13 Adjunctive Therapies in Pressure Ulcers

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Introduction

Standard care and management of pressure ulcers involves relieving risk factors, improving nutrition and skin hygiene, treating infections, removing necrotic tissues, and applying the appropriate dressings. However, some cases are not responsive to the above treatment. This fact clearly demonstrates that, well-documented, promising, and inexpensive methods from adjunctive therapies are still necessary.

According to the newest "National Pressure Ulcer Advisory Panel, European Pressure Ulcer Advisory Panel and Pan Pacific Pressure Injury Alliance. Prevention and Treatment of Pressure Ulcers: Clinical Practice Guideline" [1] published in 2014 a few forms of biophysical agents have been examined for healing pressure ulcers.

Electrical Stimulation

One of the proposed adjunctive method in this document is electrical stimulation with the strongest evidence (grade A—Table 13.1) and with the highest recommendation level.

The first report of electrical stimulation in the medical field is 63AC Scribonius Largus a greek chief physician uses an electric fish for pain control. Roman takes the torpedoes in the treatment of non healing (torpid) ulcers. In 1843,

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M. Romanelli et al. (eds.), *Science and Practice of Pressure Ulcer Management*,
https://doi.org/10.1007/978-1-4471-7413-4_13

Table 13.1 Strength of evidence according to NPUAP, EPUAP and PPPIA guideline [1]

A grade The recommendation is supported by direct scientific evidence from properly designed and implemented controlled trials on pressure ulcers in humans (or humans at risk for pressure ulcers), providing statistical results that consistently support the recommendation
B grade The recommendation is supported by direct scientific evidence from properly designed and implemented clinical series on pressure ulcers in humans (or humans at risk for pressure ulcers) providing statistical results that consistently support the recommendation
C grade The recommendation is supported by indirect evidence (studies in healthy humans, humans with other types of chronic wounds, animal models) and/or expert oipnion

Table 13.2 Activity of ESTIM from literature

Function	Result
Chemotaxis	Increase
Incretions of GF (VEGF)	Increase
Blood flow	Increase
Small vessels (granulation tissue)	Increase
Macrophages activity	Increase
Fibroblast activity	Increase
Muscular tropisms	Increase
Wound contraction	Increase
Scar elasticity	Increase
Pain	Reduction
Bacterial growth (in vitro)	Reduction

Dubois-Reymond reported a current of an intensity of 1-mA exiting human skin wounds. It was later confirmed that wounds create a surrounding electric field, the "current of injury," which was found to be of an intensity less than 1 mA. In 1885 Guillaume Duchenne notes that the alternating current is more effective in inducing muscle contractions.

The mechanisms [2, 3] that explain how electric current promotes wound healing based on evidence from many animal studies and very few controlled studies conducted in humans. It has been shown that electrical stimulation induces cellular actions in almost every phase of the wound healing cascade, including the stimulation of several fibroblast activities, such as enhanced collagen and deoxyribonucleic acid synthesis, adenosine triphosphate production and calcium influx, and an increased number of growth factor receptor sites. The *in vitro* studies on macrophages, epithelial cells, and fibroblasts have demonstrated that stimulation promotes the migration and activation of key cells within the wound site. Additionally, *in vivo* studies involving animal models have shown that electric stimulation results in more collagen deposition, enhanced angiogenesis, greater wound tensile strength, and a faster wound contraction rate. Electric current has also been shown to improve tissue perfusion and reduce edema formation, indirectly stimulating healing by improving oxygen delivery to the tissue. However the activity of ESTIM are known (Table 13.2), but the modality of action are not so certainly defined, Afargan propose a role of brain stimulation but it is based on sthocastic type of Estim [4], Kloth that work mainly on DC suggest e role on cell migration and activation.

The recommendation from the NPUAP, EPUAP an PPPIA guideline [1] is supported by six randomized controlled clinical trials.

The article from 2011 published in *Wounds* [5] showed significant progress in the healing of pressure ulcers of stage I–III in 29 participants treated with electrical stimulation. The mean area and the mean duration of pressure ulcers were 4.45 cm^2 and 3.17 months respectively in electrical stimulation group and 4.93 cm^2 and 2.80 months in the control. All patients received the same standard wound care (SWC). After six weeks the mean surface wound area decreased significantly in both groups ($p < 0.001$ in stimulated group and $p = 0.002$ in control group). In the electrical stimulation group eight of 29 pressure ulcers closed versus only four of 29 ulcers in the control group. A mean decrease in surface wound area was 85.38% in stimulated group versus only 40.08% in control group ($p < 0.001$). The obtained results were supported by our another clinical study investigating electrical stimulation compared with SWC for treating 50 patients with pressure ulcers in stage II–III [6].

To perform the electrical stimulation procedure in pressure ulcers special device and equipment is needed (Fig. 13.1). Electrodes should be made of silver or conductive carbon rubber. Usually, the active electrode size ought to be matched to the wound size, and placed on saline soaked gauze (3–5 mm thickness) directly into the wound. The return electrode should be positioned on intact periwound skin. The exampled placement of electrodes is presented in Fig. 13.2.

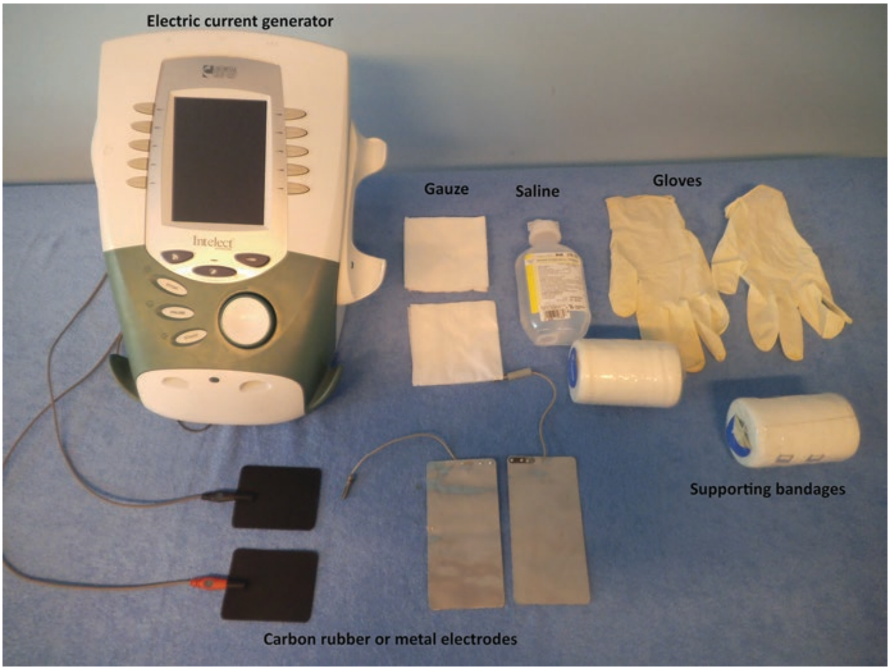


Fig. 13.1 Equipment for electrotherapy in pressure ulcers

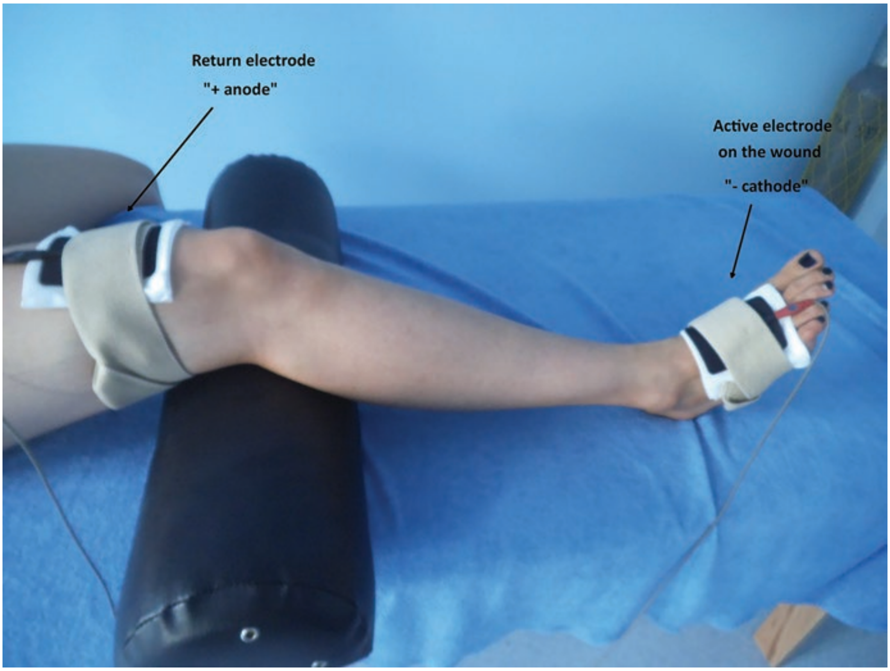


Fig. 13.2 Sample electrode placement in pressure ulcers

Table 13.3 Different type of current

Current		Wave	Energy
Pulsed	Monophasic		
	Biphasic	Symmetrical	
		Asymmetrical	Balanced
			Unbalanced
Alternated		Symmetrical	
		Asymmetrical	Balanced
			Unbalanced
Direct			

ESTIM is a definition that collect different type of current, with different level of target and action, in Table 13.3 are summarized the different current applied in Human body.

Some time is difficult for clinicians well understand the “electrical concept”, but we have to consider that electricity is in the Human body, and it determine our activity at every level through nerve transmission. Collins [7] well define the different type of treatment with ESTIM (Table 13.4).

At this state of art (Table 13.5) two electrical procedures with Direct Current are the most recommended in pressure ulcer therapy:

1. High Voltage Peaks Current (HVPC)—Table 13.6,
2. Low Voltage Monophasic Peaks Current (LVMPC)—Table 13.7.

Table 13.4 Different typology of ESTIM from Collins modified

Type	Acronyms
Low intensity direct current	LIDC
Low intensity pulsed direct current	LIDPC
High voltage pulsed current	HVPC
Decubitus direct current treatment	DDTC
Simulated biphasic ES	SSES
Asymmetric biphasic electrical stimulation	ABES
Simmetric biphasic electrical stimulation	SBES
Frequency rhytmic electrical modulation system	FREMS

Table 13.5 Electrical stimulation dosage range in pressure ulcer healing

IMPORTANT!
According to newest estimations [19] an electrical stimulation seems to be efficient in pressure ulcer therapy, when the dosage range **is** [a]**250–500 µC/s**, which represents a small window of electrical energy that has been shown to produce very favorable wound healing results

[a]Electric charge is a physical property of matter (e.g., wound tissue with endogenous electric field) that causes it to experience a force when near other electrically charged matter. Charge is measured in units called coulombs (C), representing a specific quantity of electrons, that is, electrically energy. The dosage or charge delivered into wound tissues through a treatment electrode to enhance healing is in the µC range, which flows in time (per seconds)

Table 13.6 Characteristics of HVPC

PRACTICAL MESSAGE—How to prepare a therapy!
1. Waveform: monophasic, double-peaked spike impulses 2. Frequency: 100 pps 3. Voltage: 100 V 4. Impulse duration: 100 µs 5. Current amplitude: with the intensity on sensory level, below the level of muscle contractions (usually from 20 to 40 mA, patient should only feel a mild tingling sensation) 6. Electrode placement and polarization: cathode "–" on the wound, anode "+" as a return electrode (usually in a distance of 30–50 cm from the ulcer) 7. Methods: 50–60 min a day, five times a week (from Monday to Friday)

The HVPC represents usually the electric charge from 250 to 350 µC/s. The LVPMC delivers the dosage range 300–500 µC/s. Both are useful in pressure ulcer healing, only if the generated by electric device parameters are precisely correct. The helpful for verification of signal characteristics is an oscilloscope. The oscilloscope is an instrument that can be used to identify and verify the characteristics of electrical signals that are produced by generator. The oscilloscope is useful in identifying signal characteristics, because it can reliably display a wide band of frequency ranges and a large range of amplitude. The oscilloscope can be used to verify that the voltage and frequencies that a stimulator applies to the patients' wound are in the expected range (Fig. 13.3).

There are also some contraindications to electrical stimulation in patients with pressure ulcers (Table 13.8), which wound therapist should always consider during the treatment process.

Table 13.7 Characteristics of LVMPC

PRACTICAL MESSAGE—How to prepare a therapy!
1. Waveform: monophasic, single rectangular impulses 2. Frequency: 64 or 128 pps 3. Voltage: 20–35 V 4. Impulse duration: 132 μs 5. Current amplitude: with the intensity on sensory level, below the level of muscle contractions (usually from 20 to 40 mA, patient should only feel a mild tingling sensation) 6. Electrode placement and polarization: cathode "−" on the wound, anode "+" as a return electrode (usually in a distance of a few centimeters from the ulcer). In some cases is allowed alternate polarity (+/−) at least every week, based on stage of healing. 7. Methods: 50–60 min a day, five times a week (from Monday to Friday)

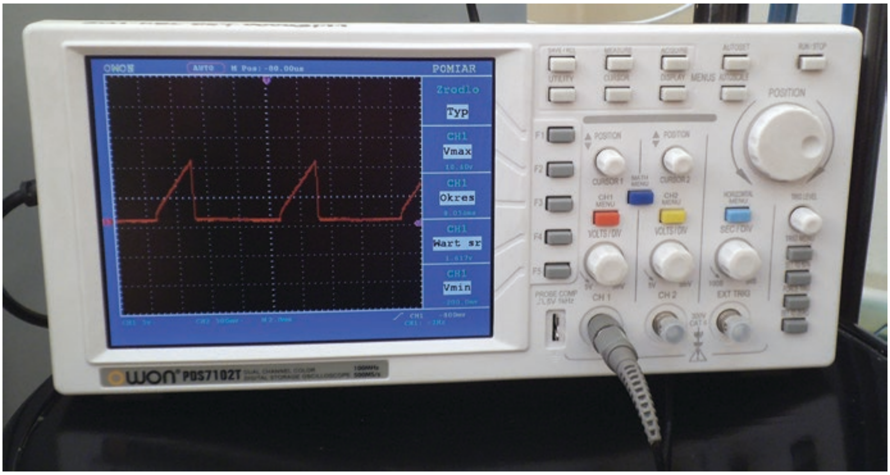


Fig. 13.3 An oscilloscope for elecrical device calibration

Table 13.8 Contraindications for electrotherapy

WARNING!
REMEMBER, NOT TO apply to the thoracic area (or transthoracically) of a patient with arrhythmia, congestive heart failure, recent myocardial infarction, and other heart conditions REMEMBER, NOT TO apply anywhere on the body of a patient with a demand-type implanted cardiac pacemaker or defibrillator or deep brain stimulator REMEMBER, NOT TO apply through the carotid sinus area (at the bifurcation of the common carotid artery); it may cause a rise in blood pressure, reflex vasodilatation and slow the heart rate REMEMBER, NOT TO apply transcerebrally (thru the head) at a milliamp level because it may cause changes in brainwave patterns. EXCEPTION: Only, microcurrent can be applied transcerebrally REMEMBER, NOT TO apply through cancerous (malignant) tissue REMEMBER, NOT NOT apply near or touching protruding metal such as surgical surface staples or external pins because they are excellent conductors of electricity REMEMBER, NOT TO use on any patient who reacts very negatively to the experience or to the sensation of stimulation REMEMBER, NOT TO apply to patients who cannot provide adequate feedback concerning the level of stimulation (infants, individuals with mental disorders)

The HVPC and LVMPC are supported by literature, but the scientists all over the world still have been looking for another new electrical procedures in wound healing [8]. In recent years, newer technologies are miniaturized, disposable bioelectric dressing-like devices with imbedded electrical circuitry that have been cleared by healthcare regulatory agencies for wound healing in the European Union and for an antibacterial effect on wounds in the United States. The former battery-powered dressing device, Posifec stimulator delivers micro-amperage electric current. The latter bioelectric dressing device, Procellera is powered by 25 micro-batteries that when activated by wound moisture deliver from 0.6 to 0.7 V at 10 μA to the wound surface. Further studies are still needed.

At present, the extremely interesting experiment is conducted in China too. Zhang et al. [9] evaluate the effectiveness of electroacupuncture for the treatment of patients with pressure ulcers. This study consists of a randomized controlled trial with two parallel arms: a control group and an acupuncture group. Both groups will receive standard wound care (including changing position, using mattresses and cushions, and a good diet) of five sessions per week for a total of 40 sessions during the 8-week treatment period. In addition to standard wound care, all participants in the treatment group will receive electroacupuncture treatment. Hanyi needles (0.17 × 7 mm) and a Micro Plus transcutaneous electrical nerve stimulator (TENS) will be used in the trial. Two needles will be punctured into the skin of the local wound. One needle will be inserted into the wound center with a 90° angle and connected with the negative pole, while the other needle will be punctured in the normal skin 0.5 cm away from the ulcer margin with a 45° angle and connected with the positive pole. Both needles will be applied without lifting, thrusting, or rotating. The electric stimulator will be turned on with 500 μA, 0.5 Hz, 30 min each time, for five sessions per week for 8 weeks. The following outcome measurements will be used in examination of participants: wound surface area (WSA), visual analogue scale (VAS), and the proportion of ulcers healed within trial period (PUHTP). All the outcomes will be evaluated at the start of the study, at the end of the fourth week, at 2 months after randomization, and 4 weeks after treatment cessation.

The DDCT wave-form has been processed from electrical activity that was observed and measured around healing wounds. The type of ESTIM is a stochastic signal close to the signal present in human body [10]. Electrodes are placed on healthy skin surrounding the wound (Fig. 13.4), time treatment is 30 min, 2 session a day. Adunski and Ory, [11] in an RCT reported an increase in healing rate and speediness in treated group vs control group. Afargan suggested a role of nerve system. The Frems is another type of stochastic E-STIM, based on a predefined asymmetrical wave, determine an increase of blood flow (vasomotion) and an increase of healing rate (Fig. 13.5).

In conclusion the electrical stimulation seems to be the most efficient therapy in alternative methods with the strongest evidence. However, there are some other interesting biophysical agents, but at this moment with much smaller recommendation level (laser stimulation, extracorporeal shock wave therapy or hyperbaric oxygen treatment).

Fig. 13.4 BST method

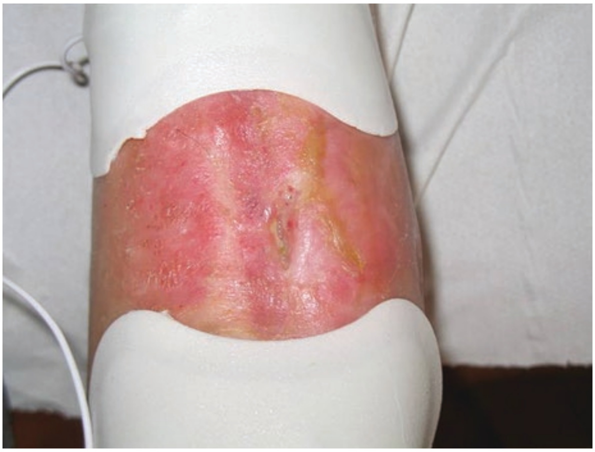
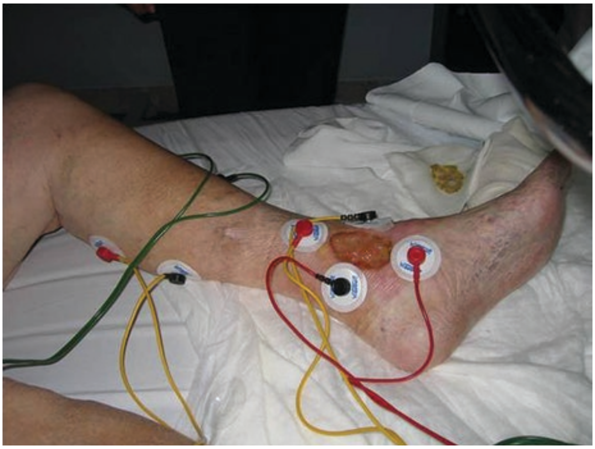


Fig. 13.5 FREMS method



Laser Therapy

Laser therapy has been used to accelerate wound healing since the late 1960s, but its results are still controversial. Due to current insufficiency of evidence to support or refute the use of laser irradiation in the treatment of pressure ulcers, laser therapy is recommended in newest guideline [1] with only relatively poor grade “C”.

Woodruff et al. [12] performed a metaanalysis of 24 animal and clinical studies on the effectiveness of laser (including infrared-based units) on wound healing in variety of ulcer on both animals and humans. They concluded that laser therapy studies had numerous methodological limitations.

In view of the absence of randomized studies with sufficiently large sample sizes, our research team assessed the efficacy of lasers for treating pressure ulcers. Taradaj et al. [13] performed in 2013 a prospective, single-blinded, and randomized clinical trial to assess the effect of laser therapy as a potential alternative to standard care. We wanted to compare a few common wavelengths in pressure ulcer therapy in a well-prepared and well-planned research program. The primary endpoint in this trial included both the percentage reduction of the ulcer surface area and the percentage of completely healed wounds after one month of therapy (ulcer healing rate). The secondary endpoint was the ulcer healing rate at the follow-up evaluation (3 months after the end of the study). In total, 72 patients with stage II and III pressure ulcers received laser therapy once daily, 5 times per week for 1 month using a (GaAlAs) diode laser with a maximum output power of 50 mW and continuous radiation emission. Three separate wavelengths were used for the laser treatment: 940 nm (group I), 808 nm (group II), and 658 nm (group III). An average dose of 4 J/cm^2 was applied. In group IV, a placebo was applied (laser device was turned off). The results of our study showed that the wavelength of the laser beam is extremely important during the wound-healing process (and perhaps this is one reason for the many controversies). In this trial, we found no evidence that justifies using laser therapy at wavelengths of 940 and 808 nm as an adjuvant to the future consensus pressure ulcer treatment. However, in our opinion the wavelength of 658 nm (dose 4 J/cm^2, 5 times a week, once daily) is interesting adjunctive therapy and efficient in pressure ulcer healing (the sample results before and after monthly therapy is presented in Figs. 13.6 and 13.7).

Fig. 13.6 Pressure ulcer before laser therapy

Fig. 13.7 Pressure ulcer after 4 wks of treatment

Extracorporeal Shock Wave Therapy

Extracorporeal shock wave therapy (ESWT) is a modern, adjunct medical procedure aimed to improve the skin condition of patients with chronic and acute soft tissue wounds. ESWT is defined as a sequence of biphasic, high-energy acoustic pulses that generate transient pressure disturbance and propagate rapidly in three-dimensional space; this therapy is associated with a sudden rise of pressure applied directly into tissues without any damaging effect.

ESWT utilizes two basic types of generators: radial and focused. They differ in terms of shock wave propagation and the physical characteristics of the energy. Radial ESWT is produced by pneumatic devices located inside the generator that create linear pressure with low energy values. The energy is produced by the pressure wave, while compressed air accelerates the cartridge strikes at the top of the applicator. The energy generated by the pressure wave is absorbed into the skin approximately 3 cm deep and spreads a wider beam to a larger target area. Focused ESWT is generated by electromagnetic, electrohydraulic, and piezoelectric sources. Pressure pulses rise rapidly in range of 10–100 MPa and concentrate the acoustic energy beam with a penetration depth of approximately 12 cm.

Our research team [14] described a third type of defocused ESWT: an acoustic planar wave generated by electromagnetic and electrohydraulic devices. It is characterized by lower energy values delivered into the soft tissues and a superficial and quite large (3–5 cm^2) impact zone. ESWT types have been differentiated on the basis of the level of energy applied at the focal point per one pulse during treatment session—i.e., energy flux density (EFD), which is determined as low energy when <0.12 mJ/mm^2 and high energy when >0.12 mJ/mm^2. The following type of ESWT seems to be very attractive for wound healing and is a serious chance for a new promising therapy in pressure ulcers.

ESWT is not indexed in NPUAP, EPUAP an PPPIA guideline [1], because it is very new biophysics agent. Probably, it will be discussed in updated 2019 edition of the guideline. At this stage the recommended parameters of ESWT in pressure ulcers are:

– Type of generator: defocused
– Frequency: 5–10 Hz
– EFD: 0.1 mJ/cm^2
– Number of pulses: $100/cm^2$
– Methods: three sessions (3–4 days interval between treatments)

Table 13.9 Modality to administer oxygen in wound treatment

Type		Oxygen	
Hyperbaric oxygen therapy	HBOT	2.4 atmosphere intermittent	
Topical oxygen therapy	TOT	1.03 atmosphere intermittent, 6 LPM, intermittent	TOCT TWO2
Transdermal continuous oxygen therapy	TCOT	1 atmosphere, > 2 mL/h, continuous	Natrox (15 mL/h) Epiflo (3 mL/h)

Table 13.10 Comparison between different wound oxygen therapies

	Hyperbaric	Local perfusion	TOCT
Local oxygen levels at wound during treatment	1800	800	350
Daily oxygen exposure	1.5 h	5 h	23 h
Average oxygen levels over a week	114	183	336

Topical Oxygen Therapy

A continuous supply of oxygen is required for any aspect of life and obviously also for wound healing. The needs of oxygen during the healing process increase 50 time, it work as substrate, but also as signal, reduce bacterial growth and increase collagen deposition.

Oxygen therapy can be administered in different way (Table 13.9), with different amount (Table 13.10). There is not a clear evidence on use of Oxygen in wound [15]. The HBOT is well defined in treatment of diabetic foot [16], in other wound, we can obtain some indication from the ECHM-ETRS guide line 2006 [17], but level of evidence is not so strong. Wild et al. [18], in a review on topical Oxygen Treatment conclude: *"The effectiveness of Topical Wound Oxygen (TWO2) has been shown in a significant number of studies. However, there is a clear need for well designed RCT to measure the true advantage of TWO2 compared to other modalities like Hyperbaric Oxygen or advanced wound care"*. At this moment, new devices are available, and result will be evaluated in future. Figure 13.8 shows the device Natrox put in place.

Fig. 13.8 A TOCT device positioned on a wound with foam as a secondary dressing

Summary

The electrical stimulation is the most recommended adjunctive therapy of pressure ulcers. At present, this biophysics agent is an algorithm for wound healing, which is strongly supported by literature. There are also other promising therapies, like HBO, laser irradiation or acoustic waves as EWST. Future studies are provided, which assess their usefulness in pressure ulcer care.

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