Non-Thermal Plasma for Acne Treatment and Aesthetic Skin Improvement

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ABSTRACT: Non-thermal plasma/cold atmospheric plasma (NTP/CAP) technology, which can generate low-temperature plasma in normal atmosphere, has been recognized widely as a new emerging tool with potential applications in life science and biomedical fields. During the last 10 years, many reports have published regarding NTP, confirming its safety and efficacy in health care and various medical applications. The promising future of NTP technology has aroused our interest to study a novel NTP device in detail. The device generates dielectric barrier discharge (DBD) with direct contact or noncontact at a few-millimeter gap between electrode surface and skin. NTP is generated by ionizing the surrounding air on the electrode surface, discharging directly to the targeted tissue.

We have conducted clinical trials of this device called the "BIOPLASMA Cell Modulator" (developed by Photo Bio Care, Thailand) as a new application for acne and aesthetic skin improvement.

KEY WORDS: Nonthermal plasma/cold atmospheric plasma, new Bioplasma source, direct DBD, aesthetic skin improvement, acne vulgaris.

I. INTRODUCTION

Many reports and reviews in recent publications have confirmed the safety and efficacy of nonthermal plasma/cold atmospheric plasma (NTP/CAP) technology in biomedical applications.[1,2] Details of this new technology have been clearly reviewed by Alexander Fridman in *Applied Plasma Medicine*.[3] This technology offers a new method of noninvasive, selective targeting therapy to biological tissue at the molecular level. This method has great potential for new medical applications in bacterial eradication, dermatology/aesthetic skin, chronic wound care, stimulation of tissue regeneration, and a new approach to cancer therapy.[4–10]

Fridman et al. have reported very high efficacy of direct plasma compared with indirect Plasma on bacterial eradication.[11] Danil Dobbrynin and a team of researchers from Drexel Plasma Institute[12–14] have identified and summarized the details of physical and biological mechanisms of nonthermal plasma and biological tissue interaction

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in their reports. Various plasma parameters and doses have been established. These studies have guided the development of a new bioplasma source for medical and therapeutic applications.

Previous studies on direct DBD plasma have shown that, at a very low dose (<1 J/cm^2), inactivation and/or sterilization occurs in a few seconds at a high power setting (0.8W/cm^2) or 6–10 seconds for a low power setting (0.4W/cm^2) without side effects to normal tissue. Sterilization is achieved at doses <2.5 J/cm^2. At a low setting, tissue can tolerate energy up to 5 minutes at 120 J/cm^2 without damage.

At an intermediate dose (2–6 J/cm^2), reparable DNA damage of normal cell occurs in 24 hours, including release of cell growth factors, stimulation of wound healing, and tissue regeneration. Increases in proliferation and migration, as well as controlled development of apoptosis in cancer cells has also been observed. At this dosage level, a sublethal effect occurs, with 10–15% apoptosis of normal cells. Cancer cells are is more sensitive, and their DNA becomes irreparably damaged at this dosage.

At higher doses (>7 J/cm^2), normal cell death occurs with 60–70% apoptosis. Tumor or abnormal cells become more sensitive and are irreversibly destroyed.

With very high doses (>10 J/cm^2), cell necrosis occurs at a high power density (0.31W/cm^2) for 40 seconds.

Notably, tissue moisture (not wet) improves efficacy of direct plasma bacterial eradication at much lower doses than in a dry environment (1 J/cm^2 to 16 J/cm^2). Direct plasma bacterial eradication in moist tissue occurs at 1 J/cm^2; with indirect plasma, bacterial eradication occurs at approximately 7 J/cm^2.

In addition to such discoveries, NTP can also induce platelet activation and blood coagulation, and can stimulate cell immune response and tissue regeneration. Plasma induces chemical changes on cellular lipid membrane properties by lipid peroxidation. Plasma induces reversible DNA damage, temporarily enhances skin permeability, and enhances macromolecule penetration. It activates the cell surface for increased adhesion of hydrophilic substances and changes the properties of the skin surface.

Discoveries regarding low-temperature atmospheric plasma tissue interactions are opening avenues for new investigation of its potential application in health and many medical fields. We have investigated the potential benefit of this new bioplasma source for treatment of common skin problems, such as acne vulgaris and its complications, by testing such a device in our clinical trial.

II. ACNE VULGARIS: HEALTH CONCERN AND PATHOGENESIS

Acne vulgaris is a common skin condition in adolescents. The prevalence of acne is thought to vary among ethnic groups and countries. Bhate et al.[15] reported that moderate-to-severe acne affects approximately 20% of young people in the United States. Acne is one of the most common skin problems among young people. It is estimated that 30–40 million people in the USA suffer from acne. Acne persists in ~64% of those

in their 20s and in ~43% of those in their 30s. In the United States, the cost of acne treatment is >$3 billion per year in terms of treatment and loss of productivity.[15]

A study was conducted on 17,345 subjects in six cities of China, a country with a population >1 billion. The prevalence of acne was ~46.8%, mostly in the 19-year-old age group. Of these acne-affected cases, 68.4% had mild acne; 26.0% had moderate acne, and 5.6% had severe acne.[16]

III. PATHOGENESIS OF ACNE

Acne is a chronic inflammatory disease of the pilosebaceous unit, mostly affecting the sebaceous follicles. Four main pathogenesis mechanisms are increased sebum productions, abnormal keratin adhesion with follicular hyperkeratinization, abnormal *Propionibacterium acne* (*P. acne*) colonization, and the use of products that induce inflammation.[17]

Early acne arises from abnormal keratinocyte differentiation, and increased sebum leads to increased adhesion and formation of keratin plugs, resulting in microcomedone formations. These increase with the *P. acne* bacteria growth, leading to subsequent formation of acute symptomatic suppurative acne. The progression of acne can be characterized as follows:

- Microcomedone formation is derived from increase keratin adhesion. Sebaceous gland orifice blockage enhances *P. acne* multiplication.
- Sebum productions increase.
- *P. acne* colonization increases abnormally.
- Inflammation and immune reactions are triggered by *P. acne* multiplication with release of toxic waste.

Treatment includes various topical or systemic medications. Antibiotic resistance is a major problem of acne infection. Acne treatment with surgery using different types of technology has proven to be an alternative to medications. These treatments include electroradiosurgery, chemical and mechanical peeling, intense pulsed light (IPL), lasers, light, and photodynamic therapy (PDT) and have shown variable success rates.[18] No other nonthermal plasma technology trial for acne treatment has been reported.

IV. NEW NON-THERMAL PLASMA SOURCE CHARACTERISTICS

There are many reports of different types of nonthermal atmospheric pressure plasma sources in the literature.[19–22] However, dielectric barrier discharge (DBD) atmospheric pressure, room air plasma[23] has great potential for acne and skin surface improvement.

In his report, Fridman, G[11] has concluded that direct plasma is much more potent in bacterial eradication than indirect type. However, a direct plasma source using the DBD technique can work only at very small millimiters distance, the gap between the powered electrode and skin as second electrode. The problem with using

a DBD electrode on a nonuniform skin surface is that the geometry and variation of skin electrical properties make it difficult to apply the flat planar floating electrode clinically. It is difficult to maintain and fix small-millimieter gap distances to create a uniform and stable homogeneous plasma beam without uncontrollable streamer discharge.

We have conducted clinical trials using a novel device called "Bioplasma Cell Modulation" (developed by Photo Bio Care, Thailand).[24] The device can create a low-temperature, sustained, homogeneous microfilament beam that emits a round shape from the specially designed dielectric electrode when it comes in direct contact with a dry or mildly moist skin surface. The round shape of the dielectric electrode tip can be varied from a few millimieters up to 25 mm. The electrode used in this study is 18 mm in diameter. Such geometry creates regular, small gap distances once the electrode is mildly pressed to the skin surface and is moved constantly (Fig. 1).

The power generator drives high-frequency sinusoidal waves in the range of 15–20 KHz. Peak-to-peak voltage is ~6–7 kV, delivered as pulsing and adjustable from 10 to 110 Hz. The maximum input from a normal household socket is 40W. Power intensity is adjustable from 1 to 10. The plasma power output is in the range of 0.2–1 Watts, adjustable according to intensity and repetitive pulse setting. The automatic preset is at level 05 intensity at 50 Hz, with average power output of 0.62 Watts. The system is set at a duration limit of 20 minutes per treatment.

The system has a small compact movable platform using room air as the discharge gas medium. Uniform, homogeneous microplasma filaments are generated by ionizing surrounding air on electrode surface and discharging it directly to target the skin tissue with direct skin contact (Fig. 2).

The outcome of this plasma treatment of the skin surface is that a superficial layer of keratins and various attachments is removed in a smooth, nonablative, and painless manner while the electrode surface rolls across and gently rubs the dry skin surface. Such maneuver creates superficial skin peeling by plasma cellular detachment. The skin debris can be wiped off totally with a clean, alcohol-soaked swab (Fig. 3). After this procedure, the treated skin usually becomes clean and smooth, showing mild whitening and a reddish pink color. There is a mild-to-moderate skin tightening effect, with an improvement in line folds; some degree of facial contour change can also be seen after the treatment. The procedure is easy to perform and delivers a warm-to-mild heat sensation. Immediate skin texture improvement is usually noted. Subsequent changes are also observable after repeated treatment (Fig. 4).

The powered electrode also can be applied without direct contact with skin, with a floating gap of 1–3 mm. A dense and strong streamer filament of 2–6-mm beam size discharges to the skin surface, creating a very high power density. This technique is used to coagulate superficial skin lesions, such as pustular acne, with few seconds of repeated strokes on the lesion (Fig. 5).

Plasma skin interaction has shown potential benefits in aesthetic dermatology in many studies.[25] With the new BioPlasma source device, an improvement in associated acne conditions occurred, along with aesthetic improvement in skin texture (Fig. 6).[26]

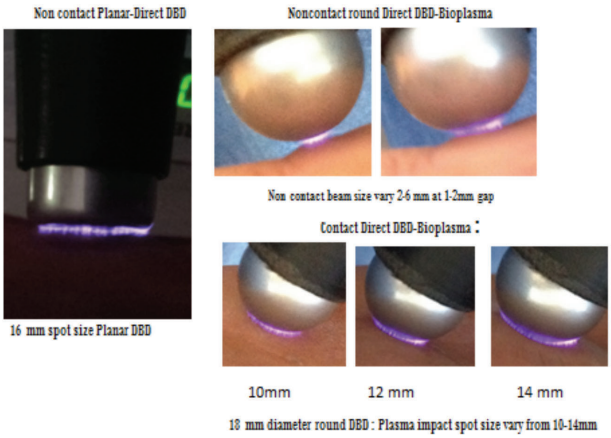

FIG. 1: Direct DBD plasma in different shapes: planar and round. Noncontact or contact application. Note microfilaments uniformity for planar electrode on flat surface at the few-millimeter gap. Round shape in noncontact mode beam size varies with gap distance. Contact mode impact beam varies with pressure apply to skin

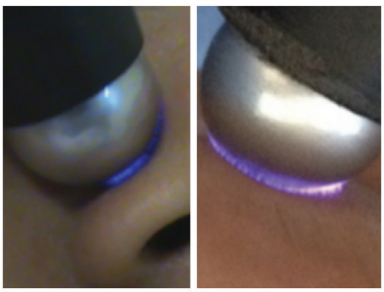

FIG. 2: Microfilament discharge patterns Rx and after Alcohol wipe out

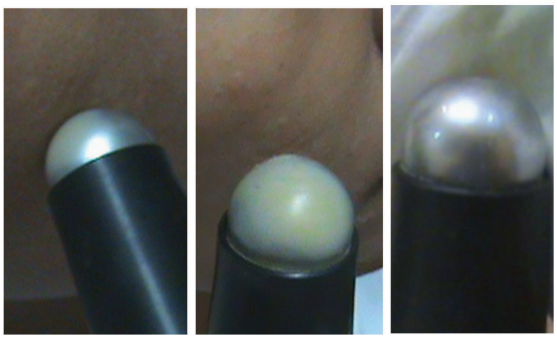

FIG. 3: Exfoliated skin debris post

These results led us to conduct a clinical control trial of the novel Direct DBD air plasma contact skin-type electrode for acne treatment.

V. CLINICAL OUTCOME OF ACNE STUDY WITH NEW BIOPLASMA SOURCE

The clinical evidence from this and other studies supporting the use of the BioPlasma device for acne therapy is as follows:

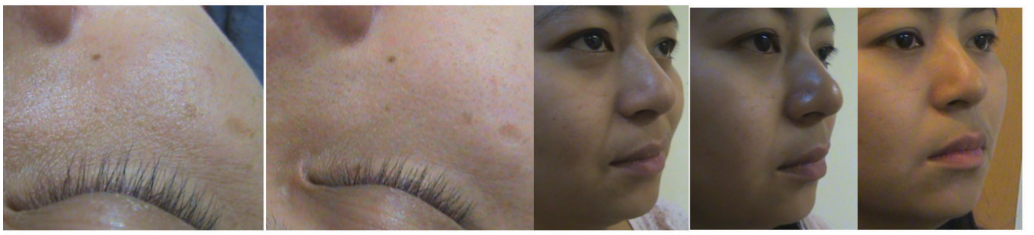

FIG. 4: Skin texture changes observable immediately after treatment: before treatment, 1 week after first treatment, and 1 day after second treatment

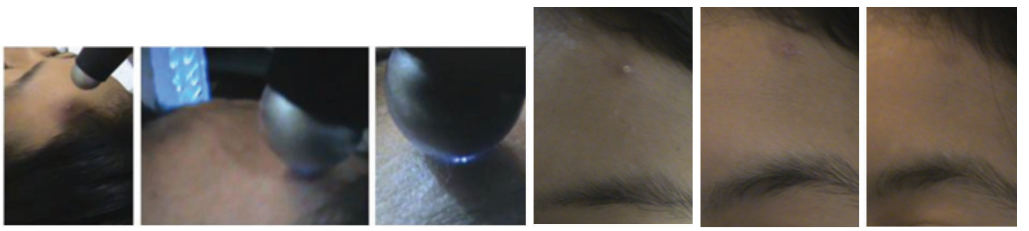

FIG. 5: Application floats near contact with the acne lesion for a few seconds a few times: before treatment, 1 day after treatment, and 7 days after treatment

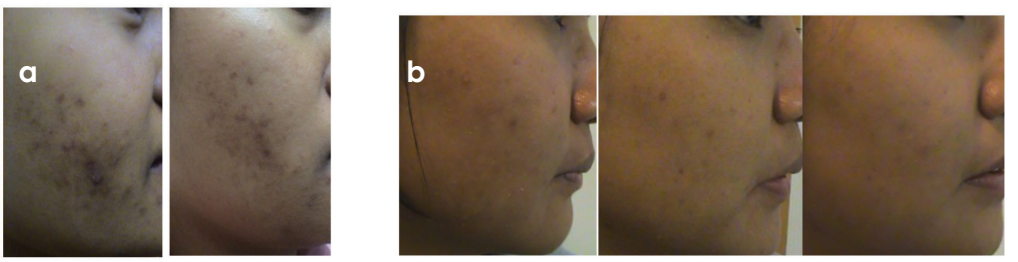

FIG. 6: (a) Before and post 2Rx, 6 week follow-up (b): before 2-week post 1Rx, 4 weeks post 2Rx

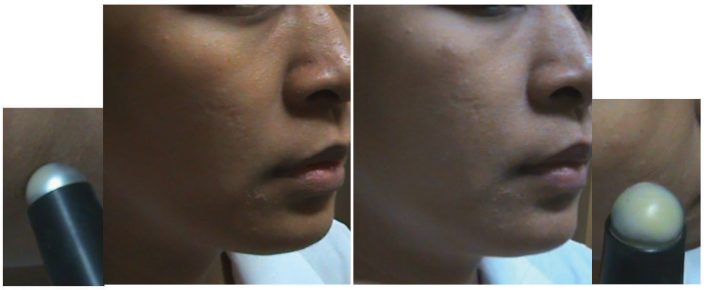

FIG. 7: Before and after bioplasma skin peeling. Note exfoliated skin on electrode surface

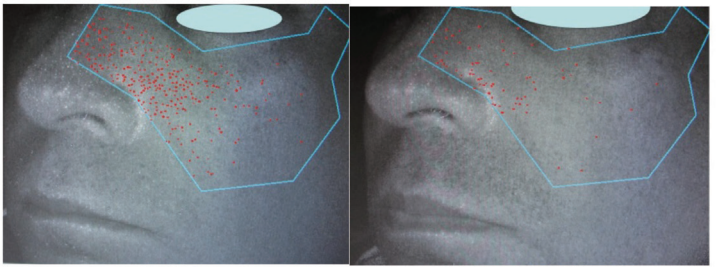

FIG. 8: Porphyrin count with Visioscan UV camera (for *P. acne*). Reduction from 270 to 70 (75%) after 1 treatment at 1 week follow-up. Courtesy of Prof. Niwat Polnikorn, MD

BioPlasma treatment helps exfoliate upper keratin and cleans out skin contamination non-invasively (Fig. 7). This proves the ability of BioPlasma to remove keratin plugs and the dead keratin layer gently without any skin damage, through noninvasive plasma skin peeling.

BioPlasma treatment helps reduce the amount of *P. acne* colonization. Prof. Niwat Polnikorn demonstrated a 75% reduction of fluorescence (which represents *P. acne* measured by a Visioscan UV camera) 1 week after 1 BioPlasma treatment (Fig. 8).

Dr. Wasinee et al. from MFU (Mae Fah Luang Unversity,Thailand.) conducted a study on the efficacy of a DBD plasma device for adjunctive therapy of acne vulgaris with 31 volunteers with acne who were treated once per week for 6 weeks. Significant improvement of ~75% in the acne count score evaluation was reported. The effect was more pronounced for inflammatory acne lesions. Minor complaints were reported in ~35% of cases, such as dry skin and skin debris retention. The global satisfaction score was 100%, and 75% of cases were markedly impressed with the treatment. She concluded that this new BioPlasma device appears to have a role in the management of acne and may be beneficial for the treatment of mild-to-moderate acne.

Another study was conducted by Dr. Treenuch et al. from MFU on the effectiveness of a nonthermal plasma device for reducing sebum production on oily facial skin.

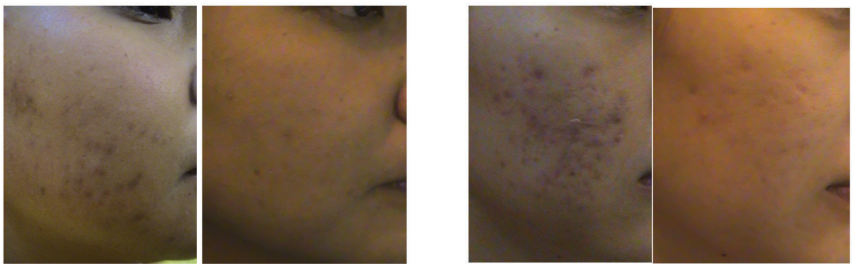

FIG. 9: 20070516 pre 20090429 2years Follow up 20100930 pre 20121227 2years Follow up post4Rx. Pictures of long term follow up of cases treated with Bioplasma: Direct DBD atmospheric Plasma technique

In this study, half of the face of each of 30 volunteers was treated with BioPlasma once per week for 4 weeks. Significant sebum reduction in up to 80% of cases was measured by sebumeter. The oil reduction effect lasted 4 weeks after the treatment was stopped.

VI. CONCLUSION

From these findings, it can be concluded that the new BioPlasma source, which provides integrated solutions to acne remedy by solving all four causative factors, can offer a new choice for acne treatment. Additionally, BioPlasma treatment helps regenerate new and healthy skin as an additional benefit to the patient. Thus, BioPlasma treatment offers a new method for acne therapy with physical NTP. It is a highly effective method that is simple and involves minimal cost and very minor side effects. effects.Long term follow up over 2 years (Fig 9) reveals progressive improvement with healthier skin condition.

Our results imply that this device can be used to combat acne, which is one of the most common skin problems affecting large populations worldwide. Once implemented, this CAp treatment will help reduce the global economic burden of acne. We hope that this report will help stimulate interest and support to bring NTP technology into widespread practice in medicine and health care.

However, further detailed studies are needed to completely elucidate the mechanism of action to standardize a treatment protocol and parameters that can further improve treatment outcomes.

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