DERMA

plasma care®

Cold plasma therapy

CAP for treatment of bacterial/fungal skin infections

SAVE AND RELIABLE

SUITABLE FOR PATIENTS WITH PACEMAKERS

PORTABLE AND EASY-TO-USE

plasma derma care® –
new chances in dermatology

The plasma derma care® is a mobile medical device for the treatment of acute and chronic bacterial or fungal skin diseases or certain skin dysplasias/ neoplasias such as actinic keratosis.

This portable device generates cold atmospheric plasma (CAP) by supplying high energy to the ambient air. CAP effectively inactivates bacteria (independent of type and level of antibiotic resistance) and human pathogenic fungi.

Furthermore, CAP has other positive effects that promote healing of dermatological diseases – e.g. an antipruritic (anti-itch)[1] effect.
By stimulating the immune system locally, CAP is potentially effective for treatment of precancerous skin, too.[2,3]

Most dermatological diseases are caused by pathogens such as bacteria and fungi or are associated with those. Patients often suffer from a high level of psychological strain. Apart from this, various pathogens can also lead to a more severe course of disease. The use of **plasma derma care®** device provides a completely new treatment approach for dermatologists offering effective opportunities without side effects.

▲ Fig. shows female patient with severe atopic dermatitis on both hands and wrists.

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Our vision of cold plasma in medicine

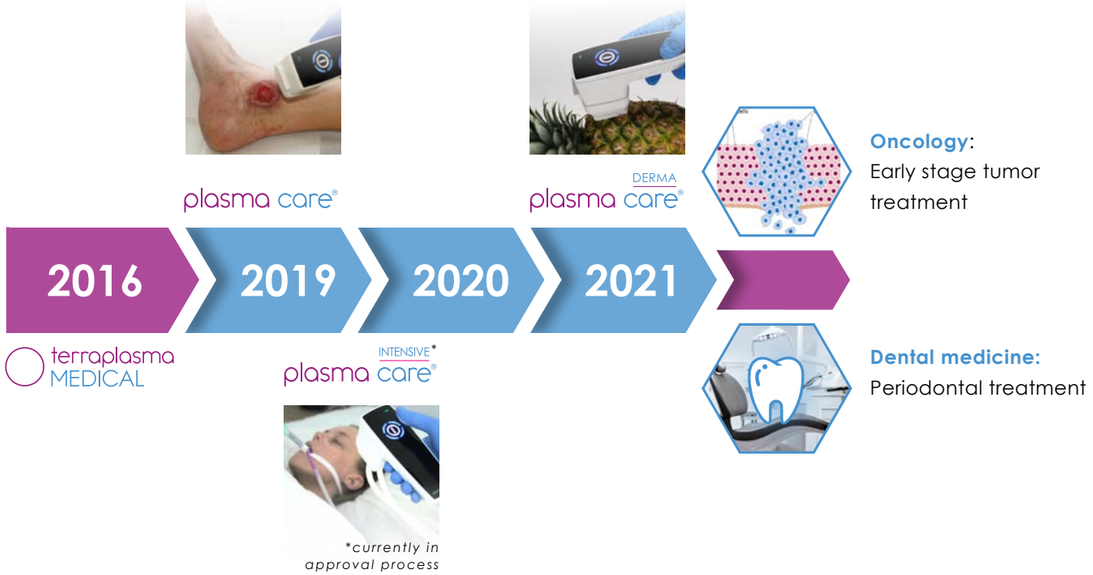
terraplasma medical GmbH looks back on many years of experience in the development of plasma technologies and their application in various fields.

As a spin-off of Max Planck Institute for Extraterrestrial Physics headed by Prof. Dr. Dr. Gregor Morfill and Dr. Julia Zimmermann, **terraplasma GmbH** was founded in 2011.
Terraplasma GmbH still focuses on the development of various plasma technologies for applications in medical technology, hygiene and air pollution control.
In 2016, **terraplasma medical GmbH** was founded as an independent subsidiary which since has developed and researched medical devices based on plasma technology.
The **plasma derma care®** uses cold atmospheric plasma designed by terraplasma medical GmbH and already applied in various medical devices to inactivate microorganisms (bacteria incl. MRE and human pathogenic fungi).
For years, plasma technology has already been established in wound treatment through the use of **plasma care®**.

Apart from this, another medical device – the **plasma intensive care®** – was pre-launched at the beginning of 2021 for treatment of ventilated COVID-19 patients.

The main goal of terraplasma medical GmbH is to convince the medical world of the innovative and promising plasma technology and to support patients in activating the body's own healing processes through a modern therapeutic approach - and this against the background of increasing antibiotic resistances and allergies.

DERMA plasma care®



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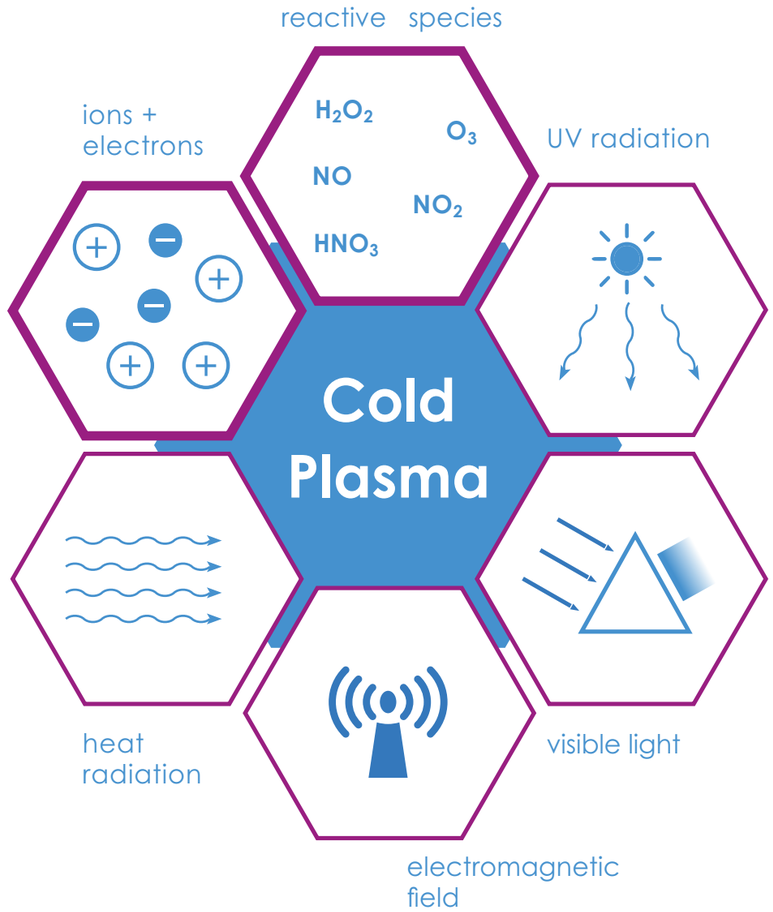
Cold plasma technology

The **plasma derma care®** provides an effective therapy option for the treatment of various skin diseases or against their progression.
It works on the basis of cold plasma technology, which has already been used successfully for the treatment of chronic and acute wounds.

Plasma can be explained as a ionized gas – the so called fourth state of matter after solids, liquids and gases. In general it is generated when gas is subjected to further energy (i.e. heat). Plasma which occurs in nature has normally very high temperatures (up to 100.000 °C). The sun – a huge plasma ball – and lightening – short electrical discharges – are some examples of natural plasmas.

▲ *Figure 1: Plasma is a 4th aggregate state*



▲ *Figure 2: Components of the „plasma cocktail“*

DERMA plasma care®

The **plasma derma care®** generates a locally ionized cold atmospheric plasma by means of controlled microdischarges from the ambient air.
The gas molecules are only partially ionized at atmospheric pressure, that means i.e. only one particle of 1* 109 particles is ionized. The advantage of these cold atmospheric plasmas is that, on the one hand, they are „cold“, which means they are at body temperature, and on the other hand they could be generated at atmospheric pressure on earth.

When microplasma is generated, a chemical non-equilibrium process is initiated resulting in a reactive „plasma cocktail“ which consists of electrons, ions, excited atoms and molecules, reactive oxygen and nitrogen species (such as O_3, NO, NO_2, etc.) as well as low levels of UV radiation (cf. fig.).

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Effects of cold plasma

Cold atmospheric plasma (CAP) does not cause any unspecific cell damage due to its low temperature and therefore is generally suitable for medical application.

The active components (reactive species) generated by cold atmospheric plasma can interact with cells in various ways.
The effects are physical (e. g. recombination or de-excitation of excited molecules/atoms at the surface) as well as chemical (e. g. hydrogen denaturation by reactions of hydroxyl radicals).

Plasma is known to have a strong antimicrobial and antiviral effect while preserving human tissues and cells.
In bacteria (prokaryotic cells) – or more precisely their cellular macro-molecules (including DNA) - a direct destruction takes place.
This effect **also applies for bacteria with antibiotic resistance**.[4,5,6] Furthermore, an antiviral effect of the reactive oxygen species produced by cold atmospheric plasma has been observed.[7]
This is presumably based on a modification of viral proteins leading to the inactivation of the viruses.

In eukaryotic cells, such as human cells, DNA is protected by nucleus and its membrane as well as cytological repair mechanisms. In addition, those cells are protected within cell compounds. This means that there is no risk of cell damage.

Quite the opposite, **in human cells a local immune response is triggered and cell growth and division are stimulated**, thus promoting the regeneration of skin or mucous membrane.[8,9,10]
This effect is locally limited to the uppermost cell layer. Among other reasons, this is due to a very short half-life of the reactive species, which will have already completely reacted by interacting with the upper cells or surrounding cell milieu.[11,12]

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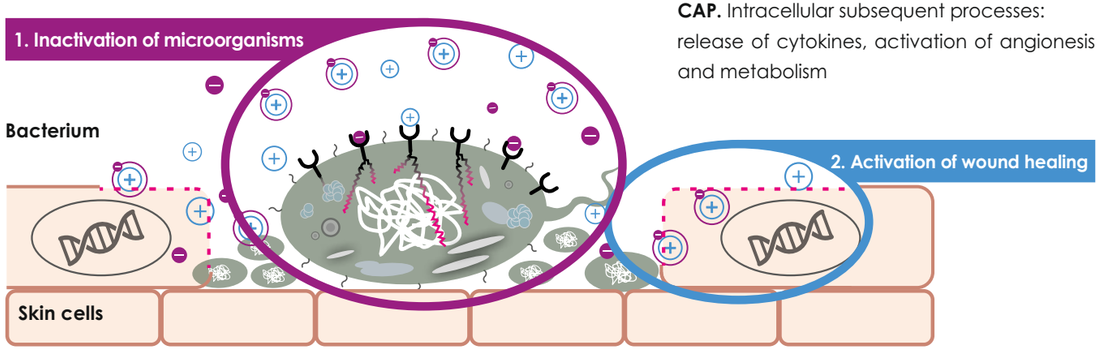
Cold plasma

CAP interacts with microorganisms, inactivates the cell and prevents cell proliferation destroying the DNA

Cell separation in healthy cells is **stimulated by CAP.** Intracellular subsequent processes: release of cytokines, activation of angionesis and metabolism



▲ *Figure 3: Biological plasma effect*

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Recent study results confirm high effectiveness

Preclinical evaluations prove the antimicrobial and antifungal effectiveness of the **plasma derma care®** (see table).

Most of the tested microorganisms are resident on our skin and thus are predestined to cause certain infections. The development of perioral dermatitis, for example, is mostly triggered by micro-organisms.[13,14]
Acne, on the other hand, is mainly caused by propionibacterium acnes.[15] Staphylococcus aureus is a highly resistant bacterial strain that causes nosocomial infections[16] and is often identifiable in bacterial superinfections in atopic dermatitis as well as many other skin diseases.[17]

On agar, 99.999 % of tested bacteria and of the yeast C. albicans were killed within 60 seconds.
Moreover, the **plasma derma care® was effective upon application to biofilms** of E. faecalis (99.9 % reduction within 1 minute). Under more life-like conditions in ex vivo models of pig skin and human skin, 69 to 83 % of bacteria were killed within the same period.

Apart from the described studies of effectiveness, **plasma derma care®** has also been thoroughly tested with regard to its safe use and the occurrence of side effects. However, plasma treatments of up to 3 minutes had no impact on vitality, viability or migration behavior of primary fibroblasts and keratinocytes. Nor did "normal" or "sensitive" skin from healthy donor biopsies display any histological or pro-apoptotic changes. Mutagenicity studies (HGPRT test using V79 cells) provided no evidence of any genotoxic potential of CAP, too.
The results of these preclinical studies by **terraplasma group** also correspond to the study results of recent publications.

	pathogenes	achieved log reduction after 1 min plasma treatment	associated skin diseases
bacteria	Fusobacterium Nucleatum	4,4	perioral dermatitis
	s. aureus / MRSA	5,6 / 6,0	acne, neurodermatitis
	p. acnes	.....	acne
	p. aeruginosa	5,9	acne
	s. agalactiae	6,5	Various superficial skin infections, wound infections, bacterial superinfections
	s. constellatus	5,8	
	e. coli	5,8	
	s. constellatus	5,7	
fungi	c.albicans	4,6	candidiasis
	t. rubrum	.....	dermatophytoses
	m. furfur	.....	tinea versicolor

▲ *Table 1: Investigated human pathogens with achieved log reduction*

Acne and actinic keratosis have already successfully been treated with cold atmospheric plasma.[18,19]
Cold atmospheric plasma was found to be an extraordinary effective treatment for patients with actinic keratosis – a non-bacterial/fungal associated skin disease. This effect is presumably based on the activation of local immune processes and the destruction of degenerated cells by the plasma – as already mentioned on left page.

Reports about tissue sensitivity or side effects caused by plasma treatment have not yet occurred in studies.[20]
Moreover, the **effectiveness of plasma treatment in bacteria appears to be independent from their level of resistance to antibiotics or the species type**.[21,22,23]

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A wide range of indications:
From acne to atopic dermatitis

The multiple mechanism of plasma action provides treatment for a wide range of dermatological diseases (see table 2).
Due to its flexible biocompatible foam layer, even hard-to-reach treatment areas could be easily accessed by plasma derma care® spacer.

Mycoses and **bacteriosis** are some of the most common dermatological diseases and - in case of delayed or inadequate therapy – they may develop severe clinical symptoms.
It is also worth to emphasize that **acne vulgaris**, with a prevalence of about 70-95%, is among adolescents[24] the most frequent dermatological disease worldwide.

Currently, **bacterial infections** are mainly treated with antibiotics. However, prolonged antibiotic treatment is not recommended due to the risk of developing resistances.
Mycoses are usually treated with topical antifungal agents. Therapy may cause side effects such as skin irritation, redness or hypersensitivity reactions; recurrences are very common.

Due to its antibacterial and antifungal effect, treatment with **plasma derma care®** is a suitable alternative for the local therapy of mycoses and bacteriosis.

The treatment of **atopic dermatitis** as a chronic constitutional disease is difficult. The usual therapies with glucocorticoids or antibiotics should not be continued for a longer time. In contrast, treatment with cold plasma is also possible in the long term, since no development of resistances or further side effects are to be expected.

Actinic keratosis can be treated well in early stages with current treatment methods such as photodynamic therapy (PDT). However these methods are often associated with recurrences and side effects such as severe pain symptoms[25] These treatment methods are often used in combination to have synergistic effects in combating the disease.
At this point, **plasma derma care®** can be used as an add-on therapy.

	INDICATIONS	ESTABLISHED THERAPIES	**plasma derma care®**
bacterial infections (bacteriosis):	akne vulgaris	antibiotics, antiseptics, glucocorticoids, retinoids, azelaic acid & benzoyl peroxide (for acne vulgaris) ⊖ retinoids with strong tetratogenic effect ⊖ antibiotics involve the risk of resistances ⊖ glucocorticoids can only be used for short periods	antibacterial, promotes wound healing, prevents superinfection and progression of inflamma- tory reactions ⊕ no resistances ⊕ long-term use possible
	perioral dermatitis		
	soft-tissue infections (folliculitis, boils, abscesses)		
	impetigo contagiosa		
fungal infections (mycosis)	pityriasis versicolor (tinea versicolor)	antifungal agents (azoles, polyenes, allylamines, etc.) – when used locally often associated with skin redness and irritations	antimycotic alternative/ combination therapies ⊕ prevention of recurrences and superinfection
	dermatophytosis (tinea)		
Other skin diseases	atopic dermatitis (neurodermatitis)	calcineurin antagonists, glucocorticoids, antibiotics, hyposensitization	antipruritic, antibacterial, wound healing (in case of excoriations (skin-picking))
	actinic keratosis	cryotherapy, 5-fluorouracil, laser therapy, photodynamic therapy (PDT) ⊖ severe pain symptoms especially with PDT	activation of local immune processes, destruction of degenerated cells ⊕ without side effects, ⊕ treatment painless
	viral skin diseases with bacterial superinfection (e.g. herpes labiales)	antivirals (aciclovir, ganciclovir, etc.), antibiotics (for bacterial superinfections)	in combination therapy for the prevention/ treatment of bacterial superinfections

▲ *Table 2: Indications for* **plasma derma care®**

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How to use –
simple, effective and painless*

The **plasma derma care®** is a portable, battery-operated and therefore mobile medical device. Accordingly, it can easily be used in the clinical or practice sector, but also by outpatient care services. Treatment with the **plasma derma care®** only requires a few minutes and its´ use is very intuitive.

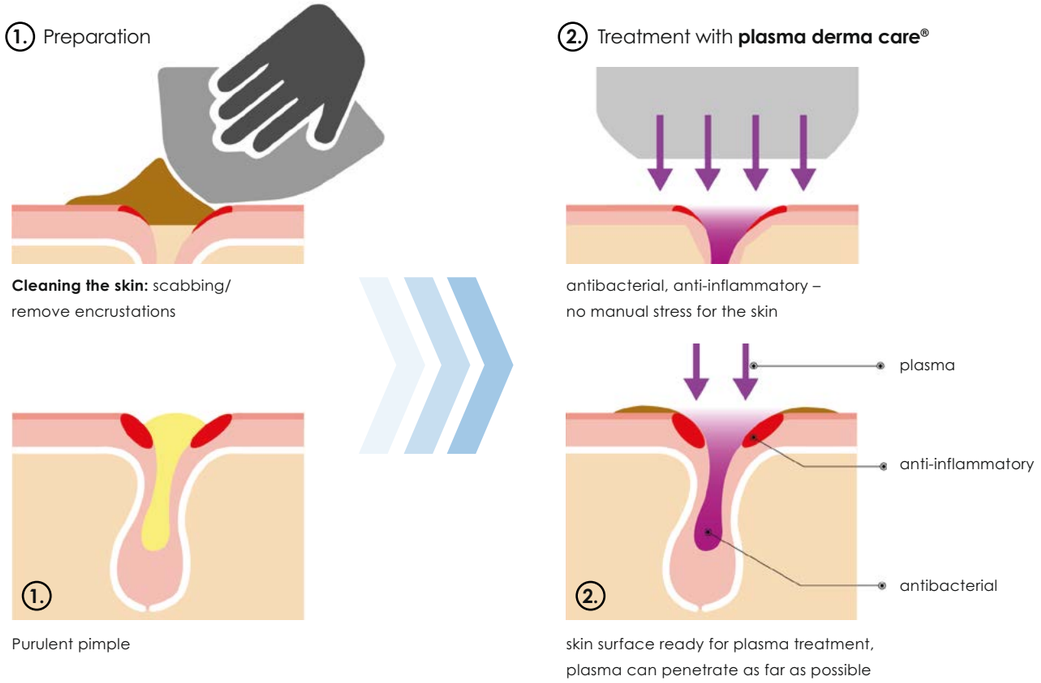
Plasma therapy does not exclude treatment with other therapeutic agents. Topical/systemic glucocorticoids, retinoids, phototherapy, etc. remain an effective add-on and may also be used depending on the individual patient profile. However, topically applied preparations should be removed prior to plasma treatment in order to avoid possible interactions.

In general, the use of the device is similar for all indications listed in table 2.
The affected skin area is cleaned prior to treatment and any existing crusts or pus are removed before the flexible biocompatible foam spacer is placed on the skin. The gaseous plasma can thus optimally penetrate the affected areas and exert its effect directly on the skin surface (see figure 4).

An antiseptic can then be applied to provide a long-term antibacterial effect. The recommended treatment time is 1 -3 minutes per affected area.

The affected skin area is only exposed to minimal contact (application of the spacer), which means a reduced pain potential compared to other topical treatment options.
Areas close to eyes and mouth/nose openings should be treated very cautiously.
Plasma should not enter the respiratory tract or get into direct contact with the eyes; if necessary, aids such as nasal plugs and protective glasses can be used.

Patients described treatment with the* ***plasma derma care®* *as free of pain.*



▲ Figure4: treatment sequence with the **plasma derma care®**

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The advantages at a glance

As mentioned before, **plasma derma care®** represents a completely new therapeutic approach for the treatment of many different chronic and acute skin diseases and offers a lot of advantages in comparison with conventional therapeutics.
In particular, there are no contraindications, the application is free of side effects, and at the same time treatment is highly effective.

Due to numerous benefits, such as activation of a local immune response, antimicrobial as well as antipruriginous effects, CAP can contribute in different ways to symptomatic relief or recovery.

Treatment with **plasma derma care®** is quick and easy to perform, painless, cost effective and economical. Thus it may effectively be added to or even replace conventional therapies.

- highly beneficial antiseptic efficiency
- wide range of applications in dermatology from acne to neurodermatitis
- „broad spectrum effectiveness“ - it inactivates all bacteria on the skin
- no adverse events, tissue intolerances and long-term risks[20]
- no resistances[6] or allergies
- treatment of affected skin area requiring only minimum contact (application of the spacer) and thus considerably reduced pain potential compared to topical antiseptics
- inactivation of bacteria through plasma treatment is independent of resistance level to antibiotics or species [21,22,23]
- also non-flat skin areas or areas on the face can be easily treated with flexible foam spacer

Notes

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