHz sinusoidal and ns-pulsed settings, to identify optimal conditions for plasma generation. Subsequently, the student will undertake a comprehensive characterization of the CAP's physical and chemical properties, focusing on the generation of reactive oxygen and nitrogen species (RONS), UV emission, and the distribution of electric fields under a variety of operational conditions, ensuring a thorough understanding of the plasma's behavior and its potential therapeutic effects. A large part of this WP will also be dedicated to the characterization of transient electrical phenomena, especially guided streamers (see illustration).



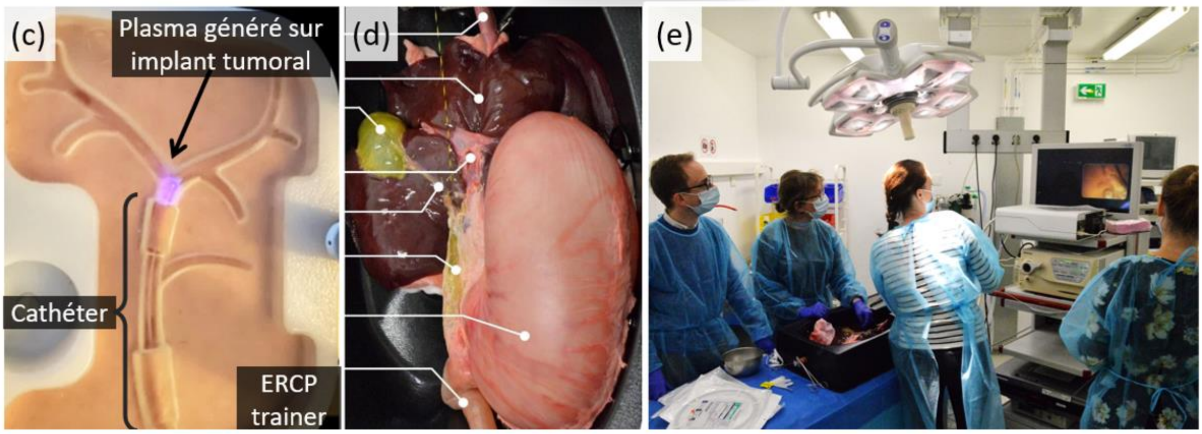
Propagation of self-organized guided streamers through jet of cold plasma

WP2: Preclinical Studies on PC and BTC Models

With the guidance of a biologist researcher, the PhD student will participate to *in vitro* experiments to ascertain the cytotoxic effects of CAP on pancreatic cancer (PC) and biliary tract cancer (BTC) cell lines, focusing on assessing cell viability, multiple cell death modes, tumor microenvironment components, oxidative stress response and the associated signaling pathways. Complementing these studies, the PhD student will assist the biologist team to carry out *in vivo* research using immunocompetent mice to observe tumor regression, analyze the tissue response, and monitor any systemic effects resulting from CAP treatment. Additionally, the PhD student will develop and implement real-time monitoring techniques to evaluate the impact of CAP on the tumor and adjacent healthy tissues throughout the treatment process, providing a comprehensive understanding of CAP's therapeutic potential and safety profile.

WP3: Safety and Regulatory Compliance

The PhD student will undertake comprehensive safety assessments to evaluate the CAP treatment's potential risks, such as dermal toxicity, intubation hazards, anesthesia-related complications, and any adverse effects on healthy tissues. In parallel, she/he t will ensure that the CAP device adheres to EU 2017/745 and IEC 62366-1:2015 regulations, demonstrating compliance with established safety and quality standards. Furthermore, the PhD student will be responsible for developing standardized treatment protocols to ensure consistent dosing and reliable measurement of the CAP's therapeutic parameters, essential for validating the treatment's efficacy and reproducibility in a clinical setting.



(a) Cold plasma delivered to the biliary tree of a human anatomical model (d) Post-mortem porcine digestive model (d) Experimental cold plasma endoscopy campaign on a post-mortem porcine model (School of Surgery at Paris).

Significance

This doctoral project is a component of the European project "MISSION PLASMA" (#01129853) that has already received funding, focusing on the critical development of innovative therapeutic approaches for treating BTC and PC. The project includes also the University of Patras (Greece) and the University of Cyprus. By advancing CAP technology from the laboratory to the clinical setting, we hope to offer a new, effective, and minimally invasive treatment option for patients suffering from these challenging cancers, ultimately contributing to improved survival rates and quality of life.

Timeline

- Year 1 : Development and optimization of the CAP device (WP1).
- Year 2 : In vitro and early in vivo preclinical studies (WP2).

- Year 3 : Advanced *in vivo* studies, safety assessments for clinical translation (WP2 & WP3).

Candidate profile

The ideal candidate will be an academically driven student, keen on developing expertise in an interdisciplinary research setting. The candidate is expected to be highly motivated, with an aptitude for scientific inquiry and a strong foundation in physical sciences.

Application process

Interested candidates should submit their academic CV and a letter of motivation to:

- Dr. Thierry DUFOUR, thierry.dufour@sorbonne-universite.fr
- Dr. Laura FOUASSIER, laura.fouassier@inserm.fr

Links of interest

• Articles

- https://doi.org/10.1051/refdp/202375024
- https://doi.org/10.3390/plasma6020019
- https://doi.org/10.1088/1361-6595/aca1da
- https://doi.org/10.1088/1361-6463/ac8c4d
- https://doi.org/10.3390/cancers12051280
- https://doi.org/10.1088/1361-6463/ab0fbb
- https://doi.org/10.1088/1361-6463/ab03b8

• PhD thesis of H. Decauchy: former student of M2-PPF, achieved in "plasma medicine": https://theses.hal.science/tel-03967323v1/document

• Thierry Dufour's homepage: https://www.lpp.polytechnique.fr/-Thierry-Dufour-
• Laura Fouassier's homepage: https://www.laurafouassier.com/