Review article / Artykuł przeglądowy

Magdalena Atta-Motte 0000-0001-7374-1617

Certifa Aesthetics Training Academy, 71 Leamington Avenue SM4 4DQ London, United Kingdom
+44 79 32857109 *magda.atta.motte@consultant.com*

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The use of lasers in the treatment of scars

Zastosowanie laserów w terapii blizn

ABSTRACT

Scar treatments described in the literature include chemical, physical and surgical methods. The treatment is primarily focused on prevention from the abnormal healing process of the skin, so and combination therapies are often used for this purpose.

The aim of the article was to present the classification of scars and the concept of laser treatment, based on the recommendations of the International Consensus of 2020 presented by the American Society of Lasers in Medicine and Surgery (ASLMS) and the results of scientific research.

Although laser therapy is one of the most effective methods, it is not possible to unequivocally state that it is the most effective in the treatment of scars. The final effect depends on many factors, including the type and age of the scar.

Keywords: scar, wound, lasers, ablation lasers, combined therapies

STRESZCZENIE

Terapie blizn opisane w literaturze obejmują metody chemiczne, fizyczne i chirurgiczne. Leczenie koncentruje się przede wszystkim na zapobieganiu nieprawidłowemu procesowi gojenia się skóry, w tym celu często stosuje się terapie łączone.

Celem artykułu było przedstawienie klasyfikacji blizn oraz koncepcji laserowej terapii leczenia blizn, w oparciu o zalecenia Międzynarodowego Konsensusu z 2020 r. przedstawionego przez Amerykańskie Towarzystwo Laserów w Medycynie i Chirurgii (ASLMS) oraz wyników przeprowadzonych badań naukowych.

Choć laseroterapia należy do jednych z najbardziej efektywnych metod, jednoznaczne stwierdzenie, że jest ona najskuteczniejsza w leczeniu blizn nie jest możliwe. Efekt końcowy zależy od wielu czynników, m.in. od rodzaju i wieku blizny.

Słowa kluczowe: blizna, rana, lasery, lasery ablacyjne, terapie łączone

INTRODUCTION

A wound is a disturbance of the continuity of skin and epidermal tissues, but also of deeper structures like fascia, muscles, blood vessels, nerves, tendons, bones, joints or their damage due to the presence of a harmful factor. The force of an injury may act only superficially and damage the epidermis, causing abrasions or tissue contusion. All wounds can be classified into one of two categories: small wounds - usually involving only damage of the layers of the skin, and penetrating wounds - in which the deeper structures are additionally damaged. Depending on the way of damage, the following wounds are distinguished as cut, stab, gunshot, bruised, lacerated, and bitten.

A scar is a skin lesion formed at the site of previous tissue damage. It consists of fibrous connective tissue, is less flexible, devoid of nerve endings, sebaceous glands, and hair follicles. According to the World Health Organization (WHO), more than 11 million burns are reported annually worldwide and require medical attention [1]. According to information published by the American Burn Association (ABA), more than 480,000 burns occur each year in the United States and require treatment [2]. The frequency of scar tissue formation, (scar formation) is unknown [3]. In some studies, the prevalence of hypertrophic scars (HTS) was estimated to range from 32% to 72%. Earlier studies indicate that scars strongly affect the quality of life of people with previous skin injuries [4].

SCAR THERAPY

Scars may have a negative impact on the quality of life [4, 5]. On the one hand, they cause disturbing sensations such as pain, tenderness, or itching, and on the other hand, functional limitations in the form of contractures, which are a consequence of problematic scars. Moreover, the aesthetics of the scar may also have a negative impact on psychosocial factors [6, 7].

Rebuilding damaged skin requires a complex sequence of physiological interactions in order to generate appropriate scar tissue and repair the skin lesion [8]. Any dysfunction of the wound healing process may lead to excessive scar tissue formation [9]. Hypertrophic or keloids scars result from such abnormal wound healing [10].

WOUND HEALING STAGES

After skin trauma, there are four linear stages to skin healing:

- the exudative (inflammatory) phase,
- purification phase,
- proliferative phase,
- the redevelopment phase.

The exudative (inflammatory) phase

It takes 1 to 6 days. The characteristic features of this phase are: redness, congestion, swelling, increased temperature, tissue soreness, and exudation. The outer clotting cascade is activated and a fibrin plug is formed. Neutrophils are attracted to the site of injury by producing cytokines, and then macrophages enter, which remove bacteria and damaged tissue by phagocytosis.

The purification phase

It can also be considered as part of the exudative phase, occurring on days 4 to 7 after tissue damage. Then the inflammatory process is slowly reduced, and the tissue is mainly affected by macrophages, which eliminate impurities by phagocytosis. Macrophages additionally support the transmission of antigens to lymphocytes and secrete cytokines, polypeptides, and growth factors.

The release of transforming growth factor β (TGF-β) activates fibroblasts up to approximately 1 week after injury, thereby initiating a proliferative phase of wound healing lasting 4-21 days. Granulation tissue (macrophages, fibroblasts, proteoglycans, hyaluronic acid, collagen and elastin) replaces the fibrin plug. TGF-β and platelet-derived growth factor (PDGF) released by macrophages activate fibroblasts to produce collagen III, ECM and initiate angiogenesis, creating immature, leaky blood vessels. Neovascularization is also stimulated by mechanical stretching.

Keratinocytes migrate from the wound margins and adnexal structures to epithelialize the wound.

The reconstruction phase

It begins after 21 days and lasts up to one year. Type I collagen replaces type III collagen, restoring tensile strength to the skin, and remodelling granulation tissue.

Disruptions in any of the wound healing phases can result in scarring. For example, when scar formation stops in the inflammatory or proliferative phase, the newly formed small blood vessels persist, clinically manifested by persistent scar erythema or granulation, and scar hyperplasia frequently occurs. TGF - β1 and TGF - β2 are overexpressed in hypertrophic and keloid scars and stimulate the excess production of collagen.

Identifying the type and origin of the scar can help predict the outcomes of various interventions and provide information on treatment recommendations.

CLASSIFICATION AND TYPES OF SCARS

According to the literature, there are two main types of scars: atrophic and hypertrophic [11].

Atrophic scars

According to the extended classification used by Jacob et al. atrophic scars can be divided into four main groups [12]:

- **Rolling valleys**. The type of rolling scar produces an undulating and deeper image that is best seen under indirect light. They occur, for example, after acne.
- **Shallow / atrophic**. Atrophic scars, are most often located in the area of the cheek and may be the result of, for example, smallpox.
- **In the shape of a boxcar**. Boxcar scars are oval or round in shape, with well-defined edges and a flat base, and their depth ranges from 0.1 to 0.5 mm. Mostly they are not adjacent to each other.
- **Skewer-shaped (icepic**k). They are often described as small scars with steep edges at the wide inlet that taper to one point at the base of the lesion. These scars, referred to as icepick, are shallow or deep, and their depth can reach the border of the dermis and subcutaneous tissue.

Hypertrophic scars

Hypertrophic scars most often arise as a result of a prolonged healing process, after burns, due to excessive collagen synthesis and its slow metabolism.

The correct classification of scars has a decisive influence on the choice of the appropriate treatment, which is later related to its effects.

According to the findings of the International Consensus 2020, these scars are divided into [13]:

- Overgrown - raised scars that remain within the limits of the original injury. Often confused with keloids, which continue to grow beyond the original boundary of the wound (fig. 1).

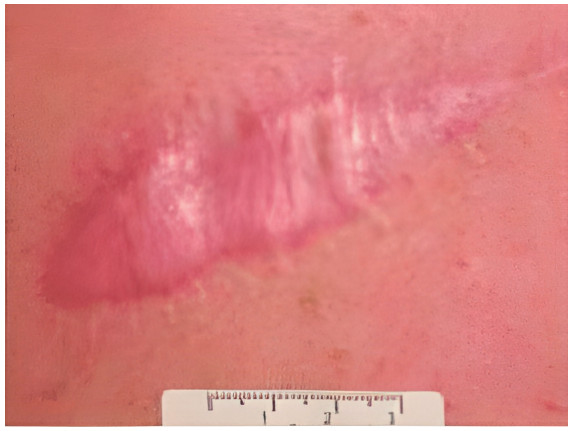

Fig. 1 The outgrown scar **Source:** [14]

- Erythematosus - pink or red (fig. 2)

Fig. 2 The erythematosus scar **Source:** [14]

- Hypertrophic - raised, located within the primary wound area (fig. 3). Such a scar grows excessively in previously damaged skin (unlike keloids which extend beyond the boundary of the wound). A hypertrophic scar consists of scar tissue that is raised above the rest of the skin surface and is dark red in color.

Fig 3. The hypertrophic scar **Source:** [15]

- With hypopigmentation - white scars with a deficiency of melanin in the epidermis (fig. 4).

Fig. 4 The hypopigmentation scar **Source:** [16]

- With hyperpigmentation - scars with increased pigmentation, there is an excessive level of melanin in the epidermis (fig. 5).

Fig. 5 The hyperpigmentation scar **Source:** [17]

- Low tension - These are the result of cuts or punctures without removing the tissue and are not found in high tension anatomy areas (like joint extensors, upper chest, and back) (fig. 6).

Fig. 6 The low tension scar **Source:** [18]

- High Tension - A type of scar that develops after large areas of skin are cut or lost. It may also occur in high-tension anatomy areas (like the extensor surfaces of the joints, upper chest, and back) (fig. 7).

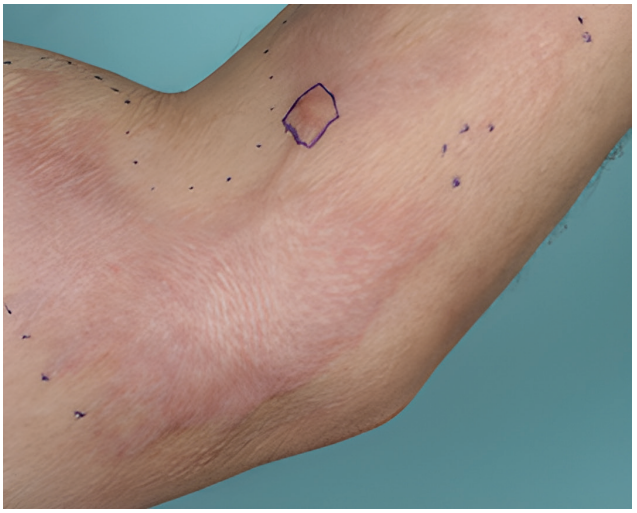

Fig. 7 The high tension scar **Source:** [19]

- Mature / Stable - this is a type of scar of receded erythema and stopped growth (fig. 8).

Fig. 8 The mature scar **Source:** [20]

- Immature / Unstable - scars with persistent erythema and active growth (fig. 9).

Fig. 9 The immature scar **Source:** [21]

OVERVIEW OF LASERS USED IN SCAR THERAPY

Scar treatments described in the literature include chemical, physical and surgical methods [22]. Physical treatment are divided into mechanotherapy, occlusive and hydrogen therapies, and light therapy, but often combination therapies are used [23]. The main goal of scar treatment is to prevent abnormal skin healing [24].

It cannot be clearly determined which of the methods is the most effective, because it depends on many factors, including the type and age of the scar. Currently, treatments with lasers of different wavelengths are one of the most effective in the treatment of scars [13].

Vascular lasers

- **Pulsed dye laser (PDL).** PDL wavelengths of 585 or 595 nm and are selectively absorbed by oxyhemoglobin. The laser coagulates the microcirculation of the scar, thus reducing the erythem. It is recommended for erythematous scars, including slightly hypertrophic (<3 mm) erythematous scars. The results are more efficient when the lesions are also treated with a corticosteroid (triamcinolone acetonide) and fluorouracil (5-FU).

  PDL reduces scarring by inhibiting fibroblast proliferation, reducing TGF-β level and connective tissue growth factor (CTGF), which promotes signal-related extracellular kinases (MAPK / ERK). The MAPK / ERK pathway (also known as the Ras-Raf-MEK-ERK pathway) is a chain of proteins in a cell that transmits a signal from a receptor on the cell surface to the DNA in the nucleus. It increases fibroblast apoptosis, which is mediated by mitogen-activated protein kinases. For optimal scar reduction results, large spot sizes and low fluency (J/cm^2) are required.
- **Potassium titanium phosphate laser (KTP**). The 532 nm wavelength is selectively absorbed by oxyhaemoglobin. KTP laser reduces scar erythema in a similar way to PDL. For optimal scar reduction results, large spot sizes and low fluency - J/cm^2 are required.

Fractional lasers

Fractional laser devices can be divided into non-ablative (NAFR) or ablative fractional laser (AFR). They are used in the treatment of mature/stable scars, older than 2 years. Treatments are performed at intervals of 4 to 6 weeks.

Fractional lasers divide a single laser beam into hundreds of micro-beams that cause minor thermal injuries, known as micro-thermal zones (MTZs), while protecting the surrounding tissue.

Tissue damage is localized in the target microfibre areas, and epithelization occurs from the structures of the appendages as well as from the intervention of unchanged tissue. There are two key parameters for partial resurfacing - pulse energy and density. The pulse energy correlates with the penetration depth of the laser beam and the resultant depth of the coagulated tissue column.

- **Non-ablative fractional lasers (NAFR)**. Wavelengths ofb1540, 1550, 1565, and 1400 nm are selectively absorbed by water without damaging the epidermis. NAFR is less effective in promoting strong tissue regeneration but has a better safety profile [25]. NAFR is the method of the first choice for immature/unstable scars, which are more likely to destabilize the wound bed with AFR. Moreover, NAFR is preferred for phototypes IV-VI according to Fitzpatrick [26]. When treating scars with NAFR, use low-density settings (10-20%) to minimize the risk of adverse events. It has been shown that low-density NAFR is as effective as high-density therapy but has a better safety profile [13]. NAFR treatments can be repeated at intervals of 4 to 6 weeks.
- **Fractional ablation (AFR)** lasers are Er: YAG (2940 nm) and CO_2 (10600 nm) erbium yag lasers. The wavelengths are selectively absorbed by water and heat the affected areas of the epidermis and dermis to over 100°C, vaporizing the target tissue. At 2,940 nm, the Er: YAG laser has a higher water absorption rate and removes thin layers of tissue (5-20 µm) with minimal residual thermal damage. Therefore, pinpoint bleeding may occur. On the other hand, the CO_2 laser is less absorbed by water and evaporates slightly thicker layers of tissue (20-30 µm) with a residual thermal damage zone of 50-130 µm. The result is a bloodless treatment area. AFR lasers are considered the standard in the treatment of mature, stable, non-proliferating hypertrophic scars. Low-density settings (5-10%) minimize side effects and the depth of treatment depends on the depth of the scar. High-energy AFR for deep root canal ablation should be performed every 8-12 weeks to allow for adequate wound healing between sessions.

Q-switched lasers

Nanosecond and picosecond lasers have ultra-short pulse durations, making them a first-line therapy targeting endogenous or exogenous pigment. Scars from accidents or those resulting in a traumatic tattoo should be treated with Q-switched lasers in the first place.

- **Nanosecond lasers**. Wavelengths: 1064, 532, 694, 755 nm. The QS Nd: YAG laser produces less hypopigmentation compared to QS ruby (694 nm) and alexandrite (755 nm) lasers, due to the lower absorption rate by melanin and deeper penetration into the skin.
- **Picosecond lasers**. The pulses in the picosecond domain have an almost complete photomechanical effect compared to nanosecond lasers, which also produce thermal effects. Therefore, there is less discomfort during treatment and the healing time is shorter.

SIDE EFFECTS OF LASER THERAPY

The use of lasers in the treatment of scars, despite the fact that it has been recognized as an effective method, is associated with the possibility of side effects. Compared to non-ablative lasers, ablative lasers have a longer recovery time and are widely believed to be associated with a significant risk of complications. The indirect method, known as fractional, uses ablative technology to remove microscopic fragments of the skin, resulting in a shorter regeneration time.

The least invasive among laser methods - non-ablative lasers, cause damage to the skin while preserving the epidermis, which results in the shortest recovery time [27]. Although more invasive ablation procedures are considered to produce better results compared to non-ablative lasers [28]. However, it is up to the person who chooses the method to decide.

Most of the side effects resulting from the therapy are of a transient nature, regardless of the method of treatment. According to the available literature, the operation of ablative lasers is characterized by fewer complications compared to non-ablative lasers [29].

Hedelund et al. enrolled 13 patients for laser treatments to remove atrophic scars in two areas, one of which was treated three times with a CO_2 fractional laser, and the other was not treated at all [30]. Before treatment, there was no statistical difference in acne scar severity, uneven texture, or atrophy. After one, three, and six months, scar texture and atrophy improved significantly ($P < 0.0001$). No serious adverse events have been reported. Transient events, including mild erythema and superficial wounds, resolved two to three days after surgery.

Li et al. and Jung et al. examined 20 and 13 patients, respectively, due to photo-damage to the skin and scars on the face. They used the CO_2 ablation laser on the area of half of the face [31, 32]. They found significant improvements in both patient satisfaction and the investigator's blind assessment of global improvement [31].

Jung et al. found that approximately 1/4 of patients reported better results of ablative treatment, with almost half reporting more pain and the other half having equal pain with both treatments [32].

No significant side effects were reported in the above studies. Jung et al. reported the most adverse events on both sides, with the exception of a few punctual bruises in one patient in the ablative half.

Kwon et al. studied 25 patients who were randomly assigned ablative laser treatments to half of the face and non-ablative fractional laser treatments to the other half in order to reduce acne scars [33]. Adverse events were reported only in the NAFR group (n = 4.16%) consisting of hyperpigmentation. It was found that half of the ablation laser users achieved a much better improvement in the appearance of acne with less severe pain and side effects ($P < 0.05$).

Lederhandler et al. analyzed the results of 10 pediatric patients who underwent fractional ablative therapy with CO_2 laser resurfacing for traumatic facial scarring, of which six received additional treatment with a non-ablative laser [34]. Improvement in the appearance and texture of scars was observed in patients undergoing fractional therapy with ablation laser. The entire surface change was well tolerated, with short-term erythema in six patients and discoloration in one patient treated with alternative devices.

Zaouak et al. described two resurfacing treatments with fractionated laser at monthly intervals for the treatment of scar after perioral burns in a 48-year-old woman [35]. The treatment reactivated HSV (herpes simplex virus) five days after the second treatment, which was treated with intravenous acyclovir for 10 days and resolved vesicular eruptions.

Brightman et al. applied an ablative fractional CO_2 laser to an 82-year-old man with recurrent basal cell carcinoma, who developed scars after reconstruction of the nasal wall [36]. After the first month, the circumference of the wings, the contour of the sidewall of the nose improved, and the postoperative scars decreased. No serious adverse events have been reported, even after 2 years of clinical follow-up after treatment.

Avram et al. presented an observation in five patients who developed scars after fractional CO_2 laser resurfacing for the treatment of photo-injuries to the neck [37]. They developed hypertrophic scars that were largely reversible with proper care using non-ablative fractional laser therapy.

SUMMARY

Laser therapy allows not only to reduce scars of various origins, appearance and age, but also to prevent their formation by stimulating the production of collagen in the skin. The most commonly used in the treatment of scars are vascular, Q-switched, ablation, ablative fractional, and non-ablative fractional lasers.

Treatments can be performed at different time intervals from the moment the scar is formed, however, it is worth remembering that usually the best results are obtained by starting the therapy at the initial stages of skin healing. Reasonable adjustment of treatment parameters allows for achieving promising results, even in difficult hypertrophic and restrictive skin scars.

Properly performed scar laser therapy is safe, and side effects are not often observed. Ablative methods provide better clinical results with fewer adverse events compared to non-ablative laser therapy, while demonstrating the safety and long-term efficacy of such interventions.

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