International Journal of Women's Dermatology 3 (2017) 131–139

Contents lists available at ScienceDirect

International Journal of Women's Dermatology

Review

# Laser treatment of medical skin disease in women

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ARTICLE INFO

*Article history:*
Received 19 December 2016
Received in revised form 9 May 2017
Accepted 9 May 2017

ABSTRACT

Laser treatment is a relatively new and increasingly popular modality for the treatment of many dermatologic conditions. A number of conditions that predominantly occur in women and that have a paucity of effective treatments include rosacea, connective tissue disease, melasma, nevus of Ota, lichen sclerosus (LS), notalgia paresthetica and macular amyloidosis, and syringomas. Laser therapy is an important option for the treatment of patients with these conditions. This article will review the body of literature that exists for the laser treatment of women with these medical conditions.



## Introduction

Dermatology is a unique area of medicine because diseases that affect the integumentary system manifest externally and are constantly on public display. In addition to providing medical therapy, dermatologists are consulted for the improvement in appearance of many of these disfiguring conditions. New research is being conducted on the use of laser alone and in conjunction with standard medical therapy in the treatment of patients with skin disease. In general, women are more likely to seek laser therapy for the treatment of their disease. This article reviews laser therapy for dermatoses that disproportionally affect women including rosacea, connective tissue disease, melasma, nevus of Ota, lichen sclerosis, notalgia paresthetica and macular amyloidosis, and syringomas.

## Rosacea

Rosacea is a common, chronic condition that primarily affects the skin of the central face and eyes. Women and patients with lighter skin types are more likely to be affected. There are four types of rosacea: erythematotelangiectatic, papulopustular, phymatous, and ocular. Patients may have one or any combination of these types (Wilkin et al., 2002). Because there is no cure for rosacea, treatment is directed at symptom management. In the arsenal of treatment for dermatologists, lasers offer a safe and efficacious way to treat some forms of rosacea.

### *Erythematotelangiectatic rosacea*

Erythematotelangiectatic rosacea is the most common form of rosacea and characterized by central facial flushing, background erythema, and persistent telangiectasias (Iyer and Fitzpatrick, 2005). This form of rosacea has the most abundant and highest quality evidence for improvement with laser therapy. Pulsed dye laser (PDL; 585nm; 595nm) is the laser of choice for most cases of erythematotelangiectatic rosacea. PDL has been reported to improve background erythema and telangiectasias in case reports, case series, and randomized controlled trials (RCTs). A range of improvements have been reported including improvement of 39 to 58% of background erythema on the cheeks (Iyer and Fitzpatrick, 2005; Rohrer et al., 2004). A study of 40 patients reported an average between moderate and marked improvement (Tan et al., 2004). There are a variety of settings that can be used to treat vascular lesions. Generally, spot sizes of 7-10 mm are used. Pulse durations in the range of 6-20ms are well tolerated and approximate the thermal relaxation time of vascular ectasias of erythematotelangiectatic rosacea (Alam et al., 2003; Tan et al., 2004). Pulse durations that are shorter than 6 ms carry a higher risk of inducing purpura. Although treatments that induce purpura offer a more rapid and effective treatment of erythematotelangiectatic rosacea (Alam et al., 2003; Iyer and Fitzpatrick, 2005), most patients prefer to avoid purpura. Pulse stacking with a lower fluence is one method to reduce the risk of purpura while maintaining high efficacy (Rohrer et al., 2004).

Intense pulsed light (IPL) has been used for the treatment of background erythema of rosacea with filters (Mark et al., 2003; Papageorgiou et al., 2008) and with exposure to the full spectrum of light (Schroeter et al., 2005). One study using a 515 nm filter

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http://dx.doi.org/10.1016/j.ijwd.2017.05.002

showed a 30% reduction in blood flow and a 21% decrease of background erythema in four patients (Mark et al., 2003). Another study with a 560 nm filter showed that 83% of 34 patients had at least a 50% overall improvement (Papageorgiou et al., 2008). IPL that ranged from 515-1200 nm had a mean clearance of 77.8% that was maintained on average for 51 months in 60 patients (Schroeter et al., 2005). A single-blinded RCT showed that there was no significant difference between non-purpuragenic 595 nm PDL and IPL with a 560 nm filter (Neuhaus et al., 2009).

The potassium titanyl phosphate (KTP) 532 nm laser has also been shown to improve the erythema of rosacea in 11 patients who had a 47% improvement compared with the untreated side (Maxwell et al., 2010). A large review of KTP laser showed that 49 of 66 patients had at least a marked improvement (Becher et al., 2014).

Treatment with the neodymium-doped yttrium aluminum garnet (Nd:YAG) laser (1064 nm) is less effective than PDL for background erythema of erythematotelangiectatic rosacea. Nd:YAG has more value in the treatment of refractory nasal vessels and larger facial vessels but should be used with caution because it carries a higher risk of scarring. One report demonstrated that 24 of 39 patients had an excellent response after treatment with long-pulsed Nd:YAG laser (Say et al., 2015). One double-blind RCT compared treatment with 595 nm PDL and 1064 nm Nd:YAG for patients with diffuse facial erythema. The results showed that the PDL treatment reduced facial redness 6.4% more than Nd:YAG and patients noticed a 52% improvement with PDL compared with a 34% improvement with Nd:YAG. Of note, the Nd:YAG treatment was associated with less pain (Alam et al., 2013).

Appropriate patient counseling and selection is important before using lasers to treat patients with rosacea. Common adverse effects are pain, purpura, and transient edema (Alam et al., 2003; Iyer and Fitzpatrick, 2005). Less commonly postinflammatory hyperpigmentation (Tan et al., 2004) and scarring can occur (Say et al., 2015) Light-based therapies and especially PDL offer a safe and efficacious treatment option for patients with erythematotelangiectatic rosacea that can significantly improve the quality of life of patients (Bonsall and Rajpara, 2016).

### *Papulopustular rosacea*

Papulopustular rosacea is characterized by inflammatory papules and pustules primarily on the central area of the face (Wilkin et al., 2002). Evidence is sparse for the application of lasers to treat this type of rosacea. One study noted that treatment with IPL showed an improvement in acneiform breakouts in 64% of treated patients (Taub, 2003) while another study on PDL showed that 50% of patients who were treated remained unchanged or worsened with regard to papulopustular lesions (Berg and Edström, 2004). Treatment with the long-pulsed 1064 nm Nd:YAG laser in rejuvenation mode was reported to improve papulopustular lesions in 22 patients (Lee et al., 2015a) and another study showed that 12 of 27 patients had an excellent improvement in their papulopustular lesions (Say et al., 2015). Although there is some anecdotal evidence of laser treatment for papulopustular lesions, it would not likely be a routine consideration.

### *Phymatous rosacea*

Phymatous rosacea is more common in men and characterized by sebaceous hyperplasia of the nose (Wilkin et al., 2002). Surgical lasers offer an efficacious option to contour this hyperplasia back to the nose's normal size. A more historical approach involved treatment with an argon laser, which aimed to decrease capillary blood flow and shrink the hypertrophic tissue (Halsbergen Henning and Van Gemert, 1983). Today, it is not a favored approach because of the high risk of dermal necrosis and scarring due in part to the continuous-wave operation of this laser that makes depth difficult to control (Sadick et al., 2008). Currently, the more common approach is treatment with ablative carbon dioxide ($CO_2$) or erbium: yttrium aluminum garnet (Er:YAG) lasers.

$CO_2$ laser resurfacing offers precise sculpturing and control of tissue depth. The most serious disadvantages of this treatment are that it is time consuming and there is a risk of scar contraction with extensive vaporization. Permanent hypopigmentation is also a concern with the $CO_2$ laser and particularly when operated in continuous wave mode. Er:YAG laser resurfacing carries a lower risk of hypopigmentation but hemostasis is more challenging.

A cohort of 24 patients showed a more than 75% improvement in rhinophyma with 23 of 24 patients who noted a greater than 50% improvement when treated with a 10,600 nm $CO_2$ pulsed laser (Bassi et al., 2016). A fractionated ablative $CO_2$ laser that is set at 70 mJ and 70% density for 16-18 passes showed significant improvement after treatment in the shape, size, and texture of the nose and excellent cosmetic results in five patients with mild-to-moderate disease (Serowka et al., 2014). In summary, in experienced hands, the $CO_2$ or Er:YAG surgical lasers are an effective treatment option for the surgical reduction of rhinophyma.

## Connective tissue disease

Connective tissue diseases such as lupus erythematosus (LE), dermatomyositis (DM), and systemic sclerosis present with a variety of dermatologic manifestations that are often resistant to conventional treatments. Laser therapy offers an additional treatment modality for patients with connective tissue diseases and especially the erythema that is seen in multiple disorders. Newer fractional laser approaches are also being investigated in the treatment of fibrosis that is seen in patients with connective tissue disorders.

### *Lupus erythematosus*

Among the connective tissue diseases, LE has the greatest body of literature that documents outcomes of laser treatment. LE is a complex autoimmune condition with several distinct cutaneous forms including acute cutaneous LE, subacute cutaneous LE (SCLE), and chronic cutaneous LE including discoid LE (DLE), chilblain LE, tumid LE, and lupus panniculitis. Telangiectasias and dyspigmentation can occur as a result of several variants of LE (McCauliffe, 2001). PDL with a wavelength of 585-595 nm is the best-studied laser treatment for the management of telangiectasias of LE (Baniandres et al., 2003; Diez et al., 2011; Erceg et al., 2009; Raulin et al., 1999; Truchuelo et al., 2012). Treatment of LE telangiectasias is very similar to that of rosacea telangiectasias. In the author's (JF) experience, LE telangiectasias tend to comprise smaller diameter vessels than most telangiectasias of rosacea; therefore, they respond more readily to shorter pulse widths (Fig. 1). In all patients, a detailed examination is performed before initiating treatment. In some published studies, most patients experienced a complete resolution of their cutaneous disease (including the annular plaques of SCLE, scarring plaques of DLE, and urticarial-like plaques of tumid LE) with a reduction in clinical skin scores including the size, erythema, and edema (Diez et al., 2011; Truchuelo et al., 2012). No complications were noted. In another study, PDL resulted in a statistically significant decrease of the Cutaneous Lupus Erythematous Disease Area and Severity Index score from a mean of 4.4 to 1.3 after three treatment sessions (Erceg et al., 2009). The majority of studies that use PDL to treat cutaneous LE reported successful outcomes with no recurrence over follow-up times of 1-10 months (Baniandres et al., 2003; Diez et al., 2011; Erceg et al., 2009; Raulin et al., 1999; Truchuelo et al., 2012).

Uncommon side effects including transient hyperpigmentation, permanent pigmentation changes, and slight scarring were reported.

Ablative lasers have shown benefits in managing the scarring of cutaneous LE. The fully ablative $CO_2$ laser has been reported in two case reports to be successful in the improvement of scarring lesions of DLE with prolonged remission (i.e., 1-2 years without recurrence; Henderson and Odom, 1986; Walker and Harland, 2000). A fully ablative Er:YAG laser has also been utilized successfully in the treatment of patients with extensive cribriform scarring of the face. One patient had no hypertrophic scarring or reactivation of the disease (Tremblay and Carey, 2001). In another patient, treatment with a nonablative Nd:YAG laser also demonstrated significant cosmetic improvement without adverse effects and 1-2 years without recurrence (Park et al., 2011b).

*Dermatomyositis*

DM is an idiopathic inflammatory myopathy that is characterized by muscle weakness and specific cutaneous findings. Classical cutaneous findings of DM include a symmetric violaceous macular erythema that progresses to poikiloderma and induration. Common lesions also include periungual telangiectasias, a heliotrope periorbital violaceous eruption, and violaceous papules that are distributed over the joints (i.e., Gottron's papules; Callen, 2000).

Many of these cutaneous manifestations are particularly resistant to traditional medical therapy (Callen, 2000). PDL treatment has been noted to be highly effective for the treatment of patients with poikilodermatous erythema as observed in two patients with DM. No adverse events such as scarring or dyspigmentation were encountered in one patient while the other had transient hyperpigmentation, which resolved in 4 weeks (Yanagi et al., 2005). PDL was also utilized in the treatment of patients with Gottron's papules of the finger and elbows in one case report (Calvo Pulido et al., 2006). After three treatments every 2 months, a 70% improvement was noted without a recurrence 3 years after treatment. Argon laser has also been reported as effective in the treatment of telangiectasias in patients with juvenile DM (Zachariae et al., 1988). The results were reported as almost normal in appearance in patients who were treated. No adverse events such as scarring or dyspigmentation were reported.

Calcinosis cutis is an uncommon but troublesome complication of DM and treatment is challenging. An ongoing pilot study is seeking to determine whether the laser-assisted delivery of a topical sodium thiosulfate solution can improve the superficial cutaneous calcinosis of DM in juvenile and adult patients (George Washington University, clinical trials). Sodium thiosulfate is an intravenous medication that is used to treat calciphylaxis and tumoral calcinosis. Laser-assisted drug delivery is a recently developed technique that utilizes the ablated columns of a fractional laser to bypass the stratum corneum and enhance topical drug delivery. This phase 2 trial recently closed and we are eager to see results in the near future.

*Systemic and localized sclerosis*

Systemic sclerosis is a chronic, multi-organ system disease of connective tissue that is characterized by fibrosis of the skin, blood vessels, and internal organs. Limited cutaneous systemic sclerosis (i.e., calcinosis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia [CREST] syndrome) is characterized by Raynaud's phenomenon, sclerodactyly, and telangiectasias of the skin (Fig. 2) with systemic involvement of the gastrointestinal tract and possibly pulmonary artery hypertension. Localized scleroderma or morphea represents thickening and fibrosis that is limited to the skin, subcutaneous tissue, and rarely underlying bone or nervous system (Gabrielli et al., 2009).

Several studies have examined the use of laser therapy to treat various forms of scleroderma. PDL has been utilized in a case series of eight patients with telangiectasias in morphea (Ciatti et al., 1996). These patients were successfully treated without recurrence from 6 months to 2 years after treatment. Two other case reports of morphea have noted similar, successful improvement (Eisen and Alster, 2002; Kakimoto et al., 2009).

One study examined whether telangiectasias that are observed in systemic sclerosis were inherently different from sporadic telangiectasias and whether they would require more treatment to clear (Halachmi et al., 2014). Nineteen skin biopsy test results from patients with scleroderma were compared to 10 control biopsy test results and showed that 17 of 19 scleroderma sections exhibited thickened vessels and thickened collagen fibers. On average, telangiectasias of systemic sclerosis requires about twice as many PDL treatments as sporadic telangiectasias.

IPL has been shown to help improve microstomia that is associated with scleroderma (Comstedt et al., 2012). Four patients with systemic sclerosis and microstomia who were treated with IPL experienced softening of the perioral skin with improvement in daily functions. An increase in oral aperture was noted in 75% of patients with improvement of approximately 1 mm per treatment. The only side effects observed were transient moderate erythema and edema.

Case reports of full-field and fractional $CO_2$ laser treatments demonstrated the improvement of rhytides and calcinosis of the digits in patients with morphea (Apfelberg et al., 1998; Bottomley et al., 1996; Chamberlain and Walker, 2003). Severe Raynaud's disease with

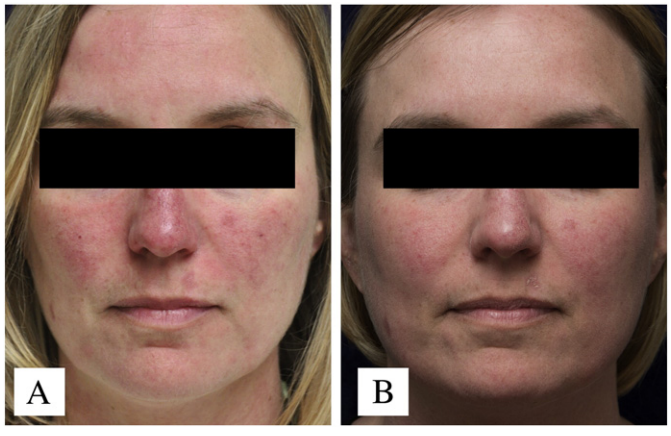


**Fig 1.** Butterfly erythema of acute cutaneous lupus erythematosus in a patient with systemic lupus erythematosus, before (left) and after four monthly treatments with 595 nm pulsed dye laser

chronic fingertip ulceration in a patient with scleroderma was successfully treated using the 1064 nm Nd:YAG laser, giving the patient improved mobility and circulation and ultimate healing of the ulcerations (St Surin-Lord and Obagi, 2008).

When cutaneous sclerosis crosses a joint, the resulting loss of function can be devastating for a patient. Traditional management paradigms include physical therapy and surgical release of the contracture. Recently, a fractional $CO_2$ laser was successfully used in the treatment of patients with morphea-related joint contracture (Kineston et al., 2011). A patient with a morphea-induced contracture across the ankle with limiting plantar flexion had failed a treatment combination of methotrexate, ultraviolet A1, topical calcipotriene, intralesional triamcinolone acetonide, and aggressive physical therapy. Almost immediately after a single treatment session with a fractionated $CO_2$ laser, the patient reported subjective improvement in range of motions. Four months after the single treatment, the patient had regained full plantar flexion with softening of the contracture on palpation without any adverse effects and this improvement was maintained at 1 year.

In summary, connective tissue diseases afflict many dermatology patients and conventional treatments may not always be successful in clearing cutaneous disease. Laser therapy may offer patients long-term benefits with a clearance or at least a reduction of the skin lesions. However, given that the formation of telangiectasias is inherent to the disease process in many connective tissue diseases, there should be an expectation of new telangiectasia development, especially if the disease is not well controlled. The majority of evidence for laser therapy is limited to small case reports and series. Therefore, large, randomized, controlled clinical trials are necessary. These trials will also assist in the evaluation and determination of parameters, techniques, and the proper placement of laser therapy in the treatment ladder for patients with connective tissue diseases.

## Sarcoidosis

Sarcoidosis is a systemic disease that is characterized by noncaseating granulomas of multiple organs, most commonly the lungs, lymph nodes, and skin. Dermatologic findings are noted in approximately 25% of patients (Haimovic et al., 2012).

Five case reports of PDL therapy for patients with cutaneous sarcoidosis were identified. Considerable-to-complete improvement was described in four cases (Cliff et al., 1999; Goodman and Alpern, 1992; Holzmann et al., 2008; Roos et al., 2009). One patient experienced ulceration in both treated and nontreated areas (Green et al., 2001). The $CO_2$ laser has been used successfully with durable responses over many years in the remodeling of lupus pernio of the nose in five patients (O'Donoghue and Barlow, 2006; Young et al., 2002). One case report discussed the use of a combination of PDL and nonablative fractional resurfacing to treat a patient with lupus pernio (Emer et al., 2014). The patient improved with minimal side effects and a maintenance for 6 months of follow-up.

Unfortunately, because of the tendency of sarcoidosis to exhibit isomorphic responses, the laser treatment of cutaneous sarcoidosis is beset with an inherently high complication rate (Kormeili et al., 2004). Caution should be exercised when treating these patients, particularly when treating with ablative devices.

## Melasma

Melasma is a hyperpigmentation disorder that affects sun-exposed areas of the skin, especially the face (Craft et al., 2013). Melasma is more common in women and can worsen in response to hormones such as during pregnancy or with the use of birth control pills (Craft et al., 2013). First and foremost in the treatment of melasma is limiting sun exposure and photoprotection with ultraviolet filters. Topical treatment with hydroquinone alone or in combination with corticosteroid medications, tretinoin, retinol, or glycolic acid are first-line therapies for patients with melasma (Craft et al., 2013). Second-line treatments include microdermabrasion, in-office chemical peels, and laser therapy. Nearly every laser in existence has been applied for the treatment of patients with melasma but a treatment regimen that consistently induces lasting remission remains elusive.

The Q-switched (QS) Nd:YAG laser has the most evidence behind its use in the treatment of patients with melasma. Treatment of Asian patients with melasma using low-fluence 1064 nm QS-Nd:YAG laser therapy yielded a 50 to 74% improvement by both patient and investigator ratings of treatment outcome (Sim et al., 2014). The melasma index (MI) and Melasma Area and Severity Index (MASI) are investigator tools that are used to measure melasma severity and improvement. A study of 50 patients who were treated with a 1,064 nm QS-Nd:YAG laser weekly for nine sessions showed improvement in both their MI and MASI scores. However, the recurrence rate was high (64%) at the 3-month follow-up mark (Zhou et al., 2011). A significant temporary improvement was also observed in the treatment of melasma using the QS-Nd:YAG in patients with types II-IV Fitzpatrick skin types (Brown et al., 2011).

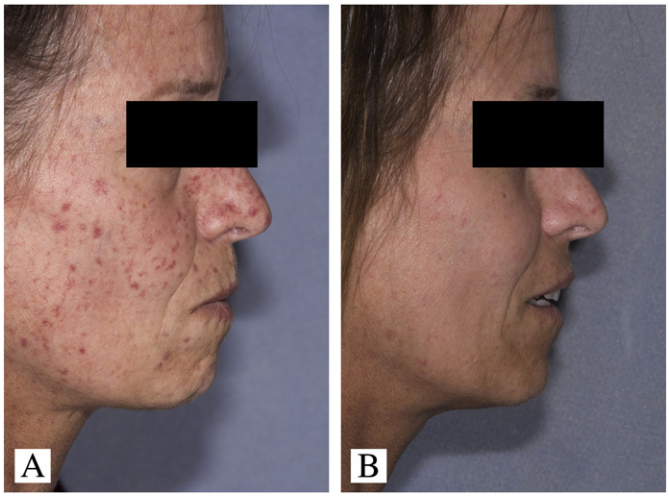


**Fig. 2.** Mat telangiectasias of calcinosis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia (CREST syndrome) before (left) and after five pulsed dye laser treatments that are spaced 1-2 months apart

The QS-Nd:YAG laser may be more effective when used in combination with other treatment modalities. The addition of oral tranexamic acid to 1064 nm QS-Nd:YAG therapy has shown to provide an additional benefit in efficacy (Shin et al., 2013). Microdermabrasion in addition to 1064 nm QS-Nd:YAG laser therapy was shown to yield a long-lasting remission of at least 6 months (Kauvar, 2012) without clinically significant side effects (Salem et al., 2009). The addition of a number of topical agents has also been shown to improve the treatment of melasma including 7% alpha arbutin solution (Polnikorn, 2010), the ultrasonic application of topical vitamin C (Lee et al., 2015b), chemical peels with Jessner's solution (Lee et al., 2014), and glycolic acid (Kar et al., 2012; Park et al., 2011a). In general, better results are observed with the use of laser therapy after treatment with a topical triple-combination cream (hydroquinone 5%, tretinoin 0.05%, and triamcinolone acetonide 0.1%) than before (Jeong et al., 2010).

Fraction photothermolysis (FP) has been employed with some success in the treatment of patients with melasma. In one study, six Chinese female patients with Fitzpatrick skin types III-IV and resistant melasma showed an improvement after treatment with three to four fractionated ablative $CO_2$ laser treatments at approximately 4-week intervals (Naito, 2007). A light microscopic evaluation after treatment with fractional photothermolysis shows fewer melanocytes and a relative absence of melanin in the surrounding keratinocytes compared with pretreatment specimens (Goldberg et al., 2008). Although fractional photothermolysis has been shown to be temporarily effective, maintenance and adjuvant therapy is needed to prolong the effect (Wanitphakdeedecha et al., 2014).

There is mixed evidence in support of nonablative fractional laser therapy for the treatment of patients with melasma both at 1540 nm and 1910 nm. Nonablative fractional laser therapy has been shown to be safe and comparable in efficacy and recurrence rate to triple topical therapy (Kroon et al., 2011). The addition of nonablative fractional photothermolysis combined with the use of triple-combination cream was successful in patients with melasma that was resistant to triple therapy alone; however, the long-term effect is limited (Tourlaki et al., 2014). A high rate of postinflammatory hyperpigmentation with nonablative 1,550 nm fractional lasers at 15 mJ/microbeam led to lower patient satisfaction (Wind et al., 2010). Finally, another study of 51 patients who were treated with nonablative 1550 nm fractional photothermolysis showed no significant improvements in the treatment of melasma (Karsai et al., 2012).

Combination laser therapy has been shown to be more effective in the treatment of patients with melasma than single laser therapy. One study treated 12 patients with fractionated IPL (IPL-F) and low-fluence (LF) QS-1,064 nm Nd:YAG laser therapy and compared the MASI scores to those of 12 patients who underwent the same number of treatments with IPL-F alone. This study found a greater improvement in the combination treatment group than those who were treated with IPL-F alone (Yun et al., 2014). Combination $CO_2$ laser therapy in combination with QS-alexandrite (alex) laser therapy showed better results than therapy with QS-alex alone but was associated with more frequent adverse effects (Angsuwarangsee and Polnikorn, 2003). No substantial added improvement was observed with the use of fractional nonablative 1550 nm erbium-doped fiber in addition to 1064 nm QS-Nd:YAG laser therapy in one study of 26 Asian patients with melasma (Kim et al., 2013). The combination of pulsed $CO_2$ laser therapy followed by QS-alex laser therapy yielded a complete resolution of the melasma according to one study (Nouri et al., 1999). This result is postulated to be effective by first destroying abnormal melanocytes with the pulsed $CO_2$ and then treating the dermal melanin with the alex laser. However, the results from this study were limited by the small sample size because this was a pilot study as well as the short follow-up period (Nouri et al., 1999).

Although some laser treatments have been shown to temporarily improve melasma, they have not been shown to be superior to topical treatment. Laser therapy is an expensive and cumbersome alternative to topical treatment, which can be easily applied by patients at home. One study compared QS-Nd:YAG laser therapy with trichloroacetic acid (TCA) and found no significant difference in efficacy (Moubasher et al., 2014). FP was also compared with TCA and again failed to show a significant improvement with respect to MASI scores or patient-rated improvements (Hong et al., 2012).

The adverse effects of treating melasma with lasers include hypopigmentation, rebound hyperpigmentation (Wattanakrai et al., 2010) and worsening of the melasma (Sheth and Pandya, 2011). There does not appear to be a significantly greater improvement in treating melasma with lasers as a first-line therapy to justify the additional cost and risk of the side effects.

In conclusion, many different lasers have been evaluated as treatment options for patients with melasma. However, due to high rate of recurrence and risk of hyperpigmentation, topical therapy is still considered a first-line treatment for patients with melasma. The use of laser therapy does offer an alternative option for some patients, especially those who are resistant to topical therapy. Combination laser therapy may yield better and longer-lasting results; however, more evidence is needed to determine the optimal regimen for treatment. Unfortunately, the recurrence of melasma is very common after a successful treatment with any modality.

## Nevus of Ota

Nevus of Ota is a hamartoma of dermal melanocytes. Originally described by Ota and Tonino in 1939, it occurs most frequently in Asian populations. The male-to-female ratio for nevus of Ota is 1:4.8 (Hidano et al., 1967). Clinically, the nevus presents as a bluish-black patch on the face in the distribution of the ophthalmic and maxillary branches of the trigeminal nerve. Nevus of Ota may be unilateral or bilateral and may also involve ocular and oral mucosal surfaces (Franceschini and Dinulos, 2015; Que et al., 2015). The first peak of onset occurs in infancy while a second peak is seen during adolescence.

Laser surgery has superseded cryotherapy, microsurgery, dermabrasion, and sequential dry ice peeling as the treatment of choice for patients with nevus of Ota. High success rates and minimal adverse effects have been reported with the QS-ruby, QS-alex, and QS-Nd:YAG lasers. Watanabe and Takahashi (1994) demonstrated an excellent response (defined as lightening of 70% or more) in 33 of 35 patients and a good response (lightening from 40 to 69%) in 2 of 35 patients who all received 4-5 treatments with a QS-ruby laser. A study of 101 patients with nevus of Ota who were treated with QS-ruby laser treatment also reported favorable results with 56% of patients achieving a 75% improvement and 36% of patients with a complete clearing. The authors noted hypopigmentation in 17% of patients while 6% of patients developed hyperpigmentation (Kono et al., 2001). Earlier treatment of children with a QS-ruby laser decreased the number of side effects and total number of treatments required (Kono et al., 2003).

A retrospective study of 806 patients who were treated with a QS-alex laser found that 94% of patients achieved complete clearance after an average of 5.2 sessions. The interval between treatment sessions was 3 to 6 months. No hypo- or hyperpigmentation was observed at the time of follow-up for 590 of these patients over an average period of 70.8 months and only 5 patients displayed a recurrence after achieving complete clearance (Liu et al., 2011). Overall, the risk for hypopigmentation tends to be the lowest with 1064 nm Nd:YAG laser therapy and one review of 176 patients found that 10.5% of patients who received QS-alex laser treatment demonstrated hypopigmentation while 7.6% of patients who received Nd:YAG laser

therapy showed hypopigmentation (Chan et al., 2000a). An additional study demonstrated that the use of a picosecond 755-nm alex laser yielded significant improvement in recalcitrant lesions that were previously treated with various nanosecond lasers. No redarkening or other adverse effects were noted with the picosecond laser. Treatment intervals ranged from 6 to 8 weeks (Chesnut et al., 2015). Recently, a retrospective study of patients with a skin of color was conducted whereby 70 patients were treated with QS-picosecond alex laser therapy, 92 patients with QS-532 nm KTP and 1064 nm Nd:YAG nanosecond, and 47 patients with QS-ruby nanosecond laser therapy. Nevus of Ota was the most common pigmentary disorder for which patients with a skin of color sought treatment (38.1%), followed by solar lentigines (23.8%), postinflammatory hyperpigmentation (9.5%), congenital nevus (7.1%), Becker's nevus (4.8%), and nevus of Ito (2.3%). Clinical efficacy was found to be comparable between picosecond and QS-nanosecond laser treatment for all lesions. Among the patients who were treated with Q-switched nanosecond, 16% displayed permanent dyspigmentation while no permanent side effects were observed in patients who were exposed to the 755 nm picosecond laser. Notably, patients with nevus of Ota were the most responsive to treatment among the pigmented lesions studied (Levin et al., 2016).

Recently, fractionated laser treatment has also been added to the options that are currently available to treat patients with nevus of Ota. The successful treatment of nevus of Ota in a 46-year-old male patient of Japanese ancestry using a 1440 nm Nd:YAG fractionated resurfacing laser has been reported. The authors noted no postinflammatory hyperpigmentation (Kouba et al., 2008). Subsequently, a 1064 nm QS-Nd:YAG laser treatment followed by a 1550 nm fractionated erbium-doped fiber laser was used to achieve near-complete clearance in two patients with nevus of Ota. The intervals between treatments were 2.3 and 3.2 months, respectively, with no evidence of recurrence (Moody et al., 2011).

In a comparison of QS-alex and QS-Nd:YAG lasers, patients reported less overall pain and discomfort with the former while the authors noted greater effectiveness of the latter (Chan et al., 1999, 2000c). A study of 31 patients who were treated with a QS-1064 nm Nd:YAG nanosecond laser found that patients who were younger than 10 years of age required a lower fluence to reach near total improvement (Seo et al., 2015a). The interval between treatments was 2 to 3 weeks.

The recurrence of nevus of Ota after laser treatment is low. Some authors have determined a recurrence rate of 0.6 to 1.2% (Kono et al., 2003) while others observed a rate of 1.2 to 5.2% (Chan et al., 2000b). Two cases of repigmentation after the treatment of nevus of Ota with a QS-alex or QS-Nd:YAG laser have also been reported (Chan et al., 2000a).

In conclusion, the response rates in patients with nevus of Ota who are treated with conventional QS-ruby, QS-alex, and QS-Nd:YAG laser therapy are generally high while the adverse event rates are relatively low. Picosecond and fractionated laser treatments may permit further decreases in dyspigmentation and recurrence rates. The best results appear to be associated with a relatively long interval between treatments (10-12 weeks) compared with the 2-4 week spacing that is typically utilized to treat other lesions of the face. Early treatment has been shown to improve outcomes but this must be weighed against the risks and stress that are associated with laser treatments in pediatric patients (Shahriari et al., 2015).

## Lichen Sclerosus

LS is a chronic skin condition that predominantly affects the anogenital skin and typically exhibits an initial inflammatory phase followed by chronic scarring and skin atrophy (Tan et al., 2017). The most commonly associated symptom of LS is pruritus (Shahriari et al., 2015). The management of LS has typically consisted of treatment with topical steroidal medications, immunomodulators, and supportive therapy including stool softeners and anesthetic medications for pain relief (Shahriari et al., 2015). A recent case report showed improvements with the use of a $CO_2$ laser (Lee et al., 2016). In this report, five female patients with hyperkeratotic vulvar lichen sclerosus that was recalcitrant to topical steroid therapy were treated. The first patient was treated successfully with an ablative $CO_2$ laser although she experienced significant discomfort for 2 weeks post-procedure. Therefore, the remainder of the patients were treated with a fractional $CO_2$ laser to achieve the same result while attempting to minimize discomfort. All five patients showed significant improvements and were able to use topical steroid medications for maintenance therapy after laser therapy. Two patients required retreatment for hyperkeratosis that recurred after 6-8 months. This case report demonstrates that fractional $CO_2$ laser therapy may provide an alternative for patients with topical steroid-resistant vulvar lichen sclerosus.

## Notalgia paresthetica and macular amyloidosis

Macular amyloidosis is a deposition disorder that can result in hyperpigmentation, pruritus, and increased thickness of the skin. A variety of treatments have been used for patients with macular amyloidosis. Pharmacologic treatments for patients with macular amyloidosis include amitriptyline (Yeo and Tey, 2013), onabotulinumtoxinA (Maari et al., 2014; Pérez-Pérez et al., 2014; Weinfeld, 2007), and gabapentin (Loosemore et al., 2007; Maciel et al., 2014). Topical treatments that have been used include tacrolimus (Ochi et al., 2016) and capsaicin (Andersen et al., 2016; Wallengren and Klinker, 1995). Other modalities including narrow band ultraviolet B (Pérez-Pérez et al., 2010), surgical decompression (Williams et al., 2010), osteopathic manipulation (Richardson et al., 2009), exercise (Fleischer et al., 2011), electrical muscle (Wang et al., 2009) and nerve stimulation (Philip et al., 2009; Savk et al., 2007), and acupuncture (Stellon, 2002).

Few studies have looked at the treatment of macular amyloidosis by laser therapy. One study of 25 patients with primary cutaneous amyloidosis used both superficial ablation and deep rejuvenation with a fractional $CO_2$ laser and found a significant reduction in pigmentation, thickness, itching, and amyloid deposition (Esmat et al., 2015). In this study, superficial ablation was preferred by patients due to decreased pain with comparable efficacy (Stellon, 2002). PDL has also shown success in the treatment of patients with macular amyloidosis. A case report of PDL treatment in a 57-year-old man with recalcitrant macular amyloidosis who was treated with three sessions of PDL at 2-week intervals showed improvement after each treatment (Barsky and Buka, 2014). This resulted from a decrease in collagen and dermatan sulfate synthesis that is similar to the mechanism behind the reduction of the size of hypertrophic scars (Esmat et al., 2015). The QS-Nd:YAG laser has also been studied in 20 patients with clinically diagnosed and pathologically confirmed macular amyloidosis who were treated with both 532 nm and 1064 nm doses in different parts or plaques. Colorimetric scores demonstrated an improvement at 8 weeks post-treatment. Both methods were effective but the QS-532 KTP was more effective in reducing the degree of macular amyloidosis and pigmentation in patients (Ostovari et al., 2008).

## Syringomas

Syringomas are benign skin-adnexal tumors that present as small dome-shaped papules and often occur in a periorbital distribution (Tan et al., 2013; Yates et al., 2015). They can also be found in the vulvar area and are associated with intense pruritus. Treatment is usually cosmetic and can be accomplished with a variety of techniques

including excision, electrocoagulation (Al Aradi, 2006), intralesional electrodesiccation (Hong et al., 2010), cryotherapy, dermabrasion, and more recently also laser therapy. Unfortunately, recurrence rates are high with any treatment modality including lasers.

Vaporization with ablative lasers such as $CO_2$ or Er:YAG is the most commonly employed laser treatment for patients with syringomas. In one study, the treatment of 10 patients with a $CO_2$ laser resulted in the elimination of syringomas in all patients. Prolonged erythema was the most common side effect. No scarring was observed with $CO_2$ laser treatment and four patients required repeat spot treatments (Wang and Roenigk, 1999). Vaporization by $CO_2$ laser also has shown success in the treatment of patients with familial syringomas (Castro et al., 1993). Another study showed excellent cosmetic results in 11 patients who were treated with multiple-drilling methods using a $CO_2$ laser without complications such as scarring, erythema, or pigmentary changes (Park et al., 2007). Another prospective study using a pinhole method with an ablative 10,600 nm $CO_2$ laser on the periorbital skin showed minimal improvement (0 to 25%) in 4 patients (13.8%), moderate improvement (26-50%) in 8 patients (27.6%), marked improvement (51-75%) in 10 patients (34.5%), and near-total resolution (>75%) in 7 patients (24.1%; Lee et al., 2015c). Patients with vulvar syringomas have also been successfully treated with a $CO_2$ laser (Huang et al., 2003). Fractional ablative lasers can be used to treat syringomas but multiple passes and consecutive treatments are required to achieve reasonable results. The treatment of periorbital syringomas in 35 patients in two sessions with a $CO_2$ fractional laser at 1-month intervals resulted in minimal improvement in 5 patients (14.3%), moderate improvement in 12 patients (34.3%), marked improvement in 15 patients (42.9%), and near-total resolution in 3 patients (8.6%; Cho et al., 2011).

Combination therapy with lasers has yielded good success. One study of 20 patients who were treated with a combination of TCA and $CO_2$ lasers showed excellent results in the majority of patients with no serious complications such as infection, scarring, or textural change (Kang et al., 1998). Another case report of eruptive facial syringomas in an African-American patient who was treated with TCA and $CO_2$ laser resurfacing showed good cosmetic results but not complete ablation and without significant side effects (Frazier et al., 2001). Another study found that the combination of $CO_2$ laser and botulinum toxin A produced better results in the treatment of patients with periorbital syringomas than $CO_2$ laser alone (Seo et al., 2015b). The combination of radiofrequency ablation and a $CO_2$ laser using low-energy parameters was found to be safe, easy, less painful, and with good cosmetic results in five patients (Hasson et al., 2012). The combination of $CO_2$ and QS-alex lasers has been studied. In one study, six patients with periorbital syringomas were vaporized with a $CO_2$ laser. Black ink was introduced to allow penetration to the dermis using iontophoresis and a QS-alex laser was used to remove the artificial tattoos. The majority of syringomas had disappeared by the time of the first follow-up 1 week after treatment and only one patient required additional treatment (Park et al., 2001). Fractional photothermolysis was used in the treatment of syringomas in one case report of two Japanese women (Akita et al., 2009). An argon laser was also used in one case report in the treatment of patients with vulvar syringomas (Kopera et al., 1999) but the treatment has fallen out of use due to the aforementioned side effects.

## Conclusion

Lasers are an important treatment option that may be used in the management of medical disease in women. Lasers are a first-line therapy for the treatment of telangiectasias in patients with rosacea and connective tissue disease and patients with nevus of Ota. Laser therapy should be considered in the disease management for patients with phymatous rosacea, melasma, hyperkeratotic lichen sclerosus, macular amyloidosis, syringomas, and sclerotic or scarring disorders such as morphea. Ongoing research will continue to define the optimal regimen for laser treatments of these conditions as well as broaden the application of lasers for other cutaneous diseases.

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