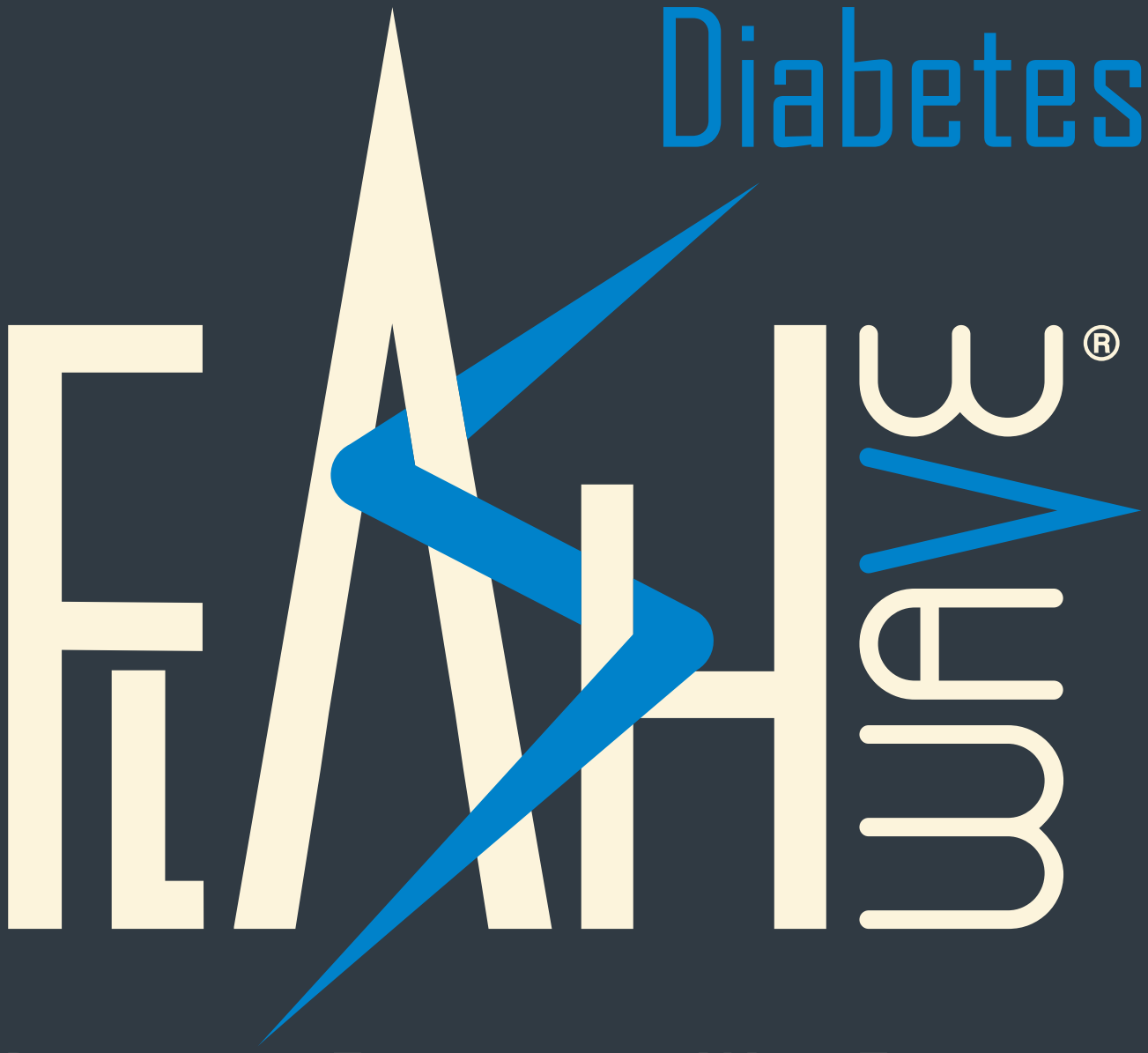


Diabetes



BIOCELLULAR TRANSDUCTIVE WAVE THERAPY
speaking the cellular language

About us

A group of highly experienced German engineers and experts, who over the last 25 years have been at the forefront of technological innovations at various companies, specializing in medical products, got together with **the goal of revolutionizing the way specific medical indications can be treated.**

All of us, while understanding the importance of surgical interventions in a multitude of medical fields, feel surgery is not the answer to many of the most common diseases and medical problems our societies face today.

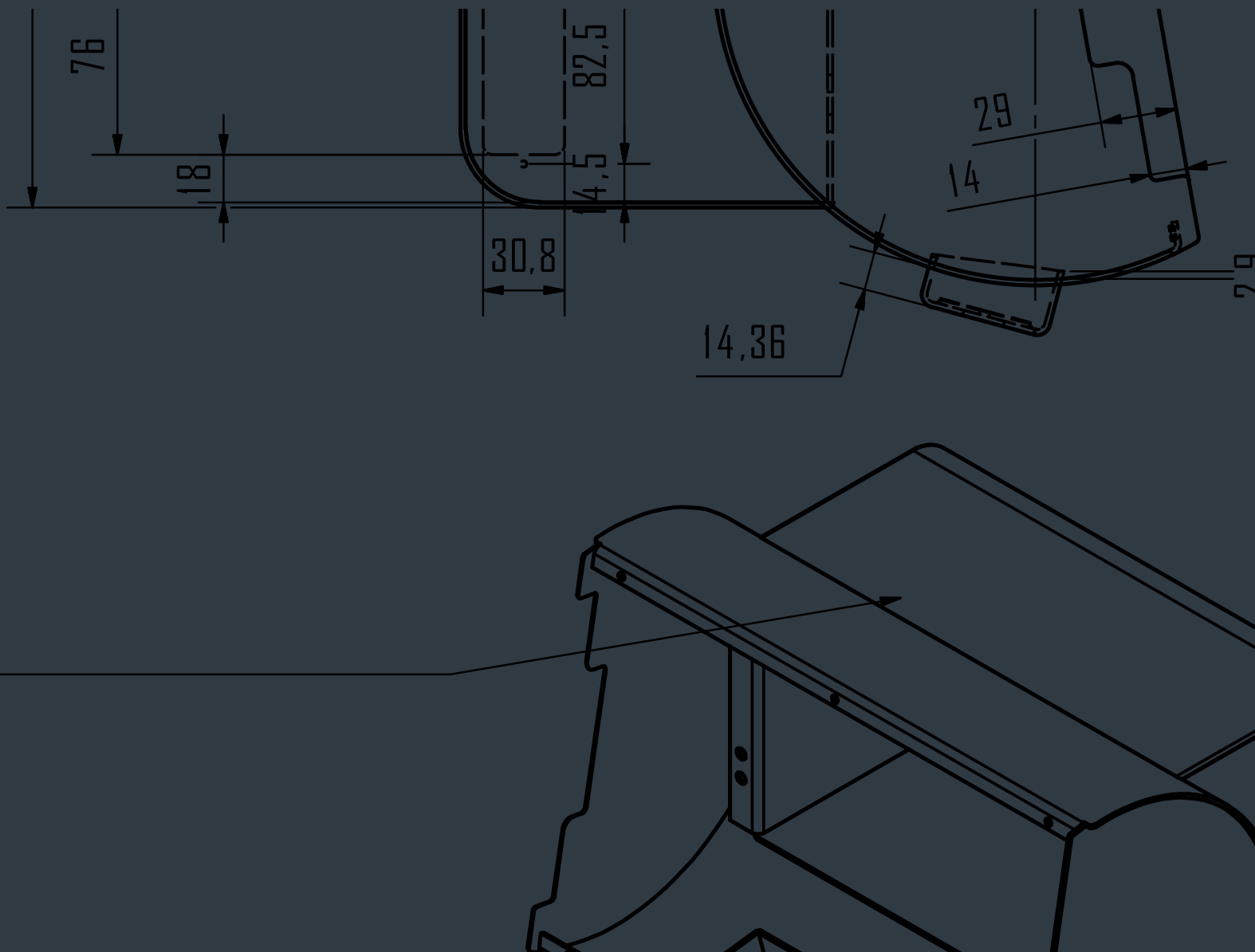
We set out to **develop a new therapy option** which allows doctors from different medical fields to treat an even wider range of medical indications without surgery, incisions, injections or drug treatments.

After gaining expertise and pushing forward technologies in the fields of laser, shockwave therapy, ultrasound and x-ray, we were searching for a technology which offers us all the technological and medical benefits we've been looking for, without any side-effects or risks for the patients treated with it.

When we started this project, our goal was to offer a pain-free, biological treatment with a cellular working mechanism, which can be carried out on an outpatient basis. Based on our previous experiences with shockwave and ultrasound we realized transduction, the physical stimulation of specific cellular receptors, was a promising starting point for our new technology and therapy idea.

Faced with the problem of achieving a therapeutic effect without physically inserting anything into or altering the body, we decided to continue our technological development along the lines of waves as carrier of the energy we're applying during treatment.

The result of our research, countless conversations with doctors from all fields of medicine, rigorous testing, feedback from patients as well as our technical expertise and dedication to pushing the boundaries of what's perceived possible, is **Flashwave® technology, the first ever Biocellular Transductive Wave Therapy available today.**



Why Flashwave®?

At the core of our technology is a high-voltage electrical discharge. The visual result of the powerful discharge in the kilovolt range is a flash, the acoustic result a bang.

To harness the energy created by the flash we're surrounding it with water, which is displaced once the flash is ignited inside the water. The displacement in the water creates the wave carrying the energy needed for the **biocellular transduction**, traveling at a supersonic velocity from our **Cellular Communication Interface (CCI®)** to the treatment area.

In nature a flash is energy, an energy signaling change:

- » Where it was dark, a flash illuminates.
- » Where it was dry, often after the appearance of a flash there's rain.
- » Where there was silence, a flash creates noise.
- » In nature a flash changes the status quo.

In medicine Flashwave® changes the status quo on how a wide range of medical indications can be treated.

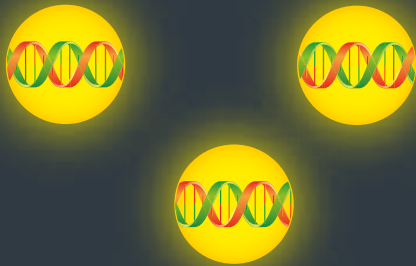
How does Flashwave® work medically?

Flashwaves® are longitudinal waves traveling to and through the body at supersonic velocity, carrying the energy of the flash which created them. The physical force of Flashwave® causes shedding of microvesicles from cell membranes without harming the cells.

1. Microvesicle shedding



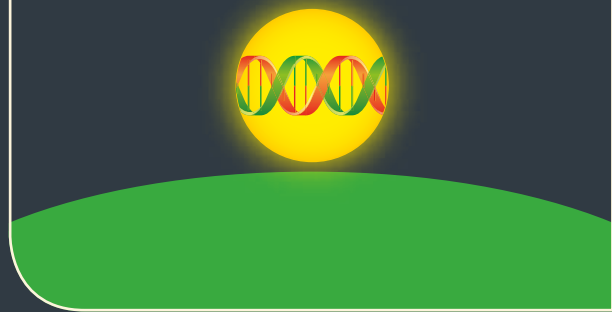
2. Microvesicles contain angiogenic cargo



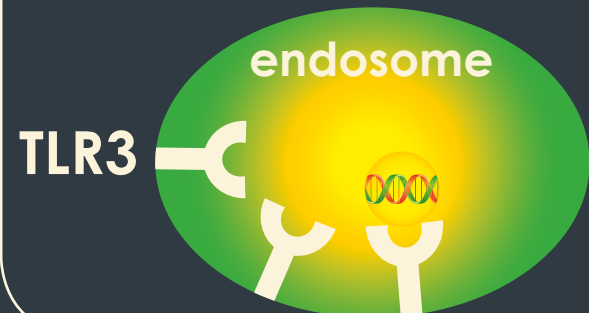
- » These microvesicles contain nucleic acids as well as proteins and other molecules that activate neighboring cells. Thereby intrinsic healing and repair mechanisms get initiated.
- » These include the release of angiogenic growth factors, leading to vessel sprouting (angiogenesis) and the recruitment of stem cells causing new vessel formation (vasculogenesis).
- » Simultaneously an increase of the metabolic activity of cells, proliferation and a positive, modulating effect on inflammation can be observed.

Flashwave® initiates communication with and among cells, activating an intrinsic repair program within the tissue – this revolutionary cellular communication is the key to Flashwave's® unique medical efficacy without any relevant side effects.

3. Fusion with plasma membrane



4. Endosomal TLR-3 activation



5. Proliferation, angiogenesis



82 years, female, insulin-dependent Diabetes, chronic renal insufficiency



traumatic wound before 1st treatment



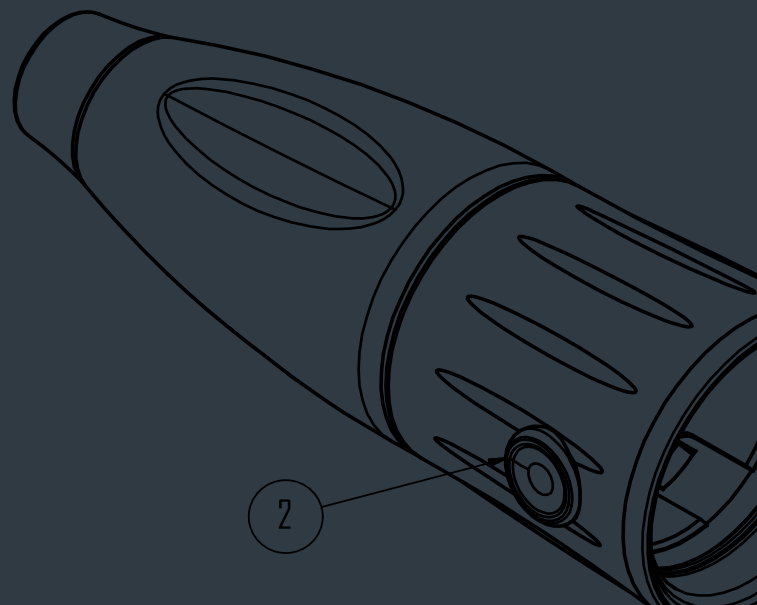
7 weeks after first Flashwave®



2 years after Flashwave®

Mittermayr, Schaden et. al

3 treatments,
combined 2.400 flashes,
overall treatment duration approx. 8 min



The Flashwave® device

In comparison to other regenerative approaches (such as traditional stem cell or gene therapy) Flashwave® is a reliable, reproducible, easy-to-use treatment and doesn't require a long and complicated learning curve for the user.

All Flashwave® devices are developed, designed and manufactured in Germany, fully qualifying as a »**Made in Germany**« product.

Our goal is to create devices which not only visually convey the latest-generation approach to medical device design, but are also compact, mobile and offer self-explanatory operation to doctors.

The significant rise of touchscreen based user interfaces and the familiarity most of our customers have with mobile devices designed in California has led to Flashwave® being the first non-invasive medical device fully operated by **a custom built App and an Apple iPad.**

Our **Flashwave® App** operates and controls the device through the touch-based user interface with intuitive icons, working smoothly on the latest generation iPads and iOS.

Both, new users and experienced therapists, will be able to use the system according to their specific requirements.

The self-explanatory icons on the clearly structured screen ensure a short learning curve.

Flashwave® devices are available for different medical fields, as well as in different configurations, allowing customers a selection of options to customize the device to their specific likings.

As a »Made in Germany« product, naturally all Flashwave® devices meet all legal and technical requirements of premium-quality medical products.



What are CCI[®]s?

Cellular Communication Interfaces (CCI[®]) are a key component of all Flashwave[®] devices. In the CCI[®]s the power generated by the device is used to create the actual Flashwave[®] and to direct it from the hand-piece on to the patient.

The multitude of medical indications which can be treated with Flashwave[®] call for different designs of CCI[®]s, as communication with different cells requires customized approaches for each indication and cell type.

We therefore **offer a range of CCI[®]s** for bespoke interaction with the specific cells we need to communicate with for optimal treatment results in each medical indication.

This unique range of cellular communication capabilities is a crucial element for the success of Biocellular Transductive Wave Therapy and Flashwave[®] devices.



A-A (1:1)

How to apply Flashwave®

Application of Flashwave® is simple and easy to learn. Even though different indications require specific treatment protocols, the application of Flashwave® basically remains the same:

1. Before the application of Flashwave® onto the treatment area, a contact medium, typically ultrasound gel, is applied directly on the treatment area.
2. The desired indication is chosen on the Flashwave® App on the device, automatically pre-setting the device with the recommended treatment parameters.
3. Flashwave® are applied by moving the CCI® over the affected area while lightly pressing the CCI® onto the skin, ensuring smooth transmission of the Flashwave® from the CCI® into the treatment area.

- » The number of Flashwave® applied depends on the indication.
- » The treatment session lasts only a few minutes and is repeated weekly/every two weeks.
- » Normally three to five treatment sessions are enough for complete regeneration/healing.

Technical Data

Power supply:
230 Volt/50 Hz or 110 Volt/60 Hz

Repetition rate:
Up to 480 flashes per minute

Weight Flashwave® device: 13 kg

CCI® energy range: 16–24 kilovolt

Flashwave® penetration depth: 0–60 mm



Diabetes facts according to the WHO's website

- » The number of people with diabetes has risen from 108 million in 1980 to 422 million in 2014.
- » The global prevalence of diabetes among adults over 18 years of age has risen from 4.7 % in 1980 to 8.5 % in 2014.
- » Diabetes prevalence has been rising more rapidly in middle- and low-income countries.
- » Diabetes is a major cause of blindness, kidney failure, heart attacks, stroke and lower limb amputation.
- » In 2012, an estimated 1.5 million deaths were directly caused by diabetes and another 2.2 million deaths were attributable to high blood glucose.
- » Almost half of all deaths attributable to high blood glucose occur before the age of 70 years.
- » WHO projects that diabetes will be the 7th leading cause of death in 2030

Diabetes and diabetes related medical complications are among the most serious medical concerns facing our societies. Treatment of diabetes related indications is a constantly growing expense, especially since many of the diabetes related symptoms are currently incurable. Diabetes mellitus is becoming one of the most chronic diseases of our times.

Flashwave® benefits in diabetes-related indications

- » Offers a cure for DFS, not just a slowdown of the progression
- » It's a non-invasive treatment
- » Easy to apply
- » Short treatment duration
- » No side-effects
- » Based on cellular communication – triggers the body's natural repair mechanism
- » Light, compact and mobile
- » Flashwave® is completely pain-free for the patient

Diabetes

Where does Flashwave® help treat diabetes related complications?

- » Diabetic Foot Syndrome (DFS)
- » Chronic wounds on patients with DFS
- » Diabetic related desensitizing of extremities
- » Diabetic related erectile dysfunction

With the unique Flashwave® technology even severely affected areas can be treated comfortably, it's bespoke CCI® allowing easy access, a high degree of accuracy and short treatment time.

Flashwave® as Biocellular Transductive Wave Therapy activates cellular communication, leading to an increase in perfusion and arteriogenesis, biofilm disruption, a pro-inflammatory response, cytokine and chemokine effects, growth factor upregulation, angiogenesis and the subsequent regeneration of tissue such as skin, musculoskeletal and vascular structures.

Diabetic-related Erectile Dysfunction (ED)

For treatment of urogenital indications Flashwave® focuses on blood vessels and neovascularization in the penis shaft and crus, helping relieve vascular deficiency, a common cause of, among other things, erectile dysfunction.

Due to the design of the bespoke Diabetes CCI® Flashwave® only have to be applied to one side of the penis or the crus, as it fully penetrates the tissue in the treatment area.

Erectile dysfunction (ED) is a sexual dysfunction that is increasingly prevalent with age. Men affected by ED are unable to develop or maintain an erection sufficient for sexual intercourse despite being sexually stimulated. Most ED cases are of vascular origin, with diabetes patients at a significantly higher risk of suffering these complications.

Unlike conventional ED treatment, such as PDE-5 inhibitors, Flashwave® does not involve the use of any pharmaceuticals. Moreover, the Biocellular Transductive Wave Therapy causes no side-effects on other organs or healthy tissue. The **non-invasive, painless** Flashwave® procedure is performed during a series of five treatments and requires no sedation or anesthesia.

Flashwave® technology is highly effective across **a wide range of medical applications**. The ability to communicate with different cells allows for treatment and management of vastly different diabetes-related medical indications, as Biocellular Transductive Wave Therapy counteracts the typical complications caused by diabetes, such as reduced blood flow, neuropathy and vascular disease.

As little as three Flashwave® treatments may suffice to show significant improvement in the aforementioned diabetes-related complications, no matter how long the patient has been suffering from them before the treatment.

Noticeable improvement may be visible within two weeks after start of the therapy. A high rate of patient satisfaction can be observed, all without reliance on PDE-5 inhibitors or antibiotics. Flashwave® has shown significant long-term effectiveness.

Vasculogenic and diabetic ED patients will benefit from Flashwave® – those who are responsive to PDE-5 inhibitors as well as those who are unresponsive. For the latter group, which includes a substantial number of severe ED patients, the only solution to date are vacuum pumps, injections and perhaps implants. Flashwave® therapy not only offers a new treatment option, but brings hope to those patients, by allowing more than 70 % of them to become responsive to PDE-5 inhibitors. As »end-stage« ED patients, they will be able to enjoy normal sexual functionality. With over 50 % of men aged 40–70 suffering from ED, and even more from transient ED, Flashwave® therapy can bring improvement in erectile function and new sexual spontaneity to millions of patients – safely, naturally, painlessly.

- » We recommend one treatment per week over a duration of five weeks.
- » If necessary, the treatment cycle can be repeated 8 weeks after the last treatment.



Diabetic Foot Syndrome (DFS)

Diabetic foot syndrome is a major complication for patients with diabetes mellitus. About 25 % of patients with diabetes will suffer from diabetic foot syndrome at some point during the course of their disease.

Diabetic neuropathy and peripheral vascular disease are the main causative factors in the pathogenesis of **chronic wounds** in patients with DFS. The mortality rate of these patients is more than twice as high as that of the average population.

Diabetic Foot Ulcers

A diabetic foot ulcer is an open wound that most commonly occurs on the foot in approximately 15 % of patients with diabetes.

25 % of costs incurred by patients with diabetes are spent on diabetic foot ulcers, and 50 % of hospital days are attributed to the treatment of the diabetic foot syndrome. **DFS is also the most common cause of non-traumatic amputations.** Both the risk of amputation and mortality are much increased in case of peripheral vascular disease.

Chronic diabetic foot ulcers are caused by small-vessel occlusion, usually compounded by neuropathy and infection. They are usually caused by several factors: Neuropathy, altered biomechanics, peripheral vascular disease (PAD) and inadequate foot wear are among the major factors. The course of the disease may be complicated by infection.

It occurs as a result of various factors, such as mechanical changes in conformation of the bony architecture of the foot, atherosclerotic peripheral arterial disease and peripheral neuropathy, all of which occur with higher frequency and intensity in the diabetic population.

Diabetic foot lesions are responsible for more hospitalizations than any other complication of diabetes, having a major impact on the patient as well as on the health care system.

Current standard of care for DFS related complications

The existing therapy approaches for complications caused by DFS are almost exclusively concentrating on prevention.

Current standards of care consist of:

- » **Prevention:** optimized insulin adjustment, professional foot care and orthopedic foot wear, patient education
- » **Early diagnosis** combined with qualified treatment
- » **Modern dressing** such as moist dressings
- » **Hyperbaric Oxygen Therapy (HBO)**

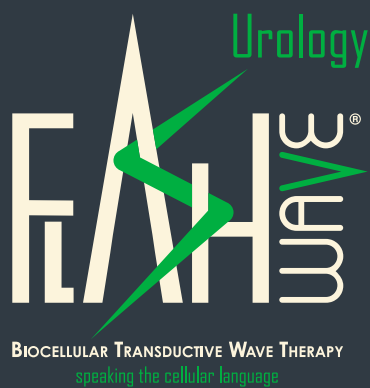
An early diagnosis combined with qualified treatment of disturbed wound healing is considered crucial for successful healing of diabetic foot ulcers too. However, therapy outcomes are often irregular and inconsistent.

Management of chronic ulcers in the lower extremity remains a challenge for patients and health providers. Therefore a therapy method with a cellular regeneration mechanism for the affected tissue is urgently required.

Flashwave® induced cellular communication activates the natural healing process of the human body, facilitating the development of new healthy tissue and offering a unique chance for a long-term healing of diabetic foot ulcers.



Flashwave® is also available for these indications:



Notes

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