Review paper

Lasers' Q-switched treatment in skin and subcutaneous lesions – review

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Adv Dermatol Allergol 2023; XL (2): 181–186
DOI: https://doi.org/10.5114/ada.2023.127636

Abstract

The numerous medical fields like dermatology, ophthalmology and surgery widely use laser therapy including Q-switched lasers. This review aims to provide information on the application and effectiveness of Q-switched lasers in dermal and vascular lesions. Q-switched lasers play a crucial part in the athlete's foot treatment and onychomycosis both in mono- and polytherapy. Laser therapy remains the gold standard for tattoo removal. Additionally, laser therapy shows high effectiveness in melasma, telangiectasias and photoaging therapy. The ability to adjust precise laser parameters like length or beam energy provides tight control of the treated area, significantly reducing the risk of adverse effects.

Key words: Q-switched lasers, onychomycosis, melasma, tattoos, telangiectasias, photoaging.

Introduction

The laser therapy era started with Albert Einstein's phrasing of the forced emission law in 1917 [1]. Lasers' electromagnetic beam penetration depends on the type of chromophore and the length of the emitted wave. The usefulness of lasers, especially scanners using the fractional technique of emitting a light beam, increases in aesthetic medicine. Non-ablative lasers, with a characteristic pulse mode, find application in medical practice because of a shorter recovery period and a lower risk of side effects than classic ablation lasers. The Q-switched lasers (ruby, alexandrite and neodymium-doped yttrium aluminium garnet (Nd:YAG)) are distinguished by 10^{-9}s pulse duration. Their precision provides the surrounding tissues' damage limitation to a minimal extent. The melanin and haemoglobin belong to molecules with the highest Q switch laser-derived radiation absorptivity. The action character makes those lasers widely used in tattoo removal or treatment of melasma, onychomycosis, telangiectasias and skin photoaging. Laser therapy also requires adjusting to the patient's skin features to maximise treatment effectiveness and minimise the risk of adverse effects [2–6]. Picosecond lasers use an acoustic effect, based on the photomechanical phenomenon, rupturing pigment elements for tattoo removal [7, 8]. However, picosecond lasers, due to their high efficacy and safety levels are used in an increasing number of dermatological indications [9, 10]. A comparison of efficacy and safety in the treatment of skin and subcutaneous lesions between Q-switched and picosecond lasers is shown in Table 1.

The paper will review Q-switched laser treatment's success rate and safety profile and follow other therapeutic options.

The purpose and the effectiveness of Q-switched laser

The length of the emitted wave, the time of exposure and the total delivered energy dose are the parameters allowing the appropriate adjustment for a particular ap-

Table 1. The advantages and disadvantages between nanosecond and picosecond lasers in the treatment of skin and subcutaneous lesions

Variable	Nanosecond lasers	Picosecond lasers
Advantages	Selective targeting in melanin lesions [3]	Good results in removing acne scarring [10]
		Lower rate of adverse effects in tattoo pigment removal [10]
Disadvantages	Poor results in non-pigmented changes and melasma alone [11]	Higher cost of the treatment [12]

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Received: 1.09.2022, **accepted:** 8.09.2022.

plication. The target tissues' absorption of emitted waves affects the laser treatment effectivity. Lasers are used in the majority of fields in medicine, especially in dermatology and ophthalmology, but also in surgery. The spectrum of Q-switched laser application mainly includes skin and subcutaneous lesions [4].

Onychomycosis

Onychomycosis is a nail infection caused by fungi, including dermatophytes, endomycetes and moulds. Furthermore, it is one of the most common lesions that affect 17–40% of adults. The most frequent signs of onychomycosis involve the altered colour and irregular surface of the nail plate [11–13]. The meta-analyses of onychomycosis treatment show the highest effectiveness of systemic antifungal therapy, including terbinafine and itraconazole [14]. However, laser therapy with 870 nm, 930 nm or 1064 nm length Nd:YAG lasers plays a non-negligible role [15].

The United States Food and Drug Administration (FDA) approved the use of lasers as adjunctive therapy for onychomycosis [16]. The 532 nm and 694 nm Q-switched lasers appear effective in destroying fungal hyphae; however, according to FDA guidelines, 1064 nm lasers are recommended [17, 18]. The action of Q-switched lasers is based on the disintegration of dermatophytes. Lasers used in the treatment of onychomycosis clean the nail plate and stimulate its growth [18]. Many studies confirmed that lasers reach excellent therapeutic results together with standard pharmacotherapy [19].

The effectiveness of 532 nm Q-switched Nd:YAG laser in a dose of 8 J/cm^2 was assessed with the average colony size of Trichophyton rubrum (T. rubrum) at 1, 3 and 6 days after a laser treatment. A decrease in the size of T. rubrum colonies appeared in the group treated with Q-switched laser from day 1 to day 6 [17].

Xu *et al.* analysed the average area of T. rubrum colony reduction after 694 nm Q-switched ruby laser therapy. The fungal colony plate was exposed to 6 J/cm^2 on the first day of colony growth. After 6 days, the authors noticed a significant difference in the size of T. rubrum colonies between irradiated and non-irradiated groups (1.84 vs. 2.59 cm^2) [20].

A Hochman's study evaluated the effectiveness of 1064 nm Q-switched Nd:YAG laser 0.65 ms pulses to treat an athlete's foot. Eight patients were treated with the Q-switched laser in 2–3 sessions at intervals of 3 weeks. The radiation dose was 223 J/cm^2. Seven of 8 patients achieved satisfactory treatment effects proved by negative cultures [21].

The study involving 120 patients with onychomycosis confirmed with direct mycological examination with KOH showed the effectiveness of onychomycosis treatment using 1064 nm Q-switched Nd:YAG laser. The radiation dose was 600 mJ/cm^2. There was a complete clinical and mycological response in all study participants without presenting adverse effects of the therapy after 9 months from a single therapeutic laser session [22].

On the other hand, a study by Kalokasidis *et al.* involving 131 patients treated with a 1064 nm/532 nm Q-switched Nd:YAG laser in 2 therapeutic sessions (days 0 and 30 of treatment), showed that 95.4% of patients after 3 months were cured of onychomycosis. The remission was evidenced with direct mycological examination and negative cultures. The Q-switched laser dose was 14 mJ/cm^2. This study revealed no adverse effects of laser therapy [23].

Additionally, a study by Kandpal *et al.* shows that the treatment with 1064 nm Q-switched Nd:YAG laser with a dose of 350 mJ/cm^2 results in faster onychomycosis disappearance compared to itraconazole treatment, assessed with direct mycological examination and negative cultures. The study included laser used for 12 weeks once a week in group 1 and the administration of 200 mg itraconazole twice a day on seven days per month for 3 months. After 12 months of follow-up, both the clinical and mycological responses (direct test with KOH and negative culture) showed a statistically significant reduction in group 1 compared to group 2 ($p < 0.05$). Moreover, in the third month of observation, 58% of the cultures from group 1 were negative compared to 12% in group 2 [24].

Afterwards, the case report by Mohanty *et al.* evidences the effectiveness of combining systemic and laser therapy. A patient with Syncephalastrum racemosum onychomycosis was treated with itraconazole pulses for 3 months and a 1064 nm Q-switched Nd:YAG laser with 600 mJ/cm^2 energy on the first, 30th and 60th day. After 12 months of observation, there was a complete clinical and mycological remission confirmed with a direct test with KOH and negative culture [25].

Melasma

Melasma is acquired hypermelanosis that appears on the skin exposed to sunlight, especially on the face [26]. Histological changes occur within the epidermis, dermis and extracellular matrix [11]. Ultraviolet (UV) radiation, genetic factors and sex hormones affect the occurrence risk [27]. Treatment of melasma includes high photoprotection, chemical peels, skin lightening agents, light and laser therapy [28]. Numerous studies confirmed effectiveness of Q-switched lasers in the therapy of epidermis and dermis hyperpigmentation [29]. In Asia, the 1064 nm Q-switched laser remains the therapeutic "gold standard" [30].

In most cases, the pigmented changes decrease after Q-switched laser radiation; however, relapses and skin hypopigmentation or hyperpigmentation may appear. Due to the adverse effects of Q-switched lasers, their use raises many doubts [30].

A study involving 50 patients, treated with 15 weekly sessions with a 1064 nm Q-switched Nd:YAG laser pulses in a dose of 2.8 J/cm^2, showed a reduction in pigmenta-

tion of lesions by 50–74%, assessed using digital photos and a pigment imaging device (Janus®, PSI Co., Ltd., Korea) after laser therapy [31].

Another study conducted by Choi *et al.* included 40 patients who underwent ten weekly sessions of the 1064 nm Q-switched Nd:YAG laser pulses in a dose of 1.2–2.0 J/cm^2. The effectiveness of the treatment was evaluated by the Melasma Area and Severity Index (mMASI) and the Physician's Global Assessment index (PGA). The average mMASI index decreased by 54.23% from the baseline value, while 75% of patients achieved an excellent, good or sufficient improvement in pigmented lesions as assessed by the PGA index [30].

Karadağ Köse and Borlu assessed 15 patients who underwent combined therapy with the 1064 nm Q-switched Nd:YAG laser pulses in a dose of 2.0–3.0 J/cm^2 and mesotherapy with biomimetic peptides. The treatment included five sessions at intervals of 2 weeks for 3 months. The evaluation was made 2 weeks after the last session. Mean mMASI scores decreased by 61% from baseline. Ten patients responded well or very well to the combination therapy. That suggests that mesotherapy with Q-switched laser usage provides an effective and safe treatment of melasma [32].

Debasmita *et al.* assessed the efficacy of a combination treatment of Q-switched Nd:YAG lasers with tranexamic acid (TA). Thirty patients underwent five monthly sessions of Q-switched laser with TA therapy applied daily. The mean decrease in mMASI in the combined treatment measured in 7 months after the first session equalled 5.12 ±2.66 to 2.33 ±1.33 ($p < 0.001$). Pain, erythema and burning were the only adverse effects of the therapy [33]. Similarly, Agamia *et al.* showed the efficacy of 1064 nm Q-switched Nd:YAG laser and TA combination therapy of melasma amongst patients treated with six sessions of laser therapy every 2 weeks and daily TA intake. Three months of combined treatment brought the mean mMASI decrease of 37.2 ±12%, 4.2 ±0%, and 41.1 ±21.7% in patients with epidermal, dermal, and mixed melasma, respectively [34].

Some studies emphasise that Q-switched lasers are not widely used, even if relapses or deteriorations of hyperpigmentation occur relatively often [5]. It is believed that in some cases, laser therapy is effective in treating changes in the course of melasma, but it has been associated with adverse effects such as dry skin and itching [35].

Tattoos

Tattoos are a form of body decoration formed by delivering a dye into the dermis in order to pigment a selected part of the skin. The word "tattoo" first appeared in the literature in the 18th century and was associated with criminals, sailors and people representing the lower social classes [36]. The process of getting a tattoo often is connected with adverse effects. Most frequently, about 20% of people who underwent the tattoo process are hypersensitive to the sunlight due to the formation of new, potentially dangerous chemical compounds in the skin resulting from the breakdown of pigment particles [37]. Further complications relate to an allergy to tattoo pigment haptens, especially in red, green and blue tattoos [38]. Depending on the colour of the tattoo pigment, it is possible to present various complications. The red pigment shows a characteristic hyperkeratosis, ulcer reaction, exanthema and urticaria. On the other hand, black tattoos are manifested by nodular-papular lesions [39].

Removing tattoos from the skin is based on breaking down of dye molecules. Lasers use the phenomenon of photoselective thermolysis to remove the pigment located in the dermis [40]. Tattoo removal is performed with nanosecond lasers (ruby, alexandrite, Nd:YAG Q-switched) and picosecond lasers [41].

Q-switched lasers are the "gold standard" in tattoo removal due to their high efficiency and safety [42–44].

The study presenting the effectiveness of laser therapy in tattoo removal included 20 patients with tattoos on various parts of the body, which were treated with a 1064 nm Q-switched Nd:YAG laser in a dose of 5.0 J/cm^2. The patients took part in 6 laser therapy sessions at intervals of 2 months. The therapy results in complete removal of the tattoo dye in all patients treated with the Q-switched laser 3 months after the last treatment session. The laser therapy ensured a minimum number of side effects limited to the erythema [45].

A study by Antony and Harland presents the effectiveness of the 532 nm Q-switched Nd:YAG laser in a dose of 1.4–6.4 J/cm^2 in removing red tattoos. The study included 7 patients who underwent six weekly cycles of laser therapy. After the end of laser therapy, flattening and depigmentation of the red ink within the tattoo area were achieved. Additionally, due to the presence of mercury sulfide in red dyes, patch tests for mercury were performed after six cycles of laser therapy, and they were negative [46].

Telangiectasias and haemangiomas

Telangiectasias are formed as a result of increased blood pressure in the capillary arteries, which leads to their permanent dilatation [47]. Predisposing factors for the development of telangiectasias are mainly individual predisposition, circulatory failure, hypertension, liver disease as well as sun exposure, solarium use, low and high air temperatures [48].

The preferred telangiectasias treatment methods are sclerotherapy, drugs containing 6-mercaptopurine and laser therapy [49]. For the most optimal results, a combination therapy consisting of laser treatments with sclerotherapy should be used [50]. The vascular lesions could be treated only with selected wavelengths. The gold standard in the most of them is the millisecond lasers – KTP laser is effectively used in the treatment of telangiectasias and erythema; however, the pulse-dye laser

provides an effective treatment for a wide variety of lesions, including vascular ones. Q-switched lasers provide optimal results with a high safety range [51].

A study involving 54 patients who received two or three cycles of treatment with polidocanol and a 1064/532 nm Q-switched Nd:YAG laser at 6–8 weeks' intervals showed excellent improvement in vascular lesions in approximately 91% of patients. The radiation dose of the Q-switched laser was 4.0–12 J/cm^2 [52].

In contrast, a study by Goldberg and Marcus compared the efficacy of two doses of 532 nm Q-switched Nd:YAG laser irradiation for telangiectasias. The study included 10 patients who underwent one laser therapy session using 3.0–4.0 J/cm^2 and 1.0–2.0 J/cm^2 against two vascular lesions present in the subjects. The vascular lesions were located on the trunk, neck, hands and face. After 180 days, applying the higher dose resulted in excellent improvement in 70% of the subjects, in comparison to 30%, when the lower radiation was given. Accordingly, a more remarkable improvement appeared when 3.0–4.0 J/cm^2 was applied compared to an amount of 1.0–2.0 J/cm^2 [53].

One of the studies proving the effectiveness of the 15–20 W Q-switched Nd:YAG laser in treating vascular lesions included 38 patients with hereditary haemorrhagic telangiectasia, in whom lesions occurred in the nasal and oral areas. Recurrence of telangiectasias appeared in 7 participants only at the same or other location during the 3-year study period [54].

Similar results occurred in other studies, summarised in the latest systematic review. These performances indicate that lasers are highly effective in treating this type of lesion. The possibility of the coexistence of telangiectasia with other skin diseases, such as rosacea, affecting the effectiveness of treatment remains worth considering [55].

Photoaging

Photoaging results from skin damage induced by reactive oxygen forms. Free radicals appear due to exposure to UV radiation [56]. Genes responsible for epidermal differentiation, neoangiogenesis and matrix metalloproteinase synthesis participate in UV-induced skin ageing. Exposure to sunlight also increases the transcription of these additionally, lipid metabolism and mitochondrial biogenesis decrease in ageing skin [57]. The most common skin lesions associated with photoaging involve wrinkles and hyperpigmentation, which satisfactorily respond to Q-switched laser treatment [58, 59].

A study by Gold *et al.* enrolled ten women with mild to moderate facial photodamage, telangiectasias, solar keratosis, sagging and dry skin. The treatment was based on a 1064 nm Q-switched Nd:YAG laser and a dose of 6.0–13 J/cm^2. Laser therapy included four sessions at 2–4 weeks' intervals. Before the treatment, patients were assessed as type II (wrinkles in motion) and III (wrinkles at rest) in a Glogau scale. Three months after treatment, the effectivity evaluation showed at least a one-point improvement in the Glogau scale in 60% of subjects. Additionally, the Q-switched laser did not cause pain during the session, and no adverse side effects of laser therapy were observed [60].

The adverse effects

The Q-switched lasers provide high safety and only a few adverse effects [61]. The most common complications include hyperpigmentation or hypopigmentation [62]. Treatment of the former includes using hydroquinone cream (not used in Poland), retinoids or peels; the latter involves using 308 nm xenon-chloride excimer laser [63]. Laser therapy also causes thermal damage [64]. Kirby *et al.* described the occurrence of blisters and burns in 3 patients after application of Q-switched Nd:YAG laser in a dose of 3.0 J/cm^2 to remove tattoos. Application of vaseline and a Band-Aid to the blisters resulted in lesions' regression [65]. The allergic reactions occurred mainly during tattoo removal with a Q-switched laser. Similarly, Harper *et al.* described the case of a patient who developed a severe cutaneous immune response. The lesions' biopsy revealed that the reaction was triggered by direct sensitisation to the ink but not the neoantigens' generation due to laser interaction with the pigment. The treatment included using local or systemic corticosteroids and antihistamine drugs [66].

Conclusions

In our work, we highlighted the role of Q-switched laser in dermatological treatment. Despite the actual broad lasers' application, there is still a need to expand their therapeutic indications. For this purpose, clinical studies need to validate the Q-switched laser as a first-line treatment.

The Q-switched lasers' efficacy evaluation showed that lasers with wavelengths of 532 nm, 694 nm and 1064 nm are preferred for the athlete's foot and onychomycosis treatment, whereas FDA recommendations suggest the 1064 nm wavelength [17, 18, 20, 21]. Moreover, Q-switched lasers present a distinctly higher efficacy in destroying fungal hyphae than traditional itraconazole treatment [24]. On the other hand, the combination therapy in onychomycosis, including itraconazole and 1064 nm Q-switched laser, showed a complete clinical and mycological improvement in a wide range of given doses [25].

The 1064 nm Q-switched lasers are preferred to remove skin lesions like melasma [31]. Presented studies show the effectivity of 1064 nm laser in a dose range of 1.2–3 J/cm^2. Combined treatment of the Q-switched laser with TA shows high efficacy with relatively few adverse effects in the melasma treatment [33, 34, 67]. Additionally, the therapy duration compared to onychomycosis treatment is noteworthy (15 weeks vs. 3–4 weeks). Due to possible recurrences, hypo/hyperpigmentation, pruritus,

dry skin, special care should be introduced while using this type of laser [5, 30, 35].

The tattoo removal "gold standard" includes Q-switched lasers due to their high efficacy and safety [44]. Studies show a variety in the choice of time and number of sessions with 1064/532 nm Q-switched laser, but all demonstrate complete tattoo pigment removal after a completed laser therapy cycle. In addition, the use of the Q-switched laser facilitated the mercury sulfide removal, a pigment component, from the skin [45, 46].

In the treatment of telangiectasias, the efficacy of combined therapy with Q-switched laser, polidocanol and two doses of radiation was compared [52]. The combination therapy and higher radiation dose variants were proven to be more effective. Millisecond lasers often appear as the first choice in vascular lesions therapy. However, many publications showed Q-switched significant therapeutic efficacy expressed with a lower recurrence rate [51].

Lesions like hyperpigmentation, telangiectasias and laxity caused by UV skin damage respond remarkably better to treatment with Q-switched lasers [56, 59]. Studies involving patients with photodamaged skin showed that Q-switched 1064 nm laser application decreased at least a one-point improvement in the Glogau scale in 60% of patients with no adverse effects of laser therapy [60].

The ability to select appropriate laser parameters such as length or beam energy gives control over the treatment and significantly reduces the risk of adverse effects compared to classical ablative lasers. Limited use of lasers in therapy sources from their low availability and the cost of the required equipment. The physician's experience plays a vital part. Nonetheless, laser techniques will continue to evolve, and it is only a matter of time before laser treatment will be performed in most dermatological offices.

Conflict of interest

The authors declare no conflict of interest.

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