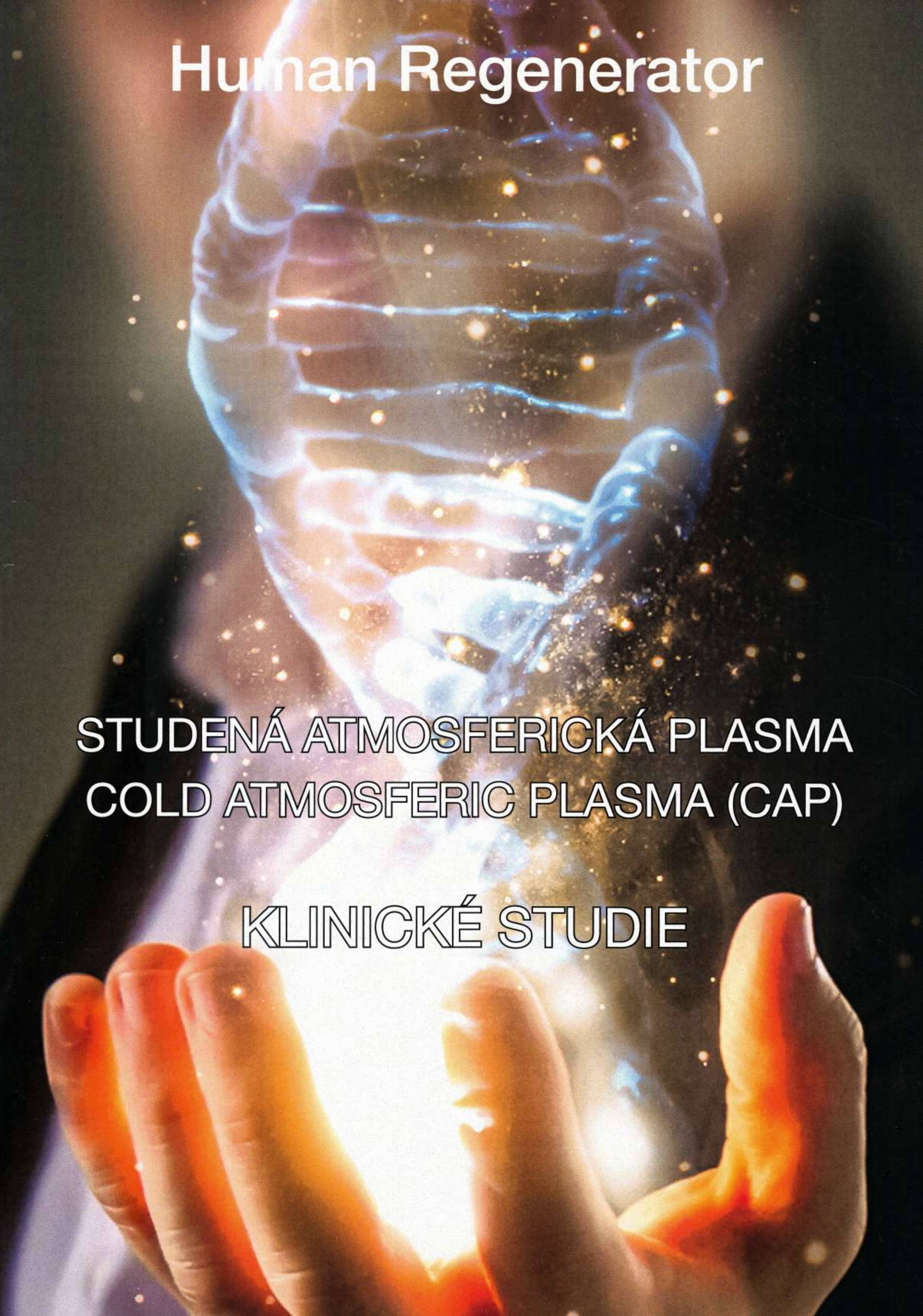
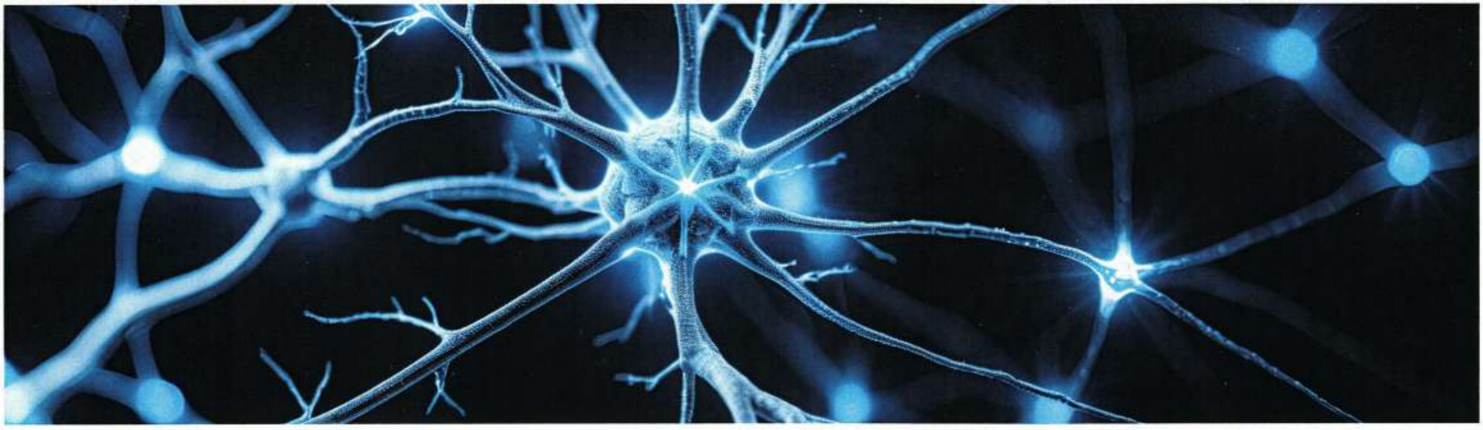
Human Regenerator



STUDENÁ ATMOSFERICKÁ PLASMA
COLD ATMOSFERIC PLASMA (CAP)

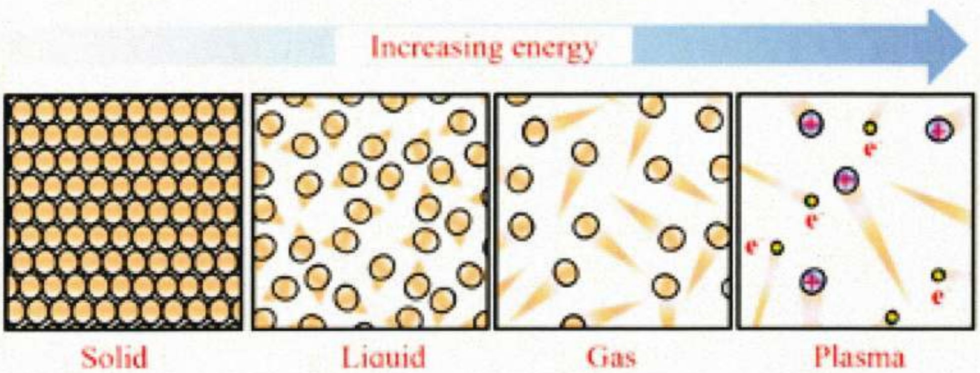
KLINICKÉ STUDIE

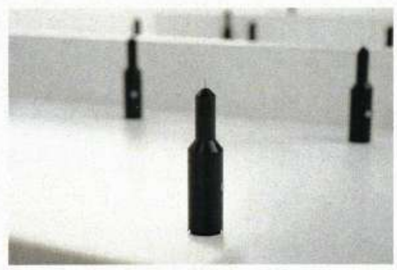


Co přesně je plazma a studená atmosférická plazma (CAP)

„Plazma“ je ionizovaný plyn – takzvané čtvrté skupenství hmoty (ostatní jsou pevné, kapalné a plynné) – a přidáním energie se zahřívá až na 100 000 stupňů, nebo i více.

Obecně platí, že jak se hmota mění z pevné látky na kapalnou, plynnou a na plazmu, teplota se zvyšuje. Teplota plazmatu je určena tepelnými pohyby elektronů a těžkých částic, jako jsou atomy a ionty. V případě běžného termálního plazmatu se všechny částice blíží tepelné rovnováze, když je hustota částic vysoká v důsledku intenzivních srážek mezi elektrony a těžkými částicemi. Teplota v takovém plazmatu je vysoká a přesahuje několik tisíc stupňů. Tyto plazmy se typicky používají za podmínek atmosférického tlaku. Na druhé straně, pokud k plazmovému výboji dochází rychle při atmosférickém tlaku, existuje další třída plazmatu, ve které jsou elektrony a těžké částice v tepelné nerovnováze.





V tomto případě je teplota těžkých částic mnohem nižší než teplota elektronů. Tato plazma se nazývá studená atmosférická plazma (CAP). Teplota těžkých částic CAP je mezi 25 °C a 45 °C. Takové plazmy lze použít v biomedicíně. V CAP se vytváří mnoho reaktivních látek, včetně radikálů na bázi kyslíku, radikálů na bázi dusíku a dalších složek. Tato komplikovaná chemie vede k řadě interakcí mezi CAP a biologickými systémy, včetně buněk.

Primární účinek regenerace buněk

Směs aniontů a elektronů nesená statickou energií zlepšuje zásobování buněk kyslíkem a stimuluje buněčný růst zdravých buněk. Stimuluje buněčné dělení a migraci buněk. Plazma má protizánětlivý účinek, zmírňuje bolest, aktivuje imunitní systém a celkově má vysoký regenerační účinek na buňky. Léčba pacientů chladnou atmosférickou plazmou je bezbolestná, Jedná se o šetrný proces bez dosud hlášených vedlejších účinků. Představte si, že každá buňka ve vašem těle je malým motorem, který potřebuje palivo k produkci energie. Toto palivo je známé jako ATP, neboli adenosintrifosfát, a je zásadní pro všechny životní funkce od myšlení až po pohyb.

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REVIEWS

Special Issue: Plasma Biotechnology

Spotlight

Cold Atmospheric Plasmas: A Novel and Promising Way to Treat Neurological Diseases

Zilan Xiong[1,*]

Cold atmospheric plasmas (CAPs) can enhance neural cell differentiation into neurons both *in vitro* and *in vivo*, which is of great interest for medical treatment of neurodegenerative diseases like Alzheimer's disease and traumatic injuries of the central nervous system. CAPs represent a promising method for future neurological disease therapy.

A neurological disease is any disease that affects the central, peripheral, and vegetative nervous system, including brain trauma, spinal injury, and Alzheimer's and Parkinson's diseases [1]. With the isolation of neural stem cells (NSCs) and the development of cloning technology, central nervous tissue (CNS) transplantation is considered to be one of the most promising therapies for neurodegenerative and neurotraumatic diseases. However, the methods for preparing the desired nerve cells are limited by the drawbacks of the existing methods, which include chemicals, Chinese medicine, hormones, and a few other treatments. These treatments may cause chemical toxicity, form glial scars after transplantation, and suffer from insufficient selectivity of specific cell type differentiation. Recently, a novel and promising method using cold atmospheric plasmas (CAPs) has been proposed to overcome these disadvantages.

Plasma is the fourth state of matter, following solid, liquid, and gas. With the development of CAPs in the past two decades, plasma medicine as a new research field has attracted significant attention worldwide [2]. Highly reactive species (reactive oxygen and nitrogen species), electrical fields, UV radiation, and charged particles generated by plasma enable this mixture to be applied in cancer therapy, skin wound healing, root canal treatment, and other biological applications, even including cell proliferation and differentiation [3]. In a recent study, Jang and colleagues [4] showed that a CAP based on a dielectric barrier discharge (DBD; an electrical discharge method used to create plasma between two electrodes separated by an insulating dielectric barrier) successfully induced neural differentiation both *in vitro* and in zebrafish, and the results showed promise for the future treatment of neurological disease (Figure 1). They also investigated the physicochemical and biological connection between the CAP cascade and the TrK/Ras/ERK signaling pathway that causes neural differentiation.

This study used mouse neuroblastoma Neuro 2A (N2a) cells for the *in vitro* investigation and a zebrafish (*Danio rerio*) transgenic embryo Tg(Huc:GFP) for the *in vivo* investigation. The treatment was conducted with a DBD plasma, using a mixture of N_2 and O_2 as a working gas, with input power ~1 W. The CAP-treated Neuro 2A cells increased in size to more than four times that of untreated cells, exhibiting a maximum neurite length of around 70 μm and average of 46.3 ± 1.5 μm after 24 hours under optical treatment. The neural progenitor cells terminally differentiated into mature neurons, specifically including catecholaminergic dopaminergic (DA) neurons, which are the main source of dopamine in the CNS and play an important role in the control of multiple brain functions. Furthermore, the loss of DA neurons is strongly related to Parkinson's disease.

In vivo 1-minute CAP treatment of transgenic zebrafish embryos expressing GFP only in postmitotic mature neurons showed that the *in vitro* results are also physiologically interesting. GFP started to increase in intensity after a 6-hour incubation and maintained intensity for up to 33 hours. GFP^+ mature neurons in the developing zebrafish were clearly visible in the CNS within 6 hours after 36-hours postfertilization (hpf) embryos were exposed to CAP. In later-stage embryos (60 hpf), a 1.17-fold increase in GFP^+ mature neurons was observed in the CAP-treated group.

In terms of the biological mechanism of the plasma treatment, the authors found that NO served as an upstream extracellular messenger, while mitochondrial $\cdot O_2$ and cytosolic H_2O_2 cooperatively acted

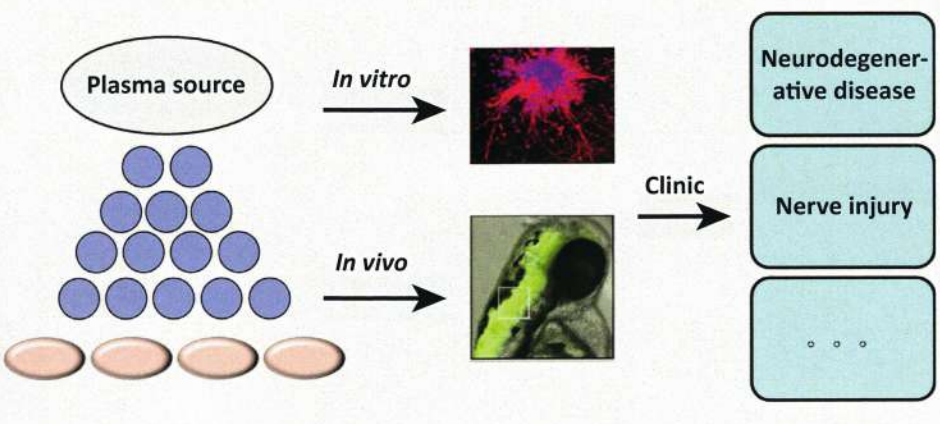

Figure 1. Promising Cold Atmospheric Plasma (CAP) Treatment for Neurological Disease. Both nerve cells and the *in vivo* nervous system treated by CAPs showed accelerated differentiation and selective differentiation into neurons, both of which may have great potential for future clinical treatment of neurological disease.

Klinické studie - Studená atmosferická plazma
COLD ATMOSPHERIC PLASMA (CAP)

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The anti-glioblastoma effect of cold atmospheric plasma treatment: physical pathway v.s. chemical pathway

Dayun Yan[1,4]✉, Qihui Wang[1,4], Alisa Malyavko[2,4], Denis B. Zolotukhin[1], Manish Adhikari[1], Jonathan H. Sherman[3] & Michael Keidar[1]✉

Cold atmospheric plasma (CAP), a near room temperature ionized gas, has shown potential application in many branches of medicine, particularly in cancer treatment. In previous studies, the biological effect of CAP on cancer cells and other mammalian cells has been based solely on the chemical factors in CAP, particularly the reactive species. Therefore, plasma medicine has been regarded as a reactive species-based medicine, and the physical factors in CAP such as the thermal effect, ultraviolet irradiation, and electromagnetic effect have been regarded as ignorable factors. In this study, we investigated the effect of a physical CAP treatment on glioblastoma cells. For the first time, we demonstrated that the physical factors in CAP could reinstate the positive selectivity on CAP-treated astrocytes. The positive selectivity was a result of necrosis, a new cell death in glioblastoma cells characterized by the leak of bulk water from the cell membrane. The physically-based CAP treatment overcomed a large limitation of the traditional chemically based CAP treatment, which had complete dependence on the sensitivity of cells to reactive species. The physically-based CAP treatment is a potential non-invasive anti-tumor tool, which may have wide application for tumors located in deeper tissues.

Glioblastoma multiforme (GBM) is characterized as a highly invasive, aggressive brain tumor[1]. Individuals with GBM face a poor prognosis, with few surviving past the 2-year mark[1,2]. A combination of chemotherapy, surgical resection, and radiotherapy is the gold standard for glioblastoma therapy, however, each component has its own drawbacks[1,3,4]. Glioblastoma tumors generally originate deep in the brain and a new treatment option, particularly a non-invasive method, is needed to enhance the anti-cancer efficacy and decrease damage to normal tissues.

CAP is a cocktail containing different reactive oxygen species (ROS), reactive nitrogen species (RNS), other charged particles, neutral particles, and electrons as well as physical factors, such as thermal effect, ultraviolet (UV), and electromagnetic (EM) waves[5–7]. CAP has wide application in many areas, ranging from plasma chemistry, surface modification, decomposition of gaseous pollutants, medical sterilization, and microbial decontamination[8–12]. CAP also shows a wide application in cancer treatment[13–16]. CAP treatment has demonstrated strong and selective anti-cancer capacity in many cancer cell lines, including breast cancer, colorectal cancer, cervical cancer, skin cancer, and brain cancer[15]. CAP also effectively inhibits the growth of subcutaneous xenograft tumors as well as melanoma by a transdermal treatment above the skin of the tumor site[17]. In addition, some recent clinical trials have started to show the promising anti-tumor effect of CAP[18,19].

To date, all reported anti-cancer effects of CAP treatment, both in vitro and in vivo have generally been regarded as the cellular responses to the chemical factors, particularly the reactive species[20–22]. Experiments using CAP-activated medium further support this conclusion[23–27]. H_2O_2 has been regarded as a key player resulting in plasma medicine being referred to as H_2O_2-medicine, but is also denoted as NO_2^-—medicine and other reactive species-based medicine in some cases[27–29].

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Review

Cold Atmospheric Plasma: A Powerful Tool for Modern Medicine

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Abstract: Cold atmospheric plasma use in clinical studies is mainly limited to the treatment of chronic wounds, but its application in a wide range of medical fields is now the goal of many analyses. It is therefore likely that its application spectrum will be expanded in the future. Cold atmospheric plasma has been shown to reduce microbial load without any known significant negative effects on healthy tissues, and this should enhance its possible application to any microbial infection site. It has also been shown to have anti-tumour effects. In addition, it acts proliferatively on stem cells and other cultivated cells, and the highly increased nitric oxide levels have a very important effect on this proliferation. Cold atmospheric plasma use may also have a beneficial effect on immunotherapy in cancer patients. Finally, it is possible that the use of plasma devices will not remain limited to surface structures, because current endeavours to develop sufficiently miniature microplasma devices could very likely lead to its application in subcutaneous and internal structures. This study summarises the available literature on cold plasma action mechanisms and analyses of its current in vivo and in vitro use, primarily in the fields of regenerative and dental medicine and oncology.

Keywords: cold atmospheric plasma; wound healing; oncology; regenerative medicine; plasma

1. Introduction

William Crookes established the fundamentals of plasma science in 1879 by experimentally ionizing gas in an electrical discharge tube by the application of high voltage through a voltage coil. The ionised gas was named radiant matter. The current plasma term was then initiated almost fifty years later in 1927 by Irvin Langmuir [1]. Plasma has since been applied in many spheres over the past few decades, including medicine [2–4]. Plasma is often defined as an ionised gas produced by disintegration of polyatomic gas molecules or the removal of electrons from monatomic gas shells [5]. However, not every ionised gas that contains charged particles can be considered plasma because of the following strict definition [5–7]: (1) Plasma must have macromolecular neutrality (quasi-neutrality). In the absence of external disturbances in plasma, the net resulting electric charge is zero. Therefore, plasma contains (almost) the same density of positively and negatively charged particles; (2) Plasma must have Debye shielding, where the charged particles in plasma are arranged to effectively shield electrostatic fields within the distance of a Debye length. This is defined as a measure of the distance over which the influence of the electric field of an individual charged particle is felt by other charged particles inside the plasma; (3) Plasma frequency. If plasma loses its equilibrium conditions, the resulting internal space charge-fields promote collective particle motion that tends to restore the original charge neutrality. This motion is characterised by the natural oscillation frequency referred to as plasma frequency. Plasma can therefore be defined as "a quasineutral gas containing many interacting free electrons and ionised atoms and molecules which have collective behavior caused by

Jedinečná technologie

Human Regenerator je celosvětově unikátní zařízení, které stojí na špici využití studené atmosférické plazmy pro podporu zdraví a vitalitu. Naše CAP+ technologie využívá ionizovaný plyn, čímž vytváří elektrostatické pole, které obklopuje uživatele a indukčně přenáší anionty a elektrony přímo do buněk. Tento proces nejenže stimuluje regeneraci a růst zdravých buněk, ale také neutralizuje volné radikály, čímž přispívá k redukci oxidačního stresu a podporuje dlouhověkost.

Human Regenerator

Human Regenerator představuje revoluční přístup v boji proti stárnutí a degeneraci buněk. Využívá unikátní technologii studené atmosférické plazmy (CAP), která je již desetiletí úspěšně používána v dermatologii pro regeneraci kožních buněk a nyní přináší své benefity do oblasti celkové revitalizace těla. Tato technologie podporuje regeneraci buněk, zvyšuje vitalitu a efektivně bojuje proti oxidačnímu stresu, který je klíčovým faktorem stárnutí a degenerace buněk.

www.HumanRegenerator.info

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