

The use of laser in keloid and hypertrophic scar

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Abstract

Keloid and hypertrophic scar are hyperproliferation of dense connective tissue characterized by the growth of fibrotic tissue. The pathogenesis of keloid and hypertrophic scar is still expanding, hence there is no optimal therapy. Laser is one of the modalities of keloid and hypertrophic scar therapy. Laser's modality which can be used for keloid and hypertrophic scar are pulsed dye laser (PDL), carbon dioxide (CO₂) lasers, neodymium-doped yttrium aluminum garnet (Nd: YAG) lasers, fractional laser as well as laser assisted drug delivery (LADD) techniques. The target of laser is the selective photothermolysis with chromophores of hemoglobin and water. The mechanism of laser causing coagulation necrosis is by generating heat, resulting in neocollagenesis, while LADD is a technique of laser to assist application of drugs, such as triamcinolone acetonide. Benefit of laser is less painful thus can be an option for extensive scar. Purpose of this study is to determine the role of lasers as a treatment modality for keloid and hypertrophic scar to improve clinical skills of clinician.

Key words

Keloid; Hypertrophic scar; Laser; Photothermolysis.

Introduction

Keloid and hypertrophic scar are benign overgrowth of fibrotic tissue due to abnormal wound healing in response to both trauma and non-trauma.¹ Keloid and hypertrophic scar can decrease patient's quality of life.^{1,2} Development of keloid and hypertrophic scar is influenced by genetic and environmental factors. Pathogenesis of keloid and hypertrophic scar results from an imbalance between increased synthesis of collagen and extracellular matrix (ECM), and decreased degradation of these products.^{1,3} Active fibroblasts responsible for increasing number of collagen and growth factors in keloid and hypertrophic scar.⁴ Several modalities for keloid and hypertrophic scar consist of corticosteroid, silicone gel, compression

bandages, cryotherapy, surgical excision, radiotherapy, and lasers.^{1,3}

Intralesional corticosteroid injection is one of the most commonly used treatments, although it causes pain, atrophy and telangiectasis.¹ Lasers can greatly improve symptoms of scar, patient satisfaction and quality of life.³ Several reports on the management of keloid and hypertrophic scar have shown therapeutic success are pulsed dye laser (PDL), fractional carbon dioxide (CO₂) laser and neodymium-doped yttrium aluminum garnet (Nd: YAG) laser, or as laser-assisted drug delivery (LADD).^{3,5} Mechanism of laser is selective photothermolysis from light energy emitted by laser. Hemoglobin and water are the main absorbing components targeted for selective photothermolysis in keloid and hypertrophic scar. The energy of the laser irradiation is transferred into heat due to the absorption of the photons by tissue components, chromophores, proteins, enzymes and water, which collagen ischemia.^{6,7}

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Keloid and hypertrophic scar

Keloid derived from the Greek word “chele” means crab claws. The term describes irregular tissue growth in areas of normal skin.⁸ Hypertrophic scar is an excessive connective tissue generally confined to the borders of original wound and tend to improve after several months, whereas keloid extend beyond the boundaries of initial wound.^{1,8} Keloid and hypertrophic scar can develop for several years after minor trauma, even form spontaneously without any trauma. Keloid persists for a long time and does not regress spontaneously.^{1,6}

Epidemiology of keloid and hypertrophic scar

Predisposing factors for keloid and hypertrophic scar include dark skin color, familial predisposition and pregnancy.^{1,8} Higher incidences are seen in African, Asian, and Hispanic, while the lowest incidence seen in albinos. The formation of keloid and hypertrophic scar occur in 4.5-16% in the African and Hispanic race population, which is associated with high melanocyte stimulating hormone (MSH).^{1,2,6} Scar tends to occur in individuals age 30 years old, rarely at younger or

older population.¹ Genetic predisposition plays a major role in keloid formation.^{1,6} Chromosome changes are associated with familial keloid, with related loci including chromosome 7p11, 2q23 and 10q23 in African, Japanese, and Han Chinese descent, respectively.⁶

Etiopathogenesis of keloid and hypertrophic scar

Trauma can cause keloid and hypertrophic scar, among others burns, surgical excision, injections, tattoo, vaccinations, inflammatory reactions and mechanical factors.^{6,8} Mechanism in keloid and hypertrophic scar occur as a result of imbalance in wound healing due to excessive collagen synthesis and ECM, and decreased degradation of these products.^{1,3} Wound healing consists of four phases, such as coagulation, inflammation, proliferative and remodeling phase.⁹ Dysregulation of fibroblast proliferation and degradation causes disruption of collagen in the ECM, leading to scar formation.^{9,10} Factors affecting keloid and hypertrophic scars can be seen in **Figure 1** and **2**.^{1,3,4} Prolonged duration of inflammatory reaction leads to excessive fibroblast activity resulting in excess ECM.³

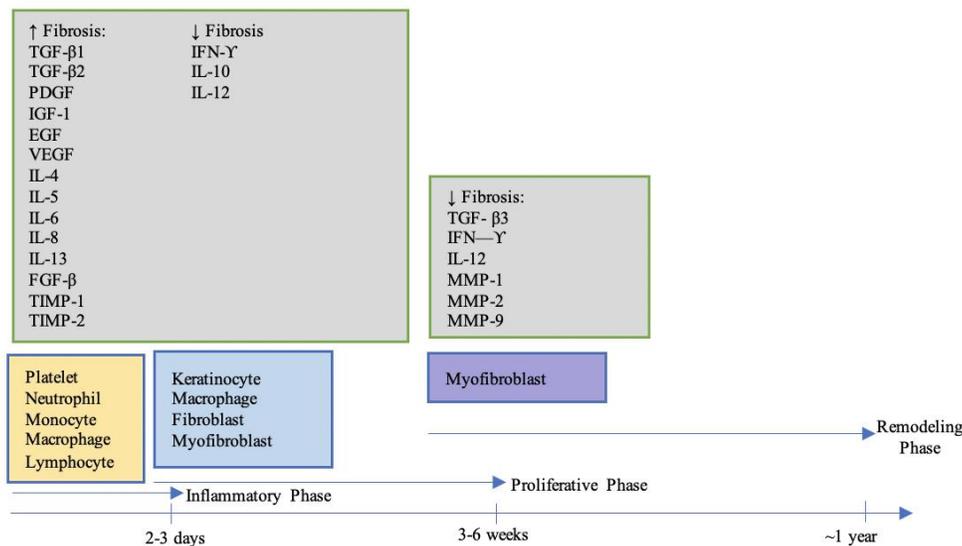


Figure 1 Factors affecting wound healing. [3]

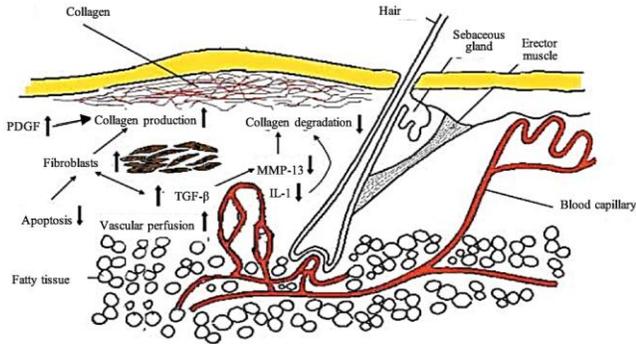


Figure 2 The role of protein and cytokines in the wound healing.[12]

Inflammatory phase in keloid and hypertrophic scar often associated with increasing growth factor transforming growth factor- β 1 (TGF- β 1), TGF- β 2, platelet derived growth factor-4 (PDGF-4) and vascular endothelial growth factors (VEGF), thereby increasing fibrosis in the wound healing process.^{4,6,8,10} TGF- β 1 plays major role in the scar formation, whereas TGF- β 3 inhibiting scar formation.^{3,11} Upregulation of VEGF and PDGF robust new blood vessels in the damaged tissue results increasing the formation of fibrotic tissue.^{3,4} Interleukins (IL)-4, IL-5, IL-6, IL-8 and IL-13 have been implicated as pro-inflammatory cytokines that cause fibrosis, while IL-1, IL-10 and IL-12 strongly linked as anti-fibrosis cytokines in keloid and hypertrophic scar.³ Fibroblast cells have been implicated as major cells in the proliferation phase.^{3,9} Macrophage activates fibroblasts and induced collagen formation in ECM through the formation of PDGF, TGF- β 1 and VEGF.^{4,9} Disturbance in macrophages downregulates proliferation and angiogenesis results interfering wound healing process.⁹ Activation of TGF- β 1 stimulates production of collagen I and collagen III.⁹ Excessive expression of VEGF enhanced capillary formation, collagen type I production, and increased scar volume.³ Angiogenesis is also stimulated by heparin, IL-8, and insulin-like growth factor (IGF)-1.¹² At the end of the proliferation phase, increased fibroblasts and myofibroblasts causing ECM accumulation in

keloid and hypertrophic scar, consist of collagen, elastin, hyaluronic acid and proteoglycans and collagen.^{3,10}

In remodeling phase abundant ECM is degraded from immature type III collagen to mature collagen type I, which results in the formation of fine scars.^{3,8,9,11} Remodeling can last for more than one year.^{3,4} Disruption of the remodeling phase interfere collagen degradation which can cause keloid and hypertrophic scar.⁹ IL-1 α is a potential stimulator for matrix degradation which may decrease in keloid and hypertrophic scar.³ Matrix metalloproteinase (MMP) is produced by fibroblasts, neutrophils, keratinocytes, and macrophages, which causes fibrotic tissue degradation.⁹ MMP-2 and MMP-9 responsible for fibrotic tissue degradation, while tissue inhibitors of metalloproteinases (TIMPs) are MMP inhibitors which increase in keloid and hypertrophic scar.^{3,12} Myofibroblasts which contain contractile actin filaments may increase in scar formation, related to wound contraction.^{3,9} An imbalance in expression between the collagen synthesis, fibroblast proliferation and MMPs, has been implicated in pathological cause of keloid and hypertrophic scar.^{4,9,10} Keloid and hypertrophic scars have a 3-fold and 20-fold increase in collagen production, respectively, compared to normal skin.⁴

Clinical Manifestations

Both keloid and hypertrophic scar appear as firm, mildly tender nodules 3-4 weeks after trauma, although keloid can develop up to 1 year later.^{1,8} Hypertrophic scar are different from keloid, which is limited to the initial site of the wound and generally regress spontaneously within 1-2 years.^{4,8,13} Both lesions are asymptomatic, but keloid may occur redness, itching, pain, and burning.^{1,10}

Keloid and hypertrophic scar develops wounds

Table 1 Keloid and hypertrophic scars.[13,14]

	<i>Hypertrophic Scar</i>	<i>Keloid</i>
Incidence	40-70% occur after surgery, up to 91% after burns There was no difference between men and women, the highest incidence was 20 to 30 years old	6-16% in African populations
Predilection area	Shoulders, neck, pre-sternal, knees and ankles Less affected: eyelids, cornea, palms, mucous membranes, genitalia and soles	Anterior chest, shoulders, earlobes, upper arms and cheeks
Onset	4-8 weeks after injury, rapid growth until 6 months, then regress after a few years	Several years after minor injury or spontaneous formation without preceding injury. Persist for a long time. No spontaneous regression
Clinical manifestations	Rarely recurs after initial hypertrophic scar excision Do not extend beyond the initial site of wound Itch, rarely painful	High recurrence after excision Extend beyond original wound site Itch, painful, discomfort
Histopathologic features	Well organized collagen type III with parallel bundle which oriented to epidermis surface Collagen type I<III Contain abundant nodules consist of myofibroblasts	Collagen types I and III are more disorganized, broad, and thick Collagen type III <I No nodules or excess myofibroblasts. Poor vascularization

Table 2 Vancouver Scar Scale (VSS).[8,13]

<i>Vancouver Scar Scale</i>						
<u>Pigmentation</u>		<u>Vascular</u>		<u>Pliability</u>		<u>Height</u>
Normal	0	Normal	0	Normal	0	Flat, Normal
Hypopigmentation	1	Pink	1	Supple	1	< 2 mm
Hyperpigmentation	2	Red	2	Yielding	2	2-5 mm
		Purple	3	Firm	3	> 5 mm
				Banding	4	
				Contracture	5	

at anatomic location with high tension, such as the chest, back, shoulders, neck, and lateral upper arms, but less affected on ear lobe, which is an area with minimal skin tension.^{1,6,8} The differences between keloid and hypertrophic scar can be seen in **Table 1**.^{13,14}

Diagnosis

Vancouver Scar Scale (VSS) is the most widely used criteria to assess keloid and hypertrophic scars, consist of pigmentation, vascularity, flexibility, and wound height (**Table 2**).¹³

Laser management of keloid and hypertrophic scar

Light amplification by stimulated emission of

radiation or laser is a therapeutic modality derived from light energy sources.^{15,16} It is a minimally invasive, low-risk therapeutic approach with relatively short post-treatment recovery period. Studies have shown decreased scar thickness, pain and surgical excision requirement with improved scar pigmentation, erythema, flexibility, texture, wound height, and pruritus.^{15,16} The exact mechanism and optimal laser parameters remain unanswered, although lasers have been used for the past two decade.^{5,12}

Lasers have been shown to be effective in treating keloid and hypertrophic scars, including carbon dioxide (CO₂) laser, pulsed dye laser (PDL), Nd: YAG laser, fractional laser or laser-assisted drug delivery (LADD).^{5,17} Annabathula, *et al.* reported clinical improvement in 73%

keloid and hypertrophic scar lesions managed with CO₂ laser, PDL, and Nd: YAG laser.⁵ Lasers can also be combined with other therapeutic modalities to obtain synergistic effects on keloid and hypertrophic scar.^{5,16}

Mechanism of action of laser on keloid and hypertrophic scar

The principle of laser for hypertrophic scar is based on the vascular proliferation that responsible for keloid and hypertrophic scar formation (**Figure 3**).^{6,12} The absorption of laser energy depends on the presence of chromophores as light-absorbing compounds.^{15,17} Selective vascular photothermolysis from light energy is absorbed by hemoglobin and water, generates heat leading direct damage to target cells and results in collagen tissue ischemia.^{6,7,16,18} Selective photothermolysis induces microvascular disturbances, hypoperfusion and tissue hypoxia which interfere cell proliferation, causing scar tissue necrosis and its regression.^{6,12,13} Hypoperfusion and hypoxia may result in neocollagenesis through collagen fiber heating with dissociation of disulfide bonds and subsequent collagen fiber realignment. Formation of new collagen and reorganization of collagen fiber arrangement will form healthy skin tissue.^{5,13} Laser can also reduce fibroblast proliferation and collagen deposition.^{12,13}

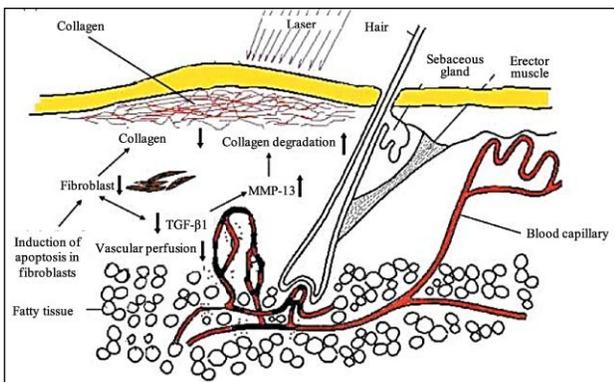


Figure 3 Laser radiation effects on keloid dan hypertrophic scar.[12]

Mechanism of laser associated with decreased vascular perfusion leading to reduced expression of TGF-β1 which induces and modulates collagen formation.^{8,12,13} It also increase fibroblasts degradation due to MMP-13 (collagenase-3) activity.^{12,13} This mechanism leads to decrease fibroblasts production thus reducing collagen formation.¹¹⁻¹³ The mechanism of lasers in keloid and hypertrophic scar is similar, although there are differences that affect therapy due to histopathological features differences. Keloid has denser and more hyalinized collagen collection, forming coarse collagen accumulations, hence the laser is more limited to keloid than hypertrophic scar.^{12,16} The main clinical effect of vascular laser therapy is to reduce erythema and pruritus. Laser is modality of choice for keloid and hypertrophic scar because the laser beam reaches scar vascularization.²⁷

Type of laser used for keloid and hypertrophic scar

Several laser options can be used for treatment of keloid and hypertrophic scar (**Table 3**).

Pulsed Dye laser

In 1986, the U.S. Food and Drug Administration (FDA) approved PDL as modality for skin vascular disorders. Selected wavelength 585 nm of this laser is absorbed by hemoglobin, thus can inhibit keloid and hypertrophic scar growth.¹³ PDL is the most recognized encouraging therapeutic option for hypertrophic scars and keloids, with level of evidence I.^{8,21}

Mechanism of action of PDL is down regulation of TGF-β levels, decreasing proliferation through thermal necrosis so that the proliferation of fibroblasts and collagen decreases, and collagen remodeling occurs.^{13,22,23} PDL specifically targeting hemoglobin as

Table 3 Commonly used laser treatments on different type of keloid and hypertrophic scars.[13,20]

Characteristics	Variables	First line
Skin type	Type I-III	PDL, CO ₂ laser, fractional laser, Nd:YAG laser
	Type IV-VI	Fractional laser
Etiology	Burn scar	PDL, fractional laser
	Surgical scar	Fractional laser, PDL, CO ₂ laser
	Acne scar	Fractional laser
	Erythematous, small	PDL
	Large, firm	Fractional laser, Nd:YAG laser
Patient choice	Minimal downtime	Nd:YAG laser
	Moderate downtime	Fractional laser
	Can tolerate downtime	CO ₂ laser

chromophores, cause vascularization reduced, also reduce erythema and pruritus.² Pulsed dye laser is gold standard for erythematous scars.²² Systematic review De Las Alas, *et al.* in 2012 showed that PDL improved scar texture, flexibility, and reduced erythema, size, pruritus, and pain.²⁴ Several studies have shown pruritus is reduced due to changes in neuropeptide Y, vasoactive intestinal peptide (VIP) substance, or calcitonin gene-related peptide (CGRP) in mechanism of pruritus.⁸ Several studies have shown clinical improvement with PDL in keloid and hypertrophic scar.^{6,8,16,25}

Parameters of PDL for keloid and hypertrophic scars range from a fluence of 3.5-9 J/cm², pulse duration 450-600 μs, and spot size 7-10 mm.^{7,23} The use of smaller spot size means fluence must be increased, although initial procedure preferably started with lower fluence. Furthermore, patients with Fitzpatrick skin type IV-VI is recommended with lower fluence (3–3.5 J/cm²) and spot size 10 mm to reduce complications.²³ PDL laser procedures can be repeated every 3–4 weeks.⁸

A comparative randomized split scar trial by Al-Mohamady, *et al.* in 20 patients compared PDL 595-nm with fluence of 7-9 J/cm², pulse duration of 1.5 ms and spot size of 10 mm to 1064 nm Nd: YAG laser on the contralateral side using fluence of 30-35 J/cm², pulse duration of 20 ms, and spot size of 14 mm for six sessions at one-month interval. The outcome

showed that the improvement of VSS in PDL significantly higher than Nd: YAG, which was 55.14% and 65.44% in PDL and Nd: YAG, respectively (**Figure 4**).²⁵ The results suggested PDL and Nd: YAG provide significant improvement for keloid and hypertrophic scar with insignificant difference between both modalities.²⁵

Side effects of PDL therapy on keloid and hypertrophic scar are generally mild to moderate pain.^{15,23} Other side effects of PDL are burning sensation and itching resolving within a few days.²³ Purpura also often occurs immediately after procedure and lasts for 7- 10 days.^{12,23} Hyperpigmentation has been reported in 1-24% patients.¹² It is associated with epidermal thermal injury due to melanin absorption and more common in dark-skinned individuals.^{12,16} Other rare side effects are blisters and crusts.^{12,17,23}

Carbon Dioxide Laser

CO₂ laser with a wavelength of 10,600 nm is an

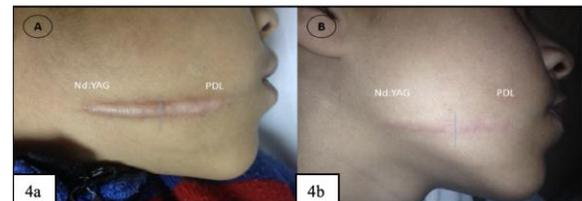


Figure 4. Clinical features of submandibular region hypertrophic scar lesions (a) before PDL and Nd: YAG laser (b) after 6 sessions of PDL and Nd: YAG treatment²⁵

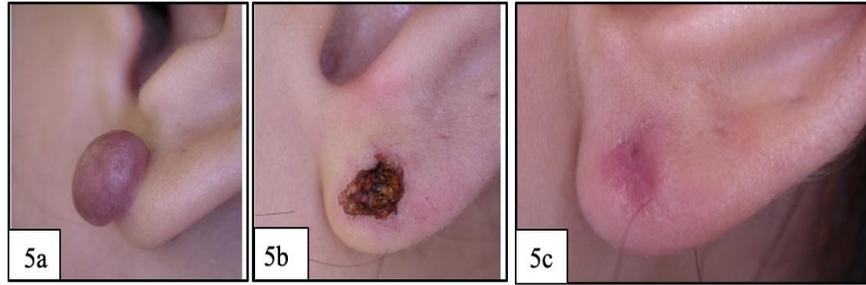


Figure 5 Keloid cases in the ear lobe due to piercing (a) before therapy (b) direct effect after therapy (c) one month after therapy.[27]

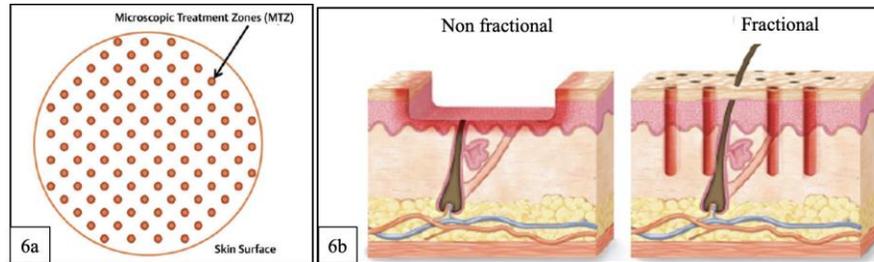


Figure 6 Fractional CO₂ laser (a) microscopic treatment zone (MTZ)[28] (b) Fractional and non-fractional CO₂ laser.[15]

ablative laser that was originally used for tissue excision.¹³ This laser target chromophore is water which found abundantly in the skin.⁷ Water in the target tissue absorbs laser energy, causing heat and vaporization, including surrounding tissue.²⁶ Evidence for the use of CO₂ lasers for keloid and hypertrophic scar is limited.¹⁰

The mechanism of action of the CO₂ laser is that ablation causes the release of protein from laser heat, and activation of MMP, TGF- β 3, and myofibroblasts, and decreases TGF - β 1, causing scar remodeling.^{13,22}

The fluence required for the CO₂ laser for tissue vaporization is in the range of 5 J/cm². CO₂ laser with a pulse duration of 1 ms and a fluence range of 5 J/cm² causes tissue vaporization to a depth of 20–30 μ m.^{26,27} Energy delivery typically used is 10-50 mJ.²⁶ Studies show a CO₂ laser to be effective in treating resistant mature scars compared to PDL therapy.¹³ The use of conventional ablative lasers is not recommended in patients with a history of keloid and

hypertrophic scar because they have a high recurrence rate.² The use of CO₂ lasers without additional therapy has a 74-100% recurrence rate. Additional therapy with intralesional corticosteroids has shown improvement of the scar after CO₂ laser.¹⁰

Chan YC, *et al.* treated keloid from a piercing wound on the left ear using CO₂ laser with a fluence of 7 J/cm² to excise the base of the keloid within the keloid (**Figure 5**). Intralesional injection of corticosteroid (triamcinolone acetonide) 40 mg/ml administered to the base to prevent keloid formation at one month after laser treatment. Alternatively, an intralesional steroid injection can be performed during laser ablation. In this case, post-laser treatment keloid had good resolution.²⁷

Side effects of CO₂ lasers are more common because they are ablative.²² CO₂ lasers generally cause pigmentation disorders such as erythema, post-inflammatory hyperpigmentation and hypopigmentation, as well as moderate-severe edema and pain.²² Post-inflammatory

hyperpigmentation generally occurs in dark skin types, such as Asian skin and disappear in 4-6 months.²⁷ Other rare side effects are blisters and crusts.⁷

Fractional Carbon Dioxide Laser

The fractional carbon dioxide (CO₂) laser ablates the skin and delivers laser energy to the skin by forming a microscopic column pattern called the microscopic treatment zone (MTZ) and leaving the surrounding tissue unharmed (**Figure 6**).^{13,28} Fractional laser is a newer modality with the concept of fractional photothermolysis which first described in 2004.²⁹ Fractional ablative laser ablates the skin and scar in a columnar pattern, destroying irregular ECM proteins resulting in reepithelization and deposition of new collagen.^{13,15} It has the ability to stimulate collagen remodeling and protein denaturation due to laser heat.^{13,30} The advantages of using fractional ablative lasers are that they require fewer sessions than non-ablative lasers and minimal damage compared to conventional ablative lasers.¹³

The CO₂ fractional laser showed better results on hypertrophic scar than on keloid. Similar findings were reported by El-Zawahry, *et al.*, Tawfic, *et al.*, and Waibel, *et al.*, which suggest CO₂ fractional laser is the option for hypertrophic scar (**Figure 7**).^{22,30,31} El-Zawahry, *et al.* compared histopathologic and clinical



Figure 7 Clinical features of hypertrophic scars over the breast (a) scar divided into upper part (control) and lower part before treatment (b) 3 sessions of fractional CO₂ laser treatment of the lower part showing improvement in texture and pigmentation.[31]

manifestation using CO₂ fractional laser in 11 keloid patients aged 16-58 years with 30 mJ energy, showed improvement in VSS and histopathologic features of keloid and hypertrophic scar. The effect of laser therapy on the dermal papillae and reticular dermis causes collagen to become less dense and horizontal and parallel in arrangement (**Figure 8**).³¹

The randomized controlled trial by Waibel *et al.* using 3 sessions of CO₂ fractional laser in 19 patients with hypertrophic scar, with 500-800 μm, at eight-week intervals, showing histopathologic improvements in the form of reduced blood vessels, reduced fibrosis, repair of elastin fibers, and prevention. excess keratin formation.³⁰ Waibel *et al.* also suggested early intervention of acute burns with fractional ablative lasers to achieve better results.³⁰ Tawfic, *et al.* also conducted a randomized controlled trial using ablative CO₂ fractional lasers with a fluence of 40 J/cm², pulse duration 300 μs, spot size 5 mm, and 3 passes, indicating the CO₂ fractional laser as an optimal modality for solid scar types.²²

Neodymium-doped yttrium aluminium garnet laser

Neodymium-doped yttrium aluminum garnet (Nd: YAG) laser with a wavelength of 1064 nm causes heat to deposit into the dermis and is absorbed by hemoglobin and melanin, as well as to a lesser extent water. This photothermolysis

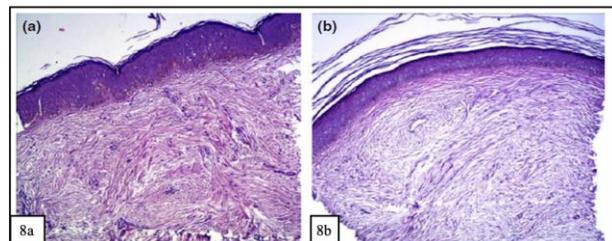


Figure 8 Histopathologic features of collagen (a) before CO₂ fractional laser (b) after CO₂ laser.[31]

effect will heat up collagen and vascular in the dermis.^{22,28} Nd:YAG laser was developed for the treatment of vascular disease, pigmentation lesions, hair removal and skin rejuvenation.^{16,22} The mechanism of the Nd: YAG laser on keloid and hypertrophic scar targets deeper vasculature in the dermis thereby inhibiting scar neovascularization and inducing hypoxia which prevents abnormal collagen deposition.^{16,22} Tissue heating also increases MMP production accompanied by abnormal collagen degradation leading to initiation of physiological wound healing processes with the formation of new collagen.³²

The parameters of the Nd: YAG laser for the treatment of keloid and hypertrophic scar depend on the product of Nd: YAG laser and the type of the scar. Fluence of 14-75 J/cm² can be used with 5 mm spot.^{3,32}

Several studies have proven Nd: YAG laser in the therapy of keloid and hypertrophic scar. Tawfic, *et al.* conducted a randomized controlled trial using an Nd: YAG laser with a fluence of 40 J/cm², a pulse duration of 300 μ s, and a spot size of 5 mm for 3 passes for four sessions at intervals of 4-6 weeks, showed a significant decrease in VSS and optimal improvement of erythema scar vascularization.²² Another study by Koike, *et al.* in 2014 to 102 patients using Nd: YAG laser every 3-4 weeks for one year using fluence 65-75 J/cm², spot size 5 mm, pulse duration 250 μ s, and 3 passes showed significant improvement in keloid and hypertrophic scar (**Figure 9**), although there were three cases of keloid in the anterior trunk unresponsive.³²

The Nd: YAG laser was generally well tolerated by patients. Several side effects due to Nd: YAG laser includes mild to moderate pain, transient erythema and hyperpigmentation.^{17,23} Other side effects are rare such as blisters appearing one day after the procedure.²⁵



Figure 9 Clinical features of keloid in deltoid (a) Before Nd: YAG laser (b) 1 year after Nd: YAG laser which showed an improvement in texture.[32]

Laser Assisted Drug Delivery

Laser assisted drug delivery (LADD) is a method of application of drugs using laser as a modality to enhance drug permeation.²⁹ Lasers can increase the absorption and allow deeper penetration of drug molecules by disrupting the stratum corneum (SC) barrier.³³ The most commonly used lasers for LADD are CO₂ and erbium lasers: yttrium-aluminum-garnet (Er: YAG).^{29,33}

The enhancement mechanism of LADD is based on ablation of the stratum corneum, epidermal, or dermal barriers.³³ Some drugs have large molecules and hydrophilic thus they cannot cross the skin barrier and do not reach the desired target tissue (**Figure 10**).^{29,34} Topical drugs should pass across lipid bilayers of SC, which is the outer layer of the skin for percutaneous drug absorption.²⁹ The use of LADD is an alternative to injection or other methods to enhance drug absorption in the skin. The advantage of the fractional laser for LADD is minimal to moderate pain and faster healing process, which increase patient's compliance.^{29,34}

The mechanism of fractional laser ablation is to increase drug penetration through direct ablation, photomechanical waves, and photothermal effect.³⁴ Fractional ablation will penetrate the skin barrier through the formation

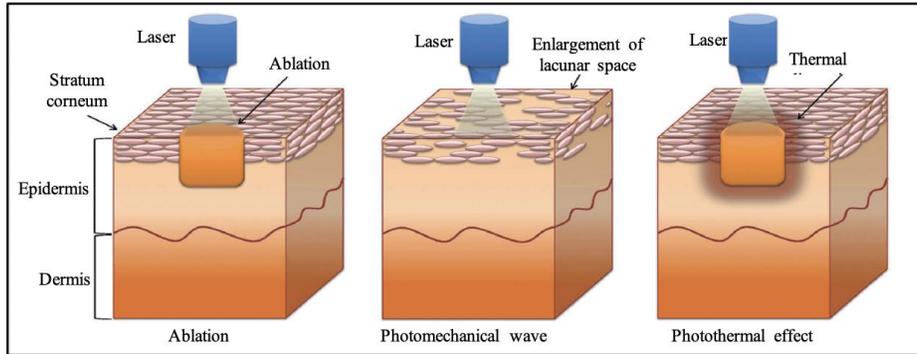


Figure 10 The mechanisms of laser for assisting drug delivery.[34]

of micropores in which drug molecules is released into the microchannels.^{33,34} Another mechanism is through photomechanical waves causing increased permeability superficial skin through the expansion of the lacunar space between cells thus intracellular lipid disruptions occur and allow drug penetrate into the deeper cutaneous layers.³⁴ The third mechanism is a photothermal mechanism which damages the skin barrier through the transformation of light energy into heat when absorbed by the chromophore causing denaturation and coagulation resulting in skin barrier damage.^{29,33,34} These effects cause vertical diffusion of the drug molecules to reach deeper skin layers. Moreover, the lateral diffusion also occurs causing the drug to diffuse into the surrounding tissue by a lateral pathway.³⁴

As the fractional lasers ablate the skin, the laser generates microbeam and creates a microscopic vertical channel which is called MTZ.^{29,34} This zone is surrounded by healthy tissue, although some degree of damage to adjacent tissues can occur.^{20,33} Furthermore, the microchannels serves as the pathways, thus drug molecules can penetrate the epidermal layer with less barrier dysfunction and minimize recovery time.²⁹

CO₂ laser (10,600 nm) provides a greater thermal effect than Er: YAG laser (2,940 nm), as it can cause an increase in the permeability of the stratum corneum.²⁰ Er: YAG laser and CO₂

laser are strongly absorbed by water in the epidermis.²⁹ Er: YAG laser provides ablation effect with minimal depth of penetration and least heat generation resulting in slight thermal damage.²⁶ Fractional Er: YAG laser requires more therapy sessions with less satisfactory improvement even though it has less downtime compared to fractional CO₂ laser.³⁵

Ablative fractional laser therapy with the LADD method is often combined with topical triamcinolone acetonide.⁷ Fractional CO₂ laser combined with immediate topical application of triamcinolone acetonide suspension at 10 mg/mL concentration synergistically improve scars.²⁹ The advantage of this technique is a more evenly distributed drug penetration in which it can reach the dermis layer with minimal pain.³³ Triamcinolone acetonide can suppress the inflammatory and proliferative processes of wound healing by inhibiting the migration of inflammatory cells, phagocytosis, and vasoconstriction effects, which improve the scars. Corticosteroids also reduce the activity of growth factors, such as TGF- β 1 and TGF- β 2, and inhibit fibroblast proliferation and collagen synthesis, thus affecting the composition of ECM.^{3,6,8}

Conclusion

Management of keloid and hypertrophic scar remains a challenge in the field of dermatology.

Laser is a treatment modality for keloid and hypertrophic scar, but there is still little evidence-based on laser management of keloid and hypertrophic scar. Types of lasers that can be used are PDL, CO2 laser, Nd: YAG laser, fractional laser or LADD technique. The mechanism of action of the laser is selective photothermolysis using light energy emitted by the laser through the chromophores of blood vessels and water, causing collagen necrosis resulting in neocollagenesis. The success of keloid therapy and hypertrophic scar using a laser is influenced by various factors. Further research is needed to determine the effectiveness of lasers against keloids and hypertrophic scars.

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