Penetration mechanisms of cold atmospheric plasma through biliary and pancreatic tissues for digestive cancer treatment

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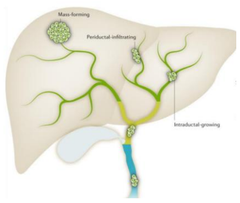
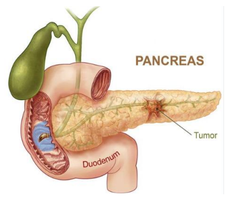
NON-INVASIVE SURGICAL PLATFORM FOR BILIARY AND PANCREATIC CANCER

Poor prognosis cancers

Biliary tract cancer (BTC)



Pancreatic cancer (PDAC)



Usual therapies

Surgery

Radiotherapy

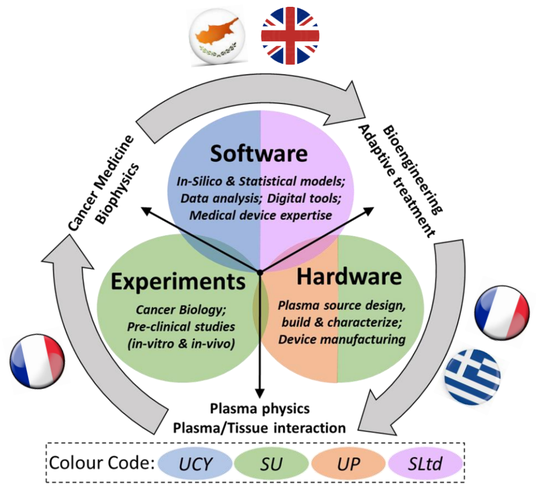
Chemotherapy ± immunotherapy

Late diagnosis: asymptomatic cancers in early stages

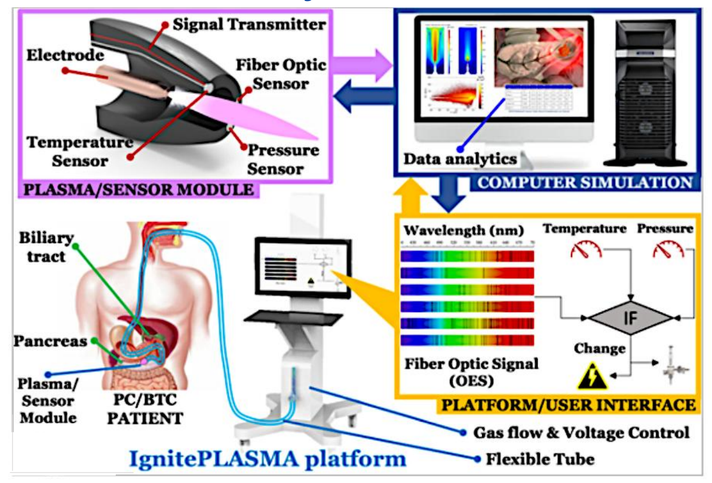
Treatments:

- Damaging healthy cells
- Depending on patient eligibility
- Not locoregional

Consortium



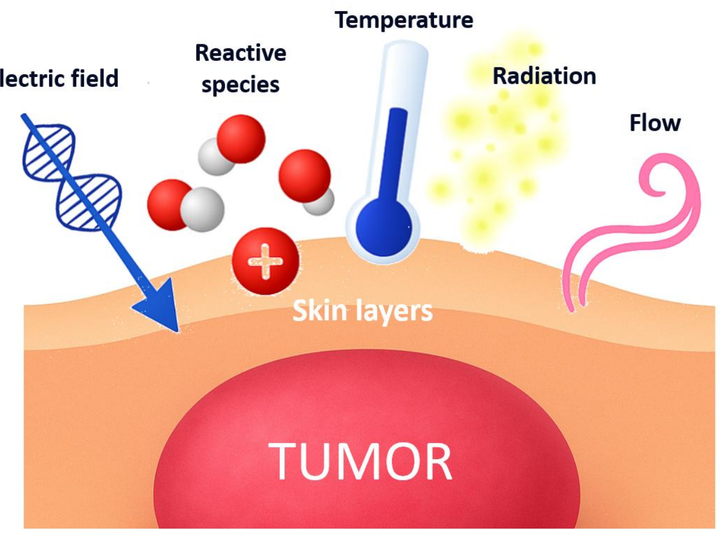
Objectives



- Develop a minimally invasive cold atmospheric plasma (CAP) delivery platform to precisely target digestive tract tumors.
- Enable personalized treatment by integrating patient diagnostics with *in silico* modeling to control plasma therapy.
- Demonstrate therapeutic efficacy and safety via *in vitro* and *in vivo* animal experiments.

DECIPHERING THE PHYSICO-CHEMICAL AND BIOLOGICAL MECHANISMS INDUCING ANTITUMOR RESPONSE

Cold atmospheric plasma (CAP) alternative

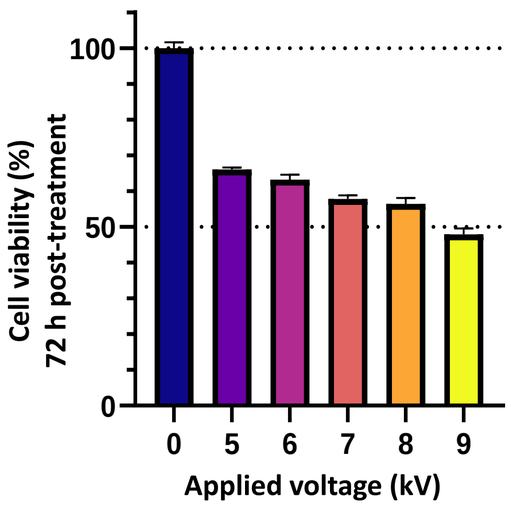


Antitumoral action:

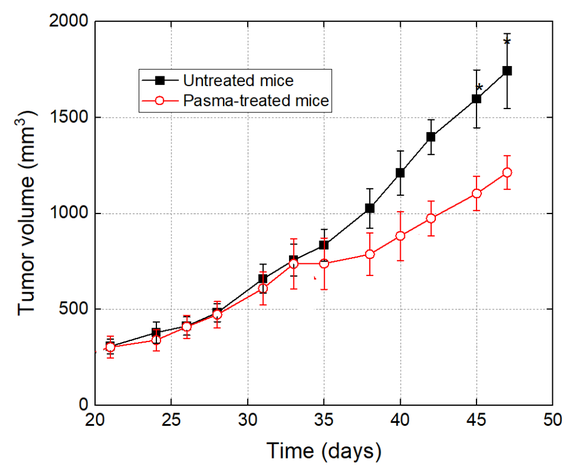
- Oxidative stress
- Immune system activation
- Cell death

Antitumor response of cold plasma on BTC

Cell viability (2 min)



Tumor growth



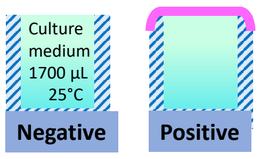
Judée et al. (J. Phys. D: Appl. Phys., 2019)

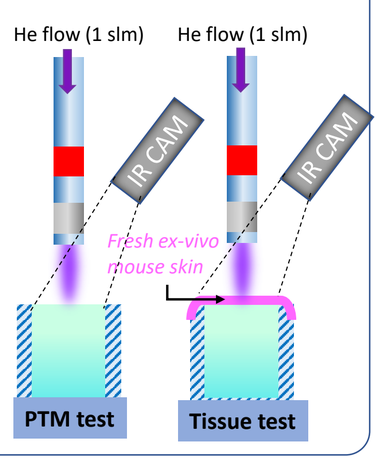
INVESTIGATING MOUSE SKIN TISSUE AS A BARRIER TO REACTIVE SPECIES DIFFUSION

Experimental setup

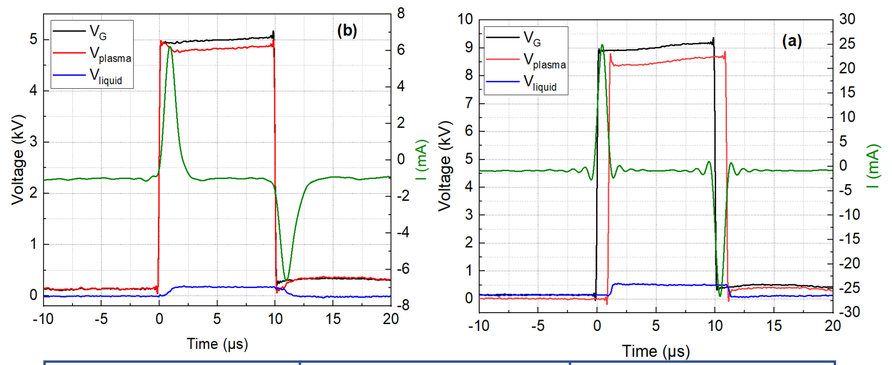
Post-mortem skins of albino mice (C57BL/6j-Tyr c)
Skin thickness: 450 µm
Plasma treatment time: 2 min

Controls



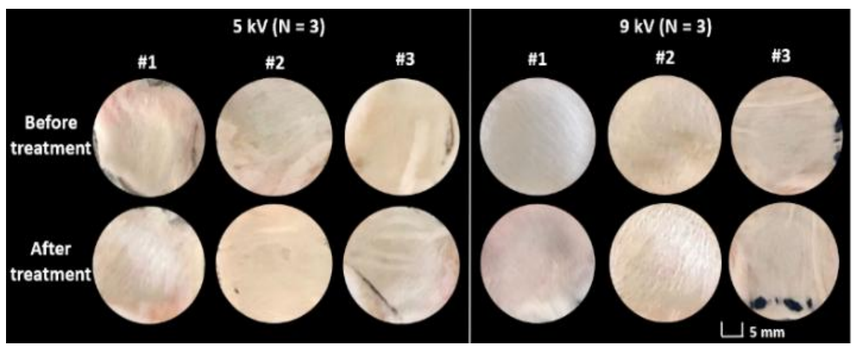


Electrical characterization of the culture medium



Generator voltage (V_G)	5 000 V	9 000 V
Liquid voltage (V_{liquid})	200 V	500 V
Current (I)	6 mA	25 mA

Macroscopic observation of skin samples

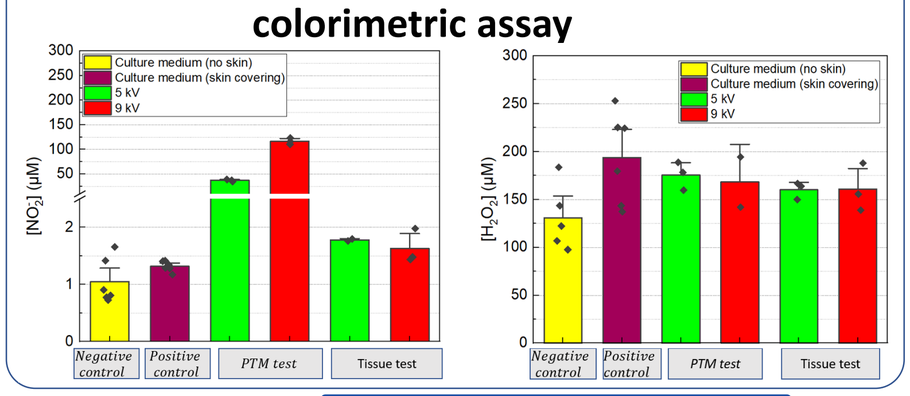


Here, we measured two long-lived reactive plasma species: Nitrites (NO_2^-) and Hydrogen peroxide (H_2O_2).

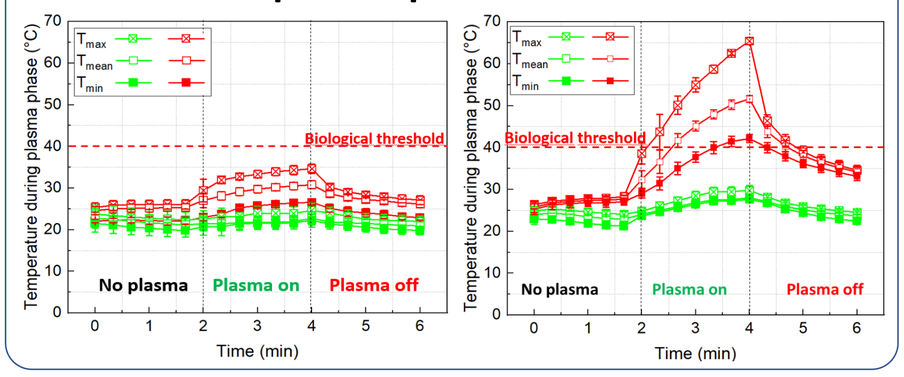
The results indicate that, under the tested conditions (2 minutes, 5 kV and 9 kV CAP), these species do not effectively cross murine skin, suggesting a significant limitation to passive diffusion.

The biological temperature threshold (40°C) is exceeded at the 9 kV voltage, which makes this experimental condition unsuitable for living preclinical models. In contrast, this threshold is not reached at 5 kV. Moreover, no macroscopic adverse effects are observed on the skin.

Reactive species concentration profiles by colorimetric assay



Sample temperature kinetics



PERSPECTIVES

- Optimizing key plasma parameters (applied voltage and exposure time) to maximize therapeutic efficacy while minimizing unintended tissue damage
- Refining plasma delivery strategies
- Exploring other mechanisms of action such as electric field effects, and assess the long-term biological impact of CAP treatment