IAEA
International Atomic Energy Agency

Technical Meeting on Emerging Applications of Plasma Science and Technology

Plasma medicine: current status and perspectives

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PlasTHER
THERAPEUTICAL APPLICATIONS OF COLD PLASMAS
CA19110
Plasma applications for smart and sustainable agriculture

IPCS
International Plasma Chemistry Society

SIB Società Italiana Biomateriali

PMIS
INTERNATIONAL SOCIETY FOR PLASMA MEDICINE

From the meeting website

Overview

The IAEA looks forward to support existing and novel applications of plasmas and plasma related technology, facilitate information exchange and help strengthen Member States' research programmes in this field.

Objectives

The purpose of the event is to **gather information and build a common understanding of emerging applications of plasma science and technology**, fostering practical ideas and proposals for joint initiatives aimed at **fostering longer-term collaboration through IAEA mechanisms (such as coordinated research projects, networks and technical cooperation projects)** for addressing global challenges.

Target Audience

Tthe target audience for this event comprises, but is not limited to:

- **Research scientists engaged in plasma-based research;**
- **Plasma technologists;**
- **Entrepreneurs or stakeholders involved in applications of plasma-based technology;**
- **Policymakers.**

Previous talks in the MEDICINE session

Michael Keidar, George Washington University, USA
Adaptive plasmas for biomedical applications

Kenji Ishikawa, Nagoya University, Japan
Low temperature plasma life innovations: functional reaction networks of radical chemistry

Agenda

- **Plasma Medicine – Technical aspects in a nutshell**
- **Plasma Medicine – Challenges**
- **The International Society for Plasma Medicine**
- **The International Conference on Plasma Medicine**
- **Plasma Medicine in the European Community – The PlasTHER project**

Plasma Medicine - Technical aspects in a nutshell

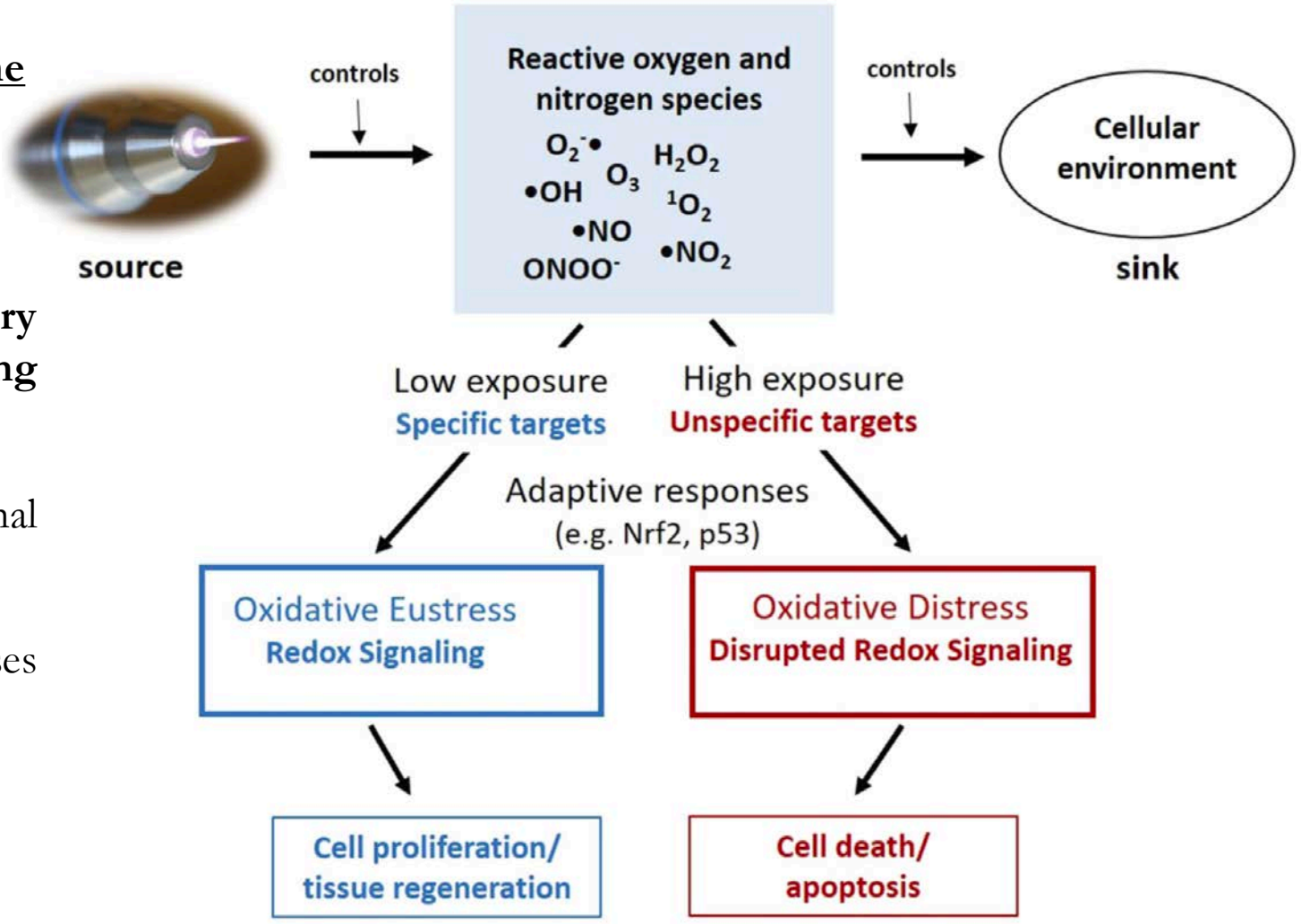
Redox biology as scientific basis of plasma medicine

ROS: Reactive Oxygen Species
RNS: Reactive Nitrogen Species

ROS and RNS play an important role as regulatory mediators in signaling processes and as signaling molecules for other physiological functions.

At 'physiological' levels ROS and RNS activate signal pathways and initiate physiological processes.

At higher, 'supraphysiological' levels damaging processes are caused.



Foundations of plasmas for medical applications
Plasma Sources Sci. Technol. 31 (2022) 054002

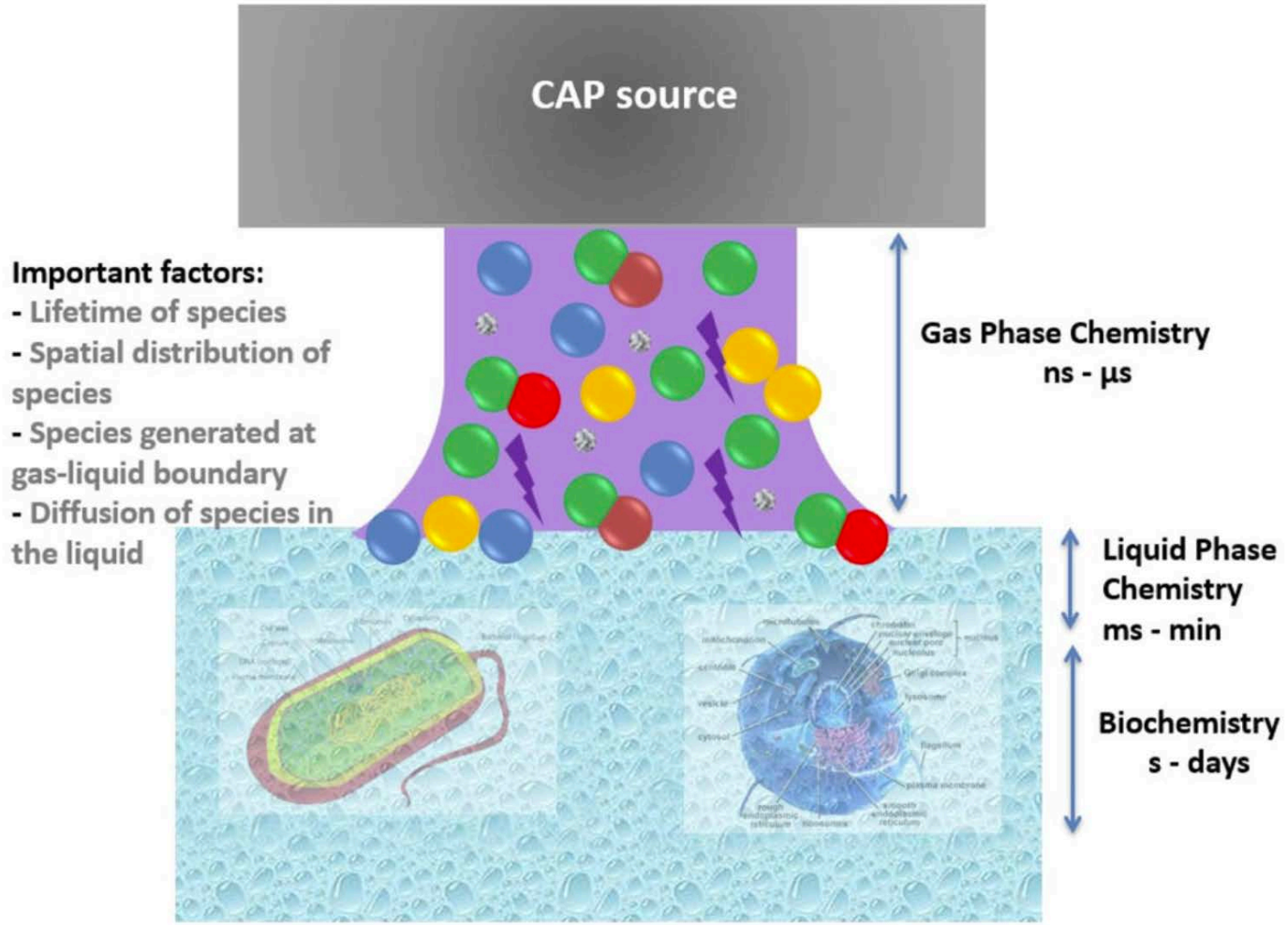
Plasma Medicine - Technical aspects in a nutshell

Reactive species generated in the plasma/gas phase have **to be transported to the biological target** and, subsequently, have to be exposed to biological structures to react with.

The transport and effective range of reactive species from the plasma/gas phase in the biological environment and their biological impact strongly depends on the **extracellular matrix composition.**

The extracellular space contains **proteins, carbohydrates and other components** that are potential reaction partners for plasma-generated reactive species.

Note: other agents may also participate in the biological response (e.g. electric fields, UV radiation, ...)

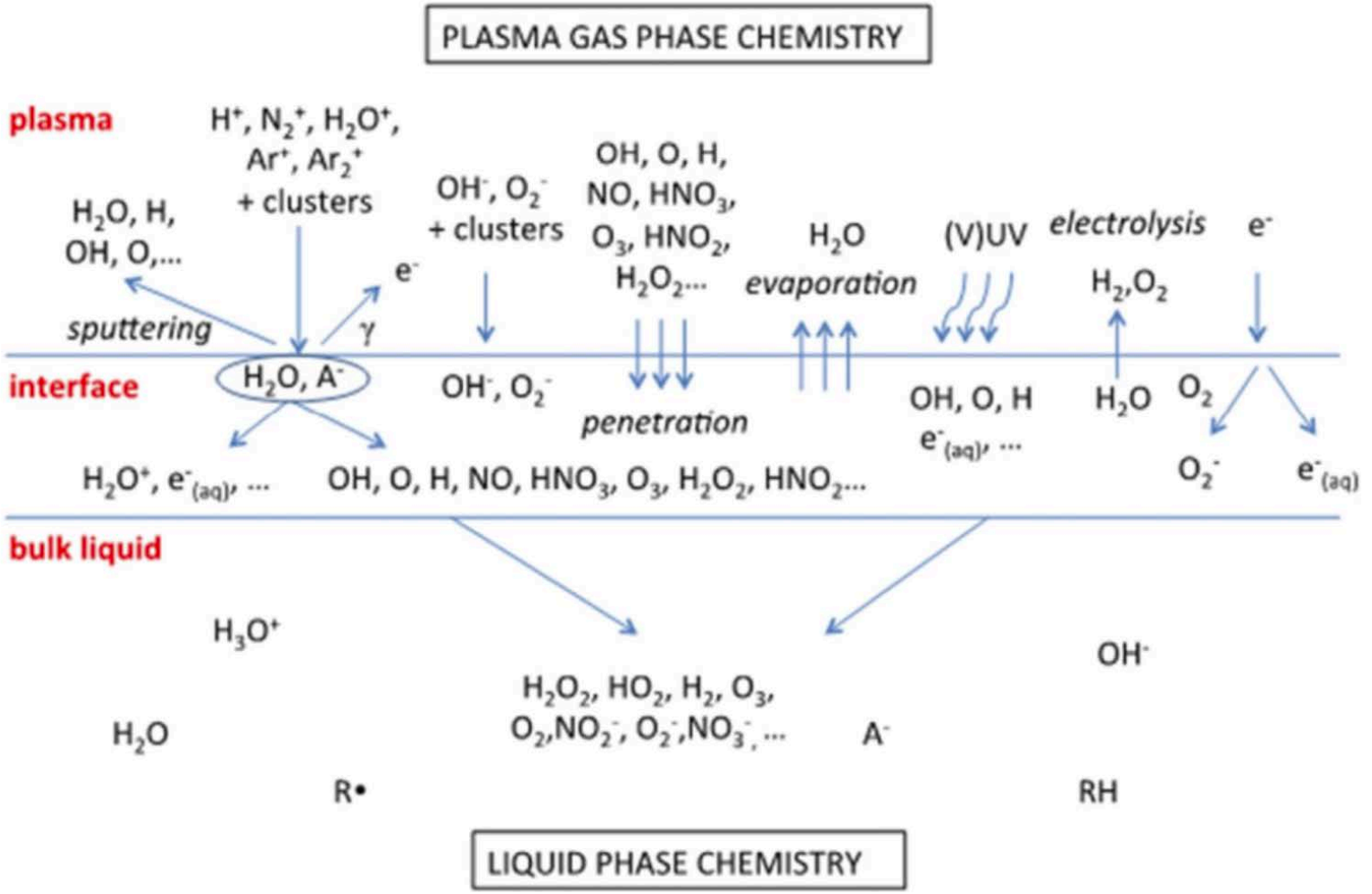


Foundations of plasmas for medical applications Plasma Sources Sci. Technol. 31 (2022) 054002

Plasma Medicine - Technical aspects in a nutshell

The dimension of the liquid layer around cells as well as its composition strongly influences the free range of reactive species, which is otherwise determined by their reactivity.

Provided that there is an albeit thin liquid phase between the plasma/gas phase and the biological target (cell), different processes have to be taken into account : **(i) gas phase transport of reactive species; (ii) processes at the plasma/gas–liquid interphase; (iii) processes inside the liquid.**



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Plasma Medicine – Examples of devices on the market

J-Plasma (US)

Rhytec portrait (US)

PlasmaCare (D)

SteriPlas (UK)

PlasmaDerm (D)

Jonix (I)

kINPen (D)

Plasma Medicine - Challenges

The regulatory challenge

Regulations of medical devices are intended to guarantee their safety and are rooted in the analysis of associated risks.
ISSUE: local nature of regulations, often different from country to country.

DIN SPEC 91315: specification registered by the German Institute of Standardization introduced in 2014 and indicating standards for the characterization of plasma sources in order to:

- obtain systematic and comparable results from researchers all over the world;
- produce results that could be checked against the safety limits imposed by regulations not specifically developed for plasma technology and that could vary from country to country.

Proposed measurements: temperature, UV irradiance, emitted gas species, chemical species in liquids, leakage current, antimicrobial activity and cytotoxicity.
ISSUES:

- the DIN SPEC 91315 considers risks for plasma devices intended for dermatological applications; as a consequence, the indicated methodologies do not specifically address plasma devices intended for intra-body medical procedures.
- the DIN SPEC 91315 does not cover the regulatory aspects of plasma-treated liquids (***pharmaceutical compounds?***)

Foundations of plasmas for medical applications, Plasma Sources Sci. Technol. 31 (2022) 054002

Plasma Medicine - Challenges

The cavity challenge

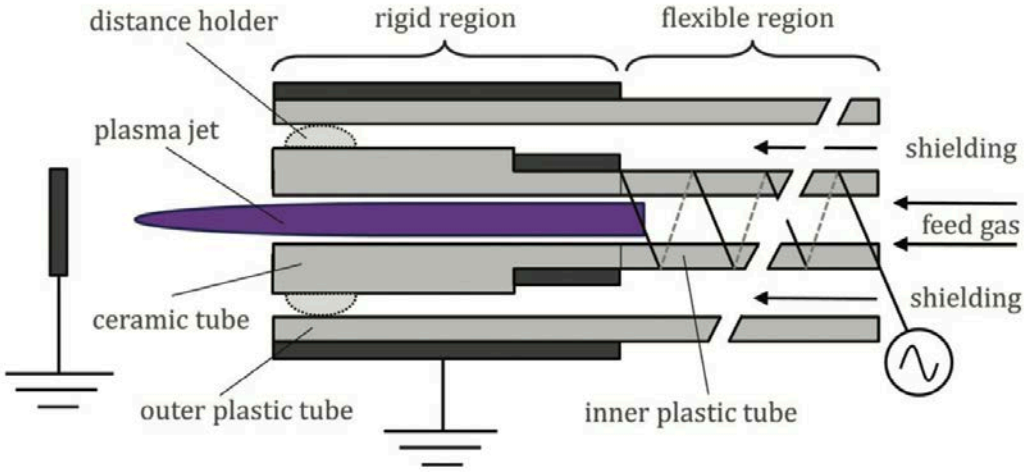
Several prospective medical applications (e.g. cancer treatment) of plasmas envision intrabody plasma delivery.

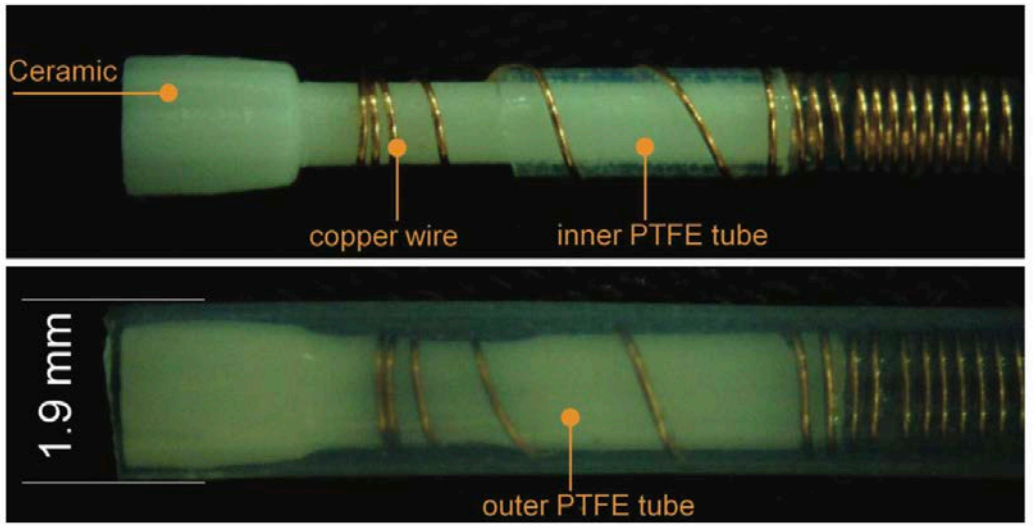
ISSUES:

- variability of conditions at the site of application;
- requirements for plasma devices:
  - flexibility;
  - limited rates of erosion;
  - electromagnetic compatibility, limited leakage currents;
  - gas delivery and plasma stability.

Some recent outcomes:

- need for an electronegative shielding gas to prevent the jet-to-glow transition of the discharge;
- formation of parasitic discharges within the plasma device and at the high voltage connections is a critical aspect.





Foundations of plasmas for medical applications, Plasma Sources Sci. Technol. 31 (2022) 054002

Contrib. Plasma Phys. 2018;58:404–414

Plasma Medicine - Challenges

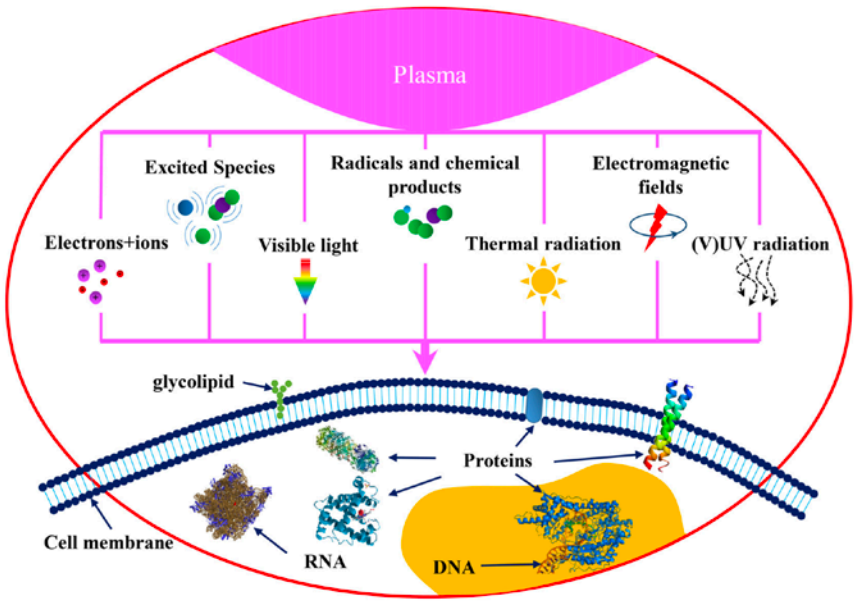
The dose challenge

Dose: the quantity of a therapeutic agent or of radiation, in the case of radiotherapy, administered to the patient during a treatment.

- employed when considering the therapeutic window of a certain drug/treatment;
- useful standard to compare different treatments and a suitable control parameter, connecting the inputs (the administered quantity of therapeutic agent) with the outputs (the biological effects) of the process.

ISSUE: ***plasma dose*** not yet defined

- initially referred to the interrelated parameters of treatment time, power coupled with the discharge and dissipated energy;
- increased understanding challenged these assumptions;
- equivalent total oxidation potential (ETOP)?



ETOP considers

- RONS in gas phase;
- other plasma oxidating agents;
- synergistic effects.

ETOP limitations:

- requires real time RONS measurements;
- quantification of non-RONS OP is complex;
- quantification of synergistic OP would require complete comprehension of the processes;
- disregards OP of liquid phase RONS.

Phys. Plasmas 27, 063514 (2020)

Foundations of plasmas for medical applications, Plasma Sources Sci. Technol. 31 (2022) 054002

Plasma Medicine - Challenges

The monitoring and control challenge

Clinical applications of plasmas require repeatable and safe treatments.

Typically the relation between the plasma parameters and the biological effects is non linear (feedback control is required).

Controlling strategies, in principle, require an understanding of:

- which are the relevant parameters controlling the process;
- what is the relationship between inputs and outputs of the process;
- monitoring those inputs and outputs.

In the case of plasma technologies, each of these points is a challenge in itself.

From the previous talks:

Michael Keidar: '*We will explore possibilities and opportunities that the* ***adaptive plasma therapeutic system*** *might offer. We shall define such an adaptive system as a* ***plasma device that is able to adjust the plasma composition to obtain optimal desirable outcomes*** *through its interaction with cells and tissues*'

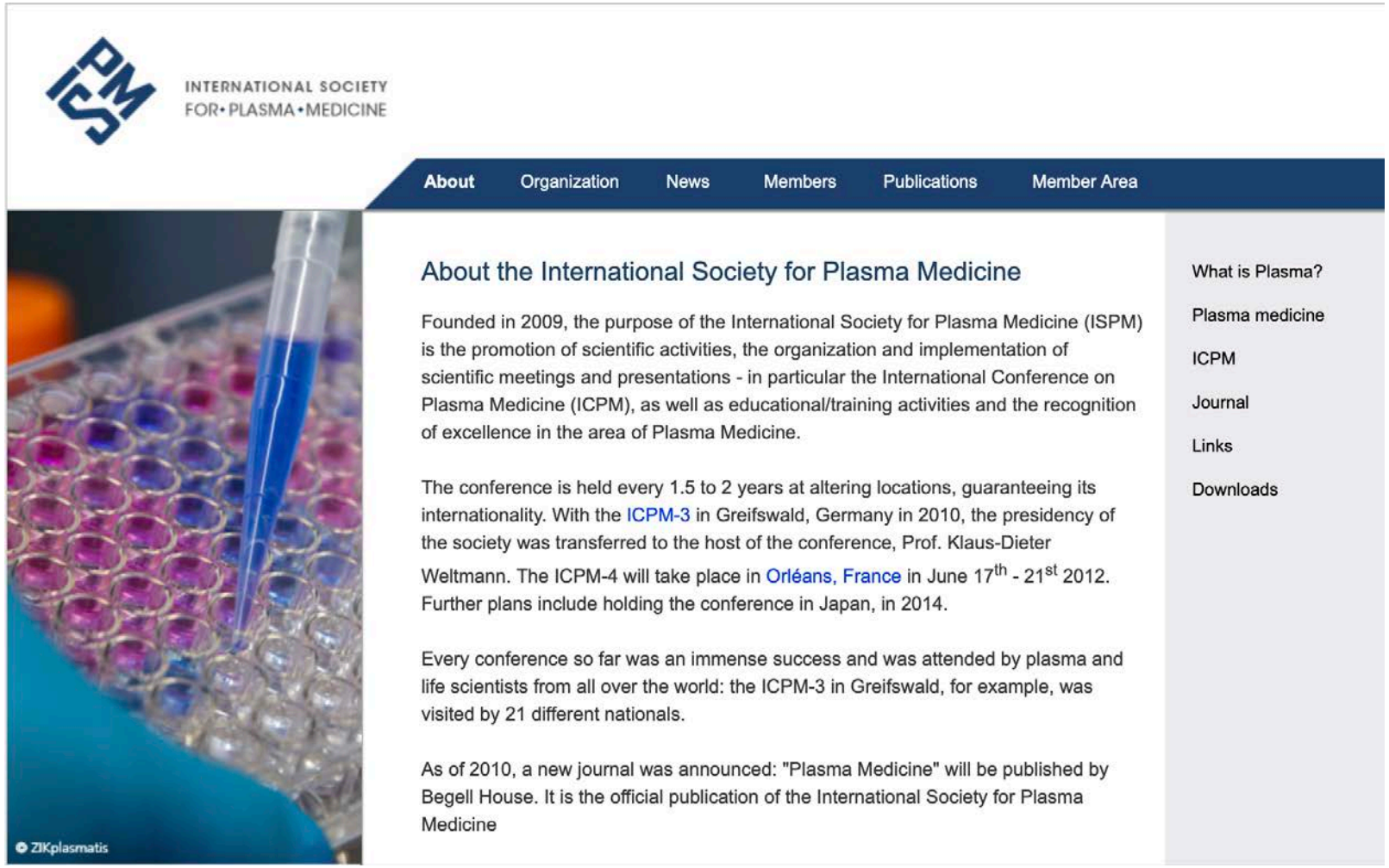
Kenji Ishikawa: '*This paper stressed the importance of* ***understanding the dynamics of complex networks based on kinetically-driven reactions*** *in nonequilibrium states, using empirical data. On this basis, it should be possible to* ***control the functionalization of living organisms*** *by employing common principles associated with the spatiotemporal atomic scale localization of reactive species*'

The International Society for Plasma Medicine (ISPM)

Founded in 2009

ISPM purposes:

- the promotion of scientific activities;
- the organization and implementation of scientific meetings and presentations - in particular the International Conference on Plasma Medicine (ICPM);
- educational/training activities;
- the recognition of excellence in the area of Plasma Medicine.



Plasma Medicine as defined by the ISPM

- Plasma medicine can be subdivided into three main fields:
  - plasma-assisted modification of bio-relevant surfaces;
  - plasma-based bio-decontamination/sterilization;
  - ***direct therapeutic plasma application*.**
- The aim of therapeutic plasma application as the central field of plasma medicine is to bring physical plasmas ***directly on or in the human (or animal) body*.**
- In order to treat living tissue, ***the plasma source must be artificially generated and at room temperature and pressure*.** Central to all medical applications are the ***antimicrobial as well as surface altering effects of plasma*.** These characteristics make it very attractive for different medical purposes, such as ***wound healing, dentistry, dermatology or implant medicine*.**
- ***It is crucial to comprehend the biological effects*** and support, as well as accompany, the ***transfer of atmospheric pressure plasma sources to medical-experimental research and further clinical trials*.**
- ***The successful interplay of medicine, biology and physics requires reciprocal understanding to be able to realize the full potential of medical plasma applications*.**

ISPM Board of Directors

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- Thomas von Woedtke, Germany
- Sander Bekeschus, Germany
- Eric Robert, France
- Paula Burke, Ireland

International Conference on Plasma Medicine (ICPM)

icpm9

From June 27th to July 1st 2022, Utrecht, The Netherlands

9th international conference on plasma medicine

TU/e EINDHOVEN UNIVERSITY OF TECHNOLOGY

The ICPM brings together professionals from the fields of plasma, medicine, biology and biochemistry in order to develop a common language, to better define key challenges and open questions and to move toward effective solutions.

The 9th International Conference on Plasma Medicine (**ICPM9**), was held in the Jaarbeurs in Utrecht, The Netherlands, from June 27th to July 1st 2022.

International Conference on Plasma Medicine (ICPM)

Topics

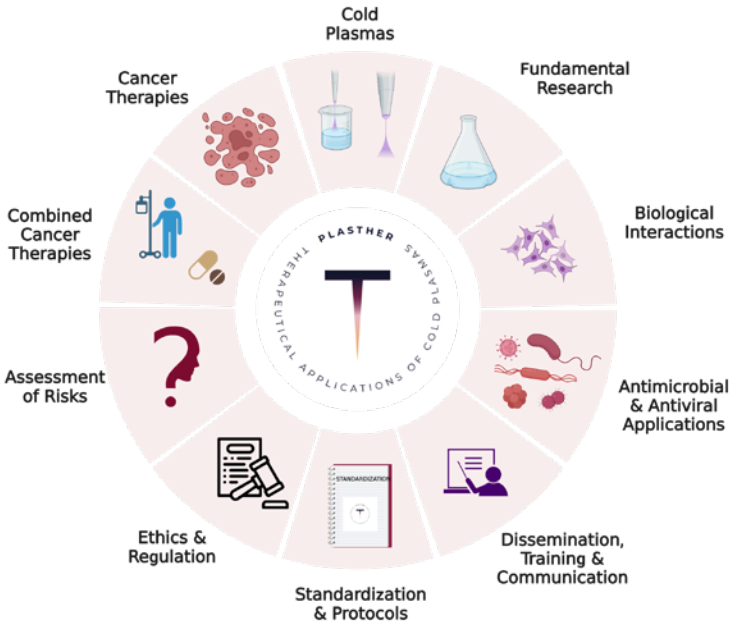
- Fundamentals of atmospheric plasmas
- Plasma for pharmaceutical applications, biochemical and biomolecular engineering
- Plasma liquid interactions, plasma activated liquids
- Plasma medical applications - clinical and animal studies
- Plasma sources for biomedical applications
- Plasma-based decontamination and sterilization
- Plasma-cell and plasma-tissue interactions - biological and biochemical reactions
- Plasma-surface interactions/modifications for biomedical applications Regulatory issues in plasma medicine
- Plasma agricultural applications

Plenary talks

- Julia Bandow, Plasma-driven biocatalysis: challenges and opportunities
- Peter Bruggeman, Plasma Regulated Biology: A Pathway Towards Defining a 'dose' in Plasma-Medicine
- Cristina Canal, Lessons learnt with plasma-treated liquid therapies for bone cancer: opportunities for Plasma Medicine
- Yuzuru Ikehara, Understanding and using the plasma effects as what interacts with the biomolecules having the electric charge
- Katharina Stapelmann, Plasma and Plasma-liquid chemistry in the presence of organic matter

Plasma Medicine in the European Community – The PlasTHER project

- The Action is concerned with the ***medical and biomedical applications of cold atmospheric plasmas***.
- The main aim of the PlasTHER COST Action is to exploit the unprecedented possibilities of atmospheric pressure plasmas in medicine to *share, develop and consolidate suitable therapies currently under investigation to make Europe's science and healthcare world leaders in this field*.
- In this sense, PlasTHER COST Action aims at ***establishing a synergistic network that articulates researchers, the medical community, industry and patient associations***, among others, and ***coordinate the European activity in this domain to foster the leadership of Europe in this emerging field***.



Plasma Medicine in the European Community – The PlasTHER project – Core group and Working Groups

Spain	Dr Cristina CANAL	WG1: Fundamental plasma-biological interaction mechanisms
France	Prof Sarah COUSTY	WG2: Antimicrobial effects of plasma
Belgium	Dr Abraham LIN	WG3: Tissue regeneration
Italy	Dr Romolo LAURITA	WG4: Plasma cancer therapy
Italy	Dr Eloisa SARDELLA	WG5: Combination therapies
Germany	Dr Sander BEKESCHUS	WG6: Regulatory, ethics, dissemination & technology transfer
Ireland	Dr Joanna SADOWSKA	
France	Dr Sara LAURENCIN-DALICIEUX	
Portugal	Dr Susana SÉRIO	
Serbia	Dr Nikola SKORO	

Plasma Medicine in the European Community – The PlasTHER project

WG1 – Fundamental plasma-biological interaction mechanisms

Leaders

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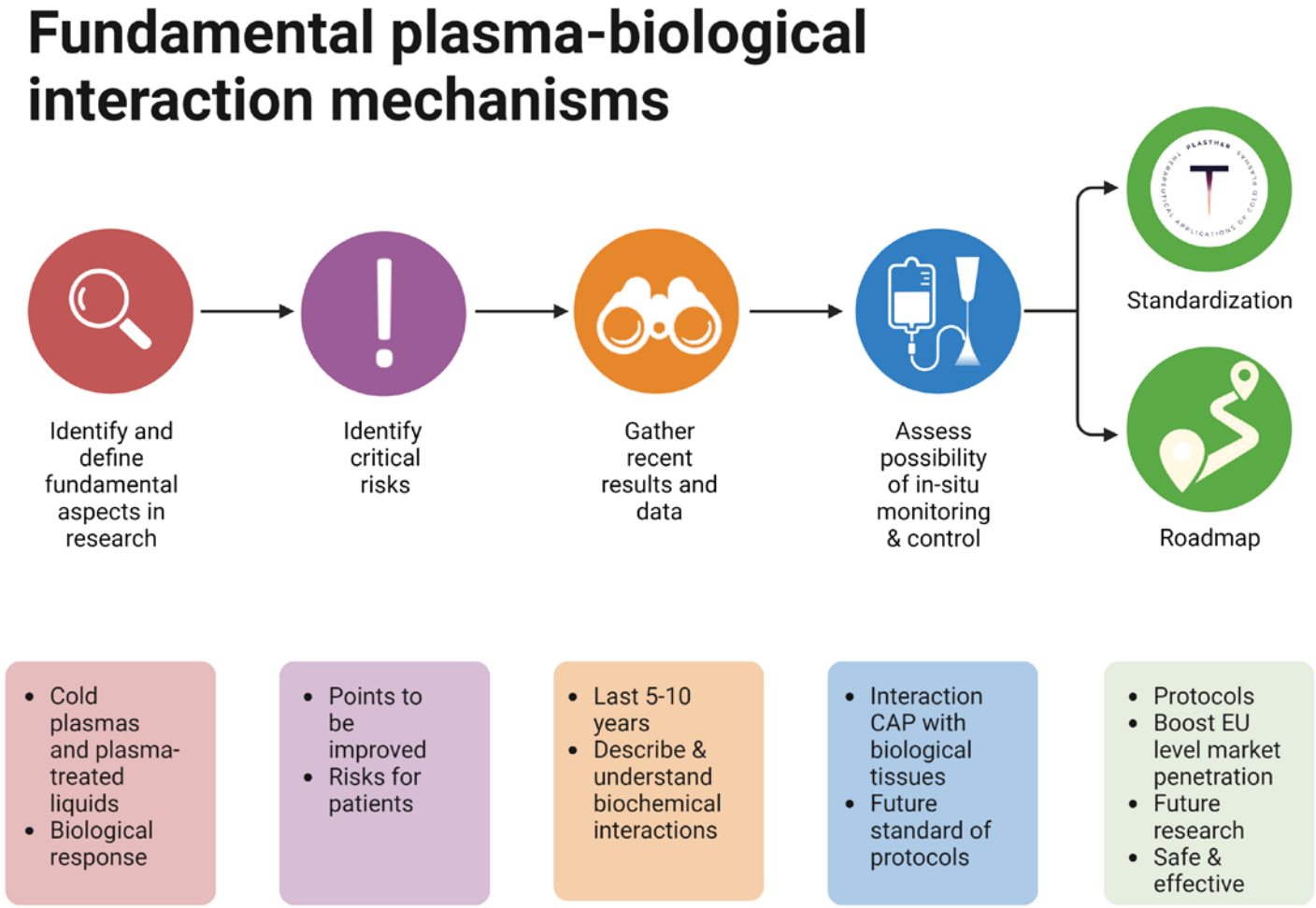

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Plasma Medicine in the European Community – The PlasTHER project

WG2 – Antimicrobial effects of plasmas

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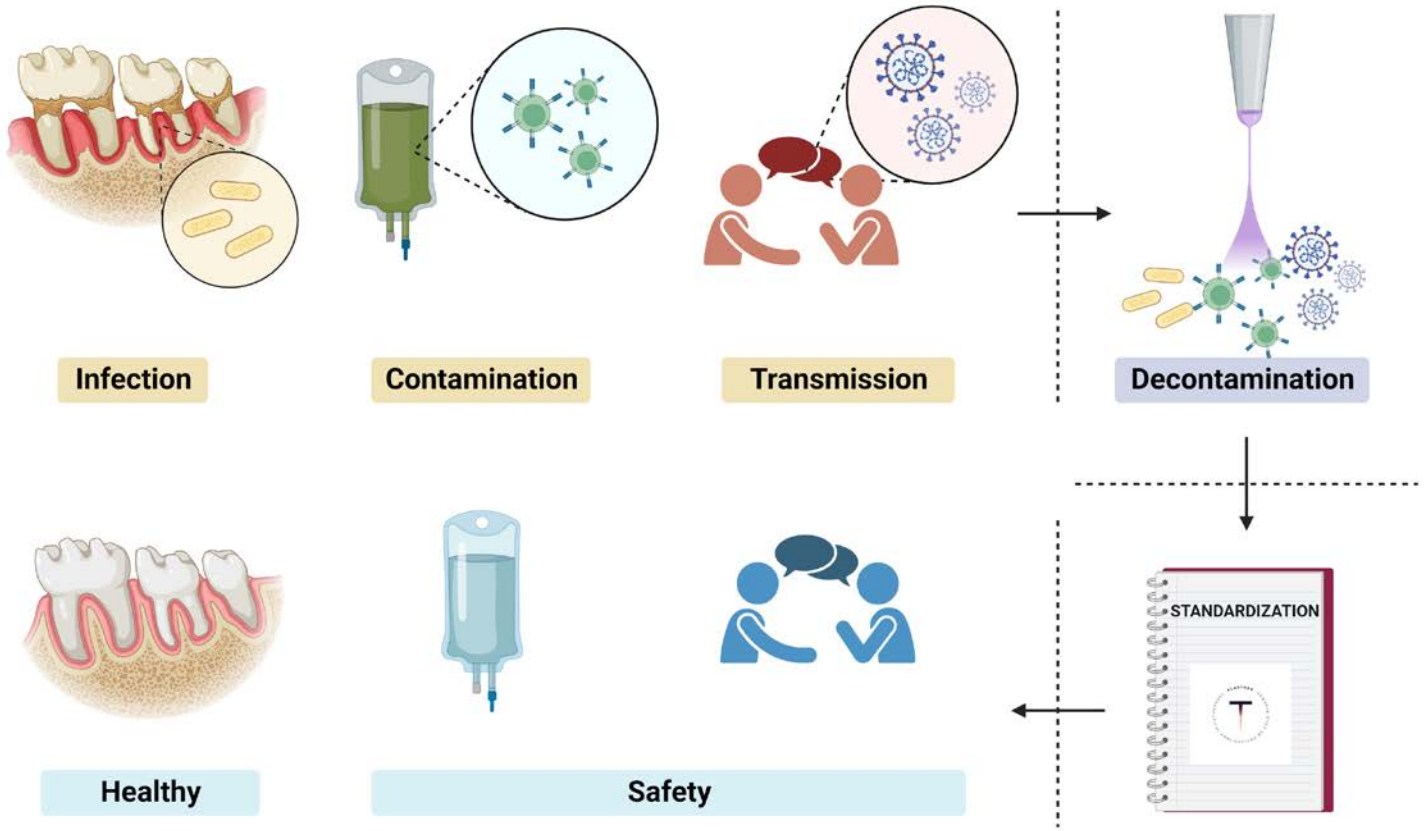

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Plasma Medicine in the European Community – The PlasTHER project

WG3 – Tissue regeneration

Leaders

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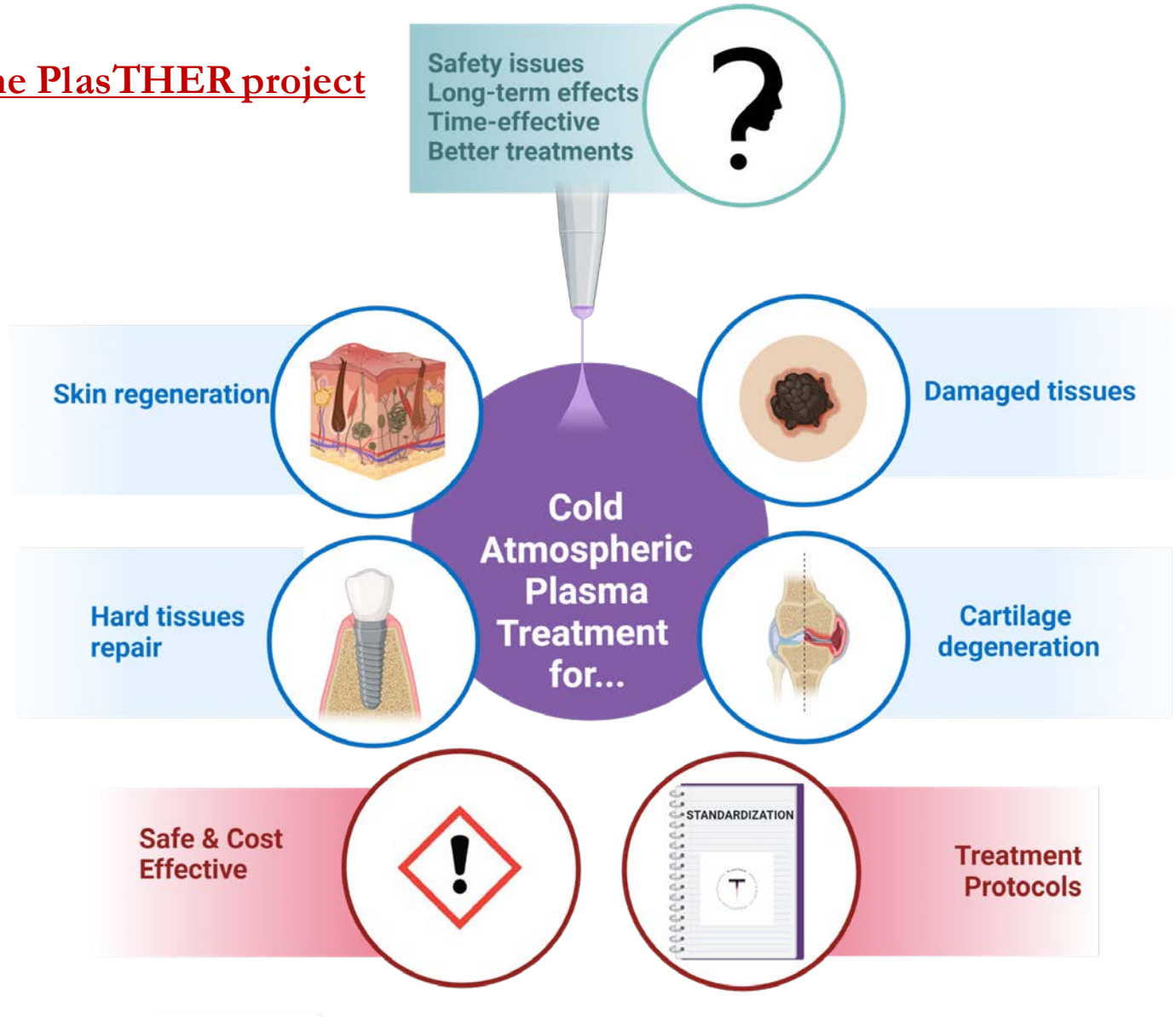

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Plasma Medicine in the European Community – The PlasTHER project

WG4 – Plasma cancer therapy

Leaders

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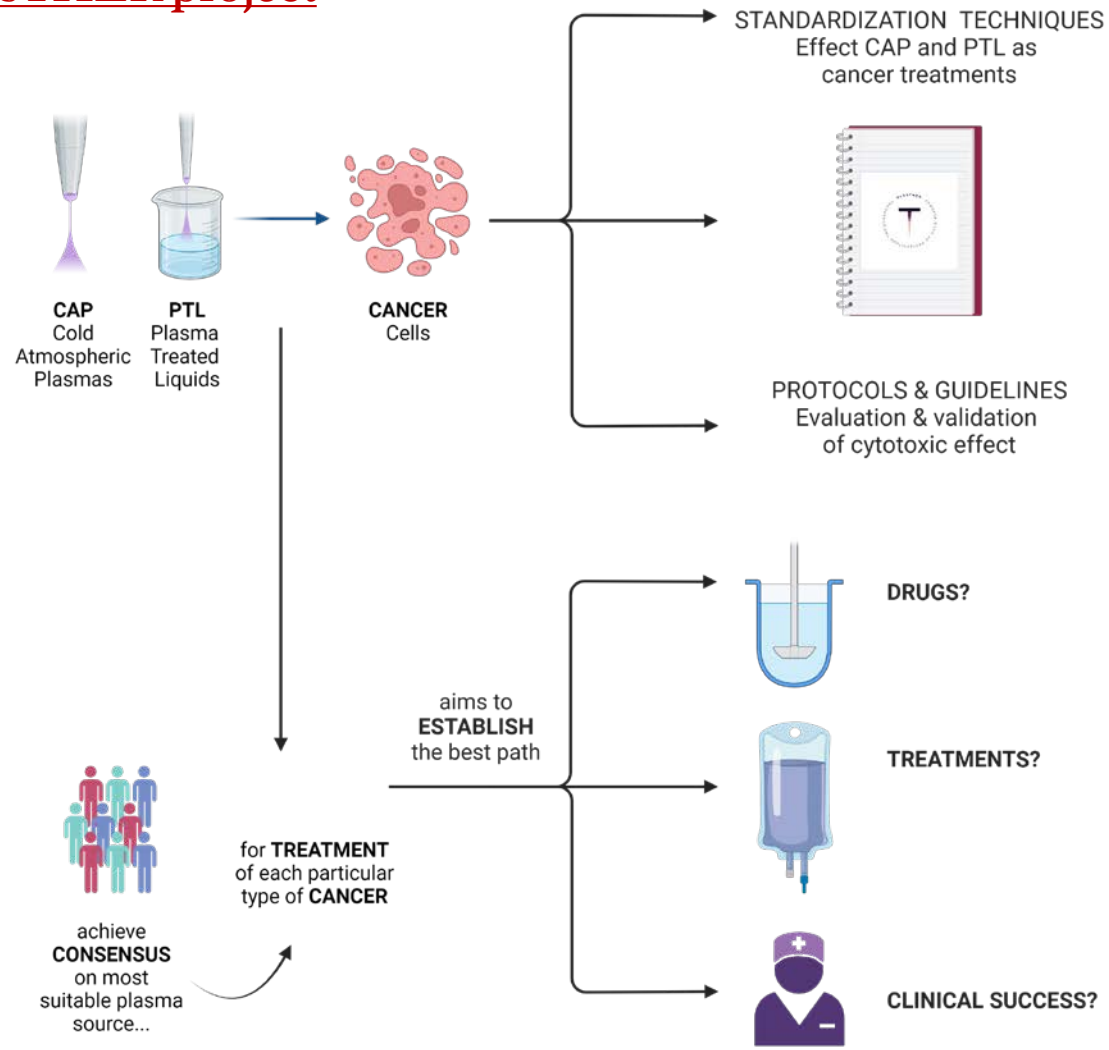

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Plasma Medicine in the European Community – The PlasTHER project

WG5 – Combination therapies

Leaders

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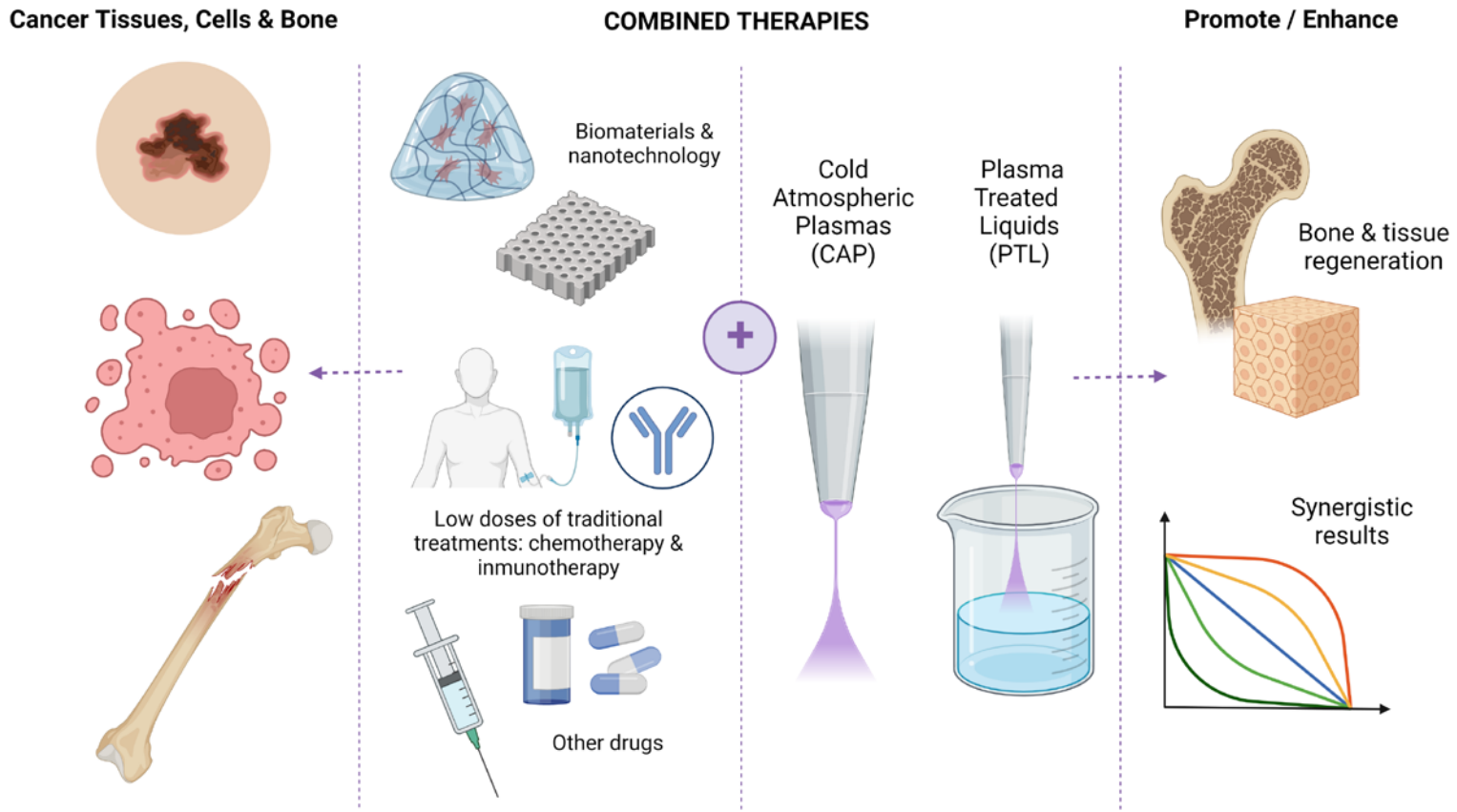

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Plasma Medicine in the European Community – The PlasTHER project

WG6 – Regulatory, ethics, dissemination & technology transfer

Leaders

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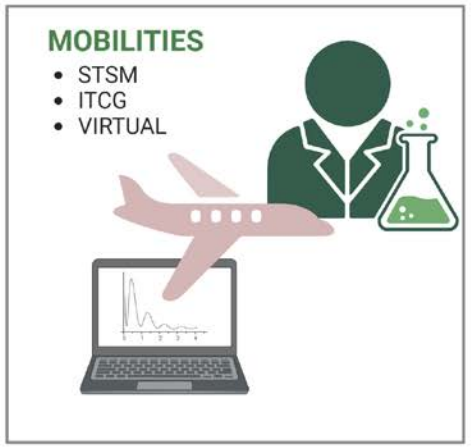

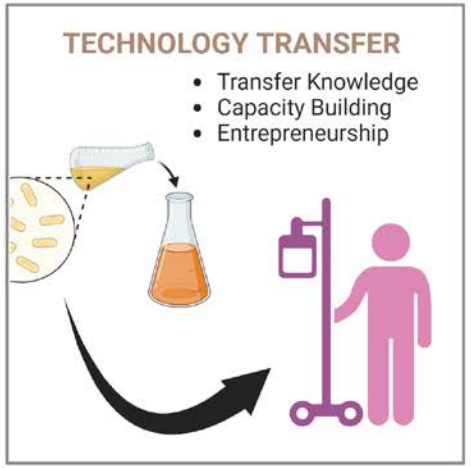

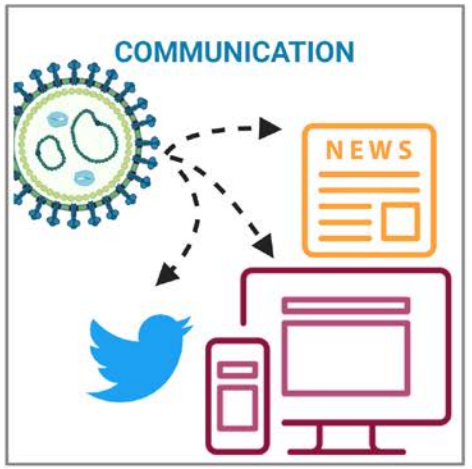

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Thank you for your attention!

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