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2018 update on dermatologic laser therapy: Part 1 – epilation, vascular lesions and pigments

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Summary

Technical advances in recent years have led to new dermatologic laser systems, light sources, and treatment concepts. Commonly used wavelengths – generated today with LED-based devices – allow for the combination of various tissue effects and are associated with improved outcomes. Laser hair removal has become more efficient with the use of diode lasers that emit multiple wavelengths simultaneously. In the near future, novel LED-based lasers will also be introduced for the treatment of vascular lesions. Here, too, the combination of different wavelengths promises to be beneficial. Picosecond lasers have led to advances in the field of pigment removal (tattoos).

Introduction

Technical innovations have facilitated the development of new laser systems, light sources, and treatment concepts. While novel usable wavelengths have hardly played any role in these advances, it is largely potent laser diodes able to emit established wavelengths with sufficient power that have come to the fore. More powerful laser diodes enable more compact designs of laser devices, new types of laser heads, and – likely – a lower rate of malfunction. Moreover, laser diodes may be combined to generate systems that allow for simultaneous application of multiple wavelengths. Next-generation lasers for hair removal already take advantage of this concept by combining the benefits of all wavelengths relevant for this indication. The same treatment approach is conceivable for vascular lasers. Such a system might combine the positive effects of a blue argon wavelength, a "green" 532 nm system, and of a yellow wavelength commonly used in dye lasers. However, such devices are still a long way off, given that laser diodes still have technical limitations with respect to power and short pulse durations (single-digit millisecond range). Short pulse durations are particularly important when dealing with small pigments such as those found in tattoos. Although ideal for this indication, picosecond lasers have not gained general acceptance, mainly because they offer only marginal benefits but are associated with high costs.

Epilation

The demand for hair removal treatments has been increasing worldwide. Patients frequently request the removal of nearly all visible hairs, except for scalp hair [1]. Technical progress has been made especially with respect to laser diodes as they have allowed for traditional flashlamp-pumped epilation lasers to be replaced. Showing fully comparable effectiveness, alexandrite lasers were the first to achieve this goal [2]. In addition, the 1,064 nm laser has become available in the form of a diode laser; thus, every wavelength relevant for hair removal can now be generated by diodes (Figure 1). What is more, devices that contain a combination of laser diodes with different wavelengths now make it possible to simultaneously apply multiple wavelengths. This concept is currently being used in next-generation hair removal lasers. There have also been advances in the field of high-energy flashlamps and home devices. The multitude of devices and applications available is not only beneficial as it will become more challenging to stay current and knowledgeable on all new developments [3]. This is particularly important with respect to the high complication rate associated with laser epilation [4–7]. In this context, it is essential to ask patients about any medication they may be taking in order to avoid known photochemical interactions. Any adverse effect and other complications require proper management [8]. Given

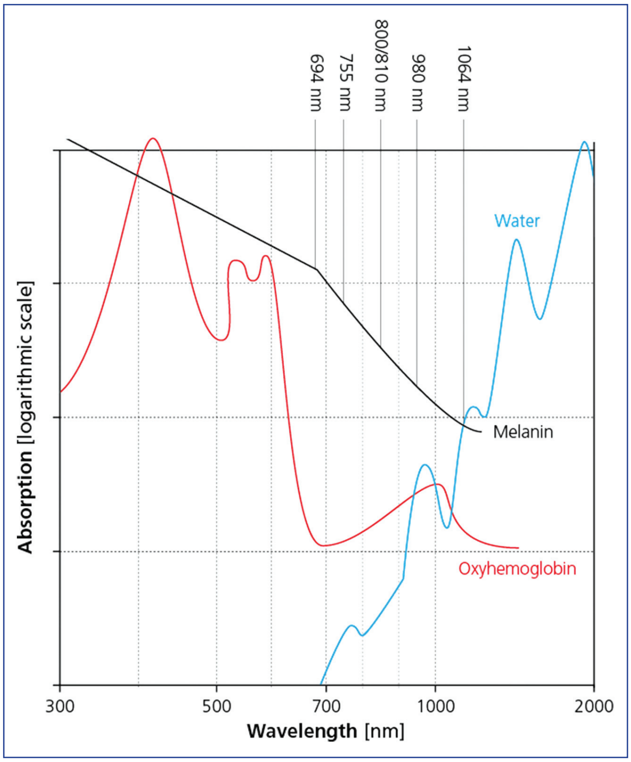

Figure 1 Melanin absorption curve and corresponding wavelengths frequently used for laser hair removal.

the numerous known and sometimes common side effects, it is recommended to use checklists [9] to prevent complications and, in particular, any interactions with the patient's current medication. In addition, specific cofactors that might increase this risk should be known and observed [8].

Conceptually, two options have proven useful: singular high-energy pulses or repetitive low energy pulses. The latter has been implemented both in the form of linear-scanning devices as well as movable laser heads (Super Hair Removal, SHR). Repetitive treatment of the hair-bearing skin using low fluence (dynamic mode) enables continuous heating of the hair down to the root and is similarly effective as the traditional static mode [10]. Undesired heating of adjacent tissue is the most common cause of adverse effects and complications. Such heat-related effects are prevented by allowing the epidermis to cool down in between laser pulses (stacks). Given that the overall amount of energy per pulse is much lower, epidermal cooling may ideally not be required and the pain associated with the procedure is dramatically reduced [1]. In routine practice, however, it is still recommended to provide sustained epidermal cooling. The 810 nm diode laser has been shown to result in hair reduction of 90.2 % up to six months post treatment [11].

The concept of simultaneous application of 755 nm, 810 nm, and 1,064 nm wavelengths for laser hair removal in the *SHR mode* is based on the assumption that such a combination will combine the benefits of high melanin absorption (755 nm), deeper penetration and lower risk for darker skin types (810 nm, 1,064 nm), and greater thermal effects (1,064 nm) to lead to improved hair removal results. While this combination has been shown to be practicable and safe, comparative studies on its efficacy are still lacking. It has also been demonstrated (in a prototype) that movement of the laser head, which is essential to the SHR technique, can be carried out by a robot. In theory, it is expected that this is associated with more homogenous distribution of laser energy and – consequently – improved outcomes. What is more, it is conceivable to equip the device with modern optical sensors to prevent unwanted irradiation of melanocytic skin lesions.

By contrast, the classic long-pulsed 1,064 nm laser is recommended for the treatment of hidradenitis suppurativa [12]. As regards axillary hair removal, it may be important to know that simultaneous treatment of hyperhidrosis (if present) with botulinum toxin is not negatively affected [1, 13]. If it is intended to employ a combination of eflornithine and laser hair removal, the former should be used after laser therapy [14, 15].

The number and acceptance of home devices available has increased in recent years. They have proven to be an effective alternative when used on a regular basis [16]. As the fluence emitted by home devices is significantly lower to prevent risks and adverse effects, the therapeutic effects are more transient and less effective, at least initially. Regular (weekly) use if therefore required [1]. One – potentially major – risk that has emerged is the fact that self-treatment by patients may be associated with chronic exposure to laser radiation of pigmented skin lesions that should not be treated with lasers [17]. From a dermatological perspective, this development continues to give rise to concern [1]. Other, albeit clinically less common risks include the release of gaseous and particulate matter [18] as well as the induction of Fox-Fordyce disease [19].

Vascular lesions

Although there are today laser diodes for numerous wavelengths suitable for the removal of vascular lesions (Figure 2), only relatively few new developments have gained acceptance in the field of vascular diode lasers in recent years. As optical coherence tomography (OCT) and confocal microscopy (reflectance confocal microscopy, RCM) allow for excellent visualization of cutaneous vessels, they have been increasingly used in laser dermatology.

Established and commonly used lasers for the treatment of superficial telangiectasia, hemangioma, and other vascular lesions are the 488/514 nm argon (cw, pulsed), the 755 nm alexandrite (pulsed), the 1,064 nm Nd:YAG (pulsed), the

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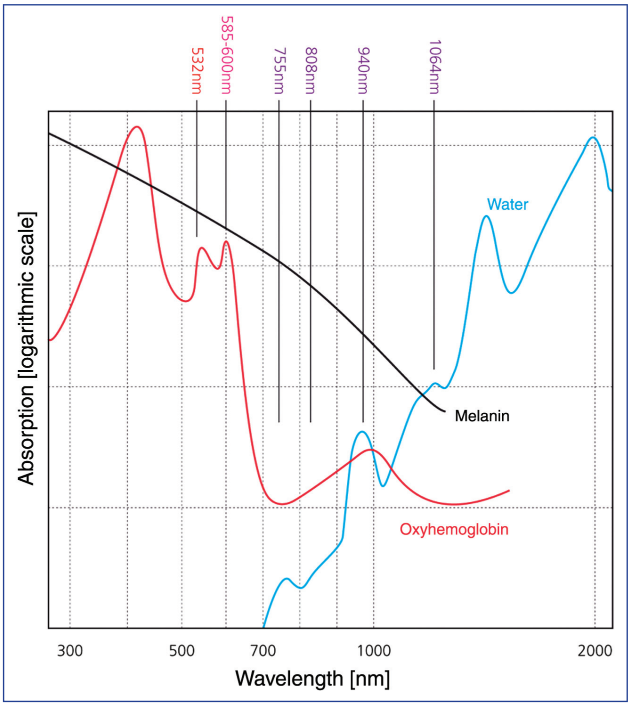

Figure 2 Oxyhemoglobin absorption curve and corresponding wavelengths frequently used for the treatment of vascular lesions [37].

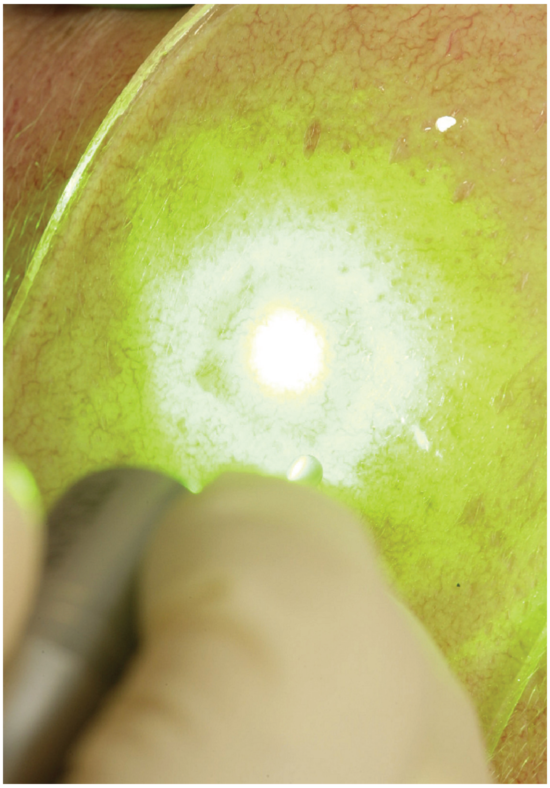

Figure 3 Typical green light emitted by a 532 nm KTP or LBO laser [37].

585/595/600 nm dye (pulsed), and the 532 nm potassium titanyl phosphate (KTP) or lithium borate (LBO) (cw, pulsed) lasers [1].

As argon lasers emit wavelengths of 488 nm and 514 nm (blue-green), they are associated with very good oxyhemoglobin absorption. Scar formation and persistent post-treatment hyperpigmentation are common. Against this background and due to the increasing shortage of spare parts, the era of argon lasers is drawing to an end. Superior successors are based on KTP or LBO crystals and exclusively emit wavelengths of 532 nm (green light) (Figure 3) in the low-energy range [1]. Both systems employ the concept of frequency doubling (or wavelength halving), thus converting invisible wavelengths of 1,064 nm into 532 nm wavelengths, which are readily perceived as green light (Figure 3). The required KTP and LBO crystals can be designed as discs and incorporated into very thin fibers. Given that the energy emitted by LBO lasers is higher than that emitted by KTP lasers [1], the former can be effectively used to treat even small hemangiomas (Figure 4). Apart from the usual measures aimed at cooling the skin, hydrogel cooling pads can even be applied during treatment to minimize potential side effects [20].

More recently, laser diodes emitting wavelengths in the blue light spectrum of argon lasers have garnered attention. However, it remains to be seen whether they will attract widespread use. Another newly available diode laser emits yellow light (577 nm). The aforementioned possibility of easily combining different wavelengths may also lead to progress in the field of diode-based vascular lasers. Conceivable options include systems that use optical methods to determine the location, density, and size of vessels as well as blood flow and hemoglobin content, and that automatically select the most effective combination from a spectrum of wavelengths (405 nm, 532 nm, 577 nm, 810 nm, 940 nm, 1064 nm etc.). In principle, scanners (linear-scanning, galvanometer scanner) can be used for this purpose. Such an approach would also facilitate treatment of larger areas and – possibly – improve treatment of small vessels. The latter have traditionally posed a therapeutic challenge as the long-pulsed alexandrite laser (755 nm, up to 20 ms), diode lasers with various wavelengths (755 nm, 800 nm, 810 nm, 930 nm, 10–250 ms), and the Nd:YAG laser (1064 nm, pulse duration up to 100 ms) have been shown to be insufficiently effective.

Recalcitrant, dark, and hypertrophic/tuberous areas of port-wine stains respond well to treatment with the long-pulsed Nd:YAG laser due to its greater hemoglobin absorption and deeper penetration with larger spot sizes. While this is an option if there is no more clinical improvement using the pulsed dye laser, long-pulsed Nd:YAG lasers are associated with an increased risk of scarring (Figure 5). Another beneficial aspect of the latter laser type is its suitability in the treatment

Figure 4 Hemangioma before and immediatly after 532 nm laser treatment (27 J/cm², 29 ms, 1 mm spot, 5 pulses) .

of darker skin, although the therapeutic range is very narrow. Using sufficiently long pulse durations, this system may also be used to treat large hemangiomas (Figure 6) and larger leg veins [1].

Another established concept includes the sequential use of different wavelengths. It has been shown that port-wine stains and telangiectasias can be successfully treated with a combination of 595 nm and 1,064 nm wavelengths. Treatment of port-wine stains with a special laser device that emits two pulses (at 595 nm and 1,064 nm) at an interval of 500–1,000 ms resulted in a clinical response of 25–50 % in almost half of the cases [1].

Pigment removal

In recent years, no new wavelengths have become available for the removal of pigment from the skin. As regards endogenous and exogenous pigment removal, the introduction of picosecond lasers has given rise to new approaches. Currently, these lasers use pulse durations of several hundred picoseconds (ps) and should therefore rather be referred to as sub-nanosecond lasers [21]. Although technically advanced

Figure 5 Pulsed dye lasers emit wavelengths of 585–600 nm, corresponding to yellow light [37].

and marketed for several years, these systems have not gained widespread acceptance due to identical efficacy profiles and very high costs. Given the shorter pulse duration, it has been postulated that the primary mechanism of action is based on further reduction of thermal effects in favor of a greater photomechanical effect [22]. What is more, these systems have become increasingly powerful (gigawatt range). On the electron microscopic level, these devices have been shown to actually "break down" tattoo dye particles, whereas treatment with traditional Q-switched pigment lasers (with pulse durations in the nanosecond range) tends to result in vacuolization of the pigment-containing tissue (Figure 7). On light microscopy, intraepidermal necrotic areas are found that are reminiscent of MEND (microscopic epidermal/exudative necrotic debris) associated with fractional lasers. The underlying mechanism is referred to as *laser-induced optical breakdown* (LIOB). Given this effect and the lower risk of postinflammatory hyperpigmentation even in darker-skinned individuals, it was a logical step to expand the indication to include treatment of endogenous pigments [23]. Using novel optics, current approaches are aimed at using picosecond lasers for the treatment of wrinkles and scars.

When 755 nm picosecond lasers were first introduced, it became apparent that they were more effective (than previous lasers) at removing certain blue dyes [24]. This was followed

Figure 6 Large-vessel hemangioma before and immediatly after treatment using 1,064 nm, 90 ms, 200 J/cm², 8 pulses, contact cooling.

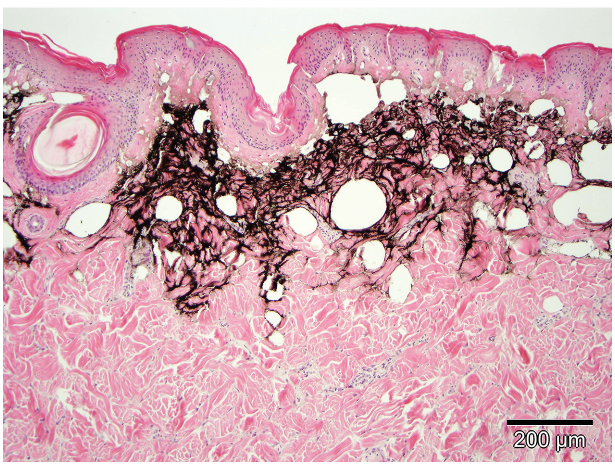

Figure 7 Tattooed skin explant treated with a 1,064 nm Nd:YAG qs laser (8.2 Jcm², 8 mm spot, hematoxylin-eosin stain).

relatively soon by picosecond lasers emitting wavelengths of 532 nm [25], 758 nm, 795 nm, or 1,064 nm (or a combination thereof), which were supposed to address a broader spectrum of tattoo dyes. However, it is important to note that the wavelengths available do not match the absorption spectra of common tattoo dyes [21] and that, despite all modifications, the side effect spectrum is largely identical to that of traditional Q-switched nanosecond lasers [26]. With some restrictions, both system classes can also be used for tattoo removal in dark-skinned individuals [27, 28].

Although data on laser treatment of tattoos is sketchy, it is safe to assume a clearance rate of 70–100 % after 7–10 sessions. The only well-controlled study available on this topic concluded that picosecond lasers were not superior to common nanosecond lasers, neither for untreated nor for pretreated tattoos [29].

In summary, current data suggests that the introduction of picosecond lasers in the treatment of tattoos has not resulted in major progress compared to nanosecond lasers, although fewer sessions are likely required [30]. A novel system has recently become available that is able to use pulse durations in both the nanosecond and picosecond range. Such a device could be used to precisely explore the potential clinical benefits of shorter pulses.

At the same time, attempts have been made in the field of traditional Q-switched nanosecond lasers to achieve faster results by applying repeat treatments at short intervals (four laser treatments every 20 minutes); treatment success was not consistently reproducible [31]. Another option is the application of transparent perfluorodecalin-containing silicone gels (PFD patches). These patches are supposed to reduce the typical formation of intraepidermal gas blisters and might increase the tolerability of the aforementioned treatment with multiple laser passes at short intervals. However, no conclusive study data is currently available. For the sake of completeness, general risk assessment of tattoo removal should also include the potential formation of highly toxic byproducts [32], even though no clinical effects have been reported to date. In one case, the patient experienced an anaphylactic reaction after tattoo removal [33].

In Asian patients, fractional Q-switched lasers have been shown to be more effective in the treatment of melasma [34]. In this context, it is important to use gentle laser settings: lowest fluence possible and a relatively low density of individual spots; in addition, expectations have to be realistic. When observing these precautions, melasma as well as dyspigmentation associated with classic CO_2 resurfacing can be successfully treated.

Numerous studies have shown that fractional ablative CO_2 laser resurfacing for wrinkle treatment will also result in a reduction of pigment irregularities and resolution of solar lentigines. Dyspigmented scars, too, respond well to this form of treatment. If larger amounts of particles – as observed, for example, in traumatic tattoos – require removal, fractional ablative CO_2 laser treatment can be used in combination with Q-switched lasers [35]. It remains to be seen whether the therapeutic effects achieved with fractional lasers are indeed better than those currently obtained with Q-switched systems. Irrespectively, fractional CO_2 lasers, too, should not be used to treat melanocytic lesions [1].

Fractional lasers

Apart from the treatment of dyspigmentation, non-ablative and ablative fractional lasers have become established modalities for a host of dermatologic indications. Special wound repair mechanisms (mediated by heat shock proteins) facilitate skin remodeling and eventually lead to healthy skin with normal epidermis, connective tissue, vessels, nerves, and pigments. Recent experiments suggest that heat shock proteins (HSP70) also induce immunological homeostasis by activating regulatory T cells. This finding will likely lead to interesting developments in the fields of allergic disorders, vaccinations, and chronic inflammatory dermatoses. Initial results obtained from vulvovaginal application of these lasers confirm that such treatment may be able to modulate chronic skin inflammation.

The concept of early intervention with non-ablative fractional lasers throughout all phases of wound healing is based on these mechanisms and is supposed to induce physiological wound closure and scar formation. The results of studies currently being conducted will show to which extent 'early intervention' may contribute to preventing or even healing pathologic scars.

There has been an increase in the number of important indications for ablative laser treatment. Apart from their use in aesthetic dermatology to repair scars and contractures, there have been dynamic developments in the field of laser-assisted drug delivery (LADD). Given the importance and scope of these novel applications of ablative fractional lasers, these topics will be discussed in part 2 of the 2018 laser update.

Onychomycosis

As the initial euphoria regarding the potential for pathogen eradication by contact-free laser treatment has dissipated, there is currently no news to be reported on. Given the data published, it has turned out that laser therapy is not superior to other options already available [36]. Furthermore, the criteria issued by the Food and Drug Administration (FDA) have completely changed, now calling for nail growth of at least 12 mm per year. From our own experience, heat-based systems along with medical pedicure (debulking of nails [urea paste 40 % NRF 11.30, milling] as well as peeling, abrasion, and topical treatment in the palmoplantar region) are quite effective in individuals who do not tolerate systemic treatment. There has been a steady uptick in the number of these patients, given the increased life expectancy as well as morbidity and polypharmacy associated therewith. Apart from the pure heat effect of the devices most commonly used, changes in nail composition may be responsible for the therapeutic effect by depriving the pathogen of its nutrient supply and thus the prerequisite for its proliferation. Clearance of up to 80 % of the nail plate is realistic after 4–6 combination treatments over a period of 9–12 months. Without any further treatment, there will be a visible increase in the area of the nail plate affected. As nearly all wavelengths used by hair removal lasers have been successfully employed in the treatment of onychomycosis, it remains to be seen whether the new multi-wavelength devices mentioned above will provide any benefits in this indication, too. In theory, one might expect beneficial effects due to the different depths of penetration into the nail plate. Other exciting developments might include the use of LADD in onychomycosis. Regular permeation of the nail plates every four weeks improves the efficacy of water-based topical agents to such an extent that – at least in isolated cases – normal nail growth may be possible in previously incurable patients.

Outlook

The last five years have seen dynamic developments in the field of laser dermatology. This is reflected not least by the almost 3,500 new publications on this topic. There is a constant stream of new and more powerful laser diodes, which can be easily combined to generate multi-wavelength devices. The potential for synchronous application of multiple wavelengths has facilitated the development of new laser therapies and has already led to improvement of existing concepts. As a consequence, numerous options for further refinement of treatment protocols using other lasers, light sources, devices, and interventions have been identified.

Additional development opportunities result from new possibilities provided by optical methods such as optical coherence tomography (OCT), confocal microscopy, and multiphoton laser scanning microscopy (MSP). Combining these techniques may give rise to a truly new generation of lasers.

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