Scar Treatment with Lasers: A Review and Update

Ru'aa Al Harithy · Kucy Pon

Abstract Scars affect millions of people every year with a great impact on patients, both physically and psychologically. Treatment of scars poses a great challenge for physicians. The evolution of lasers has provided a treatment option for many types of scars. In this paper we review the literature on different laser treatment option for scars and comment on our practice.

Keywords Lasers · Scar · Treatment · Management

Introduction

Scars are a very common complication of acne, burns, surgeries, and traumatic injuries affecting millions of people every year. The appearance of scars can be very disturbing to patients both physically and psychologically. Many treatment options and modalities have been employed for reduction and prevention of scar formation, including topical steroids, intralesional steroids, cryosurgery, interferon, 5-flurouracil, silicone gel, radiation, and surgeries. There is no general consensus in the literature as to what is the optimal treatment. The evolution of lasers in the last few decades has showed clinical and cosmetic benefits for patients and may be a good treatment option for many types of scars.

R. Al Harithy · K. Pon (✉)
SunnyBrook Health Sciences Centre,
2075 Bayview Avenue Suite M1-700,
Toronto, ON M4N 3M5, Canada
e-mail: kucy.pon@utoronto.ca

R. Al Harithy
e-mail: Ruaa.alharithy@utoronto.ca

Pathophysiology of Scar Formation

Understanding the pathophysiology of scar formation is important for the clinician who deals with scar treatment. Wound healing progresses through three stages: inflammation, proliferation, and maturation. Inflammation occurs immediately after injury with the activation of the coagulation cascade. Platelets are the first cells to appear after wounding. They release chemoattractive factors and vasoactive mediators that stimulate migration of inflammatory cells including neutrophils and macrophages. Neutrophils produce matrix metalloproteinases (MMPs) and collagenase, which cause excessive tissue loss in the wound area, leaving an area of tissue devoid of matrix that is subsequently replaced by scar tissue during the remodeling phase [1].

After 48 to 72 h the healing process transitions into the proliferative phase that lasts 3 to 6 weeks. Fibroblasts and endothelial cells migrate and proliferate within the wound site to form a connective tissue rich in blood vessels. Simultaneously, keratinocytes grow inward from the wound edges to cover the wound with a new epithelial layer. After the deposition of an early extracellular matrix (ECM), this matrix starts to remodel its collagen framework by cell apoptosis and cell maturation to obtain the scar ultimate strength. This process can last up to 2 years after the initial injury [2].

Excessive inflammation in healing tissue is responsible for increased scar formation. Scarring acne shows a predominantly CD45RO+memory T cell immune response, which is initially small and ineffective, but later becomes increased and activated in resolving lesions. In contrast with non-scarring acne, the cellular infiltrate is large and active with few memory T cells in early lesion, which subsides in the resolution phase [3].

Classification of Scars

Proper classification of scars is essential for determining proper laser treatment choice and protocol. Scar type, texture, morphology, and color determine the choice of laser parameter and help predict the number of treatments required. For the purpose of this article we discuss scars in three main categories: 1) hypertrophic scars and keloids, 2) acne atrophic scars, and 3) burn scars.

Laser Treatment of Scars

Lasers were first used in the treatment of scars in 1978. The first laser used to treat hypertrophic scars and keloids was the continuous wave argon [4]. Despite encouraging early reports, subsequent studies showed limited efficacy and high incidence of side effects [5]. Then, the neodymium: yttrium-aluminium-garnet (Nd:YAG, 1064 nm) laser and continuous wave CO_2 laser (10,600 nm) were described in the early 1980s as an alternative to argon by selectively inhibiting collagen production [6]. However, results showed failure to inhibit keloid formation and recurrence of lesions 1 year after treatment [7]. The theory of selective photothermolysis, which was introduced in early 1980s, has resulted in the invention of pulsed lasers that provided target selectivity, reducing the thermal damage and scarring [8].

More recently, the concept of fractional photothermolysis (FP) was introduced in 2003 as an option for low risk, effective resurfacing techniques. Fractionated lasers work by thermally altering a "fraction" of the skin, leaving up to 95 % of skin untouched, which repopulates the ablated columns of tissue permitting rapid epidermal repair. FP induces small three-dimensional zones of thermal damage known as microscopic treatment zones (MTZs). Water is the target chromophore for all available fractional devices on the market at this time. For FP, as the energy of the treatment is increased, the depth of penetration increases, and as the treatment level is increased, the density of the spots is increased. Densities can be reported as either percentage of coverage or number of MTZs per square centimeter [9, 10•]. Fractionated lasers are divided into ablative and non-ablative fractional resurfacing based on the wavelength affinity for water. Ablative fractional resurfacing (AFR) lasers have high affinity for water and these include the fractionated CO_2 10,600 nm, erbium:yttrium aluminum garnet (Er:YAG 2990 nm) and yttrium scandium gallium garnet (YSGG 2790 nm) lasers. Those with less affinity for water are classified as non-ablative fractionated lasers and include the following wavelengths: 1410 nm, 1440 nm, 1540 nm, and 1550 nm [10•, 11•].

Lasers for Hypertrophic Scars and Keloids

Hypertrophic scars are firm, red or pink raised scars confined within the margins of the original injury. They are usually most prevalent within the first month after injury and may regress over time. In contrast, keloids are raised, reddish-purple, nodular scars, firmer than hypertrophic scars, and keloids extend beyond the margins of the original wound and do not regress over time [13].

Many different lasers have been tried in the treatment of hypertrophic scars and keloids with variable efficacy. The most common laser used in the treatment of hypertrophic scar and keloids has been the pulsed dye laser (PDL 585–595 nm), which is considered the laser of choice in treating pigmented and hypertrophic scars [12••]. The most likely mechanism by which PDL works is through selective photothermolysis in which energy is absorbed by oxyhemoglobin leading to coagulation necrosis [8, 14, 15]. It has also been shown that PDL treatments increase MMP-13 activity and reduce TGF-beta expression, fibroblast proliferation, collagen type III, and controls the degree of angiogenesis within the wound and assists in minimizing scarring [16, 17]. Furthermore, PDL has been recently shown to up regulate P53 expression, which arrests fibroblast proliferation cell cycle [18]. When treating hypertrophic scars and keloids, PDL is used primarily to reduce erythema but has also been shown to reduce scar volume and improve scar texture as well as reduce pain and pruritus [15]. When comparing results of the two different PDL wave lengths it has been shown in a systematic review by Vrijman et al. [19••] that PDL 585 nm has a low efficacy for the treatment of hypertrophic scars when compared to PDL 595 nm, which has moderate efficacy [19••]. Keloids do show minimum improvement with PDL but seem to show enhanced clinical results when combined with intralesional corticosteroids or 5-fluorouracil injections [20].

The parameter used for hypertrophic scars and keloids are non-overlapping pulses ranging from 6 to 7.5 J/cm^2 (7 mm spot) or 4.5 to 5.5 J/cm^2 (10 mm spot), which should be applied over the entire surface of the scar (Table 1) [21]. Reducing pulse duration from 40 ms to 0.45 ms has been shown to be more efficacious in reducing scar volume and improving pliability but showed no difference in scar erythema [22]. Energy density should be decreased by 10 % in darker-pigmented patients or when treating scars in sensitive areas, such as anterior chest and neck [23]. The most common post-PDL treatment side effects are purpura that can last up to 3 to 7 days, blistering can occur, as well as pigment alteration, which is more common in darkly pigmented skin. Treatments are typically done at 6- to 8-week intervals to allow for adequate healing time, but longer intervals may be needed for darker pigmented patients and patients with sensitive area scars [24••]. Most hypertrophic

Table 1 Summary of laser choices and settings for different scar types

Scar type	Laser choice	Settings
Hypertrophic scars and keloids	PDL (585–595 nm)	7 mm spot, 6.0–7.5 J/cm^2 10 mm spot, 4.5–5.5 J/cm^2 0.45 ms
	QS Nd:YAG 532 nm	3–4 mm spot, 1.8–2.8 J/cm^2, 10 ms
	Non-ablative fractional (1540/1550 nm)	40–70 J/cm^2, treatment level 5–9, 14 %–27 % coverage, 8 passes
Atrophic acne scars	Nd:YAG (1320 nm)	10 mm spot, 12–20 J/cm^2, 350 ms
	Nd:YAG (1064 nm)	12 mm, 50 J/cm^2, 50 ms
	Diode 1450 nm	6 mm, 8–14 J/cm^2, 250 ms
	Er:glass(1540 nm)	35–40 mJ/MTZ, treatment level 7–10
	Fractionated CO$_2$	20–100 MJ, 200–1600 MTZ/cm^2, 30–70 mJ, treatment level 4–11, 20–50 mJ off face
Post-burn scars	PDL (585–595 nm)	7 mm spot, 5.0–8.8 J/cm^2, 10 mm spot, 4.0–5.0 J/cm^2, 1.5 ms
	Non-ablative fractional (1540 nm)	21–40 J/cm^2, 10 mm, 15 ms

scars require an average of two laser treatments to achieve a 50 % to 80 % improvement in redness and thickness [12••].

Other non-ablative lasers that have been reported in the treatment of hypertrophic scars and keloids are the 532 nm and 1064 nm Nd:YAG. Although the long-pulsed 1064 nm Nd:YAG showed mixed and conflicting results in the treatment of hypertrophic scars and keloids [25], the Q-switched 1064 nm Nd:YAG and frequency-doubled Nd:YAG 532 nm showed promising results by selectively suppressing collagen production in the fibroblast and inducing collagen remodeling by thermal damage [26, 27]. The 532 nm Nd:YAG has a wavelength that is close to the oxyhemoglobin absorption peak and has been shown to have a comparable favorable result when compared to 585 nm PDL [28].

Ablative laser resurfacing with CO$_2$ or Er:YAG lasers has showed moderate improvement of hypertrophic scars and keloids [19••]. These ablative lasers target water in the tissue, resulting in tissue vaporization. However, these lasers are falling out of favor due to the prolonged downtime and side effects [9].

Fractional lasers on the other hand are gaining popularity and have been successfully utilized in the treatment of hypertrophic scars. In a recent randomized controlled trial the efficacy of 1550 nm erbium-doped fiber laser (Fraxel Restore laser [Solta Medical, Hayward, CA]) was assessed in the treatment of hypertrophic scars. Results showed an overall improvement in scars after 4 treatments at 2-week intervals. Change in scar texture showed the most significant improvement compared to erythema and pigmentation. Treatments benefits were more pronounced at 3 months of evaluation compared to 1 month post-split scar and treated half was better, so there was additional benefit from laser. This study also showed younger scars, defined as scars less than 2 years, showed better overall improvement compared to older scars (over 6 years), and low-density settings (40 mJ, treatment level 5, 14 % coverage) were as effective as high-density settings (40 mJ, treatment level 9, 26 % coverage) [29]. Fractional laser treatments work by inducing a wound response mediated by several heat shock proteins, proliferation of fibroblasts, and subsequent new collagen formation [30].

Limited head-to head comparative studies exist. A comparative randomized split scar study was conducted by Tierney et al. [31•]. In this study, the 1550 nm erbium doped fiber laser (Fraxel RS [Reliant Technologies, Mountain

View, CA]) at 70 mJ (23 % coverage) was found to be superior to PDL (7.5 mJ, 10 mm, 0.45 ms) with an overall global improvement of 75 % in scars treated with Fraxel RS compared to PDL, which showed 53 % improvement [31•].

In our clinic, we typically treat hypertrophic scars with a combination of pulsed dye laser followed by intralesional triamcinolone injection during the same visit (Table 2). Patients typically require three to five sessions with treatments being spaced out at 4- to 6-week intervals. For stubborn hypertrophic scars that do not respond to a series of pulsed dye laser treatments, Fraxel is offered as second-line treatment.

Atrophic Acne Scars

Acne scarring can be broadly categorized based on the two causes of acne scar formation. Increase tissue formation, which leads to hypertrophic scars and keloids, or the more common cause, loss or damage of tissue, which leads to the formation of atrophic scars [32].

Jacob et al. [33] further classified atrophic acne scars into three types: ice pick, rolling, and boxcar scar (Fig. 1). The ice pick scar is narrow (< 2 mm), deep with tracts to the dermis or subcutaneous tissue; these are commonly seen on

Table 2 The authors' practice of treating scars

Indication	Options
Atrophic scars (ice pick, rolling, and boxcar)	If deep, the best choice is excision or subcision followed by injectable filler. For boxcar, punch elevation may be an option. Fully-ablative lasers (CO$_2$, Er:YAG) can help, especially if shallow. Fractional ablative lasers can be helpful if full ablation is not possible. Deep ice pick scar may benefit from CROSS.
	If there is redness, PDL may be used after ablative laser treatment is complete.
Hypertrophic scars	Thickness is best managed with ILK. PDL-595 is a second choice option for thickness, and first choice for redness. If ILK is chosen, it may be preferable to wait until the thickness is reduced before treating the redness, as ILK itself may induce telangiectasia that may be amenable to PDL.
Surface/superficial bumpiness/textural problems	Ablation with CO$_2$ is the treatment of choice, with fractional an option if full ablation is not tolerable. Other ablative techniques like dermabrasion or chemical peels are alternatives. PDL may provide color improvements if used at least 6 weeks after ablation is complete.

CROSS chemical reconstruction of skin scars

Fig. 1 Atrophic acne scars

the cheeks. Rolling scars are 4 to 5 mm in diameter, caused by abnormal fibrous strands anchoring the dermis to the subcutaneous tissue, leading to superficial rolling of the overlying skin. Boxcar scars are 1.5 to 4 mm round or oval depressions with sharply demarcated edges. These can be subdivided into shallow (< 0.5 mm) or deep (> 0.5 mm) [33]. In atrophic scars, the goal of laser treatment is to smooth the scar texture and stimulate collagen formation.

Ablative lasers were the first lasers used to treat atrophic acne scars. CO$_2$ and Er:YAG lasers work by targeting intra- and extra-cellular water. These laser systems emit high-energy densities within short pulses that affect tissue vaporization with limited thermal conduction to surrounding skin. A predictable amount of epidermis and papillary dermis is vaporized, leading to eventual remodeling of the dermal collagen and elastin and neocollagenesis [34]. CO$_2$ laser resurfacing vaporizes tissue at a depth of 20 to 60 μm and zones of thermal necrosis ranging another 20 to 50 μm. At the cellular level, CO$_2$ laser enhances upregulation of procollagens I and II, interleukin 1-b, TNF-alpha, TGF-beta1, and matrix metalloproteinases (MMPs)-1, -3, -9, and −13 [35].

Er:YAG (2940 nm) is 10 times more selective for water than CO$_2$ laser due to its shorter wavelength, reduces residual thermal damage [36]. Er:YAG at 5 J/cm^2 vaporizes tissue at depth of 20 to 25 μm with an additional 5 to 10 μm zone of thermal necrosis [37]. CO$_2$ laser resurfacing has improved moderate to severe atrophic acne scars in 50 % to 80 % with an ongoing collagen remodeling going on afterwards for 1 year [38]. Treatments with ablative lasers require prophylactic antimicrobial therapy, and have been associated with extended recovery periods, prolonged erythema, and transient hyperpigmentation. Re-epithelialization takes 4 to 7 days with Er:YAG and 7 to 10 days with CO$_2$ laser. Head-to-head studies of the CO$_2$ and Er:YAG lasers showed that CO$_2$ has superior results but Er:YAG is better tolerated with less downtime [9, 34].

Non-ablative lasers induce thermal injury to the papillary and reticular dermis with preservation of the overlying epidermis. This allows for scar remodeling without the extended recovery times. Nd:YAG 1320 nm, Q-switch Nd:YAG 1064 nm, diode laser 1450 nm, and erbium glass 1540 nm lasers has been used in atrophic acne scar treatments. PDL 585 nm has not been shown to be effective in treating atrophic scars due to its shorter wavelength, which can not penetrate deep enough to stimulate sufficient collagen remodeling [23].

The most widely used non-ablative lasers used for atrophic scars treatment are Nd:YAG 1320 nm and diode 1450 nm. Treatment usually involves three consecutive

monthly treatment sessions with the greatest improvement noticed between 3 and 6 months after the final laser treatment. Improvement 40 % to 45 % has been observed after either 1320 nm Nd:YAg or 1450 nm diode laser treatment. Degree of improvement was validated by clinical assessment, patient satisfaction survey, histologic evaluations, and skin texture measurements [23].

Fractional ablative and fractional non-ablative lasers has been used with variable success in the treatment of atrophic scars [39]. The first fractionated laser used and the one most studied is the 1550-nm non-ablative fractionated device that uses an erbium doped fiber laser (Fraxel Restore [Reliant Technologies, San Diego, CA]). Other available non-ablative fractionated lasers are LUX 1540 nm (Palomar Medical Technologies, Burlington, MA,USA) and Affirm 1440 nm Nd:YAG (Nd:YAG, Cynosure Inc, Westford, MA, USA). The latter two use stamping technology as opposed to scanning mode used in the Fraxel. Their mechanism of action and basic theories however are similar, and few studies compare the different fractional non-ablative devices making it difficult to state which one is superior.

Alster et al. [10•] reports a 25 % to 50 % improvement in atrophic acne scars appearance after a single treatment with the 1550 nm erbium-doped fiber laser and a 51 % to 75 % improvement in 87 % of patients who received at least three treatments.

During treatment, patients experience pain requiring pre-treatment topical anesthesia and cooling of the skin surface during treatment. Post-treatment side effects vary based on used treatment setting. In general, mild erythema and edema is experienced 1 to 3 days post-treatment followed by bronzing and slight scaling of the skin.

Following ablative fractionated treatments, patients can expect longer duration of erythema and edema, bleeding and oozing and downtime can be up to 14 days. Other reported side effects are acneiform eruption, activation of herpes simplex, and post-inflammatory hyperpigmentation in darker skin types, which may be avoided by using conservative setting and reduce treatment density (percentage coverage) [40, 41].

Atrophic acne scars have shown improvement when treated with fractional ablative CO_2. A mean reduction of 66 % in atrophic acne scars depth was seen following 2 to 3 treatments, with the maximum improvement seen several months after treatment [34, 42]. Fractionated CO_2 lasers offer the advantage of inducing thermal dermal coagulation at depths extending greater than both traditional ablative and fractionated non-ablative devices. Up to 1 mm in depth can be achieved with fractionated CO_2, thus inducing greater collagen production and dermal remodeling than non-ablative fractionated photothermolysis [42]. Persistent collagen remodeling with wound healing response occurs up to 3 months after in vivo fractional CO_2 ablative laser [43].

The combination of ablative fractional CO_2 laser and a non-ablative long-pulse 1064 nm Nd:YAG laser has allowed for a lower setting of the fractional CO_2 laser and has yielded the best results, with fewer complications compared to fractional CO_2 laser alone [44].

We agree that the most improvement of atrophic acne scars is seen with ablative laser treatments; however, due to the higher incidence of side effects and adverse events, and the prolonged down time, ablative treatments are not practical for most patients. We typically treat with the fractionated erbium doped fiber (Fraxel Restore) or fractional CO_2.

Burn Scars

Burn scars are some of the most disfiguring scars seen in clinical practice. These scars are often partially or completely deprived of adnexal structures, which are important for re-epithelialization of ablated skin surface [45].

The use of PDL (585–595 nm) in burn scars has been shown to significantly improve pruritus and pain within the scars [46], improve scar pliability and texture, reduce erythema and histologically reduce sclerosis without change in number of fibroblast [47]. Despite the positive results of PDL therapy in some burn scars, PDL laser penetration is limited to approximately 1.2 mm, which limits its effect in thick hypertrophic scars (> 1 cm) when used alone [46, 48]. PDL is best introduced in burn patients 3 to 6 months post-burn. Results show decreased erythema after 1 to 2 treatments and best candidates are patients with lighter skin types (Fitzpatrick types I-III). Prophylactic treatment of patients within the first few weeks post-burn injury showed better cosmesis of scarring, faster resolution of scar stiffness and erythema, but no significant difference was seen in long-term assessment (post 3 months) [48, 49].

Fractional non-ablative and ablative laser resurfacing has been utilized to treat burn scars. In a randomized control trial the effectiveness of 1540 nm fractional erbium:glass using Lux 1540 nm (StarLux-300TM; Palomar Medical Technologies, Burlington, MA) laser was assessed. Patients were treated with 3 treatments, at 4-week intervals using 10-mm handpiece, 15 ms, 21 to 40 J/cm^2, 3 to 4 passes, and results showed moderate to significant improvement in skin texture compared to untreated controls. The authors noticed that superficial burns did better than deep burns, which could be a result of the utilized laser's ability to cause thermal damage to a depth of 400 to 1000 nm, leaving the deeper fibrous tissues unaffected [50].

Ablative fractional resurfacing has the ability to remove both epidermal and dermal tissues, which theoretically can remove burn scar tissue, and subsequent collagen remodeling could normalize the texture, elasticity, and color of the scar [51]. Few case reports have shown that ablative

fractional resurfacing is safe and effective in treatment of burn scars; however further studies are needed to determine parameters [45].

Treatment with ablative full field CO_2 and Er:YAG has been used but has been associated with prolonged recovery times and contradicting results [52]. Burn scars, especially ones that are new, need to be treated gently. In our clinic, we typically use the pulsed dye laser first to improve erythema and texture. After a series of treatments, and as the burn scar matures, fractional ablative and non-ablative lasers may be used to further improve scar texture (Table 2).

Conclusions

Lasers represent one of the most successful modalities for scar treatments. Sufficient knowledge of efficacy, safety, and limitation of different lasers available is essential for physicians treating scars. It is important to discuss with patients that currently there is no treatment that offers complete resolution of scars and often more than one modality may be necessary to reach satisfactory results.

In this review we have examined the literature on scar treatments with lasers; most data are based on case reports and only limited randomized controlled trials are available. Furthermore, there is no consensus on what "improvement in scars" means. Different authors use different scales and outcome measurements, which makes comparing results impossible. More controlled trials are required, universal scale of scars improvement levels is needed, as are comparative studies.

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