

#### **REVIEW ARTICLE**

## Laser therapy for cutaneous sarcoidosis: A review

## Teo Soleymani<sup>1\*</sup>, Michael Abrouk<sup>2</sup>

<sup>1</sup>The Ronald O. Perelman Department of Dermatology, New York University School of Medicine, New York, USA

Abstract: Sarcoidosis is a systemic, multi-organ disease of unknown etiology characteristically defined by the development of non-caseating granulomas. The development of sarcoidosis has been associated with a number of environmental and microbacterial factors coupled with genetic susceptibility. Depending on the type, location and distribution of disease, sarcoidosis can cause functional impairment, symptomatic distress, scarring and disfigurement. The advent of lasers as precise, minimally destructive surgical tools has allowed for their development as promising alternatives that minimize the morbidity associated with current therapies. In this paper, we reviewed the role of laser therapy in the treatment of cutaneous sarcoidosis. A comprehensive search of the Cochrane Library, MEDLINE and PUBMED databases was performed to identify relevant literatures investigating the role of laser therapy in the treatment of cutaneous sarcoidosis. In our opinion, laser therapy, particularly PDL, appears to be an effective, safe and generally well-tolerated modality for the treatment of cutaneous sarcoidosis and should be considered in patients with localized cutaneous disease that is refractory to conventional treatments. Less is known about the efficacy and tolerability of ablative laser therapy for the treatment of cutaneous sarcoidosis, though the limited data appears promising as well. With that said, however, the data is limited and warrants a need for additional larger, randomized controlled studies to further investigate the utility and efficacy of laser therapy in the treatment of cutaneous sarcoidosis.

*Keywords*: Skin cancer; basal cell carcinoma; squamous cell carcinoma; lasers; PDL; ablative lasers; vascular lasers; CO<sub>2</sub> laser

*Citation*: Soleymani T and Abrouk M. Laser therapy for cutaneous sarcoidosis. J Surg Dermatol 2016; 1(1): 4–12; http://dx.doi.org/10.18282/jsd.v1.i1.20.

\*Correspondence to: Teo Soleymani, The Ronald O. Perelman Department of Dermatology, New York University School of Medicine, New York, USA, Teo.Soleymani@gmail.com

Received: 15<sup>th</sup> December 2015; Accepted: 25<sup>th</sup> January 2016; Published Online: 28<sup>th</sup> March 2016

### Introduction

Sarcoidosis is a systemic, granulomatous disease of unknown etiology that is characteristically defined by the presence of noncaseating granulomas. While numerous organs may be involved, the skin, lungs and lymph nodes are the most common organs involved. Its pathogenesis is unknown but it is suspected that sarcoidosis develops after exposure to one or more inciting "trigger" antigens in a genetically susceptible individual, resulting in the

activation and overstimulation of inflammatory pathways that promote the formation of sarcoidal granulomas<sup>[1]</sup>. Studies have found an elevated risk of sarcoidosis in individuals who have been exposed to microbial agents and environmental antigens<sup>[1-3]</sup>. Disease susceptibility is genetically linked to some degree, and several associated genes of the HLA family have been identified<sup>[1]</sup>. Cutaneous sarcoidosis, the "great imitator," may stump even the most astute clinicians because of its diversity in manifestation.

Copyright © 2016 Soleymani T and Abrouk M. This is an Open Access article distributed under the terms of the Creative Commons Attribution-Non Commercial 4.0 International License (http://creativecommons.org/licenses/by-nc/4.0/), permitting all non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

<sup>&</sup>lt;sup>2</sup>Department of Dermatology, University of California, School of Medicine, Irvine, California, USA

The prevalence of sarcoidosis varies by geographic location, race and gender. In United States, the disease prevalence is estimated to be between 10–40 cases per 100,000, with a much higher annual incidence in African Americans (35.5–64 cases/100,000) than in whites (10.9–14 cases/100,000)<sup>[4-6]</sup>. The Scandinavian countries have the world's highest prevalence at 50–60 cases per 100,000 whereas the annual incidence in Japan is only one to two cases per 10,000<sup>[7,8]</sup>.

Sarcoidosis is characteristically a multi-organ disease. Cutaneous disease is present in at least 20% of cases and is the initial manifestation in nearly one-third<sup>[1,9-11]</sup>. Depending on the type, location, and distribution of disease, sarcoidosis can cause functional impairment, symptomatic distress, scarring and disfigurement. Numerous therapeutic options are available for the treatment of cutaneous sarcoidosis but with varying degrees of success. Furthermore, powerful immunosuppressive treatments such as methotrexate and the biologics are not without inherent side effects, including long-term risks of infection, hepatotoxicity and potential malignancy.

Since the advent of the first lasers, their use has been expanded tremendously in the field of medicine. What initially precipitated from the need for a better treatment of port wine stain birthmarks (PWS) led to the development of "selective photothermolysis" [12,13]. Selective photothermolysis was based on the concept that light passes through space until it is absorbed by a structure which contains light-absorbing molecules that coincide with the delivered wavelength. Intense pulses of light at preferential wavelengths absorbed by these "target" structures will initiate selective thermal damage<sup>[12,13]</sup>. Confinement of thermal damage within the target lesion is achieved if a laser wavelength with selective absorption and with sufficient but not overwhelming energy is delivered with pulse duration shorter than the time it takes for the target to cool off<sup>[12,14]</sup>. The advent of lasers as precise, versatile and minimally destructive surgical tools has allowed for their development as an alternative treatment option that minimizes the morbidity associated with current therapies used to treat cutaneous sarcoidosis. In this paper, we reviewed the role of laser therapy in the treatment of cutaneous sarcoidosis.

### Vascular lasers for treatment of cutaneous sarcoidosis

The clinical manifestations of cutaneous sarcoidosis are highly variable and consist of various subtypes including papular, plaque, lupus pernio, scar, psoriasiform, subcutaneous including erythema nodosum, and others. Of importance, lupus pernio is a very commonly presenting variant and is characterized by chronic and violaceous induration with associated telangiectasias, found predominantly on the nose and cheeks, that can often progress into disfiguring ulcerative nodular plaques on the nose and cheeks<sup>[1,15,16]</sup>. Lupus pernio can produce considerable disfigurement with significant morbidity and is often associated with chronic, progressive multi-organ systemic disease<sup>[1,15,16]</sup>. Notably, lupus pernio is frequently resistant to both topical and systemic immunosuppressive therapy<sup>[1,16,17]</sup>.

The presence of increased vasculature and telangiectatic vessels are classic clinical features of lupus pernio<sup>[1,15-17]</sup>. These microscopic vessels are both ectatic and fragile, making them an ideal target for selective photodamage. It has been hypothesized that vascular selective lasers such as pulsed dye lasers (PDL) can be used to selectively target a structure's vascular supply. The flashlamp-pumped pulsed dve laser was the first laser specifically developed for the treatment of vascular lesions and works based on the principle of selective photothermolysis as described above. The current PDL is able to vary different parameters such as spot size, pulse duration and energy fluence, which has increased in recent years because of the development of protective cooling systems. The most frequently used wavelengths are 585 and 595 nanometers (nm), allowing the penetration depth to be a maximum of 1.5-2 mm.

The potential advantage of photothermal vascular targeting over conventional excisional treatments is greater preservation of surrounding normal tissue. By selectively targeting the aberrant vasculature in lupus pernio, this approach may be an effective treatment alternative in order to minimize morbidity. It is important to note, however, that although it has been theorized that PDL treatment specifically targets blood vessels, this has not been definitely proven. Furthermore, high energies are often used (compared to, for example, treatment of telangiectasias) in combination with multiple passes and in some cases, without epidermal cooling, which may result in the injury being non-selective.

Although the data is limited, several studies have investigated the role of vascular selective PDL therapy for the treatment of cutaneous sarcoidosis. The first ever reported case of laser treatment for lupus pernio came from the Department of Dermatology and Beckman Laser Institute at the University of California, Irvine in 1992<sup>[18]</sup>. A 39-year-old Caucasian woman with a 5-year history of stable, diffuse, violaceous erythema with scattered granulomatous papules limited to the nose was treated with 1 pass of PDL utilizing a 585 nm wave-

length, 5 mm spot size, 0.46 ms pulse duration at a fluence of 5–8 J/cm<sup>2[18]</sup>. There was no mention of cooling or anesthesia used.

At the 4-week follow-up visit, significant fading of the erythema was noted with greatest improvement at areas that received 8 J/cm<sup>2[18]</sup>. There was no atrophy, scarring or hypopigmentation reported and the patient was pleased with the cosmetic outcome. The authors noted regression in the papular components of her pernio as well<sup>[18]</sup>. The authors reported that a second full treatment session was necessary after 7 months due to the recurrence of erythema and papules, upon which at 6-month follow-up after the second treatment, a 75% overall improvement over baseline was observed<sup>[18]</sup>. As a result from the follow-ups, the authors observed that great improvements were seen for 6-10 months after each laser treatment. However, the laser effects were temporary, which was unsurprising in a chronic granulomatous inflammatory disease. The authors concluded that performing laser treatments at periodic intervals would be an acceptable, safe and well-tolerated treatment option to provide significant improvement in the appearance of lupus pernio<sup>[18]</sup>.

The second reported case of laser treatment for cutaneous sarcoidosis was published several years later in 1999<sup>[19]</sup>. In this report, a 62-year-old Caucasian woman presented with biopsy-proven lupus pernio defined clinically by violaceous induration and blanchable erythema with ectatic telangiectasias limited to the nose. The patient underwent six treatments of 585 nm PDL, each spaced 6 weeks apart, utilizing a single pass with 5-mm spot size at an average of 6.6 J/cm<sup>2[19]</sup>. There was no mention of pulse duration and no cooling or anesthesia was used. The authors reported a dramatic cosmetic improvement at the end of the 6 sessions with no evidence of scarring, atrophy or other cosmetic side effects<sup>[19]</sup>. Remarkably, a repeat biopsy from the nose taken from an area that demonstrated cosmetic improvement after laser treatment showed a paucity in vascularity within the superficial dermis compared to the initial biopsy but with a persistence of noncaseating epitheliod granulomas within the deep dermis<sup>[19]</sup>. The authors concluded that this finding was not unexpected, as the pulsed dye laser treatment likely resulted in selective thermolysis of blood vessels within the papillary and reticular dermis, which in turn reduced the clinically visible erythema but did not affect the granulomatous process.

In another similar case, a 63-year-old Caucasian woman with biopsy-confirmed cutaneous sarcoidosis defined clinically by progressively enlarging erythematous nodules on her back underwent 585 nm PDL treatment using a 12 mm spot size, 0.5 ms pulse duration at 6 J/cm<sup>2</sup>. There was no mention of cooling or anesthesia. After 4 weeks, there was complete resolution of the nodules; however, subtle persistent erythema remained<sup>[20]</sup>. The patient's sarcoidosis remained active and the patient subsequently required systemic corticosteroid treatment with prednisone for developing necrobiosis lipoidica and iridocyclitis of her eyes. Consequently, her ocular findings and necrobiosis lipoidica resolved with steroid treatment; importantly, there was no recurrence of new nodular lesions or of the original lesions that had completely resolved through laser treatment before starting prednisone, and the patient remained free of nodular lesions 13 months after the steroids were discontinued, indicating that primary efficacy was derived from the laser treatment and not from steroids<sup>[20]</sup>.

Scar sarcoidosis is characterized by the infiltration of noncaseating sarcoidal granulomas in surgical scars, tattoos, skin piercings and other sites of trauma<sup>[1]</sup>. Scar sarcoid may be difficult to be distinguished clinically from a granulomatous foreign body reaction in a scar, hypertrophic scars, keloids, or other similarly appearing cutaneous conditions. Scar sarcoid is often refractory to topical and intralesional therapies and surgical excision provides only variable success and is often associated with significant morbidity. A recently published case reported the first successful treatment of pediatric scar sarcoidosis with PDL. In this case, a 10-year-old Caucasian boy presented with a 4-year history of a 1.0 cm × 1.0 cm isolated inflammatory, violaceous, ulcerated plaque on the left buccal cheek that had developed at the site of a previous atrophic scar secondary to a primary VZV infection at age six. The lesion was biopsied and confirmed to be scar sarcoid with no evidence of polarizing foreign body material, mycobacteria or fungal infections.

The patient underwent PDL treatment utilizing a 595 nm wavelength, 7 mm spot size, 0.5 ms pulse duration at a fluence of 7.7 J/cm<sup>2[21]</sup>. Cold air cooling was provided using an air-cooling device at setting 3 (SmartCool, Cynosure)<sup>[21]</sup>. Two to four pulses were delivered per session and neither pulse stacking nor double passing was used<sup>[21]</sup>. The patient received three treatments, given at 6-week intervals. No local anesthetics or systemic analgesics were needed during laser treatment<sup>[21]</sup>. The authors reported that immediately after treatment, mild to moderate purpura was observed, followed by minimal crusting<sup>[21]</sup>. After the first two treatments, the authors observed significant flattening of the lesion; after three treatments, complete clearance was achieved<sup>[21]</sup>. The authors reported that the treatments

were well tolerated and no treatment associated side effects were noted. At one-year follow-up, there was no evidence of lesion recurrence, although the varicella scar became much more visible after the sarcoidosis resolved<sup>[21]</sup>.

One of the biggest shortcomings of PDLs is the shallow depth of penetration: pulsed dye lasers penetrate up to 2 mm into the skin with yellow light wavelengths that are strongly absorbed by both oxyhemoglobin and deoxyhemoglobin [22]. Other vascular targeting wavelengths allow greater depths of penetration to target deeper vasculature. Lasers such as long-pulsed 1064 nm Nd: YAG and 755 nm Alexandrite lasers penetrate 50% – 75% deeper into the skin than PDL. Additionally, the conversion of oxyhemoglobin to methemoglobin after irradiation with PDL creates a second target chromophore for the Nd:YAG laser. However, these lasers have a much lower absorption coefficient in blood than PDL, requiring use of higher fluences [23].

In a more recently published study, a 57-year-old Caucasian woman with a 17-year history of biopsy-confirmed cutaneous sarcoid defined clinically as lupus pernio by violaceous infiltrating plaques on her cheeks was treated with two sessions spaced 7 months apart with frequency-doubled Nd:YAG at a wavelength of 532 nm, using a 50 ms pulse duration at 12-16 J/cm<sup>2[23]</sup>. There was no mention of spot size or cooling. After the second treatment, the patient had near complete resolution of her violaceous ervthema, and follow-ups for three years demonstrated no sign of relapse<sup>[23]</sup>. There was no evidence of atrophy, hypo- or hyperpigmentation, scarring or other side effects related to treatment [23]. This presents a notable finding: compared to the cases mentioned above which were treated using PDL, this patient experienced much longer lasting treatment efficacy with the utilization of Nd:YAG. This may be attributed to the greater depth of penetration of Nd:YAG lasers compared to PDL, resulting a more efficient targeting and selective photothermolysis of deeper vasculature, and/or attributed to the use of much higher fluences in this Nd:YAG case compared to the PDL cases mentioned above (Nd:YAG lasers have a lower absorption coefficient than PDL, thus inherently requiring the use of higher fluences, as mentioned earlier). However, it would be premature to draw any definitive conclusions on comparative efficacy between PDL and Nd:YAG as these are only case reports and much larger randomized controlled trials would be needed to make a decisive conclusion.

# Ablative lasers for treatment of cutaneous sarcoidosis

Ablative lasers, consisting primarily of carbon dioxide

(CO<sub>2</sub>) and Erbium Yittrium Aluminum Garnet (Er:YAG) lasers, have wavelengths that lie within the infrared range (10600 nm and 2940 nm, respectively) and thus target tissue water as the intended chromophore<sup>[24]</sup>. Although many describe ablative lasers as "selective" given that water is the targeted chromophore, it is important to understand that these lasers work by ablating tissue through vaporization of tissue water. Their precision lies in the minimization of "spillover" damage of tissue not in the treatment area. Delivery of high fluences with short pulse duration allows for a more precise control of tissue vaporization with minimal non-specific thermal damage to surrounding tissue.

For  $CO_2$  lasers, depth of tissue ablation is superficial, in the 20  $\mu$ m range<sup>[24-26]</sup>. At depths where adequate fluence is reached for heat vaporization of water, tissue is precisely ablated. At deeper depths, fluence drops and tissue is no longer vaporized but is instead coagulated, which provides associated hemostasis and collagen synthesis stimulation<sup>[24]</sup>. For Er:YAG lasers, depth of tissue ablation is even more superficial, approximately 2  $\mu$ m in depth<sup>[27]</sup>. The water affinity of the Er:YAG laser is roughly 15 times greater than that of the  $CO_2$  laser<sup>[24]</sup>, which allows for greater tissue vaporization but minimal coagulation. Hemostasis and, to a lesser extent, collagen stimulation are significantly reduced with Er:YAG as compared to  $CO_2$  lasers<sup>[24]</sup>.

In the first ever published case series investigating the role of ablative CO<sub>2</sub> laser resurfacing for the treatment of cutaneous sarcoidosis, two patients with longstanding and gross disfiguring lupus pernio refractory to medical therapy were treated with ablative CO<sub>2</sub> laser with excellent subsequent post-operative outcomes<sup>[28]</sup>. The first patient was a 37-year-old Afro-Caribbean woman who presented with a 20-year history of progressively disfiguring lupus pernio of her nose that was refractory to medical therapy. The patient had significant concomitant progressive systemic disease. She underwent CO2 laser ablation scanning back and forth repeatedly with the defocused manual hand-piece at 20-25 W continuous wave to produce even removal without deep dermal injury<sup>[28]</sup>. There was no specific mention of model, spot size, pulse duration or fluence for the first patient in this case series. Treatment was continued until a natural nasal profile was achieved. The authors reported an excellent response to treatment that was maintained for 7 years post-operatively, without further re-treatment<sup>[28]</sup>.

The second patient was a 52-year-old Afro-Caribbean woman who initially presented with a three-month history of disfiguring lupus pernio limited to her nose. Unlike the first patient, this patient did not have conco-

mitant systemic disease. The patient underwent a trial of medical management including topical, intralesional and systemic immunosuppressive therapy (duration unknown), to which no response resulted and her nasal lesions progressed, prompting a trial of CO<sub>2</sub> laser ablation. For this patient, the authors used the Sharplan Silk Touch Flashscanner<sup>TM</sup> CO<sub>2</sub> laser attachment and resurfacing hand-piece (Sharplan Laser Industries Ltd, Israel; distributed by medical equipment distributors Litechnica Ltd, Heston, Middlesex, UK) on repeat pulse (pulse duration 0.2 s) at 4 mm spot size, 19 J/cm<sup>2</sup> and 6 mm spot size, 18 J/cm<sup>2</sup>, respectively<sup>[28]</sup>. Treatment was continued until a natural nasal profile was achieved<sup>[28]</sup>. For this patient as well, the authors reported an excellent post-operative outcome with no lesion recurrence over a 32-month follow-up period (as of publication of the case series, the patient's follow-up was being continued)<sup>[28]</sup>. The authors did not report any evidence of side effects such as atrophy, hypo- or hyperpigmentation, or scarring in either patient<sup>[28]</sup>.

A more recently published case series investigating the role of CO<sub>2</sub> laser therapy for the treatment of cutaneous sarcoidosis reported three patients with biopsy-confirmed cutaneous disease limited to the nose who underwent treatment with a CO2 laser (ESC/Sharplan 40C) utilizing a 6 mm spot size at 18 W in 'paint mode' under local anesthetic<sup>[29]</sup>. There was no mention of pulse duration or cooling. Additionally, the epidermis in patient 1 and patient 3 was ablated for cosmetic reasons using a subsequent resurfacing pass with the CO<sub>2</sub> laser with a 6-mm spot size at 14 W in 'feather mode' [29]. Residual lesional tissues at the wound base was present in patient 1 and patient 3 and were injected intralesionally with triamcinolone acetonide (TAC) 5 mg/mL in an attempt to prevent recurrence. Patient 1, a 55-year-old Indian woman with a 4-year history of biopsy-confirmed nasal lupus pernio maintained results 6 years after treatment with the desired contour and only subtle hypopigmentation observed over the treated area<sup>[29]</sup>. Patient 2, a 57-year-old white male with a two-year history of biopsy-confirmed cutaneous sarcoidosis was treated for a nodule on the nasal bridge. The new nasal contour remained stable when last examined 14 months after treatment<sup>[29]</sup>. There was an 8 mm pale, pink, slightly atrophic scar visible at treatment site. Patient 3, a 58year-old Afro-Caribbean woman with a 10-year history of biopsy-confirmed sarcoidosis was treated for nasal lesions of lupus pernio. She obtained good cosmetic result with CO2 laser remodeling and maintained this for more than nine months<sup>[29]</sup>.

## Combination lasers for treatment of cutaneous sarcoidosis

Combination therapies can be utilized to improve treatment efficacy and/or cosmesis, particularly when attempting to simultaneously treat various cutaneous topographic features such as erythema, telangiectasias, nodules and hypertrophy. This can be particularly beneficial when treating conditions that have both epidermal and dermal components in disease pathology. In a recently published case, a 54-year-old Caucasian woman with a 9-year history of biopsy-proven cutaneous sarcoidosis defined clinically by papular, erythematous to violaceous plaques on the elbows, knees, and dorsum of the nose underwent treatment with an intense pulsed light system (Photoderm-Vasculight) utilizing a 590 nm cutoff-filter in combination with 1064 nm Nd:YAG laser utilizing a double pulse (T1: 2.8ms, T2: 2.8ms, no mention of spot size) at 37 J/cm<sup>2</sup> delivered with 20 ms delay between pulses<sup>[30]</sup>. No cooling or anesthesia was used. The sessions were conducted over a two year period but there was no specific mention of the interval duration between treatments. In each session, the energy was slightly increased up to a fluence of 45 J/cm<sup>2[30]</sup>. After the final treatment, the patient exhibited near-complete resolution of her lupus pernio with excellent cosmetic outcome without any treatment-associated side effects<sup>[30]</sup>. The patient remained asymptomatic without recurrence at the two-year follow-up without any further treatment.

A more recently published paper reported a case of lupus pernio refractory to topical, oral and intralesional corticosteroids as well as oral hydroxychloroquine and allopurinol treated with combination PDL and non-ablative fractional CO<sub>2</sub> laser<sup>[31]</sup>. No specific patient demographics or past medical history were reported. The patient was treated using a combined laser therapy with PDL and non-ablative fractional resurfacing. PDL was utilized at 595 nm performed first in single pulses using a 7 mm spot size with approximately 10% overlap, 0.45 ms pulse duration, and 8 J/cm<sup>2</sup> fluence<sup>[31]</sup>. Anesthesia was 30% lidocaine ointment under plastic wrap occluded for 90 min before the procedure, and there was no mention of cooling. Immediately after PDL laser treatment, non-ablative CO2 fractional resurfacing was performed with the Fraxel Dual laser 1550 nm at 70 mJ, treatment level 6, with 8 passes<sup>[31]</sup>. There was no mention of spot size, pulse duration or cooling. Ice packs were applied for 10 min after the procedure [31]. Prophylactic hydroquinone 4% cream was applied twice daily for two weeks prior to the procedure and one week after the procedure for the prevention of dyschromias. The authors reported significant cosmetic improvement after the first procedure, which became more apparent in the following months. Improvement was maintained for 6 months of follow-up<sup>[31]</sup>.

There was no mention of any reported side effects such as atrophy, hyper- or hypopigmentation, scarring or return of pernio. **Table 1** illustrates a comprehensive technical case summary of laser therapy for the treatment of cutaneous sarcoid.

Table 1. Comprehensive technical case summary of laser therapy for the treatment of cutaneous sarcoid

Author	De- mographics	Diagnosis	Laser	Number of treatments	Wavelength	Spot Size	Pulse Duration	Fluence	Cooling and Anesthesia	Results	Side Effects	Follow-up
Goodman et al. <sup>[18]</sup>	39-year-old white female	5 year hx of stable, diffuse, violaceous erythema with scat- tered granuloma- tous papules limited to the nose	PDL	One pass, two sessions	585 nm	5 mm	0.46 ms	5-8 J/cm <sup>2</sup>	None reported	75% improve- ment over baseli ne	None reported	Great improvements were seen for 6–10 months after treatment
Cliff et al. <sup>[17]</sup>	62-year-old white female	Biopsy- proven lupus pernio	PDL	6 sessions	585 nm	5 mm	none reported	6.6 J/cm <sup>2</sup>	None reported	"Dramatic cosmetic improvement"	None reported	A repeat biopsy from the nose taken from an area that demonstrated cosmetic improvement after laser treatment showed a paucity in vascularity within the superficial dermis compared to the initial biopsy but a persistence of noncaseating epitheliod granulomas within the deep dermis
Roos et al. <sup>[20]</sup>	63-year-old white female	Biopsy- confirmed cutaneous sarcoidosis	PDL	None reported	585 nm	12 mm	0.5 ms	6 J/cm <sup>2</sup>	None reported	Complete resolution of nodules	Subtle persis- tent erythema	Free of nodular lesions 13 months after systemic corticosteroids were discontin- ued
Holzmann et al. <sup>[21]</sup>	10-year-old white male	Biopsy- confirmed scar sarcoid	PDL	Three sessions	595 nm	7 mm	0.5 ms	7.7 J/cm <sup>2</sup>	Cold air cooling, no local or systemic anesthesia	Complete clearance after third treatment	Mild to moderate purpura, minimal crusting	No evidence of lesion recur- rence at one-year follow-up
Ekback et al. <sup>[23]</sup>	57-year-old white woman	17-year history of biopsy- confirmed cutaneous sarcoid	Nd: YAG	Two sessions	532 nm	None report- ed	50 ms	12–16 J/cm <sup>2</sup>	None reported	Near complete resolution	None reported	Follow-ups for three years demonstrated no sign of relapse

(To be continued on the next page)

### (Continued)

												(Commueu)
Author	Demographics	Diagnosis	Laser	Number of treatments	Wavelength	Spot Size	Pulse Duration	Fluence	Cooling and Anesthesia	Results	Side Effects	Follow-up
O'Dono-ghue et al. <sup>[29]</sup>	55-year-old Indian woman	4-year history of biop- sy-confirme d nasal lupus pernio	CO <sub>2</sub>	Two sessions	10600 nm	6 mm	None reported	18 W	Local anesthetic, no cooling reported	Desired outcome achieved	Subtle hypopig- popig- mentatio n	6 years after treatment, desired outcome was maintained
	57-year-old white male	Two-year history of biop- sy-confirme d cutaneous sarcoidosis	$CO_2$	One session	10600 nm	6 mm	None reported	18 W	Local anesthetic, no cooling reported	Desired outcome achieved	8 mm pale, pink, slightly atrophic scar visible at treatment site	14 months after treatment, outcome re- mained stable
	58-year-old Af- ro-Carribean woman	10-year history of biopsy- confirmed sarcoidosis	CO <sub>2</sub>	Two sessions	10600 nm	6 mm	None reported	18 W	Local anesthetic, no cooling reported	Good cosmetic result	None reported	Results maintained for more than 9 months
Emer et al. <sup>[51]</sup>	None reported	None reported	PDL	One session	595 nm	7 mm	0.45 ms	8 J/cm <sup>2</sup>	Anesthesia was 30% lidocaine ointment under plastic wrap oc- cluded for 90 min before the proce- dure. There was no mention of	Improve- ment noted after the first procedure	None reported	Improvement maintained at 6-month fol- low-up
			Fraxel	1 session with 8 passes immedi- ately following PDL	1550 nm	None report- ed	None reported	70 mJ	nention of cooling. Ice packs were applied 10 min after procedure			
Rosende et al.[30]	54-year-old white woman	9-year history of biop- sy-proven cutaneous sarcoidosis	IPL Nd:YA G	None reported	590 nm 1064 nm	None report- ed None report- ed	None reported  Double pulse T1: 2.8 ms T2: 2.8 ms 20 ms delay between pulses	None reported 37 J/cm <sup>2</sup>	None reported	After final treatment there was near complete resolution with excellent cosmetic outcome	None reported	Asymptomatic without recur- rence at 2-year follow-up
Young et al. <sup>[28]</sup>	37-year-old Af- ro-Caribbean woman	20-year history of biopsy- confirmed nasal lupus pernio	CO <sub>2</sub>	Numerous passes, one session	10600 nm	None report- ed	None reported	20–25W	Local anesthetic, no cooling reported	"Excellent cosmetic outcome"	None reported	Improvement maintained at 7-year fol- low-up
	52-year-old Af- ro-Caribbean woman	Unclear duration of biop- sy-confirme d nasal lupus pernio	$CO_2$	Numerous passes, one session	10600 nm	4 mm, 6 mm	0.2 s	18–19 J/cm <sup>2</sup>	Local anesthetic, no cooling reported	"Excellent cosmetic outcome"	None reported	Results maintained at 32-month follow-up, follow-up still ongoing.

### **Conclusion**

In conclusion, laser therapy, particularly PDL, appears to be an effective, safe and generally well-tolerated modality for the treatment of cutaneous sarcoidosis. Less is known about the efficacy and tolerability of ablative laser therapy for the treatment of cutaneous sarcoidosis, though the limited data appears promising as well. It is important to note that although these outcomes show potential, the data is limited, hence requiring further investigation with a greater number of patients. While these laser treatments provide an excellent option for cutaneous sarcoidosis, potential complications should be considered. The most common immediate side effects of PDL are erythema and mild edema, and long term complications consist mainly of hyper- or hypopigmentation and atrophic scarring, though these are often transient. For ablative lasers such as CO2 and Er:YAG, common immediate side effects include oozing, bleeding and crusting while long term side effects consist of hyper- or hypopigmentation, scarring and secondary bacterial or fungal infection. In our analysis of the literatures, the vast majority of complications after laser therapy were minimal, consisting primarily of mild pigmentary changes. Also, it is important to note that although the vast majority of literatures indicate an improvement of cutaneous disease after laser treatment, a few reports have described a new development or worsening of cutaneous sarcoidosis after laser treatment<sup>[32,33]</sup>.

Given that the guidelines for the treatment of cutaneous sarcoidosis remain undefined as no high-powered randomized controlled trials have been conducted to establish them (as is the case with conditions such as psoriasis, for example), dermatologists are left to utilized their expert judgement to tailor individual treatment based on disease severity, related comorbidities, and possible adverse outcomes. In our opinion, laser therapy for the treatment of cutaneous sarcoidosis appears to be an effective, safe and generally well-tolerated treatment modality and should be considered for patients with localized cutaneous disease that is refractory to conventional treatments. However, expert discretion should be utilized. Additional randomized controlled studies are needed to further investigate the utility and efficacy of laser therapy in the treatment of cutaneous sarcoidosis.

### **Conflict of interest**

The authors declared no potential conflict of interest with respect to the research, authorship, and/or publication of this article.

### References

- Haimovic A, Sanchez M, Judson MA, Prystowsky S. Sarcoidosis: A comprehensive review and update for the dermatologist: Part I. Cutaneous disease. J Am Acad Dermatol 2012; 66(5): 699.e1–699.e18; quiz 717–718. doi: 10.1016/j.jaad. 2011.11.965.
- Brownell I, Ramirez-Valle F, Sanchez M, Prystowsky S. Evidence for mycobacteria in sarcoidosis. Am J Respir Cell Mol Biol 2011; 45(5): 899–905. doi: 10.1165/rcmb.2010-0433TR
- 3. Chen ES, Moller DR. Sarcoidosis Scientific progress and clinical challenges. Nat Rev Rheumatol 2011; 7(8): 457–467. doi: 10.1038/nrrheum.2011.93.
- Hosoda Y, Sasagawa S, Yasuda N. Epidemiology of sarcoidosis: New frontiers to explore. Curr Opin Pulm Med 2002; 8(5): 424–428. doi: 10.1097/00063198-200209000-00014.
- Rybicki BA, Major M, Popovich J Jr, Maliarik MJ, Iannuzzi MC. Racial differences in sarcoidosis incidence: A 5-year study in a health maintenance organization. Am J Epidemiol 1997; 145(3): 234–241. doi: 10.1093/oxford-journals.aje.a009096.
- Reich JM, Johnson RE. Incidence of clinically identified sarcoidosis in a northwest United States population. Sarcoidosis Vasc Diffuse Lung Dis 1996; 13(2): 173–177.
- 7. Bresnitz EA, Strom BL. Epidemiology of sarcoidosis. Epidemiol Rev 1983; 5: 124–156.
- Pietinalho A, Hiraga Y, Hosoda Y, Lofroos AB, Yamaguchi M, et al. The frequency of sarcoidosis in Finland and Hokkaido, Japan. A comparative epidemiological study. Sarcoidosis 1995; 12(1): 61–67.
- Mana J, Marcoval J, Graells J, Salazar A, Peyri J, et al. Cutaneous involvement in sarcoidosis. Relationship to systemic disease. Arch Dermatol 1997; 133(7): 882–888. doi: 10.1001/archderm.1997.03890430098013.
- Lodha S, Sanchez M, Prystowsky S. Sarcoidosis of the skin: A review for the pulmonologist. Chest 2009; 136(2): 583–596. doi: 10.1378/chest.08-1527.
- Costabel U, Guzman J, Baughman RP. Systemic evaluation of a potential cutaneous sarcoidosis patient. Clin Dermatol 2007; 25(3): 303–311. doi: 10.1016/j.clindermatol.2007.03. 008.
- Anderson RR, Parrish JA. Selective photothermolysis: Precise microsurgery by selective absorption of pulsed radiation. Science 1983;220(4596): 524–527. doi: 10.1126/science.6836297.
- Anderson RR. Lasers for dermatology and skin biology. J Invest Dermatol 2013; 133: E21–E23. doi: 10.1038/skinbio. 2013.181.
- 14. Jalian HR, Avram MM, Stankiewicz KJ, Shofner JD,

- Tannous Z. Combined 585 nm pulsed-dye and 1,064 nm Nd:YAG lasers for the treatment of basal cell carcinoma. Lasers Surg Med 2014; 46(1): 1–7. doi: 10.1002/lsm.22201.
- Sanchez M, Prystowsky S. Sarcoidosis of the skin [Internet]. Basow D (editor), Waltham (MA): UpToDate Online;
   2010. Available from: www.uptodate.com.
- James DG. Lupus pernio. Lupus 1992; 1(3): 129–131. doi: 10.1177/096120339200100302
- 17. Cliff S, Felix RH, Singh L, Harland CC. The successful treatment of lupus pernio with the flashlamp pulsed dye laser. J Cutan Laser Ther 1999; 1(1): 49–52. doi: 10.1080/14628839950517101.
- 18. Goodman MM, Alpern K. Treatment of lupus pernio with the flashlamp pulsed dye laser. Lasers Surg Med 1992; 12(5): 549–551. doi: 10.1002/lsm.1900120515.
- 19. Shaw M, Black MM, Davis PK. Disfiguring lupus pernio successfully treated with plastic surgery. Clin Exp Dermatol 1984; 9(6):614–617.
- Roos S, Raulin C, Ockenfels HM, Karsai S. Successful treatment of cutaneous sarcoidosis lesions with the flashlamp pumped pulsed dye laser: A case report. Dermatol Surg 2009; 35(7): 1139–1140. doi: 10.1111/j.1524-4725. 2009.01202.
- 21. Holzmann RD, Astner S, Forschner T, Sterry G. Scar sarcoidosis in a child: Case report of successful treatment with the pulsed dye laser. Dermatol Surg 2008; 34(3): 393–396. doi: 10.1111/j.1524-4725.2007.34077.x.
- Izikson L, Nelson JS, Anderson RR. Treatment of hypertrophic and resistant port wine stains with a 755 nm laser:
   A case series of 20 patients. Lasers Surg Med 2009; 41(6): 427–432. doi: 10.1002/lsm.20793.
- 23. Ekbäck M, Molin L. Effective laser treatment in a case of lupus pernio. Acta Derm Venereol 2005; 85(6): 521–522. doi: 10.1080/00015550510027423.
- Zachary CB, Rofagha R. Laser therapy. In: Bolognia JL, Jorizzo JL, Schaffer JV (editors). Dermatology. 3<sup>rd</sup> ed. London: Mosby; 2012.

- 25. Humphreys TR, Malhotra R, Scharf MJ, Marcus SM, Starkus L, et al. Treatment of superficial basal cell carcinoma and squamous cell carcinoma in situ with a high-energy pulsed carbon dioxide laser. Arch Dermatol 1998; 134(10): 1247–1252. doi: 10.1001/archderm.134.10.1247.
- Trelles M, David L, Rigau J. Penetration depth of ultrapulsed carbon dioxide laser in human skin. Dermatol Surg 1996; 22: 863–865. doi: 10.1111/j.1524-4725.1996.tb005-89.x.
- Sakamoto FH, Avram MM, Anderson RR. Lasers and other energy technologies – Principles & skin interactions. In: Bolognia JL, Jorizzo JL, Schaffer JV (editors). Dermatology. 3<sup>rd</sup> ed. London: Mosby; 2012.
- Young HS, Chalmers RJ, Griffiths CE, August PJ. CO<sub>2</sub> laser vaporization for disfiguring lupus pernio. J Cosmet Laser Ther 2002; 4(3–4): 87–90. doi: 10.1080/14764170-2321136255.
- 29. O'Donoghue NB, Barlow RJ. Laser remodelling of nodular nasal lupus pernio. Clin Exp Dermatol 2006; 31(1): 27–29. doi: 10.1111/j.1365-2230.2005.01960.x.
- Rosende L, del Pozo J, de Andrés A, Pérez Varela L. Intense pulsed light therapy for lupus pernio (Spanish) [Tratamiento de lupus pernio con luz pulsada intense]. Actas Dermosifiliogr 2012; 103: 71–73.doi: 10.1016/j.adengl.2011.02.004.
- 31. Emer J, Uslu U, Waldorf H. Improvement in lupus pernio with the successive use of pulsed dye laser and nonablative fractional resurfacing. Dermatol Surg 2014; 40(2): 201–202. doi: 10.1111/dsu.12376.
- 32. Kormeili T, Neel V, Moy RL. Cutaneous sarcoidosis at sites of previous laser surgery. Cutis 2004; 73(1): 53–55.
- Green JJ, Lawrence N, Heymann WR. Generalized ulcerative sarcoidosis induced by therapy with the flashlamp-pumped pulsed dye laser. Arch Dermatol 2001; 137(4): 507–508.

12