PLASBELLE®
activates your skin

Extract clinical data

1. Pre market clinical investigation

Between 2011 and 2012 a first clinical investigation (Brehmer et al. 2015) was performed to investigate safety and clinical performance in the application of the PlasmaDerm VU2010 device for ulcers in chronic venous insufficiency.

The investigation was designed and executed as single center, prospective randomized trial after approval by the responsible ethics committee and the BfArM. The investigation was performed to assess safety and, as secondary endpoints, efficacy and applicability of 45 s/cm2 dielectric barrier discharge cold atmospheric plasma as adjuvant therapy against chronic venous leg ulcers in addition to conventional wound treatment and compression therapy.

Subjects were randomized in two groups. The control group received standardized modern wound care (n = 7). The treatment group received in addition DBD-CAP 3x per week for 8 weeks. The following parameters were analysed:
The ulcer size was determined weekly (Visitrak®, photodocumentation). Bacterial load (bacterial swabs, contact agar plates) and pain during and between treatments (visual analogue scales) were assessed. Patients and doctors rated the applicability of plasma (questionnaires).

2 SAEs and 77 AEs were recorded and approximately equally distributed among both groups. Two AEs were probably related to plasma. Plasma treatment resulted in a significant reduction in lesional bacterial load (P = 0.04, Wilcoxon signed-rank test). A more than 50% ulcer size reduction was noted in 5/7 and 4/7 patients in the standard and plasma groups, respectively, and a greater size reduction occurred in the plasma group (plasma -5.3 cm2, standard: -3.4 cm2) (non-significant, P = 0.42, log-rank test). The only ulcer that closed after 7 weeks received plasma. Patients in the plasma group quoted less pain compared to the control group. The plasma applicability was not rated inferior to standard wound care (P = 0.94, Wilcoxon-Mann-Whitney test). Physicians would recommend (P = 0.06, Wilcoxon-Mann-Whitney test) or repeat (P = 0.08, Wilcoxon-Mann-Whitney test) plasma treatment by trend.

DBD-CAP was evaluated to display favourable antibacterial effects. The investigation demonstrated that plasma treatment with the PlasmaDerm VU-2010 device is safe and effective in patients with chronic venous leg ulcers.

To achieve larger treatment area and accommodate the need to provide disposable sterile devices the development of the PlasmaDerm Flex and Cutan devices were initiated.

Brehmer, Franziska; Haenssle, H. A.; Daeschlein, Georg; Ahmed, R.; Pfeiffer, S.; Görlitz, A. et al. (2015): Alleviation of chronic venous leg ulcers with a hand-held dielectric barrier discharge plasma generator (PlasmaDerm VU-2010): results of a monocentric, two-armed, open, prospective, randomized and controlled trial (NCT01415622). In: Journal of the European Academy of Dermatology and Venereology : JEADV 29 (1), S. 148–155. DOI: 10.1111/jdv.12490.

2. Pivotal clinical studies

In a first investigation in healthy volunteers (Heuer et al. 2015) the increase of microcirculation after application of DBD-CAP (PlasmaDerm) was investigated and observed in tissue depth up to 6-8mm depths. The study also qualified and quantified reactive nitrogen gas species created by the PlasmaDerm device and its distribution in the tissue as well as the temporal impact on skin pH (acidification).

Heuer, Kiara; Hoffmanns, Martin A.; Demir, Erhan; Baldus, Sabrina; Volkmar, Christine M.; Röhle, Mirco et al. (2015): The topical use of non-thermal dielectric barrier discharge (DBD): nitric oxide related effects on human skin. In: Nitric oxide : biology and chemistry 44, S. 52–60. DOI: 10.1016/j.niox.2014.11.015.

The positive effect on elevation of microcirculation was confirmed in a study in 20 healthy volunteers (Kisch et al. 2016a) who received 90s DBD-CAP (PlasmaDerm) treatment. Oxygen saturation increased immediately after the treatment about 24% and remained elevated for 8 minutes after application. Similar results were observed for the increase of microcirculation which increased by 73% and remained elevated for 11 minutes.

Kisch, Tobias; Helmke, Andreas; Schleusser, Sophie; Song, Jungin; Liodaki, Eirini; Stang, Felix Hagen et al. (2016): Improvement of cutaneous microcirculation by cold atmospheric plasma (CAP): Results of a controlled, prospective cohort study. In: Microvascular research 104, S. 55–62. DOI: 10.1016/j.mvr.2015.12.002.

The effect of repetitive DBD-CAP application on microcirculation and tissue oxygen saturation was investigated in another study in 20 healthy volunteers who received 3x 90s DBD-CAP (PlasmaDerm) treatment with an intermediate gap of 10 minutes between the treatments respectively (Kisch et al. 2016b). Tissue oxygen saturation and postcapillary venous filling pressure significantly increased after the first application and returned to baseline values within 10min after treatment. After the second and third applications, both parameters increased significantly vs. baseline until the end of the 40-minute measuring period. Cutaneous blood flow was significantly enhanced for 1min after the first application, with no significant differences found during the remainder of the observation period. The second application improved and prolonged the effect significantly until 7min and the third application until 13min.

Kisch, Tobias; Schleusser, Sophie; Helmke, Andreas; Mauss, Karl Ludwig; Wenzel, Eike Tilman; Hasemann, Benedikt et al. (2016): The repetitive use of non-thermal dielectric barrier discharge plasma boosts cutaneous microcirculatory effects. In: Microvascular research 106, S. 8–13. DOI: 10.1016/j.mvr.2016.02.008.

With more sensitive optical investigation technologies the microcirculatory effects of DBD-CAP was investigated in another study with 10 healthy volunteers (Borchardt et al. 2017). The effect of DBD-CAP versus pressure application by placing the electrode aloe were compared for application times of 90s, 180s and 270s respectively. Significant increases in microcirculation were only observed after plasma stimulation but not after pressure stimulus alone. For a period of 1 h after stimulation, local relative hemoglobin was increased by 5.1% after 270 seconds DBD-CAP treatment. Tissue oxygen saturation increased by up to 9.4%, whereas blood flow was doubled (+106%). Skin pH decreased by 0.3 after 180 seconds and 270 seconds DBD-CAP treatment, whereas skin temperature and moisture were not affected.

Borchardt, Thomas; Ernst, Jennifer; Helmke, Andreas; Tanyeli, Murat; Schilling, Arndt F.; Felmerer, Gunther; Vioel, Wolfgang (2017): Effect of direct cold atmospheric plasma (diCAP) on microcirculation of intact skin in a controlled mechanical environment. In: Microcirculation (New York, N.Y. : 1994) 24 (8). DOI: 10.1111/micc.12399.

The effect of plasma on physiological flora was studied in nine volunteers (four females and five males; mean age 29 years), and its effect on artificial contamination was studied in four volunteers (two females and two males; mean age 26.8 years). In this study (Daeschlein et al. 2012) the effect of a jet plasma device was compared with the PlasmaDerm VU2010 device. Both plasma devices led to a significant reduction physiological (PF) and artificially (AF) contaminated flora (Staphylococcus epidermidis and Micrococcus luteus). The maximum log reduction factors for PF were 1.3 for the DBD at 210 s and 0.8 for the APPJ at 60 s. For AF, the maximum log reduction factors were 1.7 for the DBD at 90 s and 1.4 for the APPJ at 120 s. Treatment with both devices was well tolerated.

Daeschlein, Georg; Scholz, Sebastian; Ahmed, R.; Woedtke, Thomas von; Haase, H.; Niggemeier, M. et al. (2012): Skin decontamination by low-temperature atmospheric pressure plasma jet and dielectric barrier discharge plasma. In: The Journal of hospital infection 81 (3), S. 177–183. DOI: 10.1016/j.jhin.2012.02.012.

In a short case series of three patients with chronic venous ulcers (Geimer et al. 2016) the following clinical observations were made after different application modes and durations of DBD-CAP:

	Patient 1 (female, 60 years)	**Patient 2 (male, 64 years)**	**Patient 3 (female, 80 years)**
aetiology	Ulcus cruris venosum	Ulcus cruris venosum	Ulcus cruris venosum, posttraumatic
Ulcus age before DBD-CAP	64 months	18 months	12 months
standard therapy	Polyhexanid gel, atraumatic gaze, compression bandage	Polyhexanid gel, atraumatic gaze, compression sock	Polyhexanid gel, atraumatic gaze, compression bandage
DBD-CAP treatment regimen	1x 90s per week, 8 months	3x 90s per week, 1 month	90s, daily, 10 days
outcome	Induction of granulation and epithelilisation	Complete healing of the ulcer	Reduction of inflammation, partial reepithelilisation

Geimer, Till; Blatner, Carolin; Ruzicka, Thomas, Sattler, Elke (2016): Kaltes Atmosphärenplasma zur Behandlung von Wundheilungsstörungen: Ansprechmuster und Therapieverläufe. Ludwig-Maximillians-Universität München, Klinik und poliklinik für Dermatologie und Allergologie, 2016.

A short case series of four patients with wound healing disturbance after radial forearm free flap donation (autologous skin graft) of the donation site DBD-CAP application was performed in addition to standard wound care (Hartwig et al. 2017a). In all patients, complete wound repair in terms of the absence of tendon exposure was observed within a mean treatment time of 10.1 weeks (range 4.9 to 16). No undesirable side effects were observed, and no inflammation or infection occurred.

Hartwig, Stefan; Doll, Christian; Voss, Jan Oliver; Hertel, Moritz; Preissner, Saskia; Raguse, Jan Dirk (2017): Treatment of Wound Healing Disorders of Radial Forearm Free Flap Donor Sites Using Cold Atmospheric Plasma: A Proof of Concept. In: Journal of oral and maxillofacial surgery : official journal of the American Association of Oral and Maxillofacial Surgeons 75 (2), S. 429–435. DOI: 10.1016/j.joms.2016.08.011.

In a case series of 6 patients with wound healing disturbance after different cranio-maxillo-facial- surgeries DBD-CAP application was performed in addition to standard wound care (Hartwig et al. 2017b). In all patients, complete remission in terms of wound closure was observed within a mean time of 15.5 weeks (range: 4-38 weeks). No undesirable side effects were observed, and no inflammation or infection occurred after cold plasma initiation.

Christian; Waluga, Richard; Raguse, Jan Dirk (2017): The feasibility of cold atmospheric plasma in the treatment of complicated wounds in cranio-maxillo-facial surgery. In: Journal of cranio-maxillo-facial surgery : official publication of the European Association for Cranio-Maxillo-Facial Surgery 45 (10), S. 1724–1730. DOI: 10.1016/j.jcms.2017.07.008.

In a prospective trial 15 patients with DBD-CAP treatment of 180s immediately at the end of the surgery of autologous skin flap grafts were compared with the outcome of a cohort of 51 patients with standard wound care alone (Paulßen von Beck und Mücke 2018). The study compared the rate for loss of the skin graft and the percentage of wound healing disturbance in the two groups. The data show a reduction of total skin graft loss from 31% to 13% in favour of the DBD-CAP groups and a reduction wound healing disturbances from 69% in the control group to 40% in the DBD-CAP group.

Paulßen von Beck, Felix; Mücke, Thomas (2018): Verbesserung der Wundheilung beim Einheilen von Vollhaut durch PlasmaDerm? - Eine Pilotstudie. Klinik für Mund-, Kiefer- und Gesichtschirurgie, plastische und ästhetische Operationen, Malteser Krankenhaus St. Josefshospital, Krefeld-Uerdingen. Wundkongress Nürnberg, 2018.

3. Clinical data from post market surveillance and Post Market Clinical Follow Up

312 case reports in the DBD-CAP treatment of chronic wounds and wound healing disturbances over a period of four years at 17 different sites (hospitals, office based practitioners, wound specialists) were analysed for indication, mean DBD-CAP treatment time, outcome and reported side effects. Outcome was ranked in no detectable effect, activation (phase shift of the wound healing process), conditioning and healing.

The following outcome is recorded:

Aetiology	**Number**	**Average DBD-CAP treatment (weeks)**	**activation**	**conditioning**	**cond. / healing**	**healing**	**no or not documented effect**
CVI ulcer	131	14	3	65	15	7	39
pAVK ulcer	15	26	-	2	3	6	4
mixed ulcer	34	10	3	14	8	5	4
mixed ulcer	10	31	-	3	3	3	1
DFS	46	16	1	22	8	8	7
Burns	2	10	-	1	1	-	-
other	74	4-88	3	19	13	33	8
total	312	n.a.	10	126	51	62	63

A separate analysis was performed for surgical site treatment in urological patients after prostatectomy in a single study site. 3 DBD CAP-Treatments were performed per patient and monitoring time was 6-7 days after surgery. Out of 25 patients, 24 showed a wound healing without complication. In one case a disturbed wound healing was observed.

In a case series of chronic inflammations in a sports medicine office a series of patients were treated with DBD-CAP. The summary of the treatment frequency, indications and outcome is given in the following table. The average treatment and observation time was 2-3 weeks.

Diagnosis	**No of cases**	**No of DBD-CAP treatments**	**Average pain reduction (scale 0-5)**	**Outcome**
Epicondylitis	5	3-9	2.4	significant improvement (3) moderate improvement (1) no change (1)
Achillodynia	3	5	2	significant improvement (2) no change (1)

Diagnosis	No of cases	No of DBD-CAP treatments	Average pain reduction (scale 0-5)	Outcome
Bursitis	2	4-6	2	significant improvement (1) no change (1)
Pressure pain (patella / ankle)	3	5-6	2	significant improvement (2) no change (1)
Tendinosis	1	5	5	significant improvement
Tendovaginitis	1	5	2	significant improvement

4. Clinical data with special relevance in cosmetic applications

The impact of DBD-CAP on Stratum Corneum permeabilization was investigated by Gelker et. al in three consecutive studies (Gelker et al. 2018; Gelker et al. 2019; Gelker et al. 2020) where the impact of electrode design and modulations of frequencies and voltages were investigated. The potential to improve substance uptake in epidermal and dermal skin layers was demonstrated in al publications.

5. Literature

Borchardt, Thomas; Ernst, Jennifer; Helmke, Andreas; Tanyeli, Murat; Schilling, Arndt F.; Felmerer, Gunther; Vioel, Wolfgang (2017): Effect of direct cold atmospheric plasma (diCAP) on microcirculation of intact skin in a controlled mechanical environment. In: Microcirculation (New York, N.Y. : 1994) 24 (8). DOI: 10.1111/micc.12399.

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Daeschlein, Georg; Scholz, Sebastian; Ahmed, R.; Woedtke, Thomas von; Haase, H.; Niggemeier, M. et al. (2012): Skin decontamination by low-temperature atmospheric pressure plasma jet and dielectric barrier discharge plasma. In: The Journal of hospital infection 81 (3), S. 177–183. DOI: 10.1016/j.jhin.2012.02.012.

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Gelker, Monika; Mrotzek, Julia; Ichter, Astrid; Müller-Goymann, Christel C.; Vioel, Wolfgang (2019): Influence of pulse characteristics and power density on stratum corneum permeabilization by dielectric barrier discharge. In: Biochimica et biophysica acta. General subjects. DOI: 10.1016/j.bbagen.2019.05.014.

Gelker, Monika; Müller-Goymann, Christel C.; Vioel, Wolfgang (2018): Permeabilization of human stratum corneum and full-thickness skin samples by a direct dielectric barrier discharge. In: Clinical Plasma Medicine 9, S. 34–40. DOI: 10.1016/j.cpme.2018.02.001.

Gelker, Monika; Müller-Goymann, Christel C.; Viöl, Wolfgang (2020): Plasma Permeabilization of Human Excised Full-Thickness Skin by µs- and ns-pulsed DBD. In: Skin pharmacology and physiology, S. 1–8. DOI: 10.1159/000505195.

Hartwig, Stefan; Doll, Christian; Voss, Jan Oliver; Hertel, Moritz; Preissner, Saskia; Raguse, Jan Dirk (2017a): Treatment of Wound Healing Disorders of Radial Forearm Free Flap Donor Sites Using Cold Atmospheric Plasma: A Proof of Concept. In: Journal of oral and maxillofacial surgery : official journal of the American Association of Oral and Maxillofacial Surgeons 75 (2), S. 429–435. DOI: 10.1016/j.joms.2016.08.011.

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Kisch, Tobias; Schleusser, Sophie; Helmke, Andreas; Mauss, Karl Ludwig; Wenzel, Eike Tilman; Hasemann, Benedikt et al. (2016b): The repetitive use of non-thermal dielectric barrier discharge plasma boosts cutaneous microcirculatory effects. In: Microvascular research 106, S. 8–13. DOI: 10.1016/j.mvr.2016.02.008.

Paulßen von Beck, Felix; Mücke, Thomas (2018): Verbesserung der Wundheilung beim Einheilen von Vollhaut durch PlasmaDerm? - Eine Pilotstudie. Klinik für Mund-, Kiefer- und Gesichtschirurgie, plastische und ästhetische Operationen, Malteser Krankenhaus St. Josefshospital, Krefeld-Uerdingen. Wundkongress Nürnberg, 2018.

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