INTRODUCTION

Tattoos have fascinated mankind from all cultures and strata of society for centuries. From the ancient Egyptian, Greek, and Roman cultures to the modern society we have today, skin markings have been used to enhance beauty, demonstrate uniqueness, signify belonging, and sometimes to identify, shame, or punish. It has been estimated that up to a quarter of young to middle-aged adults in the United States have at least one tattoo.\(^1\) Results from an online survey group, Harris Interactive, reported a rise in US adult tattoo prevalence from 16% in 2003 to 21% in 2012.\(^2\) As more tattoos are being acquired, increasing numbers of people are also seeking their removal. The American Society of Dermatologic Surgery reported carrying out 100,000 tattoo removal procedures in 2011, up from 86,000 in 2010.\(^3\) Motivation for tattoo removal includes new jobs or careers, the need to portray a certain image at work or in new social circles, and new, negative feelings towards old tattoos.\(^4\) Unfortunately, the removal of tattoos is generally more costly and time consuming than acquiring them.

TYPES OF TATTOOS

Tattoos are created by the introduction of exogenous pigment into the dermal skin layer and can be placed with intent, or be the result of accidents and trauma. Tattoos can broadly be divided into professional, amateur, cosmetic, traumatic, or medical tattoos. Professional tattoos are applied with a tattoo machine into the deeper layer of the dermis, and are applied to be permanent in nature. They generally require repeated treatments to remove.

Amateur tattoos are usually smaller, lighter in color and applied more superficially using handheld needles or homemade machines, which render them easier to remove.\(^5\) Cosmetic tattoos are often referred to as permanent makeup, and are increasingly popular. Permanent eyeliners, eyebrows, and lip liners are commonly applied using the process of micropigmentation to save time and enhance facial features. However, the inks used often contains pigments that are red, brown, white, or flesh colored; inks containing titanium dioxide and iron oxide\(^6\) are difficult to remove. Traumatic tattoos are deposited in the skin following abrasion, laceration, or explosive injuries. Such pressurized penetration of dark particles into the deep dermis gives rise to black or blue tattoos, depending on the depth of the pigment.\(^7\) Tattoos have also been used in the field of medicine, from corneal tattooing, radiotherapy field marking, to medical alert tattoos, where tattoos etched into the skin replaces medical alert jewellery for the purpose of alerting medical personnel during emergency situations.\(^8\)

TATTOO REMOVAL

Historically, the removal of undesired tattoos included destructive techniques such as dermabrasion, salabrasion, chemical destruction, cryosurgery, electrocautery, and surgical excision.\(^9\) Such non-selective destructive
modalities often result in incomplete removal, and varying degrees of scarring and dyspigmentation. Advances in laser and light-based technology have revolutionized tattoo removal, using various wavelengths to target different colored pigments with relative ease and fewer complications than before.

Quality-switched (QS) lasers have long been the traditional workhorse for the removal of tattoos. The laser treatment of tattoos is based on the concept of selective photothermolysis, where laser light of different wavelengths is preferentially absorbed by different chromophores. If the target chromophore is heated for no longer than its thermal relaxation time (time required for target to lose 50% of its heat), selective destruction of these chromophores can be achieved.[12] In the case of tattoos, the chromophore is exogenously-placed ink, which is found in membrane-bound granules in macrophages, fibroblasts, or mast cells.[13] Such tattoo pigment is very small, and can reach its thermal relaxation time very quickly. Rapid heating with very short pulse durations, in the nanosecond or picosecond range, is therefore required to cause photoacoustic injury and rupture of these pigment-containing cells. Phagocytosis is subsequently triggered and the tattoo fragments are packaged for lymphatic drainage and further scavenged by dermal macrophages, fibroblasts, and mast cells, leading to lightening of the tattoo.

**Potential complications**

In addition to establishing a realistic number of treatment sessions needed, it is important to highlight to patients the potential side effects of tattoo removal.

Patients should be counseled that tattoo clearance is often incomplete and a residual tattoo outline and textural changes may be seen [Figure 1]. An online questionnaire with 157 participants post tattoo removal showed that only 38% achieved complete tattoo removal. Local reactions following tattoo removal occurred in 97% of participants, and include blistering, edema, crusting, erythema, and pain. Permanent side effects can occur, and include scarring, hyper- or hypopigmentation [Figure 2], and color change of tattoo pigment. Patients with darker skin type are at a higher risk of complications.[13] Skin textural changes are not uncommon and follow multiple laser treatments post treatment [Figure 1].

Strict sun protection measures must be emphasized to all patients. Melanin in the epidermis can compete for the absorption of laser light intended for tattoo removal. This can cause destruction of the melanin containing cells and manifest as dyspigmentation, blistering or scarring. The use of longer wavelengths such as the QS Nd:YAG (1064 nm) in patients with a tan or patients with darker skin types can reduce such

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**Table 1: Kirby Desai scale for estimating number of treatment sessions needed for tattoo removal**

| Phototype | Location                | Color                                      | Ink amount        | Scarring        | Layering      |
|-----------|-------------------------|--------------------------------------------|-------------------|----------------|--------------|
| I-1 point | Head and neck-1 points  | Black only-1 point                          | Amateur-1 point   | No scar-0 points | None-0 points |
| II-2 points | Upper trunk-2 points   | Mostly black with some red-2 points        | Minimal-2 points  | Minimal-1 point  | Layering-2 points |
| III-3 points | Lower trunk-3 points | Mostly black and red with some other colors-3 points | Moderate-3 points | Moderate-3 points |              |
| IV-4 points | Proximal extremity-4 points | Multiple colors-4 points                  | Significant-4 points |              |              |
| V-5 points | Distal extremity-5 points |                                          | Significant-5 points |              |              |
| VI-6 points |                          |                                          |                   |                |              |

*The points for each column can be added up for individual tattoos to arrive at the estimated number of treatment sessions needed for laser removal, plus or minus 2.5.
absorption by epidermal melanin and reduce the risk of complications.

**Patient preparation**
The area to be treated should be cleansed thoroughly and free from any residual cosmetics or skin care products. Avoid using potentially flammable cleansing agents such as isopropyl alcohol. As removal of tattoos can be painful for the patient, topical anesthetics such as 5% lidocaine cream (LMX-5) and 2.5% lidocaine/2.5% prilocaine (EMLA) are often applied under occlusion for 45-60 minutes. The anesthetic should be completely removed prior to treatment. Other methods of reducing discomfort for the patient include the use of cool air during treatment, local infiltration of lidocaine, regional nerve block, or a combination of these modalities.

All medical personnel must wear wavelength-specific protective goggles during the laser procedure. The patient must also be provided with protective goggles or external metal eyeshields. If the area treated is on the eyelid or near the orbit, intraocular metal eyeshields should be placed for the patient.

In darkly pigmented patients, test spots can be carried out and evaluated at 4-6 weeks for efficacy and side effects. Test spots should also be considered for cosmetic tattoos where paradoxical darkening is likely to be encountered.\[6\]

**Laser treatment**
The desired endpoint of QS laser treatment (Nd:YAG, alexandrite, and ruby) is immediate tissue whitening, although this may not occur if the tattoo has faded significantly. Such whitening can last approximately 20 minutes, and is a result of rapid heating of the chromophore leading to gas formation.\[16\] 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. A low starting fluence should be used to attain this desired endpoint during initial tattoo treatment especially when the tattoo pigment density is very dark [Figure 3]. The fluence can be increased as the tattoo becomes lighter. Different wavelengths of laser can be used, depending on the tattoo color treated, previous response to laser treatment, and also skin phototype of the patient. Laser spots (3-4 mm spot sizes are used usually) are applied with approximately 10-20% overlap, aiming for immediate whitening, and minimizing pinpoint bleeding. Laser treatments can be repeated approximately every 8 weeks.

Generally, black and dark blue pigment respond best to Nd:YAG and alexandrite lasers. QS ruby laser tends to be associated with hypopigmentation in dark skin individuals. Colored pigments are generally less responsive to treatment Figure 4. Green pigment may respond to the alexandrite lasers but is recalcitrant to Nd:YAG lasers [Figure 5].

**Post-treatment concerns**
Patients should be appropriately advised to look after the treated area post-tattoo removal. Immediately after treatment, patients should expect the treated area to become red and swollen. Cold compresses can be used to minimise any discomfort. Antibiotic ointment or simple ointment-based emollients can be applied for 10-14 days after. Patients should be counseled that blisters and crusting might occur. If large blisters occur, these can be pricked with a sterile needle and dressed. Possible longer-term adverse effects such as scarring, hyper- or hypopigmentation [Figure 3], and color change of tattoo pigment should also be discussed with patients.
Types of lasers
The QS ruby laser (694 nm) was the first commercially available QS laser for tattoo removal in 1983,[17] followed by the QS Nd:YAG laser (532 nm, 1064 nm) and the QS alexandrite laser (755 nm). These are all still used today in dermatology practices. The tattoo color and patient skin type should be taken into consideration when choosing the appropriate laser for tattoo removal. A summary of the different lasers used for treating different tattoo colors are shown in Table 2.

Blue or black tattoos
Darker pigmented black or blue tattoos can be effectively treated by QS ruby, QS Nd:YAG (1064 nm) [Figure 1] or QS alexandrite laser.[18,19] Leuenberger et al. compared the three different lasers and found that QS ruby laser showed more significant tattoo clearing after 4-6 treatments compared to the QS Nd:YAG and QS alexandrite lasers. The authors attributed it to the use of a larger spot size in the QS ruby laser, which would afford greater depth of thermal injury to the targeted chromophore. The smaller spot sizes used in the QS Nd:YAG and QS alexandrite lasers may have led to more scatter and more rapid decrease in fluence, and, hence, less effectiveness.

Treatment with QS ruby laser however resulted in the highest incidence of hypopigmentation (38% for ruby, 0% for Nd:YAG and 2% for alexandrite respectively). This is due to increased absorption by epidermal melanin at this shorter wavelength, and their resultant destruction. Treatment with the longer 1064 nm wavelength results in minimal absorption by epidermal melanin and allows light to penetrate greater than 2mm in the skin, making it ideal for the treatment of dermal chromophores such as tattoo pigments.[16] In darker skin types where there is heavy epidermal melanin content, QS Nd:YAG laser is the laser of choice to reduce the risks of post-inflammatory hyper- and hypopigmentation post tattoo removal.[20]

The importance of a homogenous beam profile and large spot size in attaining better tattoo removal was further highlighted in another study by Karsai et al.[21]

Jones et al. carried out a study on eight skin type VI patients with 15 amateur tattoos treated with the 1064 nm QS Nd:YAG laser at 8 week intervals. After an average of 3-4 treatments, 8 of the 15 tattoos were rated as 75-95% cleared and 5 tattoos rated 50% cleared. Only 2 of the tattoos were associated with slight lightening of the skin. None of the other tattoos had any pigmentary or textural changes.[22]

Figure 3: Black amateur tattoo on nape of neck before and after 2 treatments with 1064 nm QS Nd:YAG laser (Photographs courtesy of National Skin Centre, Singapore)

Figure 4: Difficult to treat multi-colored tattoo on the back, before and after 4 treatments with 755 nm QS Alexandrite laser (Photographs courtesy of National Skin Centre, Singapore)

Figure 5: Show multicolored tattoo partially removed with the QS Nd:YAG laser. Note persistence of green pigment which are generally unresponsive to Nd:YAG laser. (Photograph courtesy of National Skin Centre, Singapore)

| Table 2: Tattoo pigment response to different laser wavelengths (tick indicate positive response) |
|---------------------------------------------------------------|
| QS Laser | Black | Blue | Green | Red | Orange | Purple |
|-----------|-------|------|-------|-----|--------|--------|
| Ruby 694 nm | ✓     | ✓    | ✓     |     |        | ✓      |
| Alexandrite 755 nm | ✓     | ✓    | ✓     |     |        |        |
| Nd:YAG 1064 nm | ✓     | ✓    |       | ✓   |        |        |
| Nd:YAG 532 nm | ✓     | ✓    |       |     |        |        |

Lapidoth et al. treated 404 Ethiopian patients (skin types V and VI) with blue/black tattoos with the 1064 nm QS Nd:YAG (380 patients) or QS ruby laser (24 patients), and reported a clearance of 75-100% in 92% of patients after 3-6 laser treatments (average 3.6) at intervals of at
Least 8 weeks. Most of these tattoos were carbon-based and located on the face or neck. Mild hyperpigmentation [Figure 1] lasting 2-4 months was noted in 44% of patients, and mild textural changes in 2 patients. There were no cases of scarring or permanent pigmented changes.[23]

QS alexandrite laser has also been found to be safe and effective for tattoo removal in darker skin types. Burkhari et al. treated 20 Arabic women with skin type III-IV and achieved more than 95% lightening in 5 patients, and more than 75% lightening in 10 patients. These patients were given 3-6 treatments at 6-12 week intervals. Pinpoint bleeding was observed in one case but no pigmented alteration or scarring was seen.[24]

**Red tattoos**
The light emitted from the 1064nm QS Nd:YAG laser may be doubled in frequency to produce light with a wavelength of 532 nm. Red, orange, and red-brown pigments respond well to this wavelength.[19,20] Studies comparing the QS 532 nm Nd:YAG have also found it to be superior to the QS ruby and QS 1064 nm Nd:YAG in the removal of red colors in professional tattoos.[21,22]

**Green tattoos**
Both the QS alexandrite and QS ruby laser are effective for the treatment of green tattoos, although the QS alexandrite laser is considered the modality of choice.[19,21] QS alexandrite can therefore be used effectively for the treatment of black, blue or green tattoos [Figure 2]. In addition to black, blue, and green tattoos, QS Ruby also works well for purple and violet pigments.[19]

**Light colored tattoos**
Cosmetic tattoos or pale-colored tattoos can be more difficult to treat as they often contain red, brown, flesh-colored, and white inks containing iron oxides and titanium dioxide, which may irreversibly turn black after QS laser irradiation.[29] Chemical reduction of ferric to ferrous oxide is thought to be responsible for such phenomenon. Such paradoxical darkening has been successfully treated with further QS laser treatments, sometimes requiring up to 20 sessions.[29,30] Ablative laser resurfacing with pulsed CO2 and erbium-doped YAG lasers have also been successfully used in cosmetic tattoos.[31,32]

**NEW STRATEGIES IN TATTOO REMOVAL**

**Combination laser treatment**
Non-ablative or ablative fractional resurfacing has been reported to be effective for tattoo removal, either when combined with QS ruby laser treatment or as monotherapy.[33,34] It appears to enhance pigment clearance, prevent blistering, shorten recovery and diminish treatment-induced hypopigmentation.[33] It has also been reported to be effective for the treatment of traumatic, allergic, and multicolored tattoos.[35,36] Animal models with cosmetic tattoos treated with non-ablative and ablative fractional lasers have demonstrated tattoo pigments in the microscopic coagulation zones migrating to the epidermis and becoming part of the microscopic exudative necrotic debris that can be exfoliated after 5 days.[36,37] Such fractional resurfacing can be combined with the traditional QS lasers for a synergistic effect.

**Multi-pass treatments**
The use of multi-pass treatments to reduce the number of treatment sessions has been explored. Kossida et al. first described the R20 method of tattoo removal, where accelerated lightening can be achieved by using four laser passes in one treatment session, with an interval of 20 min between the passes.[38] The 20 minutes waiting time allows for the post-laser immediate whitening to resolve completely before a second pass is given. The authors hypothesize that such repeated passes allow for treatment of pigment in successively deeper layers of the dermis. One patient developed transient hypopigmentation. Reddy et al. then demonstrated that application of topical perfluorodecalin prior to QS laser treatment allows for immediate treatment of the tattoo with repeated passes, thereby improving results while decreasing overall treatment time (R0 method).[39] Topical perfluorodecalin is a highly gas soluble liquid fluorocarbon that can resolve the whitening reaction within seconds. These studies reported superior tattoo clearance with both the R20 and R0 methods, compared to traditional single pass laser treatment.

**Picosecond lasers**
Picosecond lasers, with pulse duration of 10^-12 seconds, are the newest lasers promising fast and efficacious tattoo removal. Ross et al. first compared the use of nanosecond and picosecond lasers for the treatment of black tattoos in human patients, all other parameters being equal, and reported tattoo removal to be more effective with the picosecond pulse duration. As the common tattoo pigment is around 40nm in diameter, with thermal relaxation times of around 1 ns, the shorter picosecond pulse duration can better target the tattoo pigment with increased photomechanical breakup of the pigment.[40] These findings were further supported by Izikson et al., who also found the picosecond laser was able to deliver better results than the QS alexandrite laser during tattoo removal in a pig study.[41] The first commercially available picosecond laser was launched in 2013 and recently published studies have confirmed its efficacy. Saedi et al. reported 12 patients with darkly pigmented tattoos who completed treatment with the 755 nm picosecond alexandrite laser obtaining greater than 75% clearance. 9 of the patients obtained
75% clearance after just 2 to 4 treatments.[42] Brauer et al. also reported rapid and successful treatment with the picosecond alexandrite laser for multicolored or recalcitrant tattoos. 75% clearance of 12 blue or green tattoos was obtained after 1 or 2 treatments, with more than two thirds of these tattoos approaching 100% clearance.[43]

A recently presented, but unpublished, study by Tanghetti demonstrated significant tattoo clearing in 17 patients using the picosecond 755 nm alexandrite laser at fluences in the 1.3-2.0 J/cm² range. Gradual dose escalation of fluence based on previous responses, skin type, tanning, and melanin index increased safety by minimizing downtime and blistering. They noted that blue and green inks are often eliminated in one treatment.[44] Kilmer and Custis treated 26 tattoos with a picosecond laser, treating each half with R20 or single pass treatment. After one session, the multi-pass R20 method showed a 3.4 fold improvement from baseline, compared to 2.1 fold improvement with the single pass treatment. They concluded that the R20 method may further improve the efficacy of the new picosecond laser technology.[45]

**Microencapsulated tattoo ink**

Kitzman previously presented his unpublished data on microencapsulated tattoo ink. Such designer inks are made by microencapsulation of water soluble dye in polymethylmethacrylate beads. Removal can then be accomplished by targeting the encapsulating shell instead of more extensive disruption of the entire pigment particle. Preclinical studies in hairless rats and guinea pigs showed significantly increased ease of removal. One laser treatment effectively removed 80% of tattoo intensity, while only 20% of conventional ink was removed in a single identical laser treatment.[46] Further studies are needed to establish the safety and efficacy of such microencapsulated tattoo inks in human clinical studies.

**SUMMARY**

As the trend for tattoo acquisition increases, the demand for tattoo removal will similarly rise. The QS ruby, alexandrite and Nd:YAG lasers are established technologies against blue, black, red and green tattoos, with varying degrees of effectiveness. Other colors can be challenging to treat, although outcomes using fractional resurfacing and picosecond lasers are promising. Multi-pass treatments and picosecond technology are new strategies for faster and more effective removal of tattoo pigments. Better regulation of tattoo inks and pigments can help ensure safe application and ease of removal, but it is currently lacking.

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