Atmospheric pressure gas plasmas for biomedical applications

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1. Overview of Plasma medicine
   • Recent progress in *Plasma Medicine*
   • Plasma sources for biomedicine
   • Wound healing and cancer treatment
   • ROS/RNS in gas plasmas and biomedicine

2. RF plasma needle – bacteria interaction
   • Ring-shaped killing pattern
   • Fluid model
   • TALIF measurement

3. Concluding remarks
A brief history of gas plasmas in biomedicine

- 1893 A. d’Arsonval: compatibility of HF with nerve and muscle
- 1926 Bovie knife: the first clinical use of a electrosurgical device
- 1940 Hyfrecator (Birtcher Co): low power and no ground pad
- 1995 APC (ERBE GmbH): Ar plasma for endoscopic surgery
  Coblation (Arthrocare Co): discharge in saline solution
- 1999 M. Laroussi: E. coli sterilization (He DBD)
- 2003 E. Stoffles: non-destructive cell handling (He plasma needle)
- 2007 G. Fridman: in vitro cancer cell treatment (Air DBD)
- 2010 G. Isbary: clinical trial for wound healing (MW Ar plasma)
Potential applications

- antibacterial resistance
- nosocomial infection
- chronic wound
- dental cavity
- pandemic flu
- cancer
- hand hygiene
- drug delivery
Cancer cell treatment

**indirect-mode air DBD (in vitro)**

- HV electrode (~5kV, 10kHz)
- Glass plate
- Ground electrode
- Suspension with MCF7 cells

**direct-mode air DBD (in vivo)**

- Direct-mode air DBD
- Oscilloscope
- Voltage probe
- Current probe
- Gas pipe
- Gas
- Mass flow meter
- Reactor
- Mass flow meter
- Gas pipe
- Mouse
- Silver plate grounded

Trypan blue viability assay

![Graph showing normalized viable cells vs. exposure time](image)

Wound healing: *in vitro* study

R. A. Bryant, et al., *Acute and Chronic Wounds* (Mosby, Missouri, 2006).


**Inflammatory phase**
- ~48 hours
- bacteria sterilization/debris removal
- blood coagulation

**Proliferative phase**
- 2~10 days
- blood vessels generation
- collagen deposition from fibroblasts

**Remodeling phase**
- 1 year
- tissue reorganization/realignment
- apoptosis of unnecessary cells
Wound healing: clinical study

- Plasma health care project
- Lead by G. Morfill at Max-Planck Institute
- 19 PhDs, 11 MDs
- Germany, UK, Russia, Japan, USA

Phase-I clinical study


Microwave Ar plasma torch

Before treatment

After 11 treatments
Plasmas in ambient air at room temperature

Plasma-biomaterial interaction: possible agents (1)

- DNA damage
- etching
- sputtering

- oxidation
- signaling

- membrane disruption (~$10^9$ V/m)
- stimulation

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Cu (copper) on glass with high voltage (HV)
Plasma-biomaterial interaction: ROS/RNS

- **ROS** (reactive oxygen species): O, O₂*, O₃, O₂⁻, OH, H₂O₂
- **RNS** (reactive nitrogen species): NO, NO₂, ONOO⁻

Mass spectroscopy


phagocytes

antibiotics

radiation therapy

Abbas, Celluar and Molecular Immunology (Elsevier, 2005).
Outline

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Plasma needle: observed killing pattern

Plasma needle: fluid model

Neutral Gas flow (He, Air)

\[ \nabla \cdot (\rho \mathbf{u}) = 0, \quad \nabla \cdot (\rho \omega_{\text{air}} \mathbf{u} - \rho D \nabla \omega_{\text{air}}) = 0 \]  
(mass conservation)

\[ \nabla \cdot (\rho \mathbf{u} u_i) = -\nabla p - \nabla \cdot \mathbf{\tau} + \sum q_i n_i \mathbf{E} \]  
(momentum conservation)

\[ \nabla \cdot (-\lambda \nabla T + \mathbf{u} c_p T) = \Phi + \sum q_i \Gamma_i \mathbf{E} + Q_{el} \]  
(energy conservation)

Plasma dynamics

\[ \frac{\partial n_i}{\partial t} + \nabla \cdot \Gamma_i = S_i \]  
(mass conservation)

\[ \Gamma_i = \text{sgn}(q_i) n_i \mu_i \mathbf{E} - D_i \nabla n_i + n_i \mathbf{u} \]  
(drift-diffusion)

\[ \frac{\partial (n_e \varepsilon)}{\partial t} + \nabla \cdot \left( \frac{5}{3} \varepsilon \nabla - \frac{5}{3} n_e D_e \nabla \varepsilon \right) = -\Gamma_e \cdot \mathbf{E} - Q \]  
(electron energy)

\[ \varepsilon_0 \nabla \cdot \mathbf{E} = \sum q_i n_i \]  
(Poisson’s equation)

Plasma needle: phase-averaged species density

Mole fraction of air (log scale)

![Graph showing mole fraction of air and phase-averaged species density for plasma needle, with color scale and labels for insulator and needle.]
Plasma needle: reproduced ring-shaped emission

Mole fraction of air (log scale)

Predicted emission pattern

dark ➔ bright

Observed light emission

Y. Sakyiama et al, Plasma Sources Sci. Technol. 18 (2009) 025022
Plasma needle: flux onto bacteria

on-axis

off-axis

ROS/RNS
Model validation: O atom measurement

- **TALIF**: two photon absorbed laser induced fluorescence
- collaboration with Ruhr-Universitat Bochum (Germany)

Model validation: measured O atom density

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1. Plasma-generated ROS/RNS has enormous potential to open up a new field in biomedicine.

2. Neutral gas flow and air chemistry play significant roles in plasma medicine at atmospheric pressure.

3. Numerical modeling is a powerful tool to investigate plasma-biomaterial interaction and to understand the basic mechanisms of the interaction.
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Related publications

Reviews for plasma medicine

Plasma-biomaterial interaction in Graves group