PLASON®
NO-therapy

Medical device for NO-therapy

Medical technology on the basis of the use of air plasma and exogenous nitrogen oxide for the treatment of wounds, inflammatory processes, auto-immune diseases.

The exogenous nitrogen oxide of plasma-chemical genesis is contained in the high and low temperature gas flows (4000 °C to 20 °C), generated from atmospheric air.

The “PLASON” device doesn´t have analogous devices available worldwide.
Basic Types of the Device Usage

Fig.3. Two operational versions of the device

1 - Service block
2 - Electro-hydro-pneumatic (EHP) supply
3 - Manipulator
4 - NO-containing gas flow supply tube
5 - Variable end metallic tip
6 - Cooler socket
The therapeutic effectiveness of the exogenous nitrogen oxide (NO) is based on the properties of the endogenous NO as polyfunctional physiological regulator (the Nobel Prize for medicine in 1998) and consists of the following:

- normalization of microcirculation due to the vasodilation, anti-aggregation and anticoagulative action of NO;
- bactericidal action on its own and by peroxynitrite, which is formed in the cloths as an interaction of NO with the superoxide - anion (NO + O_2 → ONOO-);
- induction of the phagocytosis of bacteria by neutrophils and by macrophages;
- the activation of antioxidant protection;
- the strengthening the secretion anti-inflammatory and pro-regenerative cytokine and the factors of angiogenesis;
- an improvement in the nervous conductivity (neurotransmission);
- regulation of specific and nonspecific immunity;
- the direct induction of the proliferation of fibroblasts, increase in the vessels, synthesis of collagen, formation and ripening of granulating cloth, proliferation of the epithelium;
- the regulation of apoptose and averting pathologic cicatrisation.
Composition of atmospheric air

- 78% Nitrogen
- 21% Oxygen
- 1% Carbon dioxide, Argon, Water vapour and other gases

\[ N_2 + O_2 = 2NO - 181 \text{ kJ} \]
Content of Nitric Oxide depending on the distance

- Nitric oxide content in the gas stream is the determinant factor depending on the distance from output channel of manipulator.

- **Air-plasma stream flows out from special extender adapter** of manipulator (130, 200, or 350 mm of length).

- **Direct action** on biological tissue or pharmaceutical solutions.
Basic Functions of Nitric Oxide as Universal Biological Regulator

Arginine → eNO-Synthase (endothelium) → nNO-Synthase (neurocytes) → Inducible NO-Synthase (macrophages and other cells) → NO

Physiological regulation

Pathological processes
Nitric Oxide: Physiological Role

DIRECT ACTION:

• Thermoregulation: carotid body (control of $O_2$, $CO_2$, pH and $t$ through gas messengers NO, CO, $H_2S$)
• Smooth-muscle cells: relaxation (vasodilatation); proliferation;
• Hemostasis: inhibition of platelet aggregation; leukocyte adhesion, blood coagulation.

MEDIATOR ACTION:

• Synthesis of DNA and proteins;
• Apoptosis, angiogenesis
• Interneuronic communications;
• Nonspecific immunity;
• Smooth-muscle cells mediated tone of different systems of organism; cell proliferation
• Hormonal functions;
• Renal filtration and others.
Nitric Oxide: The Role in Pathological Processes

- Adaptation, stress;
- Tumor growth;
- Immune disorders;
- Inflammation;
- Wound healing and regeneration;
- Diseases of cardiovascular, pulmonary, nervous, gastrointestinal, endocrine, urino-genital systems.
The Role of Endogenous Nitric Oxide in Inflammation

- Antimicrobial action
- Stimulation of macrophages, T-lymphocytes
- Induction of cytokines and production of antibodies
- Interaction with free radicals: cytotoxic effects or cell membrane protection
Basic Facts About the Role of Nitric Oxide in wound healing

• The Nitric Oxide (NO) level is increased in the healing wound.
• Low level of NO is a typical feature of recalcitrant wounds.
• Fibroblast proliferation and collagen synthesis are depressed by inhibitors of NOS.
• Inductors of NOS increase such processes.
• NO-donors accelerate wound healing.
• Wound healing is delayed in iNOS knockout mice; transfection of iNOS gene accelerate the reparation.
Role of Endogenous Nitric Oxide in Wound Healing

- **Activation of iNOS** (in exudative and proliferative phases)
- **Activation of eNOS** (in vascularization phase and granulation tissue)

Increasing of fibroblast proliferation and collagen synthesis
Modern trends in NO-therapy

• Donors of NO *(different compounds containing nitrogen)*

• Inductors of NO-synthases: cytokines *(IL-1β, TNF-α, interferon-γ and others)*

• Inhibitors of inductors of NO-synthases *(glucocorticoids, IL-4, 8, 10; TNF-β, EGF and others)*

• NOS-blockers *(S-methylthiazol etc.)*

• Arginine *(as NOS substrate)*

• Superoxide dismutase *(prevention of NO inactivation)*

• Transfection on NOS-gene

• Inhalation of gaseous NO

• Generation of NO from atmospheric air by plasmochemical reaction *(PLASON device)*
Advantages of Plasmochemical Generation of NO by PLASON® device

1. Minimized systemic action while pronounced local effects of NO-therapy

2. Number of NO molecules in the gas stream can be dosed from 0 to 2500 ppm

3. It is possible to manipulate in visceral cavities and in lumens of hollow organs because of attaching of endoscopes, drainage tubes, puncture needles

4. It was proved that gaseous NO can penetrate through intact skin, mucous and serous membranes, eye tissues

5. It is possible to treat wounds, ulcers, inflammatory and fibrous processes

6. It is possible to combine coagulation and sterilization with NO-therapy
Application Experience of Plason® Device in Clinical Practice

- **General surgery:** postoperative wounds (stimulation of reparation and prophylaxis of suppuration); purulent wounds; abscesses; phlegmons; furunculosis; erysipelas; burns; preparation to skin transplantation and prophylaxis of graft rejection; persistent wounds, venous and arterial trophic ulcers; diabetic foot ulcers, decubitus ulcers; purulent peritonitis; mediastinitis.

- **Oncology:** radiation ulcers, chronically nonhealing wounds (including lesions against chemotherapy background), opening of sutures, radiation fibrosis, destruction of tumors, coagulation of wound surfaces.
Application Experience of Plason® Device in clinical practice

- **Traumatology and orthopedics:** open fractures, osteomyelitic fistulas; wounds raising after sequestrectomy etc.
- **Field surgery:** gunshot wounds and fractures, mine-explosive injuries etc.
- **Dermatology:** dermatitis, eczemas, lichen ruber planus.
- **Pulmonology and phthisiology:** pleural empyema, tubercular cavities, tuberculosis of bones and joints.
- **Gynecology:** cervical erosion; tubal sterility; pyoinflammatory diseases of uterus and uterine appendages etc.
Application Experience of Plason® Device in clinical practice

- **Stomatology:** periodontitis; gingivitis; aphthous and ulcerative stomatitis; post-tooth replacement state and others.
- **Otolaryngology:** strictures of larynx and trachea, sinusitis (including polypous); pharyngitis; tonsillitis; rhinitis; otitis; epistaxis; post-surgery states.
- **Ophthalmology:** traumas and burns of cornea.
- **Gastroenterology:** stomach and duodenal ulcers; fistulas of bowels; pancreatitis and pancreatic cysts etc.
Effect of NO on different parts of wound healing process

Alteration

- Microcirculatory reactions, exudation, neutrophilic increase
- Macrophagal activation
- Fibroblast proliferation, vascularization, granulation tissue growth
- Synthesis and assemblage of collagen fibrils
- Regeneration of epithelium
- Pathological scarring

Wound healing

- Decreasing
- Increasing
Mechanisms of action of exogenous NO

• Vasodilatation, antiaggregant and anticoagulation effects → improvement of microcirculation, trophism and tissue metabolism;

• Direct bactericidal or bacteriostatic effect;

• Activation of macrophages → phagocytic effect, wound cleansing, cytokine and chemokine production → vascularization, regulation of apoptosis and immune reactions; epithelization.

• Activation of antioxidant protection → membrane's stabilization;

• Direct induction of fibroblast proliferation and collagen synthesis → granulation tissue formation → completing of wound hollow, arrangement of conditions for epithelization.
Sparing coagulation of wound surfaces

- For achievement of the effect of partial drying there is no need for using of the entire temperature potential of air-plasma flow. It is sufficient to ensure temperature from 1000°C to 2000°C in the place of contact of plasma with cloth.

- The distance from the outlet of manipulator to the cloth is minimal, since the temperature does not exceed 1000°C.

- If it is necessary to realize the sparing coagulation on large surfaces, it is possible to use the coagulator.

- If it is necessary to coagulate bounded spaces, stimulator-coagulator can be used.
NO-therapy using the coagulator and the destructor

- Minimum distance from the manipulator to the object, with which it is possible to carry out the sessions of the NO-therapy by coagulator or by destructor, is 150 mm.
- The NO-containing gas flow is directed to surface at right angle.
NO-therapy by stimulator-coagulator

- Directed in the right angle to the place of treatment the flow will smoothly spread in on the surface, creating axisymmetrical region with the increased content of nitric oxide.
- Length of thermal distancer is selected so that the temperature of the NO-containing gas flow on the end of spacer would be 40±10 °C.
- In this case the concentration of the nitrogen oxide will have a value of ~750 ppm.
NO-therapy by narrowly-directed, cooled NO-containing gas flow

- The cooled flow can be supplied to the object through a flexible silicone tube and the metallic tip, which is made in the form of the thin-walled tube with a diameter of 4 mm from biologically inert materials.
- Localization and focusing is achieved by the calibration of the tip outlet. For the satisfaction of the existing tasks for NO-therapy the optimal diameter of the tip outlet is less than 1 mm.
NO-therapy of cavities by the cooled NO-containing gas flow

- The complete cooling of the NO-containing gas flow makes it possible to use it with working of cavities.
- **Variant 1.** If cavity has a form of pocket and the opening allows inserting of the metallic tip, then it is placed directly into the cavity. Air is displaced by forced NO-containing gas flow. The environment with increased content of nitrogen oxide is created after a certain time in cavity.
- **Variant 2.** Connection of metallic tip to the vent lines allows to process practically any internal cavity by nitrogen oxide. Metallic tip is connected air tightly to the vent line (supply tube) in the cavity. NO-containing gas flow is injected into the cavity, and the gas located in it escapes through another tube (discharge tube).
Destruction (dissection)

• Basic difference between the manipulator - destructor and the coagulator is the diameter of outlet channel (coagulator = 1,2 mm, destructor = 0,7 mm).
• This makes it possible to aggravate and to concentrate energy of air-plasma flow (APF) and, furthermore, to increase the speed of its expiration.
• In treatment of living biological tissues by concentrated and aggravated APF of destructor the carbon layer of necrosis is heated to the temperature of ~800°C and it begins to be decomposed into small particles - sublimates, and high-speed flow takes away the decay products of CoLN from the zone of action.
Technology of obtaining of antiseptic solution on the basis of hydrogen peroxide and nitrogen oxide

• For obtaining of the antiseptic solution on the basis of hydrogen peroxide and nitrogen oxide it is necessary to dissolve the specific quantity of NO in 3% solution of hydrogen peroxide.

• The low solubility of the nitrogen oxide in the aqueous solutions does not make it possible to prepare this solution without the application of technology of bubbling.

• The optimum time for preparation of solution depends on the volume of the prepared solution and is determined by the formula:

\[ t = 0.06 \cdot V \]

where the \( V \) is volume of the solution in ml, \( t \) - time of bubbling in min.