New lasers and light sources - old and new risks?

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Summary
Recent developments (new wavelengths, treatment concepts, and combinations) in the field of lasers, intense pulsed light (IPL), LED, as well as new energy and light sources have opened up new therapeutic options that extend beyond mere aesthetic indications. Thus, while fractional lasers used to be employed to merely treat wrinkles, the same devices – in the context of laser-assisted drug delivery – have now become important tools in the treatment of scars, field cancerization, and epithelial tumors. The requirements posed to physicians, both with respect to establishing the indication and conducting treatment, have been growing along with the increase in technological complexity as well as the rising number of comorbidities and comedinations in a patient population that continues to age.

At the same time, home-use devices have been introduced for a variety of indications. These devices are characterized by low power and special safety features aimed at preventing accidents, risks, and side effects. Despite the reduced efficacy of such self-treatment devices, there is an increased risk of misuse, given that the basic prerequisite for adequate treatment cannot be ensured, to wit, the exact diagnosis and therapeutic indication. Consequently, during hair removal or anti-wrinkle treatment, pigmented lesions and cutaneous neoplasms may be altered, thus giving rise to expected, unexpected and new side effects and complications.

In the aforementioned setting, it is important that all potential users of these new technologies be properly trained in a manner that ensures those treated a maximum of safety and efficacy in accordance with the guiding principle “diagnosis certa – ullae therapiae fundamentum”.

Introduction
Recent developments (new wavelengths, treatment concepts, and combinations) in the field of dermatological lasers, intense pulsed light (IPL) devices, LEDs (light-emitting diodes), and new light sources have opened up additional indications and therapeutic options for dermatologists. Remarkably, despite the growing number of comorbidities and comedinations in an aging society, there is an increased demand for aesthetic procedures. As a consequence, taking a precise patient history and conducting a thorough diagnostic workup prior to treatment becomes a sine qua non.

A new aspect is the merging of aesthetic treatment and therapeutic intention, for example, in the treatment of photoaged skin. Thus, while fractional lasers used to be employed to merely treat wrinkles and dyspigmentation, the same devices – in the context of laser-assisted drug delivery – have now become important tools in the treatment of field cancerization. Apart from the correct indication, safe and effective treatment requires comprehensive patient information with regard to benefits, risks, and limitations of the procedure to be performed, as well as adequate parameter selection and patient follow-up. Given that binding standards for laser therapy (in humans) do not exist [1], this challenge can only be met with thorough user training [2–5].
The most common source of complications are “health care providers” (that is, non-medical personnel). Approximately 30 % of complications, such as burns, scars, dyspigmentation, and infections, can be attributed to these individuals alone [6–8], whereas all other user groups are less commonly responsible for said adverse events. More than two-thirds of all complications are caused by incorrect parameter selection [7]. By contrast, trained dermatologists with years of experience can achieve a complication rate as low as 0.24% [9].

Against this backdrop, the recent introduction of home-use devices for epilation and the treatment of aging skin must be critically assessed. Based on published evidence, we will summarize classic, well-known, and thus avoidable risks and side effects. In addition, potential risks associated with the use of new therapeutic concepts, systems, lasers, as well as energy and light sources are highlighted.

**General hazards associated with lasers, intense pulsed light devices, and new light sources**

Long established in routine clinical practice, lasers, IPL and radio frequency devices generally represent safe technologies. Nevertheless, injuries to patients have been reported for all device classes (Medical Device Reports [MDR] in: Manufacturer and User Facility Device Experience [MAUDE] – FDA data on complications with lasers, light sources, and energy-based devices) [6, 10], in particular when operated by non-medical personnel [6, 8]. Of the 1,257 adverse events documented between 1991 and 2013, injuries to the eyes, which are particularly damaging, were predominantly caused by IPL devices [10].

In order to answer the question whether IPL treatment is potentially more harmful to the skin than laser treatment, various aspects have to be considered. On the one hand, various device generations are currently being used, with first-generation devices employing different technologies than subsequent systems (square pulse/free discharge). This affects the stability of the emitted pulse during the application cycle and thus has direct effects on the expected side effect profile [11–13]. First-generation IPL devices emit light in the infrared spectrum, often resulting in collateral damage to the epidermis and a high incidence of adverse effects. In second-generation IPL devices, the unwanted infrared component is filtered out by water, thus significantly reducing the risk of adverse events [14, 15]. This, however, does not apply to the off-label use of these devices. In this context, the use of IPL in the treatment of tattoos is particularly problematic and may even have legal implications.

Manufacture, handling, and maintenance of medical lasers as ‘medical devices’ are regulated by law. International standards apply with respect to their use, safety inspections (sicherheitstechnische Kontrollen, STK), documentation, and maintenance. Pursuant to STK Article 6 of the German Medical Device Operator Ordinance (Medizinprodukte-Betreiberverordnung [MPBetreibV]), test reports have to be prepared on a regular basis at 6-, 12-, or 24- month intervals, depending on manufacturer specifications. For each individual device, these checks include a visual inspection of the exterior of the device (protective ground wire, insulation, casing, connection cable, type label), a power-on check, power measurements including a reference value check, electrical measurements (protective ground wire resistance [R PG], insulation resistance [R Ins], U ins leakage current [I L], Δ I), and functional tests (U LN, Δ I, I V, LF).

Medical lasers are also subject to international standards with respect to their emitted radiation (measured in SI units) (Système international d'unités, international system of units): measured deviations must not exceed ± 20 % (measured in SI units).

For IPL devices, there are no such standards that have to be adhered to [16]. It is merely recommended that the data provided by the manufacturer be compared with own measurements of the handpiece and documented in an inspection book (FA ET 3 2009). However, such initial or even recurrent measurements are not mandatory. This is also true for measurements of the applied energy. It is, however, recommended to measure five key parameters in order to minimize risks associated with over- or undertreatment. Based on these parameters, service technicians are able to check performance and eliminate device malfunction [17].

The relevance of these checks is reflected by the fact that operator errors due to incorrect parameter selection and improper device maintenance are responsible for the majority of adverse events and complications. Apart from radio frequency devices, diode lasers, IPL devices, and – since 2003 – BBL (broadband light) devices have been the systems most commonly associated with side effects. The latter have most frequently been used for hair removal [10].

Ultimately, the technology behind IPL devices is one reason for their exceptionally high rate of side effects, given that their wavelength spectrum is not as precisely defined as is the case with lasers [18]. The required wavelengths are achieved by upstream cutoff filters and integrated water filters. Depending on the device generation, however, the patient’s skin may also be exposed to and damaged by infrared and blue light as well as UV radiation [14, 15, 17]. Consequently, a wide range of side effects may be expected, including erythema, skin aging, potential induction of neoplasms [19], phototoxic and photoallergic reactions, and many more (FA ET 3 2009).

Legal certainty had been expected from the Protection against Non-ionizing Radiation Act (Gesetz zum Schutz vor...
nichtionisierender Strahlung (NiSG]) passed in 2009. Article 3 of the NiSG regulates the protection of individuals during the use of cosmetic or other devices outside the medical field, including lasers or IPL devices. Article 5 of the NiSG specifies the scope of the regulations. Among other things, it is meant to regulate qualification certificates, threshold values, and technical inspections. Though highly relevant with respect to the legally compliant use of such devices in the cosmetic sector as well as to the health protection of users thereof, this regulation is still not available (German Parliament, docket number 18/2163).

Epilation

Epilation enjoys continued popularity. With the exception of scalp hair, the last remnants of body hair have – for millennia – been removed with increasingly sophisticated methods: plugging, shaving with sharpened stones, shells, and blades, epilation with resins, wax, as well as chemical procedures. The limited efficacy of conventional epilation techniques has boosted the demand for procedures with permanent or at least long-lasting results. Moreover, continued medical progress has brought about new (iatrogenic) indications for epilation, for example, due to adverse drug reactions or as a result of surgical interventions such as defect coverage with hair-bearing skin in the context of skin cancer treatment.

The discovery of selective photothermolysis and the application of this concept for effective and lasting photoepilation using various wavelengths have provided physicians with numerous highly effective laser and IPL systems. The wide range of devices and applications requires profound knowledge in order to provide patients with safe and effective treatment strategies as well as to identify potential drug interactions (Table 1) and reliably master special cases and complications (Table 2) [20]. This especially holds true in light of the fact that this particular procedure is the one most commonly associated with complications [6, 21–23]. Given the numerous known – and sometimes common – side effects, it is recommended to use checklists [24] (Table 3) In order to avoid complications and, in particular, interactions with comediations (Table 1). Moreover, physicians should be cognizant of and observe specific risk-increasing cofactors [20]. Although photosensitizing drugs are usually activated by UVA, it is always recommended to first treat only a small area and see how the skin reacts.

Commonly used devices include the alexandrite laser with a wavelength of 755 nm and the diode laser with a wavelength of 810 nm. The mode of action of both wavelengths has thus been comprehensively studied. Until now, these devices have

<table>
<thead>
<tr>
<th>Diuretics</th>
<th>Hydrochlorothiazide, furosemide, bendroflumethiazide, amiloride, etacrynic acid, triamterene, spironolactone, xipamide*2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonsteroidal antiinflammatory drugs</td>
<td>Naproxen, ketoprofen, tiaprofenic acid, piroxicam, diclofenac, phenylbutazone, mefenamic acid, indomethacin, ibuprofen</td>
</tr>
<tr>
<td>Antimicrobial agents</td>
<td>Sulfamethoxazole/trimethoprim, sulfasalazine, ciprofloxacin, enoxacin, lomefloxacin, ofloxacin, norfloxacin, oxytetracycline, tetracycline, doxycycline, minocycline, isoniazid, gentamycin, griseofulvin, nitrofurantoin</td>
</tr>
<tr>
<td>Antimalarial agents</td>
<td>Chloroquine, quinine, pyrimethamine, mefloquine, hydroxychloroquine</td>
</tr>
<tr>
<td>Antipsychotic drugs</td>
<td>Chlorpromazine, thioridazine, promethazine, chlorprothixene, perazine, fluphenazine, promazine, haloperidol</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>Amitriptyline, trimipramine, nortriptyline, desipramine, imipramine, doxepin, clomipramine*2</td>
</tr>
<tr>
<td>Cardiovascular agents</td>
<td>Amiodarone, nifedipine, quinidine, captopril, enalapril, fosinopril, ramipril, disopyramide, hydralazine, simvastatin</td>
</tr>
<tr>
<td>Antiepileptic drugs</td>
<td>Carbamazepine, lamotrigine, phenobarbital, phenytoin, topiramate<em>2, valproic acid</em>2</td>
</tr>
<tr>
<td>Antihistamines</td>
<td>Cyproheptadine, diphenhydramine, loratadine</td>
</tr>
<tr>
<td>Cytotoxic agents</td>
<td>Fluorouracil, vincristine, dacarbazine, procarbazine, methotrexate, azathioprine</td>
</tr>
<tr>
<td>Hormones</td>
<td>Corticosteroids, estrogens, progesterone, spironolactone</td>
</tr>
<tr>
<td>Systemic dermatological agents</td>
<td>Isotretinoin, alitretinoin, tretinoin, methoxsalen (8-methoxypsoralen)</td>
</tr>
<tr>
<td>Others</td>
<td>Gold salts, hematoporphyrin</td>
</tr>
</tbody>
</table>
been characterized by their technically limited spot size, resulting either in time-consuming treatment sessions or in the use of scanners. Drawbacks of scanners include the technical necessity for overlapping passes and their susceptibility to malfunction. The need for fast laser systems that can be used to treat large areas, in particular for hair removal, has been met with linear-scanning and continuous-wave diode lasers [20]. The latter are now also available with wavelengths of 755 nm and 1,064 nm [27]. Based on initial studies, classic alexandrite lasers and the aforementioned novel diode lasers are almost identical with regard to efficacy and side effects [25].

Treatment duration is markedly reduced and the energy to be applied is lower; in theory, the hair bulbs are thus exposed to heat both for a longer period of time and more evenly. For this purpose, a diode laser block is arranged in such a way that yields a “spot” with an approximate size of 1 mm x 10–20 mm. Using mobile mirrors, the spot can then be continuously passed across the skin within a diameter of up to 5 cm. Alternatively, a diode laser block sized > 1 cm² can be constructed, and continuously passed over large areas (super hair removal [SHR] concept). Both options result in very large treatment areas. In the case of linear-scanning systems, the movement speed can be adjusted by software. While this leads to exposure times (corresponding to conventional pulse durations) that are comparable to conventional systems, they are, however, less painful due to their successive application [20]. With respect to SHR, the operator plays a pivotal role as it behooves him to precisely define the size of the area to be treated and to ensure the homogeneous distribution of the total amount of energy applied. Too little energy results in therapeutic failure, and too much energy increases the risk of side effects and complications [27].

One problem of employing selective photothermolysis in the treatment of large areas is the accidental irradiation of pigmented lesions with the potential risk of inducing

<table>
<thead>
<tr>
<th>Item</th>
<th>Immediate reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>– Burns and curling of external hair components, burned smell, plume</td>
<td></td>
</tr>
<tr>
<td>– Diffuse erythema</td>
<td></td>
</tr>
<tr>
<td>– Perifollicular erythema</td>
<td></td>
</tr>
<tr>
<td>– Perifollicular edema/wheals</td>
<td></td>
</tr>
<tr>
<td>– Treatment-associated pain</td>
<td></td>
</tr>
<tr>
<td>– Cold urticaria</td>
<td></td>
</tr>
<tr>
<td>Delayed reactions</td>
<td></td>
</tr>
<tr>
<td>– (Diffuse) erythema</td>
<td></td>
</tr>
<tr>
<td>– Blistering/erosions</td>
<td></td>
</tr>
<tr>
<td>– Purpura</td>
<td></td>
</tr>
<tr>
<td>– Crusting</td>
<td></td>
</tr>
<tr>
<td>– Hyperpigmentation</td>
<td></td>
</tr>
<tr>
<td>– Hypopigmentation</td>
<td></td>
</tr>
<tr>
<td>– Folliculitis, acneiform reactions, exacerbation of acne, infections</td>
<td></td>
</tr>
<tr>
<td>– Scars</td>
<td></td>
</tr>
<tr>
<td>– Koebnerization, vitiligo, psoriasis, Lichen planus</td>
<td></td>
</tr>
<tr>
<td>– Changes in nevi after photoepilation</td>
<td></td>
</tr>
<tr>
<td>– Thrombophlebitis</td>
<td></td>
</tr>
<tr>
<td>– No effect, partial or complete hair regrowth</td>
<td></td>
</tr>
<tr>
<td>– Angular cheilitis</td>
<td></td>
</tr>
<tr>
<td>– Focal depigmentation of the lips</td>
<td></td>
</tr>
<tr>
<td>– Allergic reaction to cryospray</td>
<td></td>
</tr>
<tr>
<td>– Hyperhidrosis, bromhidrosis after axillary epilation</td>
<td></td>
</tr>
<tr>
<td>– Leukotrichia</td>
<td></td>
</tr>
<tr>
<td>– Paradoxical hair growth in the treated area or adjacent to it</td>
<td></td>
</tr>
<tr>
<td>– Pili bigemini</td>
<td></td>
</tr>
<tr>
<td>– Dry skin</td>
<td></td>
</tr>
<tr>
<td>– Reactivation of herpes simplex</td>
<td></td>
</tr>
<tr>
<td>– Bacterial infection</td>
<td></td>
</tr>
<tr>
<td>– Livedo reticularis</td>
<td></td>
</tr>
<tr>
<td>– Urticarial vasculitis</td>
<td></td>
</tr>
<tr>
<td>– Pruritus</td>
<td></td>
</tr>
<tr>
<td>– Excoriatiion</td>
<td></td>
</tr>
<tr>
<td>– Terminalization of hairs</td>
<td></td>
</tr>
<tr>
<td>– Induction of rosacea</td>
<td></td>
</tr>
<tr>
<td>– Textural changes</td>
<td></td>
</tr>
<tr>
<td>– Brightening of pigmented lesions</td>
<td></td>
</tr>
</tbody>
</table>
malignancies. The guidelines of the European Society for Lasers and Energy-Based Devices (ESLD; the European Guidelines for Care) recommend that the lesions be covered [27]. However, side effects cannot be ruled out, given the high energy used in linear-scanning systems and the successive, repetitive heating associated with SHR systems (unpublished data). The use of various cover materials has previously been reported in connection with conventional UV and laser light sources. Simple application of thick layers of zinc paste has been shown to be effective in the new, linear-scanning systems [18]. The use of various cover materials has previously been confirmed histologically [26]. As with all other cover concepts, this method cannot be used when employing epilation lasers that require skin contact, irrespective of whether they are scanned or used as SHR device. Finally, it should be emphasized that nonpigmented, yet palpable skin lesions also may represent benign neoplastic lesions [26]. This situation once more highlights the necessity for thorough assessment of the skin in the entire treatment area.

Another new development has been the introduction of home-use laser epilation systems [28, 29]. Given the greatly reduced fluence for safety reasons, one may assume that hair removal is rather transient and less effective. Here, a new and grave risk is the chronic application of laser radiation to pigmented skin lesions that should not be treated with lasers [30]. From a dermatological perspective, this development should therefore give rise to concern [27]. So far, published side effects correspond to those already known [31].

Photoepilation as such is prone to complications and even more so when IPL devices are used [6]. Avoiding UV exposure prior to and at least 24 hours after IPL treatment is of particular importance. Even the single application of > 3 SEDs (standard erythema dose) has been shown to cause numerous adverse effects such as erythema (87 %), purpura (27 %), blisters (20 %), edema (13 %), crusting (13 %), hyperpigmentation (60 %), and hypopigmentation (20 %) [32]. Due to phototoxic reactions and bulk heating, tattoos in the epilation area are a recurrent source of adverse events. “Treatment” of pigments using IPL devices almost always results in complications. It is therefore important to raise all relevant issues in the informed consent discussion (Table 4) and to use checklists prior to treatment initiation (Table 5).

In addition, the technical report IEC TR60825-9 illustrates the ocular risks associated with incoherent light sources. Nevertheless, when used correctly, IPL systems may be employed as reliably as diode lasers if the operator is adequately trained [33].

Table 4: Important items in the informed consent discussion prior to laser epilation.

<table>
<thead>
<tr>
<th>Item</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall complications</td>
<td>Are rare in case of adequate, skin type-adapted parameter selection.</td>
</tr>
<tr>
<td>Side effects</td>
<td>More common when treating dark-skinned individuals (Fitzpatrick IV–VI) [86].</td>
</tr>
<tr>
<td>Depending on the wavelength employed</td>
<td>The most common side effects include erythema, burns, blistering/crusting, hyperpigmentation, hyperpigmentation, and scarring [87].</td>
</tr>
</tbody>
</table>

Table 5: Checklist for laser epilation.

<table>
<thead>
<tr>
<th>Item</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classification of the abnormal hair growth (hirsutism, hypertrichosis, others)</td>
<td>The potential underlying pathomechanism that may also require treatment: endocrine, drug-induced, associated with a neoplasm or a syndrome, constitutional</td>
</tr>
<tr>
<td>Clinical/diagnostic evaluation as to whether there is a potential underlying pathomechanism</td>
<td>That may also require treatment: endocrine, drug-induced, associated with a neoplasm or a syndrome, constitutional</td>
</tr>
<tr>
<td>Are there any other known disorders or allergies?</td>
<td>The potential underlying pathomechanism that may also require treatment: endocrine, drug-induced, associated with a neoplasm or a syndrome, constitutional</td>
</tr>
<tr>
<td>Which drugs are taken or topically applied?</td>
<td>The potential underlying pathomechanism that may also require treatment: endocrine, drug-induced, associated with a neoplasm or a syndrome, constitutional</td>
</tr>
<tr>
<td>Sun tolerance?</td>
<td>The potential underlying pathomechanism that may also require treatment: endocrine, drug-induced, associated with a neoplasm or a syndrome, constitutional</td>
</tr>
<tr>
<td>Which steps have been taken to treat the abnormal hair growth?</td>
<td>The potential underlying pathomechanism that may also require treatment: endocrine, drug-induced, associated with a neoplasm or a syndrome, constitutional</td>
</tr>
<tr>
<td>Determination of contraindications/risk-increasing cofactors</td>
<td>The potential underlying pathomechanism that may also require treatment: endocrine, drug-induced, associated with a neoplasm or a syndrome, constitutional</td>
</tr>
</tbody>
</table>

Fractional photothermolysis

In light of an increased cumulative UV exposure in combination with a longer life expectancy, dermatologists are increasingly confronted with their patients’ request to treat their chronically photoaged skin, that is wrinkles, dyspigmentation, scars, and obvious as well as incipient neoplastic changes as a consequence of sun damage [34]. In this context, laser procedures are of particular importance as they have become less and less invasive due to technological advances.

In the past, good clinical effects were primarily achieved with CO₂ and Er:YAG lasers, which allow for the two-dimensional ablation of large areas of the skin. However, the excellent therapeutic effects of the CO₂ laser have to be weighed against the pronounced side effects and the long time required for healing (“down time” period during which the patient cannot participate in public life; also, time until re-epithelialization) [35].

Recent developments in the field of laser systems have allowed for continued conceptual advances [36], resulting in the development of fractional photothermolysis [37]. Here, the single laser beam is divided into numerous microscopic laser beams, comparable to water flowing from a shower head — and the skin treated layer by layer.
head [38]. Through nonspecific coagulation (without ablation), these lasers were initially used to create column-like defects in the skin, which resulted in clinical improvement of treated lesions (scars, sun-damaged skin) during the wound healing process [34].

Following several clinical studies [37, 39, 40], the principle of fractionated heat delivery into the skin (non-ablative fractional laser therapy; NAFXL) was approved by the US Food and Drug Administration (FDA) for the treatment of wrinkles, dyspigmentation, and the coagulation of connective tissue. The latest development combines the basic principles of fractional photothermolysis and classic ablative laser procedures by introducing microscopic channels into the skin (ablative fractional laser therapy; AFXL) [41]. The impact of the selected laser parameters on the ablation characteristics has been systematically evaluated in pigskin [42].

It has also been shown that these systems are effective in neoplastic skin [43] and that suitable suction devices ensure the safety of patients and physicians even when large amounts of tissue are ablated [44]. In clinical studies [45, 46], ablative fractional laser therapy, which is usually conducted using Er:YAG, Er:YSGG, and CO₂ lasers, showed comparable and promising results in the treatment of sun-damaged and thus potentially neoplastic skin as well as scars [47, 48].

Based on these findings, an in vitro explant model was established to study the individual and combined effects of various laser systems on the skin. HSP70 (heat shock protein 70) is a crucial trigger point for scar-free wound healing as well as the treatment of neoplastic skin using photodynamic therapy and ablative fractional lasers [49–56]. Subsequently, the spatiotemporal healing process was analyzed in vivo, and threshold values (spot size 250 μm, coverage < 50 %, fluence < 100 mJ for the Quantel Exel02 system) for safe and effective treatment were determined [57, 58]. These were then confirmed by optical coherence tomography and reflectance confocal microscopy [59].

To date, numerous ablative fractional CO₂ lasers are FDA-approved for ablation, coagulation and remodeling of soft tissue, treatment of wrinkles, dyspigmentation, vessel-related discolorations, and especially for scars, all changes related to extrinsic skin aging [60]. Today, fractional lasers are considered the standard in dermatology [41]. Nevertheless, further developments of fractional laser systems are required in order to safely establish potential areas of application in routine clinical practice [61].

Thus, the spectrum of indications for these lasers is continuously being expanded. These systems are already used for neoplasms, fibrosing skin diseases, inflammatory skin diseases, and for the removal of foreign bodies. Their potential lies in the temporary opening of the epidermal barrier (TOR) [61]. While the TOR (German for “gate”) to the skin literally has the potential to pave the way to new and intensified therapies, it has also brought to light numerous new risks [62]. Given that the concept of these new techniques, which can be summarized as laser-assisted drug delivery (LADD), is to make the skin distinctly more penetrable than usual, it is imperative that the indication be established by a board-certified specialist. The enhanced penetration of drugs is associated with an increased risk of side effects and complications due to systemic absorption and effects, inoculation of pathogens, sensitizations, and anaphylactic reactions.

Currently, LADD is employed for the sustained treatment of field cancerization. It has been shown that laser-assisted photodynamic therapy (PDT) is superior to conventional PDT in treating actinic keratosis and field cancerization, especially in immunosuppressed patients [63–66]. It does even have preventive effects [67]. In superficial and nodular basal cell carcinoma, the efficacy of conventional PDT can be enhanced as well [68, 69]. Recent studies confirm the increased efficacy of topical antineoplastic agents such as ingenol mebutate [70] and methotrexate (MTX) [71, 72], as well as other topical drugs such as 5-fluorouracil (5-FU) [62]. Essential steps in the improvement of therapeutic concepts are geared towards increased reliability and efficacy in the case of evident and incipient neoplasms in chronically photodamaged skin. Current examples include the sequential use of synergistic lasers to maximize the HSP70 response [49], the application of pressure to induce deep drug delivery following fractional ablation [73] and the use of nanotransporters [61].

Recent studies on the utilization of alternative light sources for PDT demonstrate the importance of medical supervision when using these new, highly effective therapies. PDT is always painful when used according to standard procedures. While preliminary studies show very positive results for daylight-mediated PDT (shortened incubation time) [74–76], numerous cofactors can significantly limit its efficacy [77]. Adequate medical assistance is therefore a sine qua non in any kind of LADD.

Vessels

Historically, the treatment of unwanted vessels is one of the most common interventions. Here, too, a thorough diagnostic workup prior to the intervention is crucial, given that especially malignant vascular neoplasms may show slow clinical progression. Apart from IPL devices, argon lasers (488/514 nm), alexandrite lasers (755 nm), Nd:YAG lasers (1,064 nm), dye lasers (585/595/600 nm), and potassium titanyl phosphate (KTP) lasers (532 nm) have been extensively used for the treatment of superficial telangiectases, hemangiomas, and other vascular lesions [27].

The argon laser emits a blue-green light of the wavelengths 488 nm and 514 nm with low epidermal penetration. Its use...
is commonly associated with adverse effects such as persistent postinterventional hyperpigmentation and scar formation [27]. Lasers that emit light of 532 nm are similarly effective and characterized by similar side effects. Here, the use of KTP or lithium borate (LBO) crystals results in doubling of the frequency (1,064 nm).

The long-pulsed alexandrite laser (755 nm, up to 20 ms) and diode lasers (800 nm, 810 nm, 930 nm, 10–250 ms) have been shown to be less effective in the treatment of very thin vessels [27]. Short-pulsed alexandrite lasers are characterized by very high efficacy and a very narrow therapeutic range. A rather high risk of side effects must be expected when using long-pulsed Nd:YAG lasers (1,064 nm, pulse up to 20–100 ms), although they are exceptionally effective if employed correctly [78]. Here, the competent management of potential side effects (hyperpigmentation, textural damage, hemorrhage) is of particular importance.

Recently, there has been an increasing number of publications describing the use of well-established wavelengths under certain conditions or in combination in order to improve success rates. Treatment-refractory, especially dark and hypertrophic nevus flammei pose a particular challenge. Tuberous components can be treated quite well with the long-pulsed Nd:YAG laser or the short-pulsed alexandrite laser with larger spot sizes, while accepting a higher risk of scar formation, whereas plane components are difficult to treat with these lasers [27]. Recent developments have shown good results in plane lesions using a combination with radio frequency-induced heating.

Alternatively, IPL devices can be used, in particular for extensive and small-caliber lesions. Here, too, special care must be taken when treating tanned individuals. Following treatment, UV exposure should be avoided for at least 24 hours [32].

Pigment removal

A significant innovation for the removal of unwanted skin pigmentation systems are systems that emit light in the picosecond (ps) range. However, it has been shown that these systems are no more effective in the treatment of tattoos than their nanosecond counterparts [79, 80]. In addition, there have been reports of an interaction with the epidermis (laser-induced optical breakdown; LIOB), which presents as light-induced cutaneous perforation that is smaller than the spot size of the laser (EP2366355 A1). A conclusive assessment of the effects of these interactions on healthy, artificially changed, or diseased skin is not yet possible.

Fractional lasers have also been used to remove unwanted pigment. Evidence of limited therapeutic success in melasma was provided by the detection of melanin in the elimination products occurring during postfractional wound healing [62, 81]. These findings are corroborated by reports that the pigment stored in melanophages is released following their rupture and dispersed in the tissue. There is evidence that fractional ablative interventions are well suited to treat dyspigmentation even in scars. However, it is important to keep in mind that fractional lasers should not be used in the treatment of melanocytic lesions, either [27]. Still doing so requires a clear indication established by a board-certified specialist.

Given their large wavelength spectrum, IPL systems have also been used to treat unwanted hyperpigmentation. Ultimately, the success rates are as low as for conventional Q-switched lasers that emit in the nanosecond (ns) range and are generally used for the removal of tattoos and pigmented lesions. Prior to any intervention, it is imperative to have a specialist determine whether the lesion to be treated is truly benign.

In accordance with the concept of selective photothermolysis, only systems with very short pulse durations may be used for tattoo removal in order to minimize any collateral damage. A common problem is the competing target chromophore melanin [32], which renders the procedure exceedingly prone to complications. In addition, the removal of dyes from the human skin is associated with risks such as allergic reactions (especially for red dyes), color changes, formation of toxic degradation products, scarring, and incomplete removal even after many sessions [82–85].

Adverse effects are much more severe when IPL systems are used for tattoo removal. In this case, phototoxic reactions, dyspigmentation, scars, and keloids have to be expected. Periodic use bears the risk of additional complications.

Summary and outlook

Recent developments (new wavelengths, concepts, and combinations) in the field of lasers, intense pulsed light devices, LED, as well as new energy and light sources have provided dermatologists with new areas of application, therapeutic options, and aesthetic indications.

These developments have brought about a merging of aesthetic indication and therapeutic intention. For example, while fractional lasers used to be employed solely for aesthetic indications, today these systems – in the context of LADD – have become important tools in the treatment of field cancerization. Along with greater efficacy, improved techniques, and implemented safety requirements, physicians are confronted with increasing demands, also due to potential interactions with a growing number of comorbidities and comediations in a patient population that continues to age.

In order to avoid treatment errors, it is therefore essential that the indication be established by a physician, in particular when procedures are employed that include coagulation
(vessel-occlusion), ablation, fractional treatment, pigment removal, and epilation. Access to any device that might be used incorrectly should be denied to laypersons as well as medical personnel without specific training and thus without diagnostic competence.

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