Cold atmospheric argon plasma significantly decreases bacterial load of chronic infected wounds in patients

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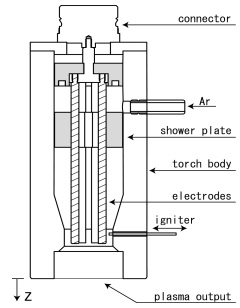
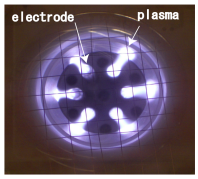
The device: MicroPlaSter ß (right)
Construction plan of argon plasma torch (below)

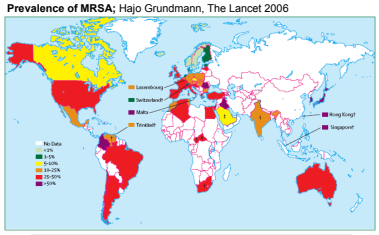


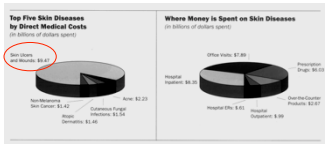


•Microwave (2.45 GHz, 86W)
•Ar (2.2 slm)
•Torch body is cooled by airflow

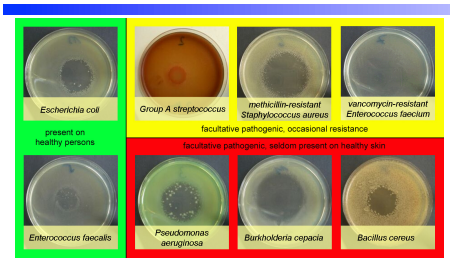
Plasma – the fourth state of matter – consists of charged particles and neutrals. Because of its physical properties plasma has a bactericidal effect due to reactive oxygen and nitrogen species (ROS and RNS), charged particles, UV, and electric fields. Cold atmospheric plasmas operate below 40°C and allow in vivo applications without damaging surrounding tissue. The benefit of this new technique is to have a safe, contact free application for "rough" surfaces down to micrometer scale which can kill bacteria efficiently, regardless the strain, and without having the problems of antibiotic resistance and allergic reactions. Furthermore it could lead to a faster wound healing itself. These properties make plasma an ideal tool for treating chronic infected wounds, which are the main reason for hospitalizations in dermatology and high costs.

Prevalence of MRSA; Hajo Grundmann, The Lancet 2006

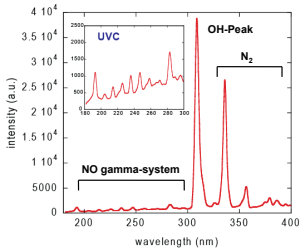




American Academy of Dermatology Report 2005



We tested the effect of 2 min low-temperature Argon plasma on different germs relevant to chronic wounds.



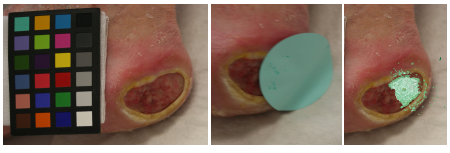
UV-spectrum of the argon plasma. Control of reactive species and UV radiation:
UVA : N_2 molecules
UVB: OH
UVC: NO

Measurements of reactive species in air revealed:
NO: < 1 ppm
NO_2: ~ 6 ppm at max
O_3: ~ 900 ppb

	UVC	UVB	UVA
Sun	1-2.5	30-50	~600
MicroPlaSter	10-16	40-60	<100

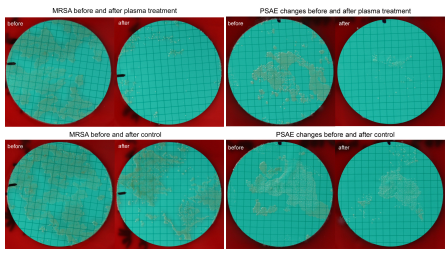
UV power (μW/cm²)

Correlation between different UV-dosages compared with standard UV, measured within the year in Garching (Germany). UVC dose produced by plasma during one minute is comparable to the dose received during 5 min of direct sunlight.

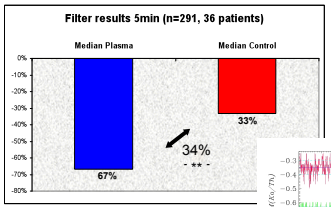


Changes in germ load were detected by nitrocellulosis filters. The filters represent „fingerprints" of the bacterial colonization.

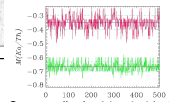
The study – argon plasma has been shown to be highly effective in vitro against different, even multiresistant bacteria (gram positive and gram negative) and yeasts, like *Candida albicans*. Safety was proven by several tests using ex vivo human skin, HeLa cells, human skin cells and blood samples. The total UV dosage of a plasma treatment is harmless according to WHO guidelines (ICNIRP). Especially reactive species (NO, NO_2, $ONOO^-$, O_2^-, O_3, $^{\cdot}OH$, H^+, H_2O_2) are estimated to play a major role in bactericidal effects. Plasma can also lead to cell proliferation in endothelial cells and is able to induce growth factors in keratinocytes and fibroblasts.
In 2005 our group started to treat patients with chronic infected and colonized wounds with cold atmospheric argon plasma. These patients received standard wound care besides a 2 to 5 minutes argon plasma treatment on randomized wound(s). The bacterial load was detected by nitrocellulosis filters. Standard swab technique failed in accuracy and reproducibility. Possible side effects like pain were noted according to a standardized WHO score. This is the first in vivo study in patients to proof a highly significant ($p<10^{-6}$) higher bactericidal effect of 34% in plasma treated wounds compared to control wounds (n=291, 36 patients) *(Isbary et al. British Journal of Dermatology DOI 10.1111/j.1365-2133.2010.09744)*. But also 2 min plasma treatment resulted in a significant higher reduction rate in bacterial load (40%, p<0.016, n=70, 14 patients). This reduction is found in all kinds of germs, even multiresistant ones like MRSA. Until now, the treatment is very well tolerated and no side effects occurred.



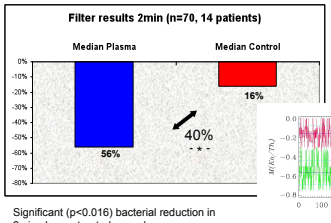
Nitrocellulosis filters after 12h of incubation. Left: Changes of MRSA colonies before and after plasma treatment on top, in comparison to changes in control area below. Right: Changes of *Pseudomonas aeruginosa* colonies.



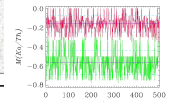
Highly significant ($p<10^{-6}$) bacterial reduction in 5min plasma treated wounds



Corresponding bootstrap test (n=500)

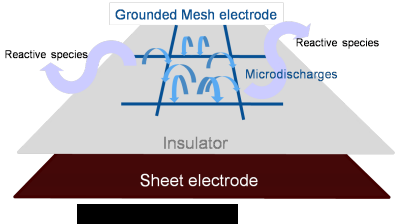


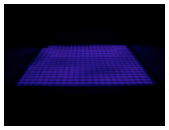
Significant (p<0.016) bacterial reduction in 2min plasma treated wounds



Corresponding bootstrap test (n=500)

Barrier Corona Discharge



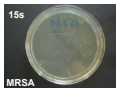


• Used gas: air
• Voltage = 18 kV
• Frequency = 12.5 kHz
• Power = 0.5 W/cm²

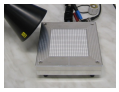
⇒ Plasma is produced through many nano- and microdischarges
Morfill et al. 2009

Future – A new technique, called Barrier Corona Discharge, opens the field of multiple new indications in health care. This method uses ambient air to produce high amounts of ROS and RNS. Plasma is generated through multiple nano- and microdischarges and needs therefore only little power input. Another benefit of this system is the possibility to bring it in any shape and size. It already proved its high antimicrobial effects in vitro within seconds and is capable to pass structures like socks or even envelopes.
Conclusion – Cold atmospheric plasmas are a new treatment option for chronic infected wounds and have the potential to treat many other pathogen related diseases or to solve hygiene problems in health care.

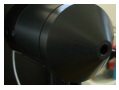
www.mpe.mpg.de/theory/plasma-med/index.html

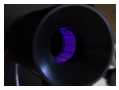


Hand disinfection (HandPlaSter)



Athlete's foot (FootPlaSter)





Oral hygiene (OralPlaSter)

Personal hygiene (DeoPlaSter)