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INVITED REVIEW

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Intense pulsed light: The early years

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Abstract

Background: Intense pulsed light (IPL) is one of the most controversial and widely used light-based technologies that had its origin in San Diego in 1992 and was approved by the US Food and Drug Administration in late 1995.

Aims: The purpose of this review is to highlight the early years' experience with IPL and development of its use over time.

Material and Methods: Articles from PubMed on this subject were reviewed and clinical experience of the authors were shared.

Results: IPL was initially developed as an improved treatment for leg telangiectasias. Its ability to successfully treat vascular lesions while minimizing purpura, a common complication of pulsed dye lasers, as well as exfoliating superficial pigmented lesions and eliminating hair, extended the clinical utility of IPL to treat both pigmented and vascular lesions, providing the basis for its role in photorejuvenation.

Discussion: IPL is an effective and safe treatment modality for a wide range of dermatologic conditions from pigmented to vascular and inflammatory disorders.

KEYWORDS
intense pulsed light, photorejuvenation, pigmented lesions, vascular lesions

1 | HISTORY

The concept of intense pulsed light (IPL) was first conceived by Goldman, Fitzpatrick, and Eckhouse in April 1992 in San Diego, CA, to improve the treatment of leg telangiectasias. Research by Goldman et al.[1,2] on rabbit ear veins and then on human leg veins by Goldman and Fitzpatrick demonstrated that a 585-nm laser pulsed at 0.45 ms could effectively cause thermal coagulation of blood vessels <0.4 mm in diameter. However, in human leg veins, it produced prolonged purpura as well as hypo- and hyperpigmentation. To circumvent these unwanted side effects, Goldman and Fitzpatrick began developing a device that could thermocoagulate a vessel and protect the epidermis. Eckhouse, an aerospace engineer from Israel, engineered the first IPL device according to Goldman and Fitzpatrick's specifications. In September 1992, Goldman and Fitzpatrick began treating rabbit ear veins with pulse durations ranging from 1 to 15 ms and energies ranging from 10 to 20 J/cm^2 using a 515-nm cut-off filter with one pulse. Photographs and biopsies were taken of the rabbit ears from 1 h to 30 days after IPL treatment. Many of the dorsal marginal ear veins disappeared and, histologically, many veins were thermocoagulated with the overlying epidermis undamaged. The results of their work were presented at the 6th Annual Congress of the American College of Phlebology in Orlando in February 1993 in a lecture titled, "Clinical and Histologic Evaluation of the ESC Vascular Lesion, Pulsed Light Source on the Dorsal Marginal Rabbit Ear Vein."[3]

Goldman and Fitzpatrick's proof of concept with rabbit ear veins led to the first human study on seven leg veins and four patients with port-wine stain (PWS) in their office in Encinitas, CA in November 1992. Single pulses of 3–15 ms and energies of 10–20 J/cm^2 were used, again with a 515-nm cut-off filter without cooling and without a light guide on leg veins ranging from 0.2 to 1 mm in diameter. Leg vein patients were followed up for 6 weeks and PWS patients for 4 weeks. Excellent resolution was seen in 60% of veins and PWS; however, epidermal burns occurred in 40% and scar formation in 20% of patients. This prompted further studies to determine

appropriate IPL parameters to minimize epidermal damage. A formal Institutional Review Board-approved human study was conducted, which developed multiple sequential pulsing using a variety of filters ranging from 550 to 570 to 590 nm to cut off lower, more superficial wavelengths with the maximal output of the flash lamp around 800 nm. Increased epidermal protection was achieved with the incorporation of a quartz light guide and cold ultrasonic gel, which allowed light to be transmitted to the targeted epidermal lesion as well as provided protection from excessive heating to the epidermis. The results from the human leg vein study were presented in a lecture titled "Can Light Be Useful in the Management of Lower Extremity Telangiectasia and Reticular Veins?" in December 1993 at the 53rd Annual Academy of Dermatology in New Orleans, LA.[3] In 1994, Goldman and Fitzpatrick published the theoretical basis for using IPL to treat benign vascular lesions in their textbook titled, "Cutaneous Laser Surgery: The Art and Science of Selective Photothermolysis."[4] After their success with leg veins, they began treating facial telangiectasias, hypertrophic scars, hemangiomas, and venous malformations in May 1995 with excellent results.

The introduction of IPL was not met without critics. In August 1995, the United States granted FDA approval for the first IPL systems. With over 20 Photoderm systems in use in various "clinical trials" in the United States and another 20 IPLs in use in Canada and Europe, many doctors reported great success with IPL systems, whereas others experienced frequent complications such as epidermal burns, leading to the derogatory term "photo-burn" to describe this technology.[3]

Goldman and Eckhouse published the first large-scale publication in *Dermatologic Surgery and Cosmetic Surgery* in 1996, detailing the excellent results of their multicenter leg vein study.[5] Drs. Robert and Margaret Weiss included an editorial in this issue discussing early complications, but they concluded that experience is often the best teacher.[6] Dover et al.[7] discussed varied results with treating leg veins with IPL, which decreased its use for leg telangiectasias. At the same time, treatment of benign pigmented and vascular lesions with IPL gained popularity as a way to rejuvenate the skin.[8,9]

In August 1996, Dr. Goldman treated a facial PWS in a male with a mustache that he was unable to successfully treat with multiple pulse dye laser sessions. The PWS cleared over 50% with one IPL treatment and the mustache only grew back 50%. What appeared to be a complication extended the clinical utility of IPL. Dr. Goldman treated his own back with IPL shortly after this discovery. Biopsies of his back demonstrated successful thermocoagulation of hair follicles. Further clinical studies were performed on male transvestites in Berlin, Germany, which helped develop an IPL with higher power and faster recharging time, which came to be known as the Epilyte™.[3]

In the early days of IPL development, many physicians struggled with the technical expertise required to produce consistent and successful results in the early days of development. *The New York Times* published an article titled, "Unsightly veins? Zap Wall St. Woes? Zap" on June 23, 1996 that was sprinkled with quotes by physicians doubting the utility and safety of the IPL. Harvey Jay, MD, published a Letter to the Editor explaining that operating an IPL can be equated to a skilled surgeon with a scalpel, that is, a novice will not produce acceptable results, but an expert will achieve great results.[3] Dr. David Green published an article in the *Journal of the American Academy of Dermatology* detailing his observations including a high degree of adverse events and patient dissatisfaction with the IPL.[10] Dr. Goldman was asked on a panel at the Annual Meeting of the American Society for Laser Medicine and Surgery why he did not agree with Dr. Green's recent article. He responded with a similar sentiment as Dr. Jay did in his Letter to the Editor. Dr. Goldman was sued for libel in San Diego Supreme Criminal Court by Dr. Green. Dr. Green was not awarded any damages for these remarks. Clearly, the early days of the IPL were not without strife.[11]

The IPL has withstood the early critics and is now one of the most versatile tools in the cosmetic surgeon's toolbox. It is used to treat benign pigmented and vascular lesions and has been incorporated into photodynamic therapy (PDT) treatment of superficial nonmelanoma skin cancer, acne, and photodamage.[12-14]

It should be noted that current systems (such as Lumenis M22) provide an optimal pulse technology, producing uniform energy throughout the entire pulse. This is a vast improvement over earlier models that produced an energy peak followed by a decline.[12]

The IPL has withstood the early critics and is now one of the most versatile tools in the cosmetic surgeon's toolbox. Comparatively low initial cost and lack of consumables make IPL a cost-effective workhorse for a busy cosmetic practice. It is used to treat benign pigmented and vascular lesions and has been incorporated into PDT treatment of superficial nonmelanoma skin cancer, acne, and photodamage.[13-15]

2 | WAVELENGTH, PULSE DURATION, AND THE CONCEPT OF SEQUENTIAL PULSING

IPL devices emit a noncoherent, polychromatic light with a broad spectrum of wavelengths ranging between 400 and 1200 nm. This allows IPL devices to target a number of chromophores (hemoglobin, melanin, and water). The wavelength of light emitted from the device can be manipulated using a number of filters including 515, 560, 590, 615, 640, 695, and 755 nm. Manufacturers add additional filters to their IPL devices, for example, Lumenis has a vascular notch filter at 530–650 and 900–1200 nm and an acne notch filter at 400–600 and 800–1200 nm. Thus, IPL devices are able to operate on the target tissue by selective photothermolysis.

There are more than 20 different IPL devices on the market. Some IPL devices have a single pulse, whereas others have multiple sequential pulsing. Furthermore, some can independently vary the pulse duration, the energy fluence, or both in each pulse. Other variables include the size of the delivered light, power outputs, pulse duration, and cooling system. One example of the commonly used IPL device systems is the Lumenis system. When filtered, the Lumenis IPL device is capable of emitting light of wavelengths ranging from 515 nm to approximately 1200 nm.

Handpiece thermokinetic cooling of the sapphire light guide is a useful feature present in some devices, and it can be employed to provide epidermal protection, while at the same time allowing greater fluences to reach deeper targets. A cold ultrasound gel should be applied to the areas being treated by IPL to protect the epidermis and diffuse the surface heat emitted from the device handpiece. Furthermore, the gel reduces the refractive index between air and skin, thus allowing better penetration and absorption of light, and it enhances the gliding ability of the handpiece from one location on the skin to another.

3 | PULSE DURATION

To limit thermal damage to the intended target, the pulse duration must be shorter than the thermal relaxation time of the target tissue. The thermal relaxation time of tissue is defined as the time necessary for the peak temperature to rise in a heated region of tissue to decrease to 37% of the total rise.[15]

Allowing proper thermal relaxation time between pulses theoretically prevents elevation of epidermal temperatures above 70°C and is an inherent advantage of "multiple sequential pulsing" of some of the IPL devices, like the Lumenis IPLs. For a typical epidermal thickness of 100 μm, the thermal relaxation time is about 1 ms. For a typical vessel, of 100 μm (0.1 mm), the thermal relaxation time is approximately 4 ms; for a vessel of 300 μm (0.3 mm), the thermal relaxation time is approximately 10 ms. Therefore, vessels >0.3 mm cool more slowly than the epidermis with a single pulse. For larger vessels, however, multiple pulses may be advantageous. The delay times between sequential pulses need to be 10 ms or longer to accommodate normal epidermal thermal relaxation times; a 20- to 40-ms thermal relaxation time is recommended for patients with darker skin types to avoid thermal damage to the epidermis.[16] We recommend supplementing the sapphire crystal cooling with cold air cooling to achieve a less painful, more efficacious result.

4 | COMMON USES OF IPL

4.1 | IPL treatment of pigmentary disorders

4.1.1 | Lentiginous disease

IPL has demonstrated efficacy in the treatment of pigmented lesions, particularly epidermal pigmented lesions such as lentigines and ephelides.[17-27] A multitude of studies have uniformly reported excellent efficacy and safety of IPL in the treatment of solar lentigines and ephelides on the face and body after an average of three to five treatments. IPL modality can be safely used in darker skin types when used in a double- or triple-pulsed mode with 30- to 40-ms delay between pulses, which allows the epidermis to remain unaffected.[27]

Kawada et al.[19] showed that an upward movement of melanocytes and their subsequent elimination occurs via desquamation of microcrusts at areas treated with IPL. The group used video-microscopic evaluation and histologic analysis to show that microcrust formation was limited to pigmented spots and that these microcrusts contained melanin, as demonstrated by Fontana–Masson staining. Furthermore, there was less melanin in the basal layer than in untreated spots. Resolution of these crusts led to the clinical clearing of the solar lentigines. Friedmann and Peterson[18] reported that the use of an IPL KTP filter (525–585) in the treatment of facial and hand solar lentigines demonstrated to be a well-tolerated effective treatment method.

One well-designed, randomized, observer-blind, right–left comparison clinical trial of 32 Taiwanese women, 17 with ephelides and 15 with solar lentigines, compared the efficacy of IPL with that of quality-switched alexandrite laser (QSAL)[27]; the latter is a commonly implemented modality in the treatment of lentigines. The study showed that both modalities resulted in significant improvement in Pigmentation Area and Severity Index (PASI) scores after one treatment with QSAL or two treatments with IPL. QSAL was more effective for ephelides, whereas IPL and QSAL were equivalent for solar lentigines. It is worth noting that post-inflammatory hyperpigmentation (PIH) occurred in eight patients with ephelides and one with solar lentigines on the QSAL-treated side, whereas none occurred on the IPL-treated side.

Lentigines can be a component of different cutaneous syndromes including Peutz–Jeghers syndrome and LEOPARD syndrome. In these syndromes, the histology is similar to that of lentigo simplex with the occasional difference of more deeply melanized melanosomes in Peutz–Jeghers syndrome[28] and larger melanosomes are found in LEOPARD syndrome.[29] Case reports showed a significant clinical improvement of lentigines associated with Peutz–Jeghers syndrome and in LEOPARD syndrome.[23,24]

IPL has consistently been shown to be a safe and effective modality for the treatment of solar lentigines and ephelides. IPL may be preferable to QSAL for the treatment of lentiginous disease in Asian patients due to a possible risk of PIH in the latter.

4.1.2 | Melasma

Data suggest that increased vascularity is one of the major findings in melasma.[30] Vascular endothelial growth factor (VEGF) may be a major angiogenic factor for altered vessels in melasma. A recent meta-analysis showed a 39% reduction of Melasma Area and Severity Index (MASI) scores with IPL-based treatment of melasma.[31] Multiple studies showed moderate efficacy for the treatment of melasma.[32-37]

In one melasma split-face comparative study,[38] one half of the face was treated with pulsed dye laser (PDL) and the other half was treated with IPL. Clinical outcomes were measured by using the hemifacial modified Melasma Area and Severity Index (mMASI) score. Tissue biopsies were performed to assess VEGF via immunohistochemical staining. The mMASI scores were significantly reduced in both groups. However, the study showed a higher efficacy of IPL in lesions with epidermal melasma or those melasma patients with a significant vascular component. The expression level of VGEF was significantly reduced in both groups.

In a randomized controlled trial conducted by Wang et al.,[36] IPL achieved significantly superior results than in a control group treated with topical hydroquinone and sunscreen (40% improvement of quantitative melanin index in the former as compared with 11% improvement in the latter group). A subsequent randomized controlled trial compared IPL treatment with a control group treated with a triple combination (TC) cream (fluocinolone acetonide, 0.01%; hydroquinone, 4%; tretinoin, 0.05%) and sunscreen, showing statistically significant improvement of MASI score in the IPL group as compared with the control group.[39] Goldman et al.[40] demonstrated that the combination of IPL and TC cream was superior to IPL alone in a prospective left–right comparison trial.

Na et al.[34] performed a retrospective comparison study that suggested that the addition of IPL to a low-fluence neodymium-doped yttrium aluminum garnet (Nd:YAG) laser was superior to the use of a low-fluence Nd:YAG laser alone in the treatment of melasma.[34] The results were consistent with a later study by Vachiramon et al.[41] Topical and oral tranexamic acid has shown promise in the treatment of melasma.[42-44] It is worth noting that IPL has not been compared in a head-to-head trial to tranexamic acid to date.

In summary, the available evidence indicates that IPL can lead to an improvement in patients with melasma who are refractory to topical therapy; however, it can be associated with recurrence unless topical therapy is maintained. Response to IPL can be also related to the type of melasma, with a more favorable response in epidermal than dermal or mixed subtypes.

4.1.3 | Poikiloderma of Civatte

IPL is also efficacious in the treatment of poikiloderma of Civatte.[45-47] These studies unanimously showed marked to significant reduction in vascular, pigmented, and atrophic skin changes in 81%–82% of patients after three to five sessions of IPL.

One histological study showed homogenization of melanin distribution after IPL treatment (86% of patients) and reduction of vessel diameter by more than 50% in the superficial vascular plexus (57% of patients). Furthermore, histological analysis showed a greater diameter of fibroblasts, an increase in nonfragmented elastic fibers, and thickening and compaction of collagen fibers.[46] In conclusion, the use of IPL for the treatment of poikiloderma of Civatte has been consistently shown to be a safe and effective option, given the fact that it addresses the three components underlying the pathogenesis of poikiloderma of Civatte, namely vascularity, pigmentation, and laxity.

4.2 | IPL in acne vulgaris and rosacea

4.2.1 | Acne vulgaris

IPL was investigated in the treatment of acne vulgaris in several studies, either as a treatment option by itself or as an activator of PDT.[48-63]

There are several proposed mechanisms of action by which IPL can impact acne. One is thermolysis of blood vessels supplying sebaceous glands. This is associated with a reduction of sebum production and gland size. This is supported by findings of Barakat et al.[64] who performed histopathological examination and measurement of the surface area of sebaceous glands at baseline and 2 weeks after six treatment sessions with IPL. The study showed a significant reduction in the surface area of the sebaceous gland following IPL treatment. IPL has also an anti-inflammatory effect by down-regulating tumor necrosis factor-alpha (TNF-α) and upregulating transforming growth factor-beta 1/smad3 signaling pathway.[65-67]

Chang et al.[48] conducted a split-face, open-label, prospective trial in 30 Korean women with mild-to-moderate acne and found that IPL treatment equipped with a 530- to 750-nm acne filter resulted in improvement of acne red macules, irregular pigmentation, and skin tone but did not affect inflammatory acne lesion counts. Those results were replicated by Yeung et al.[61] in 30 Chinese patients treated with IPL.

The vast majority of studies of IPL in acne patients resulted in a reduction of both inflammatory and noninflammatory lesions.[49,57,68] The reported efficacy of IPL on acne lesions ranged from 34% to 88% with an average improvement of 40%–60%. The number of IPL sessions in those studies ranged from four to eight.

A greater efficacy of IPL has also been demonstrated when combined with PDT compared with IPL alone in the treatment of acne vulgaris. The most commonly reported efficacy ranged between 60% and 80%.[54,58] Shaaban et al.[58] compared the safety and efficacy of PDT using intralesional 5-aminolevulinic acid (5-ALA) with IPL and IPL alone in the treatment of acne vulgaris. The authors performed an open-label split-back prospective trial in 30 patients. All patients experienced a reduction in the number of acne lesions on both sides of the back, but the reduction was significantly more, and recurrence of the lesions was significantly less in the PDT and IPL side compared with the IPL only side.

In a randomized placebo-controlled trial, Mei et al.[54] compared ALA–IPL–PDT with IPL alone in the treatment of 41 patients with moderate-to-severe facial acne and found the former to be superior in terms of reduction in global acne lesion counts and specific inflammatory and noninflammatory lesions. At 12-week follow-up after four weekly treatment sessions, there was 75% improvement of the global lesion count in the ALA–PL–PDT group, versus 51% improvement in the IPL-alone group. In a retrospective 10-year single-center study comparing multiple light sources in the sequential activation of PDT for acne vulgaris, Friedmann et al.[63] revealed that patients treated with a combination of blue light and IPL had a significantly lower rate of acne flares.

4.2.2 | Rosacea

Initial studies demonstrated the efficacy of IPL in reducing blood flow, telangiectasia, and severity of erythema in individuals with rosacea.[69,70] These data were confirmed in a prospective trial involving 60 patients

(Fitzpatrick I–IV) who underwent an average of four treatments to achieve a mean clearance of 78%. These results were maintained during a 3-year posttreatment follow-up period.[71] Papageorgiou and colleagues found that IPL was effective in significantly reducing erythema and telangiectasia in erythematotelangiectatic rosacea (ETR) after four treatments were delivered at 3-week intervals. Results were maintained for at least 6 months following treatment.[72]

In a head-to-head randomized, controlled, single-blind split-face trial comparing non-purpuric PDL with IPL in the treatment of ETR, Neuhaus et al.[73] found that both modalities were equally effective in reducing cutaneous erythema, telangiectasia, and patient-reported symptoms and that both were significantly superior to untreated controls. In another prospective right–left comparison trial, Fabi and colleagues showed that the therapeutic benefit of IPL for rosacea could be further enhanced with the addition of 15% topical azelaic acid.[73]

A case report involving a single patient demonstrated the effective treatment of granulomatous rosacea with IPL. In this patient, the disease had previously been refractory to topical clindamycin, metronidazole, azelaic acid, calcineurin inhibitor, and oral doxycycline.[74] One prospective observational study showed improvement of erythema in both patients with ETR and those with papulopustular rosacea (PPR) following three treatment sessions with IPL spaced 3 weeks apart. Physician-reported improvement of erythema was twofold in the PPR group and 1.4-fold in the ETR group.[75] Overall, IPL appears to be an effective, well-tolerated treatment option for rosacea with efficacy equal to that of PDL. Typical reported improvement was 50% on average.

4.3 | IPL treatment of vascular lesions

IPL was originally developed to treat leg veins. IPL has proven to be successful in treating a wide variety of vascular lesions and disease processes. Goldman and Raulin reported the first successful treatment of an adult PWS with IPL in 1997.[76] This PWS was refractory to treatment with PDL but resolved with four treatments of IPL. Similarly, Bjerring et al.[77] treated 15 patients with PWS refractory to treatment with IPL and were able to achieve 75%–100% clearance in 46.7% of cases. In 1999, a retrospective study including 40 PWS determined that 75% of PWS treated with IPL achieved 75%–100% clearance after one to four treatments.[78] There have been conflicting results regarding the relative efficacy of PDL and IPL for the treatment of PWS.[79] A randomized, controlled, single-blind head-to-head trial comparing PDL with IPL for the treatment of PWS showed that both modalities were effective; however, PDL was superior in terms of median clinical improvement (65% vs. 30%) leading patients to prefer treatment with PDL.[80] Babilas et al.[81] compared IPL with the standard PDL treatment used for PWS. They found IPL to be superior to short PDL (0.45 ms) and equivalent to long PDL (1.5 ms) for treatment of PWS.[81]

PDL has been the standard of treatment for telangiectasias since the 1990s.[82] PDL can produce residual purpura due to rapid heating of blood vessels with shorter pulse widths (0.45 ms) and with longer pulse widths (up to 40 ms) there is slower heating of vessels which reduces purpura but can also reduce efficacy.[83] PDL has evolved to include devices with long pulse widths (up to 40 ms), along with treatment protocols including the use of pulse stacking, multiple passes and multiple wavelengths to minimize adverse effects.[82,84-89] IPL's ability to minimize the possibility of purpura and treat large areas due to its larger spot size makes it an ideal modality for the treatment of telangiectasias.[13] A review by Wat et al.[79] found evidence demonstrating successful treatment of a wide variety of telangiectasias with IPL including benign essential telangiectasia, telangiectasia of the lower limbs, hereditary hemorrhagic telangiectasia, radiotherapy-induced telangiectasia, postsurgical telangiectasia, and telangiectasia associated with systemic sclerosis. As mentioned previously, the early days of the IPL involved the treatment of leg veins. Goldman and colleagues treated 159 patients with lower limb telangiectasias with IPL and found 79% of patients achieved 75%–100% clearance of vessels.[6] Tanghetti conducted a split-face randomized treatment of facial telangiectasia comparing PDL and IPL demonstrating equal efficacy and similar side-effect profile including erythema, post-treatment edema, and purpura which resolved within a few days. One patient had trace hyperpigmentation from the IPL which resolved within a month.[82] Clementoni and colleagues analyzed 1000 patients, Fitzpatrick skin types I–IV, with telangiectasias treated with IPL and found 89.7% of patients experienced 75%–100% improvement. Patients who underwent three or more treatments noted significant improvement in overall skin quality.[90] IPL is an effective and well-tolerated treatment for telangiectasias with the added benefit of improving overall skin quality.

4.4 | IPL treatment of premalignant and malignant lesions

Actinic keratoses (AKs) are dysplastic epidermal neoplasms resulting from chronic cutaneous exposure to ultraviolet radiation. Risk factors include increasing age, male gender, Fitzpatrick I/II skin types, sun tanning, as well as outdoor occupations and hobbies. They are commonly found on the face, bald scalp, neck, dorsal hands and forearms, and upper trunk.[91] It should be noted that 65%–97% of squamous cell carcinomas (SCCs) do develop from AKs or areas of field cancerization.[92] Warino et al.[93] found an estimated 5.2 million physician visits each year were for AKs between the years of 1995 and 2003. Due to the vast number of patients affected by AKs and the potential for progression to invasive SCC, effective treatment strategies are warranted. Many treatments exist for AKs but PDT has the advantage of being a well-tolerated, cost-effective method for treating areas with diffuse AKs with prolonged recurrence-free periods, excellent cosmetic outcomes, and without the need for strict patient compliance.[94,95]

Several studies have examined the use of IPL as an activator of photosensitizing agents for PDT of AKs. One right–left comparison study compared IPL versus IPL–methyl aminolevulinate (MAL)–PDT

which showed 60% improvement on the combination side and 55% using IPL alone. These results suggest IPL alone may be effective in the treatment of AKs but is enhanced by the addition of a photosensitizer.[96]

Four other studies also examined the use of ALA or MAL plus IPL, with AK clearance ranging from 50% to 91% after a single treatment.[97-100] Kim et al.[100] documented histologic resolution in 42% of lesions using 5-ALA–PDT and IPL as a light source. 5-Fluoruracil has also been used in combination with IPL–PDT to treat AKs successfully.[101] A randomized control trial by Haddad et al. examined the optimal fluence for treating AKs. The response was greatest in the treatment groups receiving 40 J/cm^2 (20 J/cm^2 × 2 passes; $p = .02$) and 50 J/cm^2 (25 J/cm^2 × 2 passes; $p = .02$) in combination with PDT and 5-ALA compared with IPL alone, as well as 20 and 25 J/cm^2. It should be noted that only 24% of patients had a marked response (>75% improvement).[99]

Friedmann and colleagues examined the use of multiple sequential light devices for activation of 5-ALA for PDT of AKs. They determined the combination of IPL, PDL, and blue light was superior to blue light plus IPL or blue light alone for the treatment of AKs. The addition of red light to the other devices did not lead to increased efficacy. The patients treated with the combination of IPL, PDL, red light, and blue light had lower rates of peeling, erythema, and acne flares than blue light plus IPL and less pain than blue light plus PDL.[102] Overall, IPL combined with PDT is an effective alternative that is well tolerated by patients for the treatment of AKs.

Limited studies have examined the utility of IPL for the treatment of superficial basal cell carcinoma (BCC) and Bowen's Disease. One open-label trial included 30 patients with a combination of AKs, superficial BCC, and Bowen's disease. Patients were treated with MAL pulse IPL. After two sessions of IPL (6 pulses, 1–10 s apart), all 10 patients with superficial BCC, and all nine with Bowen's disease experienced complete resolution. Another small open-label trial treated three patients with ALA plus IPL. All patients had complete resolution after two to five sessions administered every 2 weeks. ALA plus IPL offers promising results for the treatment of superficial BCC and Bowen's disease; however, current evidence is based on low-quality studies.[79,98,103]

4.5 | IPL treatment of other disorders

4.5.1 | Hypertrophic scars and keloids

Hypertrophic scars and keloids are the results of excess fibroblast proliferation and collagen synthesis due to dysregulation in the wound healing process following tissue trauma. Clinically, they are erythematous, elevated, and firm and often associated with pain and pruritis. PDL is widely accepted as the treatment of choice for hypertrophic and keloidal scars; however, it can produce unwanted purpura sometimes lasting up to 2 weeks.[104] Randomized control trials evaluating the use of IPL for treatment of keloidal and hypertrophic scars are lacking; however, there are a few studies supporting the use of IPL including an open-label trial, one retrospective observational study, and a prospective right–left comparison trial, and demonstrating effective use of IPL.[104-106] In patients undergoing cosmetic surgery purpura is an unwanted side effect. In a prospective split treatment trial, a total of 15 breast reduction and abdominoplasty scars were treated with IPL and long-pulsed PDL. IPL was associated with increased pain but produced decreased purpura compared with long-pulse PDL. Differences in scar improvement between long-pulse PDL versus IPL were not statistically significant.[104] Kontoes et al.[105] demonstrated 50% improvement in all hyperpigmented, erythematous, and proliferative scars treated with IPL after a mean of 2.97 sessions. Erol et al.[106] treated 109 patients in an open-label trial with IPL. Notably, scar height, erythema, and hardness decreased with an average of eight treatments in 92.5% of patients with keloidal or hypertrophic scars. IPL is an effective treatment for hypertrophic and keloidal scars with similar efficacy to long-pulsed PDL and a lower incidence of unwanted purpura.

4.5.2 | Sebaceous gland hyperplasia

The presence of sebaceous gland hyperplasia is cosmetically bothersome for many patients. In one investigator blinded study, 12 patients were randomly selected to receive four consecutive monthly treatments with 5-ALA (30–60 min) followed by a 15-min treatment with 405–420 nm blue light (Clearlight; Lumenis Inc.) or treatment with an IPL using a 550-nm cut-off filter (32 J/cm^2, 3.5-ms pulse duration, 20-ms pulse delay). Both treatments were well tolerated. At a 4-month follow-up, those treated with blue light had a 50.6% lesional reduction and those treated with IPL had a 48.4% lesional reduction.[107]

Microstomia as a result of systemic sclerosis has a large impact on the quality of life, making daily tasks and routine dental care challenging. The ability of longer wavelengths to penetrate the dermis lends the ability for IPL to replace sclerotic collagen with newly formed collagen and elastin. Comstedt and colleagues demonstrated treated four patients with IPL, three of four patients experienced a 1-mm increase in the oral opening. All patients noted softening of perioral skin, as well as improvement in articulation, eating, and ease of tooth brushing.[108]

Colloid milium is a rare depositional disease often located in sun-exposed areas. It can be challenging to treat. Dermabrasion, cryotherapy, and diathermy treatments have been met with limited success. Erbium:YAG laser has been used with success in one patient.[109] In one case report, a 60-year-old woman was treated with four treatment sessions of IPL (Apollo-II Shanghai Wonderful Opto-Electric Tech Co. Ltd.). Significant improvement was noted, with facial skin appearing smooth.[110]

5 | ADVERSE EVENTS

IPL was found to be well tolerated, with minimal and self-limiting side-effect profile. The most common adverse effects reported in the literature were mild discomfort, erythema, purpura, edema, blistering, and crusting. These findings typically resolve within 48 h,

however, can last up to 1 week. Posttreatment hyper- and hypopigmentation were also reported in the literature as possible adverse effects of IPL. This pigmentary alteration typically responded to conservative management but in rare cases could be long lasting (up to 18 months). Serious adverse events were exceedingly rare and consisted of one case of prolonged ulceration resolving in 30 days,[17] one case of herpes simplex labialis,[24] and two cases of hypertrophic scars.[111] IPL side-effect profile is minimal when the appropriate settings are used by a sufficiently experienced operator.

6 | CONCLUSION

IPL is an effective treatment modality for a wide range of dermatologic lesions from pigmented to vascular and inflammatory lesions. The versatility of the wavelength output of IPL and the availability of a variety of cut-off filters resulted in the versatility of skin conditions it could address. IPL is typically well tolerated by patients with minimal and self-limiting side-effect profiles. Furthermore, the relatively affordable initial cost of the device and the lack of consumables put it at an advantage when compared with other devices.

CONFLICT OF INTERESTS

Dr. Goldman received discounted equipment, performed research, and consulted for Lumenis. The remaining authors declare that there are no conflict of interests.

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