Cold Atmospheric Plasma in Pancreatic and Biliary Tract Cancer Therapy

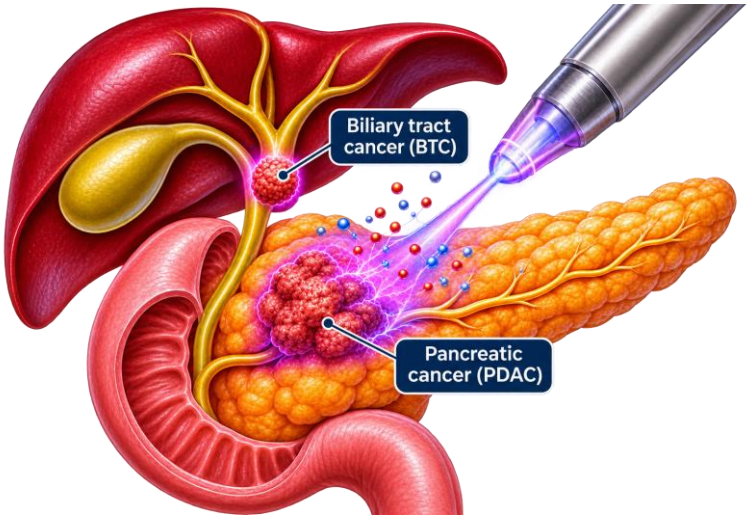
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Executive summary

Pancreatic ductal adenocarcinoma (PDAC) and biliary tract cancers (BTC) remain difficult to treat despite improvements in systemic therapy and biomarker-guided care. Cold atmospheric plasma (CAP) offers an alternative means of delivering reactive oxygen and nitrogen species (RONS), transient electric fields, ultraviolet (UV) and visible radiation, to biological targets without relying on thermal effects. Laboratory and animal studies have reported antitumour effects in PDAC and BTC models, although clinical efficacy has not been established.



A major challenge for the clinical translation of CAP is the definition and control of plasma dose. CAP exposure involves multiple interacting physical and chemical components, and treatment duration alone cannot adequately describe the dose delivered to biological tissues. Reliable dosimetry therefore requires quantitative characterisation of plasma operating conditions, reactive species delivery and the resulting biological responses.

IgnitePLASMA focuses on the direct application of CAP to cancerous tissues, with the longer-term objective of developing a controllable, minimally invasive treatment platform. Direct treatment enables investigation of the combined effects of plasma-generated reactive species, electric fields, and other short-lived plasma-associated stimuli at the treatment site. It also provides opportunities for real-time monitoring and adjustment of plasma operating conditions, which are central to the project's engineering and computational modelling approach. This white paper summarises the scientific evidence, identifies the challenges associated with reproducible dosing and safe internal delivery, and presents the IgnitePLASMA strategy for advancing CAP towards potential clinical applications.

1. Clinical context: pancreatic and biliary tract cancers

PDAC and BTC are anatomically challenging malignancies often diagnosed at advanced stages. Curative-intent resection is possible only for selected patients, and recurrence remains a major problem even after surgery. Management is multidisciplinary and depends on stage, performance status, anatomy and molecular characteristics. In metastatic PDAC, combination regimens include FOLFIRINOX, NALIRIFOX and gemcitabine plus nab-paclitaxel for appropriately selected patients. In advanced BTC, gemcitabine–cisplatin combined with durvalumab or pembrolizumab is an established first-line option; molecular profiling can identify selected patients eligible for targeted treatment, including FGFR2- and IDH1-directed approaches. These advances are important, but they do not remove the need for improved local control and more effective treatment strategies [1,2].

CAP offers a potential approach for delivering a controlled, localised physicochemical treatment that could complement established cancer therapies, particularly at accessible tumour surfaces or surgical margins. Its clinical application requires however further investigation to establish biological effectiveness, anatomical accessibility, procedural feasibility and safety.

2. What is cold atmospheric plasma?

Plasma is an ionised gas containing electrons, ions, neutral particles and excited species producing visible and UV radiation. In thermal plasmas, electrons and heavier particles can be considered in thermal equilibrium, resulting in high bulk gas temperatures. On the contrary, cold plasma (whether at low or atmospheric pressure) operates under non-equilibrium conditions, i.e., electrons can have high energies while the bulk gas remains comparatively cool. Electron-driven reactions produce reactive oxygen & nitrogen species (RONS), alongside photons, transient electric field and other discharge-related effects. Gas and target temperatures depend on the plasma source, power, treatment geometry and exposure conditions; thermal safety therefore requires assessment for each application [3].

CAP also emits electromagnetic radiation in the visible and UV spectral regions as excited atoms and molecules return to lower energy states. The emission spectrum and intensity depend on the plasma source, feed gas, surrounding atmosphere and operating conditions. UV photons may contribute to biological effects, including photochemical reactions and, under certain exposure conditions, cellular damage. Their relative contribution to the overall biological response depends on the plasma configuration, treatment geometry and surrounding environment, with RONS generally considered major mediators of CAP-induced anticancer effects.

Common CAP configurations include atmospheric-pressure plasma jets and dielectric-barrier discharges. The characteristics and biological effects of the generated plasma depend on several operating and environmental parameters, including the feed gas composition, applied voltage and waveform, distance from the treatment target, ambient humidity, surrounding liquid environment and properties of the treated tissue. These factors influence the generation and delivery of reactive species and the resulting biological response.

Two treatment modalities can be distinguished: direct CAP, where the plasma discharge or its effluent interacts with the biological target, and indirect treatment using plasma-activated liquids (PAL), where a liquid is first exposed to plasma and subsequently applied to cells or tissues. PAL contains plasma-generated chemical species but generally does not deliver the same transient electric fields and short-lived reactive species as direct treatment. Both approaches have demonstrated biological activity in preclinical investigations, although their exposure conditions and mechanisms of action differ [4,5].

IgnitePLASMA focuses on direct CAP treatment because this approach enables controlled delivery of plasma-generated reactive species together with other plasma-associated stimuli at the treatment site. It also provides opportunities to monitor plasma operating conditions during treatment and investigate how these conditions influence biological responses. These capabilities are particularly relevant to the project's objective of developing a controllable plasma source supported by diagnostic measurements and predictive computational models.

3. Experimental evidence in pancreatic and biliary tract cancer

3.1 Biliary tract cancer

Preclinical investigations have demonstrated that CAP can induce antitumour effects in cholangiocarcinoma, a malignancy arising from the biliary epithelium. Vaquero *et al.* investigated CAP in human cholangiocarcinoma cell lines and mouse xenograft models, reporting reduced tumour-cell proliferation, cell-cycle arrest, DNA damage and apoptosis. These findings support further investigation of CAP in biliary tract malignancies, although treatment selectivity, safety and effectiveness in clinically relevant settings remain to be established [6].

The potential combination of CAP with established anticancer therapies has also been investigated. Jones and colleagues evaluated the Canady Helios CAP system in combination with a FOLFIRINOX regimen in cholangiocarcinoma cell models. The study reported enhanced anticancer activity under the investigated in-vitro conditions, suggesting that combination approaches merit further investigation. However, these findings are limited to laboratory models and do not establish clinical therapeutic synergy or provide a basis for treatment recommendations [7].

Together, these studies indicate that CAP can influence cholangiocarcinoma cell survival and treatment response. They also highlight the need to understand the effects of plasma operating conditions, biological mechanisms and interactions with conventional therapies. Further studies using relevant tissue models and direct plasma delivery systems are needed to assess reproducibility and safety.

3.2 Pancreatic cancer

Several preclinical studies have investigated CAP in pancreatic cancer using direct plasma exposure and indirect treatment with PAL. These studies have reported reduced cancer-cell viability, induction of apoptosis and inhibition of tumour growth, although results depend on the plasma source, exposure conditions and biological model.

Partecke *et al.* demonstrated that direct treatment with tissue-tolerable plasma induced apoptosis in pancreatic cancer cells and produced antitumour effects in preclinical models [8]. Brullé *et al.* subsequently investigated non-thermal plasma treatment, alone and in combination with gemcitabine, in an orthotopic pancreatic cancer model, providing further evidence of antitumour activity and supporting investigation of combination approaches [9].

Other investigations have examined indirect exposure through plasma-treated liquids. Sato *et al.* studied plasma-activated lactated Ringer’s solution in pancreatic cancer models and reported antiproliferative and pro-apoptotic effects *in vitro* and antitumour activity *in vivo* [10]. Hattori *et al.* investigated plasma treatment of

pancreatic cancer cells and reported treatment-related biological effects [11]. Liedtke *et al.* demonstrated antitumour activity of non-thermal plasma-treated solutions in pancreatic cancer models [12].

Further studies have explored molecular and cellular responses. Zhen *et al.* reported that plasma-activated medium induced apoptosis in AsPC-1 cells through a pathway involving reactive oxygen species and autophagy [13]. Van Loenhout *et al.* investigated plasma-treated phosphate-buffered saline, reporting effects on pancreatic stellate cells and immunogenic cell-death responses in pancreatic cancer cells [14]. Miebach and colleagues also reported immunogenic cell-death responses following exposure of pancreatic cancer cells to plasma-oxidised Ringer's lactate [15].

Together, these studies indicate that plasma treatment can affect oxidative stress, apoptosis and other cell-death pathways. Evidence from PAL experiments must, however, be distinguished from direct CAP exposure because the delivered chemical and physical stimuli differ. This distinction is particularly important for IgnitePLASMA, which focuses on a controllable direct-treatment platform. Further research is needed to establish reproducible exposure conditions, evaluate effects on healthy tissues and assess clinical relevance.

RONS such as hydrogen peroxide and nitrogen-derived species can participate in redox signalling and, at sufficiently high exposures, contribute to oxidative damage. Reported downstream responses include DNA damage, cell-cycle arrest, apoptosis and other cell-death programmes. The outcome depends on the plasma chemistry, exposure, antioxidant capacity, tissue environment and time after treatment. It is therefore misleading to describe a single universal CAP anticancer mechanism [5,6,8,13].

Investigations outside PDAC and BTC suggest that plasma may affect drug delivery, nanoparticle uptake or immune responses; for example, preclinical studies have explored nanoparticle endocytosis and plasma-assisted immune checkpoint blockade. These findings are not evidence that those combinations are effective in pancreatic or biliary cancer. Translational evaluation must distinguish disease-specific results from evidence obtained in unrelated tumour models [16,17].

A preclinical assessment of cold-plasma endoscopy in human-like and porcine biliary-duct models examined feasibility and electrical/thermal risks, providing useful early engineering evidence for internal access. It does not establish the safety or effectiveness of repeated treatment in patients with BTC [18].

A published phase I report described intraoperative CAP application to surgical margins in a heterogeneous group of patients with advanced solid tumours, including a patient with metastatic BTC. The study is relevant as an early feasibility and safety-oriented clinical investigation, but its size and design do not establish survival benefit, local-control efficacy or a standard treatment role in PDAC or BTC using CAP [19].

Collectively, these studies provide a scientific foundation for investigating CAP in PDAC and BTC, while highlighting the importance of distinguishing direct plasma exposure from treatment with PAL. Although both approaches have demonstrated promising preclinical effects, their treatment conditions and biological mechanisms are not directly interchangeable. IgnitePLASMA builds on this evidence by focusing on the controlled delivery of CAP directly to biological targets, supported by experimental characterisation and computational modelling.

4. Challenges and limitations

4.1 Dosimetry, standardisation and safe delivery

There is no universally accepted biologically equivalent CAP “dose” applicable across plasma generators, liquids and tissues. Plasma dose remains difficult to define because CAP delivers a combination of chemical and physical stimuli whose effects depend on the source, exposure geometry, surrounding environment and biological target. Treatment time alone is therefore insufficient to compare exposures across devices. Quantitative reporting of electrical operating conditions, gas flow, treatment geometry, reactive-species measurements and relevant biological endpoints is needed to support reproducibility and meaningful comparison of experimental results [20].

Earlier European collaborative work provides an important foundation for these efforts. COST Action MP1101, Biomedical Applications of Atmospheric Pressure Plasmas, supported the development of the COST Reference Microplasma Jet, a defined research source designed to improve the comparability of plasma experiments through controlled operating conditions and well-characterised diagnostics [21]. A subsequent multi-device study assessed the reproducibility of independently constructed reference jets using electrical and optical measurements, reactive-species and temperature measurements, and a bactericidal endpoint [22]. These achievements demonstrate the value of reference sources and harmonised characterisation procedures. They do not, however, establish a universal biological plasma dose or a transferable anticancer treatment protocol for different CAP devices.

The development of CAP devices for surgical applications requires careful consideration of electrical and thermal safety, electromagnetic compatibility, gas delivery, pressure control and potential effects on surrounding healthy tissues. Particular attention must be given to electrical insulation, leakage currents, prevention of thermal injury and the sterility and biocompatibility of components that may contact patients or enter the sterile surgical field. Device development and testing should consider applicable requirements of the IEC 60601 series, together with relevant risk-management, biocompatibility and regulatory requirements according to the intended clinical application and medical-device classification.

4.2 Biological translation and clinical adoption

Cell-culture and animal studies provide valuable evidence of biological activity but cannot reliably predict therapeutic benefits in patients. Plasma chemistry and biological responses may change substantially in protein-rich liquids and tissues, while reactive-species penetration, scavenging, vascularisation, immune responses and heterogeneous tumour stroma can influence treatment outcomes. Consequently, in-silico models should define their intended context of use and undergo verification, validation and uncertainty quantification (VVUQ), including sensitivity analysis and uncertainty propagation across plasma, tissue-transport and cellular-response components. Credible computational models can help prioritise experiments, guide experimental design and potentially reduce animal testing, but they cannot substitute for independent biological and clinical validation.

Clinical translation of CAP will depend on identifying specific applications where localised plasma treatment could provide additional benefits alongside established cancer therapies. Potential applications in PDAC and BTC include treatment of accessible tumour surfaces or surgical margins following resection, endoscopic delivery to anatomically accessible biliary lesions, and local treatment combined with systemic therapies. These approaches remain exploratory and require further preclinical and clinical investigation to establish their safety, feasibility and therapeutic effectiveness.

Each application presents distinct technical and clinical requirements. Treatment of surgical margins would require controlled plasma delivery, uniform coverage of the target area and protection of surrounding healthy tissues. Endoscopic applications would require miniaturised, potentially flexible delivery systems capable of reaching internal lesions while maintaining reliable plasma generation and electrical and thermal safety. Combining CAP with chemotherapy or immunotherapy would require further investigation of treatment interactions, optimal sequencing and potential synergistic effects.

Successful clinical adoption will also require standardised treatment protocols, reproducible device performance, appropriate regulatory approval and evidence from well-designed clinical trials. Medical devices intended for internal CAP treatment must meet applicable safety and performance requirements, while their integration into existing surgical and endoscopic procedures will depend on usability, procedural compatibility and clinician training. Treatment costs, reimbursement pathways and patient acceptance will also influence their eventual adoption.

A progressive development pathway, supported by plasma characterisation, biological studies, computational modelling and relevant preclinical models, will be essential for translating CAP technologies into clinical applications. Real-time diagnostic measurements and predictive models could support more consistent treatment delivery and, ultimately, personalised treatment, provided their reliability is established through experimental validation. Continued collaboration between plasma scientists, engineers, cancer researchers, clinicians and medical-device developers will be important for advancing CAP towards safe and effective clinical use.

5. IgnitePLASMA and future perspectives

IgnitePLASMA is developing an innovative CAP platform for potential applications in PDAC and BTC treatment. The project brings together expertise in plasma engineering, cancer biology and computational modelling to investigate how plasma can be generated, controlled and delivered directly to cancerous tissues, and how its biological effects can be better understood and predicted.

A central objective is to establish relationships between plasma operating conditions, the generation and transport of RONS, and the resulting biological responses. The research combines experimental studies with multiscale *in silico* models describing plasma behaviour, reactive-species transport through biological tissues and cellular responses. Optical, electrical and thermal diagnostics are also being investigated to identify measurable indicators of treatment effectiveness and safety, with the longer-term goal of enabling adaptive control of plasma treatment.

5.1 The IgnitePLASMA source: controlled and reproducible plasma treatment

A major technological contribution of IgnitePLASMA is the development of a programmable CAP platform designed to provide precise control over plasma generation and treatment conditions. The platform incorporates a plasma reactor, gas delivery system, high-voltage power electronics, diagnostic sensors and an integrated control system. Both sinusoidally driven and pulsed plasma configurations have been developed, allowing the investigation of different electrical excitation methods and their influence on plasma characteristics and biological effects.

The pulsed configuration incorporates a custom-developed, modular high-voltage switching system that enables adjustment of voltage amplitude, pulse repetition frequency, duty cycle and pulse rise and fall times. These capabilities provide additional flexibility in controlling the electrical discharge and investigating how different operating conditions influence reactive species generation and delivery. The development of the pulsed power electronics is a particularly important innovation, providing a technological basis for more versatile and precisely controlled plasma operation.

The platform also integrates electrical, optical and thermal diagnostic capabilities to characterise plasma behaviour and monitor operating conditions. Measurements of electrical signals, optical emission and temperature can provide information on discharge stability, energy delivery, excited species and thermal conditions. Combined with chemical measurements of RONS and biological experiments, these diagnostics support the investigation of relationships between plasma operating parameters and treatment outcomes.

An important objective of IgnitePLASMA is to develop control strategies that support stable and reproducible plasma operation under different treatment conditions. The programmable source and its diagnostic capabilities provide the basis for monitoring and adjusting selected electrical and operational parameters. In the longer term, the project aims to combine these measurements with computational predictions and experimentally validated indicators of plasma delivery and biological response. Such integration could support model-guided adjustment of treatment parameters, although a fully validated biological closed-loop control system has not yet been demonstrated.

Building on the reproducibility principles established by the COST reference-jet initiative, IgnitePLASMA investigates programmable direct CAP delivery alongside electrical, optical and thermal diagnostics and measurements of biological response. Its distinct research objective is to connect source operating conditions with reactive-species transport and cellular effects through experimentally informed multiscale modelling. The COST reference jet and the IgnitePLASMA source have different designs and intended uses; reproducibility findings from the former cannot be assumed to apply directly to the latter [21,22].

The platform is currently being developed and evaluated in laboratory settings. Further research is required to establish reliable plasma dosimetry, validate the relationships between measurable signals and biological effects, and adapt the technology for safe and effective application to internal tumours.

5.2 Multiscale in-silico modelling of plasma–tissue interactions

A second major contribution of IgnitePLASMA is the development of a multiscale computational framework intended to describe the physical and biological processes involved in CAP treatment. The objective is to connect plasma generation and reactive species delivery with their transport through biological tissues and the resulting responses of individual cancer cells. In-silico modelling was used to evaluate the effects of helium plasma-jet treatment and chemotherapy on melanoma cells [23]. IgnitePLASMA extends these modelling principles towards the integration of plasma physics, reactive-species transport and cellular responses in pancreatic and biliary tract cancer models.

The computational framework comprises three complementary modelling components.

At the **plasma scale**, numerical models describe the behaviour of the plasma discharge and its interaction with the surrounding gas flow. These models investigate how operating parameters and treatment geometry influence plasma propagation, electric-field distributions and the conditions associated with reactive species generation.

The framework is implemented using OpenFOAM, with customised numerical methods for gas-flow and plasma-discharge simulations.

At the **tissue scale**, a macroscale model describes the transport, diffusion, decay and uptake of plasma-generated RONS within biological environments. This approach enables the investigation of how reactive species are distributed in tissues and how their concentrations may change with distance from the treated surface, tissue characteristics and exposure conditions. Such information is particularly relevant for understanding the spatial extent of CAP treatment and the challenges associated with reaching cancer cells located beneath the tissue surface.

At the **cellular scale**, IgnitePLASMA has developed ABM4bio, an agent-based computational framework that represents individual cells and their responses to plasma-generated reactive species. The model incorporates biological processes associated with oxidative stress, DNA damage, cell-cycle progression, proliferation and cell death. By representing individual cells, the framework can investigate how differences in cellular characteristics and local exposure conditions may influence treatment outcomes.

An important development has been the initial coupling of the tissue-scale and cellular-scale models through the preCICE coupling library, enabling the exchange of information between reactive species transport and cell-level biological responses. Further integration with the plasma discharge model is under development, with the aim of establishing a computational framework that connects plasma operating conditions to predicted biological outcomes.

The experimental investigations conducted within IgnitePLASMA provide data for model calibration and validation, including plasma operating parameters, electrical and optical measurements, RONS concentrations and cancer-cell viability. Through systematic verification, validation and uncertainty quantification, the project aims to establish the reliability and limitations of the computational predictions.

The longer-term objective is to use the integrated modelling framework to support the optimisation of plasma treatment conditions, identify potentially effective operating regimes and investigate the feasibility of model-guided adaptive treatment. Such capabilities could contribute to more reproducible plasma delivery and provide a scientific basis for future treatment planning, although their predictive accuracy and clinical relevance remain to be demonstrated.

5.3 Future perspectives and clinical translation

The next stage of IgnitePLASMA research will focus on consolidating the experimental and computational developments into a more integrated framework for understanding and controlling direct CAP treatment. A central priority is to establish quantitative relationships between plasma operating parameters, measurable physicochemical indicators, reactive species delivery and biological responses. These relationships are essential for advancing plasma dosimetry and identifying treatment conditions that produce reproducible effects.

Further experimental investigations will examine the biological responses of cancer and healthy tissues under different plasma exposure conditions, with particular attention to treatment selectivity, reactive species transport and the influence of the surrounding biological environment. The resulting data will support the calibration and validation of the multiscale computational models, including the assessment of predictive accuracy, sensitivity and uncertainty.

An additional priority is the integration of plasma diagnostics with computational modelling to investigate the feasibility of model-guided treatment control. By connecting measurable plasma characteristics with predictions of reactive species transport and cellular responses, the project aims to establish a scientific basis for more reproducible and potentially adaptive treatment strategies.

The longer-term development of IgnitePLASMA will also consider the requirements for delivering CAP to anatomically accessible tumour surfaces and surgical margins through suitable minimally invasive instruments. Progress towards clinical applications will depend on further preclinical investigations, demonstration of safety and therapeutic effectiveness, development of appropriate medical devices and carefully designed clinical studies.

Through this integrated approach, IgnitePLASMA aims to advance the scientific and technological foundations for direct CAP treatment and contribute to its future evaluation as a complementary, localised approach within multimodal cancer care.

6. Conclusions

CAP is an emerging approach to localised cancer treatment with encouraging preclinical findings in PDAC and BTC. Clinical evidence remains preliminary, and therapeutic benefit and safety in patients have yet to be established. Towards overcoming the challenges, IgnitePLASMA brings together controllable plasma sources, biological experimentation, diagnostics and *in silico* models to improve our understanding of plasma–tissue interactions and support reproducible treatment strategies. Future progress depends on standardised dosimetry, safe internal delivery, rigorous model validation and carefully designed preclinical and clinical studies. These advances may enable CAP to be evaluated as a complementary local treatment within multimodal cancer care.

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References

[1] Conroy T, Ducreux M. ESMO Clinical Practice Guideline Express Update on the management of metastatic pancreatic cancer. ESMO Open. 2025;10:104528. doi:10.1016/j.esmoop.2025.104528.

[2] Vogel A, Ducreux M; ESMO Guidelines Committee. ESMO Clinical Practice Guideline interim update on the management of biliary tract cancer. ESMO Open. 2025;10(1):104003. doi:10.1016/j.esmoop.2024.104003.

[3] Fridman A, Chirokov A, Gutsol A. Non-thermal atmospheric pressure discharges. J Phys D Appl Phys. 2005;38:R1–R24. doi:10.1088/0022-3727/38/2/R01.

[4] Yan D, Cui H, Zhu W, et al. The specific vulnerabilities of cancer cells to the cold atmospheric plasma-stimulated solutions. Sci Rep. 2017;7:4479. doi:10.1038/s41598-017-04770-x.

[5] Fang T, Chen Z, Chen G. Advances in cold atmospheric plasma therapy for cancer. Bioact Mater. 2025;53:433–458. doi:10.1016/j.bioactmat.2025.07.031.

[6] Vaquero J, Judée F, Vallette M, et al. Cold-atmospheric plasma induces tumor cell death in preclinical in vivo and in vitro models of human cholangiocarcinoma. Cancers. 2020;12:1280. doi:10.3390/cancers12051280.

[7] Jones O, Cheng X, Murthy SRK, et al. The synergistic effect of Canady Helios cold atmospheric plasma and a FOLFIRINOX regimen for the treatment of cholangiocarcinoma in vitro. Sci Rep. 2021;11:8967. doi:10.1038/s41598-021-88451-w.

[8] Partecke LI, Evert K, Haugk J, et al. Tissue tolerable plasma (TTP) induces apoptosis in pancreatic cancer cells in vitro and in vivo. BMC Cancer. 2012;12:473. doi:10.1186/1471-2407-12-473.

[9] Brullé L, Vandamme M, Riès D, et al. Effects of a non thermal plasma treatment alone or in combination with gemcitabine in a MIA PaCa2-luc orthotopic pancreatic carcinoma model. PLoS One. 2012;7:e52653. doi:10.1371/journal.pone.0052653.

[10] Sato Y, Yamada S, Takeda S, et al. Effect of plasma-activated lactated Ringer's solution on pancreatic cancer cells in vitro and in vivo. Ann Surg Oncol. 2018;25:299–307. doi:10.1245/s10434-017-6239-y.

[11] Hattori N, Yamada S, Torii K, et al. Effectiveness of plasma treatment on pancreatic cancer cells. Int J Oncol. 2015;47:1655–1662. doi:10.3892/ijo.2015.3149.

[12] Liedtke KR, Bekeschus S, Kaeding A, et al. Non-thermal plasma-treated solution demonstrates antitumor activity against pancreatic cancer cells in vitro and in vivo. Sci Rep. 2017;7:8319. doi:10.1038/s41598-017-08560-3.

[13] Zhen X, Sun HN, Liu R, et al. Non-thermal plasma-activated medium induces apoptosis of AsPC-1 cells through the ROS-dependent autophagy pathway. In Vivo. 2020;34:143–153. doi:10.21873/invivo.11755.

[14] Van Loenhout J, Flieswasser T, Freire Boullosa L, et al. Cold atmospheric plasma-treated PBS eliminates immunosuppressive pancreatic stellate cells and induces immunogenic cell death of pancreatic cancer cells. Cancers. 2019;11:1597. doi:10.3390/cancers11101597.

[15] Miebach L, Mohamed H, Wende K, Miller V, Bekeschus S. Pancreatic cancer cells undergo immunogenic cell death upon exposure to gas plasma-oxidized Ringer's lactate. Cancers. 2023;15:319. doi:10.3390/cancers15010319.

[16] He Z, Liu K, Manaloto E, et al. Cold atmospheric plasma induces ATP-dependent endocytosis of nanoparticles and synergistic U373MG cancer cell death. Sci Rep. 2018;8:5298. doi:10.1038/s41598-018-23262-0.

[17] Chen G, Chen Z, Wen D, et al. Transdermal cold atmospheric plasma-mediated immune checkpoint blockade therapy. Proc Natl Acad Sci USA. 2020;117:3687–3692. doi:10.1073/pnas.1917891117.

[18] Decauchy H, Pavy A, Camus M, Fouassier L, Dufour T. Cold plasma endoscopy applied to biliary ducts: feasibility risk assessment on human-like and porcine models for the treatment of cholangiocarcinoma. J Phys D Appl Phys. 2022;55:455401. doi:10.1088/1361-6463/ac8c4d.

[19] Canady J, Murthy SRK, Zhuang T, et al. The first cold atmospheric plasma Phase I clinical trial for the treatment of advanced solid tumors: a novel treatment arm for cancer. Cancers. 2023;15:3688. doi:10.3390/cancers15143688.

[20] Dai X, Zhang Z, Zhang J, Ostrikov K. Dosing: The key to precision plasma oncology. Plasma Process Polym. 2020;17:e1900178. doi:10.1002/ppap.201900178.

[21] Golda J, Held J, Redeker B, et al. Concepts and characteristics of the 'COST Reference Microplasma Jet'. J Phys D Appl Phys. 2016;49(8):084003. doi:10.1088/0022-3727/49/8/084003.

[22] Riedel F, Golda J, Held J, et al. Reproducibility of 'COST reference microplasma jets'. Plasma Sources Sci Technol. 2020;29(9):095018. doi:10.1088/1361-6595/abad01.

[23] Gazeli K, Hadjicharalambous M, Ioannou E, et al. Interrogating an in silico model to determine helium plasma jet and chemotherapy efficacy against B16F10 melanoma cells. Appl Phys Lett. 2022;120:054101. doi:10.1063/5.0077694.

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