plasma care®

wound treatment with cold plasma

inactivation of bacteria and fungi | activation of wound healing

SAFE –
HEALTHY TISSUE
IS NOT DAMAGED

SUITABLE FOR
PATIENTS WITH
PACEMAKERS

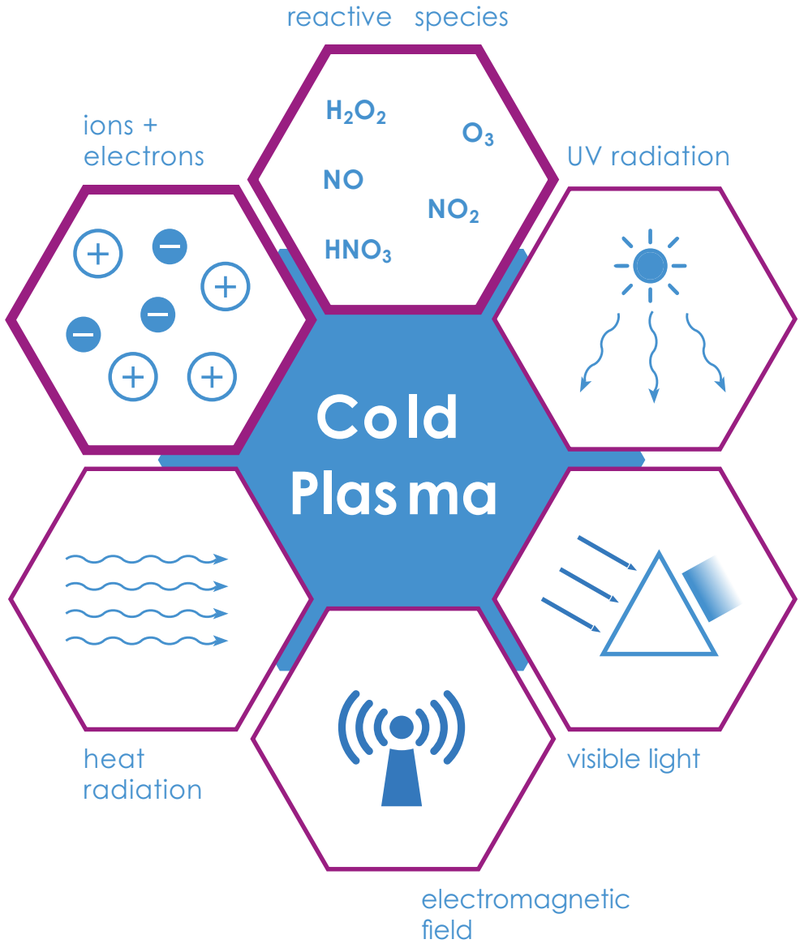
PORTABLE
AND
EASY-TO-USE

ACTIVATION
OF WOUND
HEALING

Cold plasma – innovation for medicine

When ice and water are heated up – in other words, energy is supplied to them in the form of heat – they change their state of aggregation: ice melts and water evaporates.
It´s quite the same process when gas is transformed into plasma after energy is added.
Plasma thus describes the fourth high-energy state of matter in which gas is (partially) ionized. It is defined as cold or non-thermal if only a small increase in temperature occurs during its generation and just normal ambient air pressure conditions are required[1].

Figure 1: Plasma is a 4th aggregate state.



The gas mixture that makes up the air we breathe in can be converted into plasma by adding energy.
This kind of plasma is called cold atmospheric plasma (CAP) and has properties that can be applied for the medical treatment of patients.[2,3,10,17-23,24,25-28]

Physically, CAP consists of free electrons and radicals, ions and excited molecules originating from a natural environment, the ambient air. Furthermore, electromagnetic fields, visible and ultraviolet light as well as small amounts of heat radiation are produced when CAP is generated.[1]

Ions and electrons	N^+, N_2^+, N_3^+, N_4^+, O^+, O_2^+, NO^+, NO_2^+, H^+, H_2^+, H_3^+, OH^+, H_2O^+, H_3O^+, e^-, O^-, O_2^-,O_3^-, O_4^-, NO^-, N_2O^-, NO_2^-, NO_3^-, H^-, OH^-
Reactive species	excited N_2, excited O, H, N, O, excited O_2, O_3, NO, N_2O, NO_2, N_2O_3, N_2O_4, N_2O_5, H_2, OH, HO_2, H_2O_2, HNO, HNO_2, HNO_3
UV-radiation	max. 0,00198 J/m² in 3 minutes (limit = 30 J/m² in a day)
Visible light	purple glow
Heat	ΔT = about 1°C/minute, always ≤40°C

ONLY 1 MINUTE PER APPLICATION

USER-FRIENDLY

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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 exact properties of cold atmospheric plasma depend on how it is generated.
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 processes (e. g. hydrogen denaturation by reactions of hydroxyl radicals).

As a consequence, the bacteria (prokaryotic cells) – or more precisely their cellular macromolecules (including DNA) are inactivated. Due to this reaction even bacteria that have developed antibiotic resistance are inactivated[29-31]. In this process different stable reactive species of the cold atmospheric plasma interact with the cell membrane of the bacteria[3]. Furthermore, an antiviral effect of the reactive oxygen species produced by cold atmospheric plasma has been observed. 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, eukaryotic cells are protected within cell compounds. This means that there is no risk of cell damage. Quite the opposite: the reactive oxygen species in human cells even stimulate the growth of tissue or mucous membrane, thus triggering wound healing.
The positive effect of cold atmospheric plasma on human cells is due to the stimulation of intracellular processes initiating cell growth through reactive species.[34-35]
This effect is locally limited to the uppermost cell layer. Among other reasons, this is due to a very short halflife of the reactive species, which will have already completely reacted by interacting with the upper cells or surrounding cell liquid.[36-37]

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

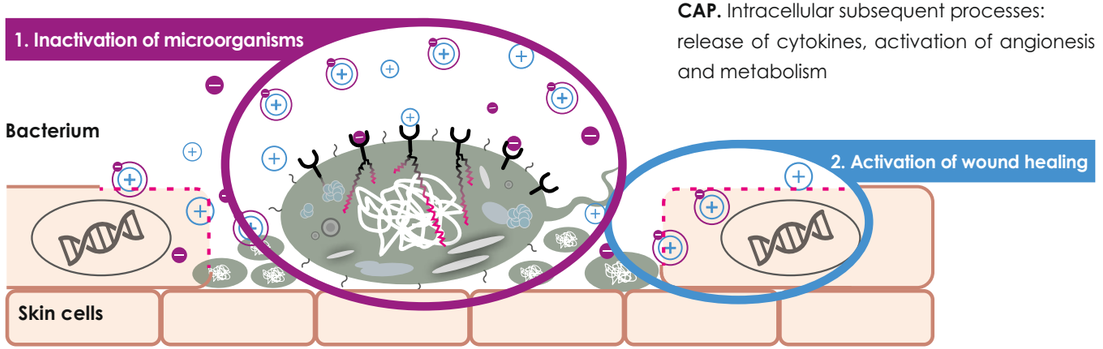

Figure 2 : biological plasma effect

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Plasma medicine to go

The **plasma care®** is a medical device used for disinfection of wounds by means of cold atmospheric plasma. It has quite the size and weight of a travel hair dryer, is rechargeable and has a battery life of at least 200 hours fully charged.
Accordingly, the device can be used both in the clinical and private practice sector, as well as in the field of ambulant care services and wound care specialists. The indications for CAP application are listed in the table on the right. **plasma care®** is charged by induction using a docking station.

INDICATION			
	Etiology/cause	Disease/condition	Symptoms and aspects
Chronic wounds	arterial, venous, infectious, diabetic, neuropathic, traumatic, vasculitic	ulcers, decubitus or pyoderma gangrenosum	potential indication of bacterial load (prophylactic), colonization and infection with bacteria
Acute, open wounds	mechanical cause	abrasions, cuts, lacerations, stab wounds, contused wounds, avulsions, fissures, bites, gunshot wounds, impalement injuries, amputation of extremities	potential indication of bacterial load (prophylactic), colonization and infection with bacteria
	thermal cause	burns, frostbite	
	surgical	surgery wounds, secondary healing surgery wounds, split-thickness skin graft sites	prophylaxis for wounds at risk of infection
CONTRAINDICATION			
Wounds with heavy and acute bleeding			
Wounds at exposed inner organs (surgical area)			
Wounds at mucous membranes			
Wounds in the head and neck area			
Children under the age of 12 years			

Table 1: Indications and contraindications for the use of the **plasma care®**.

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The treatment – simple, effective, painless*

In order to ensure sterile treatment of each individual patient and to avoid cross-contamination, individually packaged sterile spacers are used in combination with the **plasma care®** device. These spacers, easily attachable to the upper part of the device, are gently placed on the wound without causing any additional pain through pressure. The CAP is generated from the ambient air within the spacer by means of adding energy.

The **plasma care®** device contains an indirect plasma source working on the basis of SMD (Surface Micro Discharge) technology ensuring that no electric current flows through the patient.
The skin or rather wound surface only gets in contact with the therapeutically effective, stable plasma components. Healthy tissue is not damaged.
With a potential treatment area of 13 cm^2, the **plasma care®** device is suitable for most wounds. For larger or multiple wounds, a spacer can be used up to 6 times within one treatment session (total possible treatment area: 78 cm^2). Subsequently, the spacer is no longer usable and must be disposed of together with infectious waste.

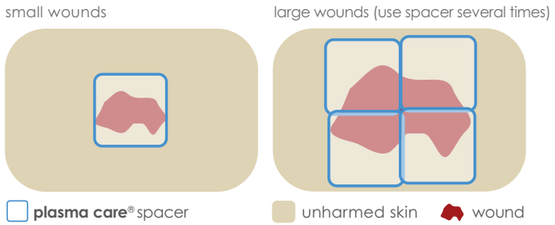

Figure 3:
Treatment scheme for wounds of different size

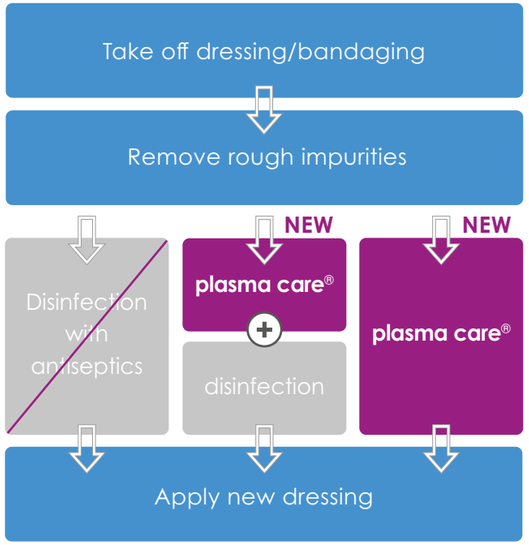

Figure 4: Wound care process

The process of wound treatment remains basically unchanged: The wound bed is prepared , i. e. mechanically debrided and cleaned. The wound is now ready for treatment with **plasma care®** , the cold plasma can flow freely onto the wound surface and deactivate bacteria including MREs.
After that the wound is dressed as usual. In addition, an antiseptic can be used to achieve a long-term antibacterial effect.

*So far, patients describe the therapy with **plasma care®** as a painless treatment.

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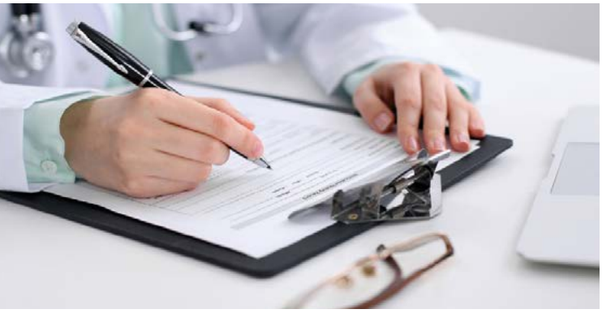
Clinical results – Effectiveness

Clinical results show that the **plasma care®** can effectively inactivate numerous bacterial strains from risk groups I and II including S. aureus, E. faecalis, P. aeruginosa, E. coli, MRSA and VRE. In this context no significant difference in their sensitivity towards CAP could be found and apart from that no resistances were developed.

On agar 99.999 % of tested bacteria and of the yeast C. albicans were killed within 60 seconds. Moreover, the **plasma 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.

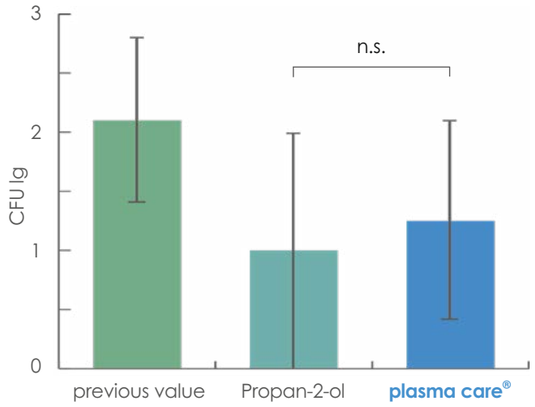


The plasma treatment is, however, not a targeted therapy, which exclusively attacks pathogens. Healthy human tissue also comes into contact with the CAP. Therefore, it was carefully examined, whether the plasma treatment causes any changes in primary fibroblasts and keratinocytes or in the skin. However, plasma treatments of up to 3 minutes (longest permissible treatment period for a single wound area within 24 hours) 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. Furthermore, mutagenicity studies (HGPRT test using V79 cells), provided no evidence of any genotoxic potential of the CAP from the **plasma care®**. For this purpose, treatment periods of up to 5 minutes were examined.

The **plasma care®** device is therefore considered to be effective and safe according to the results of the preclinical studies.
These results also correspond to the published data of the **terraplasma group**.[8,9,12–16]

The advantages at a glance

In addition, the antibacterial effect of **plasma care®** has been tested by an independent, certified testing laboratory (HygCen Germany GmbH) using a modified standard method (VAH method 13).
The resident skin flora on the upper arm of healthy volunteers was reduced by 83 % within three minutes (n = 20) after application of an artificial contamination with E. coli K12 , a 99.97 % reduction was achieved within same period (n = 5).
Thus, the effect of **plasma care®** was comparable to that of the reference product 70 % (v/v) propan-2-ol.



- Effective reduction of bacteria
- Elimination of multi-resistant pathogens
- Improved wound healing was observed
- No development of resistances
- No tissue damage
- Only 1 minute per application
- Portable and easy to use
- Also applicable for patients with cardiac pacemaker
- No noble gases
- No electric current through skin

Figure 5:
Test results for resident skin flora (n=20)

CFU = colony-forming unit
n.s. = not significant

Within 3 minutes the **plasma care®** reduces the resident skin flora on skin with a small amount of sebaceous glands (upper arm) to a comparable extent as after treatment with 70% (v/v)propan-2-ol during same time.

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plasma care®
case reports

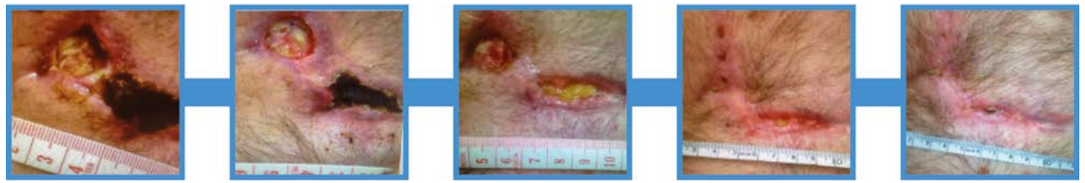
The **plasma care®** is used for patients with chronic wounds of various genesis, e. g. postoperative wound healing disorders, diabetic foot syndrome and decubitus. Here you will find some case reports:

EXAMPLE: POST-OPERATIVE WOUND HEALING DISORDER

40-year-old male patient. Resection of a liposarcoma and partial resection of the costal arches C2-C5 right and C2-C4 left. Post-operative wound healing disorder with sternal putrid (purulent) wound abscess cavity – wound revision and application of a wound sealing system unsuccessful, formation of necrosis.

Treatment course:

- Cold plasma treatment over 13 weeks with an average of 3 applications/week.
- Regular removal of crusts and necroses, necrosic areas became smaller, the wound became flatter and closed from inside and from its edges.



Initial situation, Oct 2019 → End of January 2020

EXAMPLE CASE: DECUBITUS ON THE NECK

64-year-old female patient. Post-polio syndrome, chronic respiratory and ventilatory insufficiency, Gr. III obesity, hypercapnic coma. Hypergranulating pressure ulcer on the neck, due to friction and moisture on the strap of the respiratory mask, stagnation in the granulation phase.

Treatment course:

- 7 cold plasma treatments (6 x 2 min, 1 x 1 min) over 3 weeks, first treatments were performed on 6 days in a row.
- The wound was completely epithelialized after 22 days.

(Picture documentation following page)

Continued picture documentation decubitus

Day 0, Initial situation | **Day 1,** 1 CAP treatment | **Day 8,** 6 CAP treatments | **Day 15,** 7 CAP treatments | **Day 22,** completely epithelialized

EXAMPLE: POST-OPERATIVE WOUND HEALING DISORDER

77-year-old female patient, secondary healing wound (split skin transplantation and flap wound plastic) as a result of trauma (contusion) in a car accident, wound healing disorder with known CVI and heart failure, infection with enterobacter aerogenes, additional tendency to edema formation in the lower legs.

Treatment course:

- 2 cold plasma treatments per week (1 min each).
- changeover to moist wound care to soften the incrustations and necroses
- mechanical cleaning
- after 18 treatments over 11 weeks, wound completely epithelialized except for punctual superficial skin gap (wound size: 0.22 x 0.17 cm).

Week 0, Initial situation | **Week 1,** 3 CAP Treatments | **Week 2,** 5 CAP treatments | **Week 8,** 7 CAP treatments | **Week 11,** 18 CAP treatments

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plasma care® – small medical device with big effect

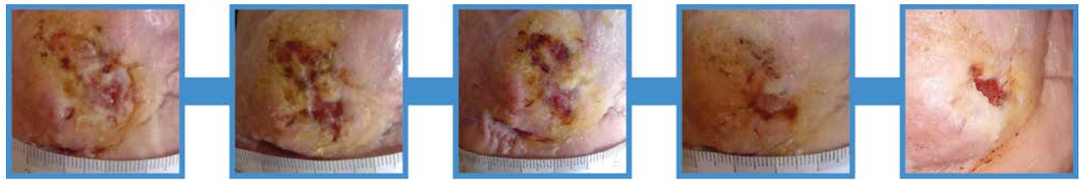
The **plasma care®** is on market since July 2019. This medical device uses cold atmospheric plasma to inactivate microorganisms including multi-resistant pathogens. Even stimulation of wound healing can also be observed in some patients. Here are some case reports on wound treatment:

EXAMPLE: POST-OPERATIVE WOUND HEALING DISORDER

63-year-old female patient with a traumatic transtibial amputation of the right lower leg, post-operative wound healing disorder on the stump (support surface to the prosthesis), followed by a flap plastic surgery, no wound healing for over 1½ years – no infection.

Treatment course:

- 9 cold plasma treatments (1 min/13 cm^2) within 3.5 weeks.
- Reduction of wound size from 2.04 cm x 1.87 cm (L x W) to 0.48 cm x 0.51 cm (L x W)



Day 0, Initial situation | **Day 1,** 1 CAP treatment | **Day 7,** 3 CAP treatments | **Day 21,** 6 CAP treatments | **Day 25,** 9 CAP treatments

EXAMPLE CASE: DIABETIC FOOT SYNDROME

50-year-old male patient with diabetic foot syndrome. Infected ulcers above the metatarsal bones (left) and necrotic 4th toe, amputation due to worsening of the wound situation, wound infection with partially resistant corynebacteria, enterococci and staphylococci.

Treatment course:

- 2 cold plasma treatments per week for the first 3 weeks, followed by application every 14 days thereafter (9 treatments in 12 weeks) as part of the dressing change
- Healing within 12 weeks after beginning of plasma therapy

(Picture documentation following page)

Continued picture documentation diabetic foot syndrome

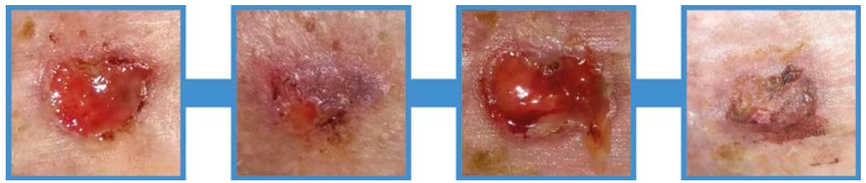
Day 0, Initial situation | **Day 2,** 2 CAP treatment | **Day 14,** 4 CAP treatments | **Day 42,** 7 CAP treatments | **Day 83,** 9 CAP treatments

EXCAMPLE CASE: ULCUS CRURIS

77-year-old female patient, bedridden due to a cervical spinal injury. Ulcus recurrence of unclear origin on the right lower leg, no edema, vascular structure unclear. Wound healing stagnated for several months, partly purulent coatings, patient suffers from severe pain during mechanical wound cleaning.

Treatment course:

- 8 cold plasma treatments (1 min) within 4 weeks resulted in significant reduction of wound size
- Progressive epithelialization, pain relief
- Interruption of CAP treatment caused ulcus recurrence
- Complete epithalization of wound 4 weeks after restart of CAP therapy (2 x 1 min/week)



Initial situation | 8 CAP treatments | Relapse after interruption of therapy | restart: after 8 CAP treatments

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Notes

ONLY 1 MINUTE
PER APPLICATION

USER-FRIENDLY

NO DEVELOPMENT
OF RESISTANCES

REDUCTION OF
BACTERIAL LOAD

SAFE –
HEALTHY TISSUE
IS NOT DAMAGED

SUITABLE FOR
PATIENTS WITH
PACEMAKERS

PORTABLE
AND
EASY-TO-USE

ACTIVATION
OF WOUND
HEALING

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NO DEVELOPMENT OF RESISTANCES


REDUCTION OF BACTERIAL LOAD