

Optimizing Outcomes of Laser Tattoo Removal

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ABSTRACT

Since the elucidation of the concept of selective photothermolysis, quality-switched lasers have been the gold standard for tattoo removal. Proper patient education prior to commencing treatment is crucial to ensure realistic expectations and compliance. This article reviews appropriate device selection and technique. Clinical pearls and pitfalls are presented, as well as cutting-edge techniques and technologies are discussed in order to enable the laser practitioner to optimize outcomes.

Key words: Q-switched, quality-switched, tattoo, tattoo removal, ablative fractional, nonablative fractional, laser, review

The first evidence of efforts to remove body art exists in the writings of Scribonius Largus (54 A.D.), physician for the Roman Emperor Claudius. He described the use of a preparation of cantharides to induce blistering and eschar formation.¹ In the early 20th century chemical methods of tattoo removal continued to predominate. A 1928 *Journal of the American Medical Association (JAMA)* review of tattoos highlighted removal methods including surgical excision and electrolysis, but concluded that 50% tannic acid yielded the best results.² Quality-switched (QS) lasers for tattoo removal (694 nm ruby) was first reported in 1965 by Goldman.³ However, it was not until the theory of selective photothermolysis was introduced in 1983 that QS lasers became the gold standard for modern day tattoo removal.⁴

In order to optimize the outcomes of laser tattoo removal, it is imperative at the initial consultation to thoroughly educate patients regarding the treatment process. It is costly, often far exceeding the expense of obtaining the body art. Amateur tattoos generally require four to six treatments and professional tattoos may need eight or more sessions. Tattoos in acral locations prove more challenging to remove than those placed on truncal sites and older tattoos respond more readily than newer ones.⁵ The procedures can be painful and may not result in complete removal. A recent retrospective review of 238 paying patients who underwent an average of 3.57 treatments (ranging between 1-18 sessions) found that 1.26% achieved total clearance of the tattoo, defined as complete absence of pigment.⁶ The authors attributed the suboptimal results to their patients being inadequately informed of the process and subsequently underwent fewer treatments. To set reasonable expectations for our prospective

patients presenting with professional tattoos, the authors suggest that 75% of pigment can be diminished, however, complete removal is difficult to achieve. Prior to initiating treatment, it is important to examine the skin and query the patient regarding whether they have a history of hypertrophic scars/keloids or infectious diseases. Q-switched laser treatments are absolutely contraindicated in patients who have received gold therapy as they induce chrysiasis. Baseline photographs are highly recommended.

Appropriate Device Selection

When approaching a patient for tattoo removal, the laser practitioner must choose an appropriate device. A QS laser is necessary to achieve selective photothermolysis, as the exposure time in the nanosecond (10^{-9}) domain is less than half the thermal relaxation time of the target pigment. This ensures that the thermal damage is spatially confined to the target chromophore, resulting in photoacoustic destruction and minimizing damage to the surrounding tissue from thermal diffusion. The four available QS laser wavelengths are in the visible and infrared domain and include the 694 nm ruby, 755 nm alexandrite, the 1064 nm neodymium:yttrium-aluminum-garnet (Nd:YAG), which when passed through a potassium titanyl phosphate (KTP) crystal will double the frequency (halve the wavelength) to 532 nm. It is essential to utilize a wavelength that will be selectively absorbed by the tattoo particle (see Table 1). Additionally, dye laser handpieces can convert 532 nm to 585 nm (sky blue) and 650 nm (green). Despite these guidelines, it is important to remember that tattoo composition can be highly variable and the pigment may not respond predictably to QS laser treatment.⁷ The QS Nd:YAG is the device of choice

Q-switched Laser	Wavelength	Pulse Duration	Tattoo Colors
Ruby	694 nm	< 40 ns	black, blue, green
Alexandrite	755 nm	50 ns - 100 ns	black, blue, green
Nd:YAG	1064 nm	< 10 ns	black, blue
KTP	532 nm	< 10 ns	red, orange, yellow, brown

Table 1: Efficacy of Q-switched lasers for specific tattoo colors

when treating tattoos on Fitzpatrick type IV to VI patients, as the 1064 nm wavelength penetrates deepest and is minimally absorbed by epidermal melanin.

Treatment and Technical Considerations

Adequate pain control is necessary to deliver a pleasant treatment experience. Depending on the size of the tattoo, its location, and the pain tolerance of the patient, the authors utilize topical anesthesia with a forced air-cooling device or intralesional anesthesia. When QS laser energy is directed at the tattoo, the desired endpoint is usually immediate tissue whitening, though this may not occur once the tattoo has faded significantly. The whitening, which lasts approximately 20 to 30 minutes, is a result of rapid heating of the chromophore leading to gas formation.⁸ The optimal fluence is the lowest possible setting that elicits this endpoint in order to minimize the risk of thermal injury, such as blister formation and scarring. Failure to choose the proper wavelength will result in no visible laser-tissue interaction. It is beneficial for practitioners to have multiple wavelengths of light in their laser armamentarium to treat the spectrum of colors in modern-day professional tattoos.

An additional consideration is to utilize the largest spot size possible when treating tattoos. Because the smaller the spot size the greater the beam scatter, an increased amount of laser energy scattering at the edge of the field results in decreased depth of penetration.⁹ There is a tendency among practitioners to reduce the spot size in order to increase the fluence in non-responding tattoos, however, this results in a more superficial delivery of energy and potentially increases epidermal damage. Treatment spots are applied with approximately 10-20% overlap and fluence is chosen to minimize pinpoint bleeding. Laser treatments are ideally spaced 4 to 6 weeks apart, however, it takes approximately 3 months for the full effect of the treatment to be realized. The authors apply a cooled hydrogel dressing (2nd Skin® Moist Burn Pads) immediately following treatment. It is important to apply emollients and an occlusive dressing to the treated area until reepithelialization is complete.

Potential Adverse Effects

The most common side-effects of QS laser tattoo removal include scarring and dyspigmentation. When therapy is done properly, the estimated incidence of these effects is approximately 5%.¹⁰ Hypopigmentation is more common with the 694 nm ruby laser as it is well absorbed by melanin, but can also occur with other wavelengths.^{11,12} As well, all QS wavelengths can produce hyperpigmentation in darker skin types.^{11,12} Moreover, because epidermal melanin serves as a competing chromophore, increasing the chance of hypopigmentation or hyperpigmentation, it is imperative that patients avoid all sun exposure at the tattoo site prior to laser treatment.

The aforementioned 1928 *JAMA* review cautioned, “Bad results follow attempts at removal by professional tattooers and advertising charlatans.”²² In fact, there are recent European reports of the increasing frequency of laser tattoo removal performed by laypeople.^{13,14} Furthermore, the literature is replete with cases of scarring and disfigurement associated with the use of intense pulsed light, long-pulsed lasers, and even radiofrequency devices to remove body art.^{2,15-17} The light devices violate the principle of selective photothermolysis by delivering energy over a longer duration than necessary, exceeding the thermal relaxation time of the pigment, thereby causing excess heat conduction to the surrounding dermis and subsequent scarring.

Caution must also be undertaken when attempting to remove pink, tan, white, yellow or other light-colored tattoos with QS lasers. These colors are often utilized in cosmetic tattoos for permanent makeup. Paradoxical darkening can occur as the titanium dioxide or iron oxide pigment is reduced by the QS laser treatment.^{18,19} It is therefore prudent to perform a test spot prior to treating the entire tattoo. When paradoxical darkening occurs, clearing can at times be achieved with additional QS laser treatment.²⁰ Another option for cosmetic tattoos is to avoid QS lasers and treat primarily with fractional carbon dioxide (CO₂) or erbium:YAG (Er:YAG) devices. Arndt and colleagues remind practitioners to question patients whether the tattoo is a “double tattoo,” with one covering the original.²¹ In such cases, failure to reduce the fluence accordingly could result in hypertrophic scarring.

There are reports in the literature of successful treatment of tattoo pigment-induced local allergic reaction with QS lasers, and the authors have performed treatments after pre-medication with oral antihistamines. However, extreme prudence is recommended as there are reports of laser tattoo removal resulting in systemization of the allergic response and anaphylaxis.^{15,22} In two recently reported cases, fractional Er:YAG with or without adjunctive QS laser therapy proved successful in treating tattoo pigment-induced allergy.²³

Advances and Future Perspectives

Research is underway to improve both the techniques and devices used for laser tattoo removal. The recently presented “R20” method suggests repeating QS laser treatment four times in a single session spaced 20 minutes apart to allow whitening to fade.²⁴ The investigators found more rapid clearing with the R20 technique versus areas of the same tattoo that received a single treatment per session. Weiss et al. found that adding nonablative fractional 1550 nm laser treatment after QS laser reduced the amount of treatment-induced hypopigmentation.²⁵ The investigators also found that fractional CO₂ laser therapy immediately after QS laser treatment enhanced the rate of pigment clearance versus

QS laser alone. The theoretical mechanisms described include the fractional CO2 laser ablation of superficial tattoo pigment and the induction of an immune response that potentiates removal of the treated pigment.

Lasers in the picosecond (10^{-12}) domain are currently under development.²⁶ Theoretically, delivering a sub-nanosecond pulse could more effectively confine the energy to the tattoo particle, resulting in increased photoacoustic breakup of the target. This would allow for effective treatment utilizing lower fluences, thereby decreasing thermal energy transfer to surrounding tissues and minimizing the risk of scarring.

Conclusion

Quality-switched lasers remain the gold standard for tattoo removal, but employing the appropriate device and technique does not guarantee a successful outcome. Practitioners must educate their patients in detail regarding the process of laser tattoo removal and reasonable post-treatment expectations in order to create a therapeutic alliance. Exciting new technologies and techniques promise to augment our ability to effectively rid patients of their unwanted body art.

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The Noncompliant Patient with Acne

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ABSTRACT

Clinical studies with topical and systemic agents for acne show remarkable improvement over a 3 month period of time, with continued progress in long-term use. However, in clinical practice it is uncommon to see these favorable results. Clinical experience and recent published data suggest that compliance, perhaps better referred to as adherence, is a major obstacle in achieving these outcomes. This article will review this problem and offer a number of suggestions, including dosing considerations and the use of laser/light devices, to better treat the nonadherent patient.

Key words: acne, patient compliance, treatment adherence

It is hard to imagine why patients with acne, particularly adolescents who are concerned with their appearance, are noncompliant with effective acne treatments that can significantly improve their condition in a 3 to 4 month period of time. In fact, recent data shows that patients in nonclinical trial settings have an adherence rate of approximately 50%.¹ These findings suggest that most of our patients are not adherent. This is accurately reflected in my clinical practice where patients in clinical trials do significantly better than patients who are on routine follow-up at 3 to 4 month intervals. Furthermore, it is a mistake to assume that patients who are distraught with their disease are more compliant than those who are not.^{2,3}

Frequency of Patient–physician Contact

A recent study demonstrated that compliance is enhanced by more frequent office visits at 1 to 2-week intervals even though the effects of the topical acne treatments take 8 weeks to significantly impact the patient's acne.¹ In this investigation, parental reminders were counterproductive, implying that “nagging” elicits opposition, which in turn causes the patient to be less compliant. Therefore, we should not underestimate the effect of a positive therapeutic relationship with positive transference between the patient and health care provider. Hopefully, dermatologists will review these data and consider more frequent visits, especially during the initiation of acne treatments and utilize electronic reminders, such as tweets, to achieve better results.

Fixed-dose Topical Combinations

In this busy world, simplifying an acne program with once-a-day treatment would help with encouraging adherence.⁴ There are a number of combination products (e.g., benzoyl peroxide with clindamycin, adapalene with benzoyl peroxide, and tretinoin with clindamycin) that utilize multi-agents with complementary modes of action. The concern with the daily use of clindamycin without benzoyl peroxide (BPO) is the well-documented occurrence of bacterial resistance with clindamycin monotherapy.⁵ The advent of fixed combination preparations consisting of BPO with a topical antibiotic assures that the patient will not use clindamycin as a single agent. The combination of a topical retinoid with clindamycin is problematic for maintenance therapy where resistance will emerge without the concurrent use of BPO. Ideally in the future, we will have a topical combination product that will include BPO, clindamycin, and a retinoid. These products do simplify the treatment regimen, but the current

array of agents are relatively weak and do not well serve our patients with moderate to severe forms of acne. In these patients, adapalene 0.3% gel and tazarotene 0.1% cream are clearly more effective.⁶ Currently, we utilize these agents in the morning/evening, or with layering techniques, though I am concerned about adherence and proper use. It would be ideal to have multi-agent products with the stronger retinoids in combination with BPO or BPO/clindamycin.

Potential for Devices in Managing Nonadherence

A device administered by a provider to treat acne has a great deal of appeal. This mode of treatment would preclude the development of bacterial resistance with a mechanical, not an antibiotic, mechanism of action. This would be convenient if the therapy could be delivered intermittently with a limited number of treatments. Finally, a machine or mechanical device would almost certainly have a better record of reliability than a teenage patient. Theoretically, it would be ideal if this device produced isotretinoin-like results with permanent or long-lived effects. An intriguing study done by Dr. Rox Anderson's group at the Wellman Center for Photomedicine with aminolevulinic acid and high-dose red light demonstrated dramatic and durable improvement that appeared to be associated with sebaceous gland destruction.⁷ Unfortunately, the inflammation elicited by the first few treatments was severe, resulting in a vigorous inflammatory response that was likely mediated by the liberation and alteration of the lipids in the sebaceous glands. Others have attempted to reproduce these results by using less light and shorter incubation periods with apparent success, but without the long-lived response that was seen in the original study. Blue light alone has limited utility.⁸ It activates the porphyrins that are generated in the skin by the host bacteria, which include *Propionibacterium acnes*, resulting in a mild photodynamic response. Unfortunately, the results are generally modest and require the addition of topical and/or systemic medication to achieve a satisfactory outcome.

Intense pulse light (IPL) devices have an effect on bacterial-derived porphyrins in acne patients.⁹ There is also a thermal effect on sebaceous glands, epidermal cells in the infundibular region of the follicle, and perhaps the inflammatory cells mediating an inflammatory cascade. From a practical standpoint, the results are modest in my experience. However, when combined with a suction device that removes the material from the follicular canal and the sebaceous gland, there is a significant improvement in

efficacy. Numerous studies have documented success in this type of device alone, and our center has worked with the combination pneumatic (vacuum) and broadband light technology, i.e., Isolaze™ and the newer updated Acleara™ instruments.¹⁰ The updated version appears to be more comfortable for patients and enhances therapeutic effects. Our experiences have demonstrated that these devices significantly enhance response in the first 5-6 weeks where the topical and systemic agents have virtually no visible effect. The weekly to every-other-week visits also provide an opportunity for encouragement and positive reinforcement.

We and other investigators have studied the utility of the pulse dye laser for the treatment of acne vulgaris.^{11,12} Yellow light activates the bacterial-derived porphyrins from the skin and diminishes sebaceous gland over-activity. Unfortunately, the penetration of this wave band of light is limited to the depth of sebaceous glands. The results of well-controlled clinical studies have failed to demonstrate a convincing response.¹¹

Non-ablative 1450 nm devices have been used to treat acne with the idea that there is significant absorption by water and sebum.¹³ Formerly, some have suggested that lasers with this wavelength could destroy or alter sebaceous glands.¹³ However, the limited depth of penetration of this wavelength permits the lasers to primarily target epidermal cells in the infundibular region of the follicle. Results of clinical studies have shown an encouraging clinical response with limited duration of activity.¹⁴

Theoretically, it should be possible to target sebaceous glands by delivering energy that has specificity for lipids. Currently, there is ongoing research with a 1200 nm and 1700 nm laser.¹⁵ Unfortunately, there is also significant water absorption around these peaks, which limits the specificity of the absorption to sebaceous glands alone. However, research is ongoing with the hope that there will be devices and methods that allow for specific sebaceous gland destruction.

Gender Differences Associated with Adherence

Some have proposed that adherence or compliance has a great deal to do with the sex of an individual, suggesting that boys by nature are less likely to apply their medication. However, this view is naïve and perhaps sexist since there is absence of data that looks specifically at application adherence with topical agents in males versus females. We have recently completed a study with topical dapsone that showed significantly superior results in females over males.¹⁶ While this could be due to compliance, there is also the possibility that females respond differently than males to certain treatments. This could result from hormonal differences, subtle compositional issues with sebum, or other yet to be discovered findings.

Other effective acne therapies are only appropriate for females. Certain oral contraceptives are FDA approved for the treatment of acne vulgaris in women. It might be wise to use these agents on those patients who are considering a form of birth control when treating their acne. In fact, it might be more tolerable and acceptable to consider systemic therapy with an oral contraceptive than with an oral antibiotic in young females with acne.

Patient-specific Dosing Considerations

Understanding the daily activities that an individual usually performs and tying acne treatment to them often ensures better

compliance, e.g., applying a topical medication in the period after a daily wash is often convenient. Alternatively, some patients do not wash regularly, but most individuals brush their teeth 1-2 times a day. Attaching the acne treatment to this type of activity often reminds patients to perform their therapeutic regimen. Finally, using topical products with emollients might be difficult for patients who apply makeup after their morning wash.

Conclusion

The noncompliant acne patient is in fact the most common patient in our practices. A strong and positive therapeutic relationship with our patients is extremely important in achieving adequate adherence to a specific treatment protocol. Even though it takes 8-12 weeks to see significant improvement in most acne regimens, an initial 3-5 week visit often can provide an opportunity to encourage our patients and reinforce the importance of the therapeutic agents and their proper use. Alternatively, a device treatment performed weekly to every other week during the first 5-6 weeks can result in more rapid results and positive reinforcement, which will lead to better efficacy. The supportive role of the physician and other providers is critical in achieving success with the noncompliant patient.

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Name/Company	Approval Dates/Comments
Belimumab <i>Benlysta</i> TM Human Genome Sciences GlaxoSmithKline	Health Canada approved this new first-in-class human monoclonal antibody in August 2011 for the treatment of systemic lupus erythematosus (SLE). Treatment is indicated for adult patients with active, autoantibody-positive SLE who are receiving standard therapy. The drug inhibits the biological activity of the B-lymphocyte protein (BLYS). Elevated levels of BLYS are associated with autoimmune disorders and are believed to contribute to the production of autoantibodies that attack and destroy the body's own healthy tissues. US FDA approval was granted in March 2011.
Generic and OTC Drugs	
Tolnaftate 1% Cream <i>Tolnaftate-D</i> TM NexMed USA Apricus Biosciences, Inc.	The US FDA confirmed that this over-the-counter antifungal compound is OTC monograph compliant for marketing in August 2011. This new formulation of tolnaftate uses the NexACT® drug delivery technology, which enhances the absorption of medications through the skin by transiently loosening the tight junction between skin cells to improve skin permeability and increase bioavailability. Tolnaftate is used to treat jock itch, athlete's foot, and ringworm.
Hydrocortisone 1% Cream <i>Hydrocortisone-D</i> TM NexMed USA Apricus Biosciences, Inc.	The US FDA confirmed that this reformulated antipruritic compound is OTC monograph compliant for marketing in August 2011. The active ingredient, hydrocortisone, is combined with the proprietary drug technology NexACT® to improve drug permeation. Uses include the treatment of itching associated with minor skin irritations, inflammation and rashes due to eczema, insect bites, poison ivy, poison oak, and psoriasis.
Ketoconazole 2% Foam Perrigo Company	The US FDA granted approval in August 2011 to market this generic version of Stiefel's antifungal product (Extina®) containing 2% ketoconazole in a foam formulation for the topical treatment of seborrheic dermatitis in patients ≥12 years of age.

Drug News

In September 2011, the US FDA announced that the boxed warning for the entire class of tumor necrosis factor alpha (TNF-alpha) inhibitors (e.g., adalimumab, certolizumab pegol, etanercept, golimumab, and infliximab) has been updated to include the increased risk for serious, and sometimes fatal, infection from two bacterial pathogens, Legionella and Listeria. A search of the FDA's Adverse Event Reporting System (AERS) database between 1999 and 2010 found 80 patients who developed Legionella pneumonia after receiving anti-TNF therapy, including 14 deaths. In addition, the drugs have been associated with 26 cases of Listeria monocytogenes, including 7 fatalities. In many of these cases, patients were also using other immunosuppressive drugs (most commonly methotrexate and/or corticosteroids). The FDA further cautions that the risk for opportunistic infection may be higher in patients on concomitant treatment with immunosuppressive agents and in individuals >65 years of age. In 2008, the FDA mandated the strengthening of label warnings on TNF-alpha antagonists to include the increased risk for histoplasmosis and other invasive fungal infections.

More information is available at: <http://www.fda.gov/Drugs/DrugSafety/ucm270849.htm>

<http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm270977.htm>