

ASDS Guidelines Task Force: Consensus Recommendations Regarding the Safety of Lasers, Dermabrasion, Chemical Peels, Energy Devices, and Skin Surgery During and After Isotretinoin Use

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BACKGROUND Currently, the isotretinoin (13-cis-retinoic acid) package insert contains language advising the discontinuation of isotretinoin for 6 months before performing cosmetic procedures, including waxing, dermabrasion, chemical peels, laser procedures, or incisional and excisional cold-steel surgery. It is common practice to follow this standard because of concerns regarding reports of sporadic adverse events and increased risk of scarring.

OBJECTIVE To develop expert consensus regarding the safety of skin procedures, including resurfacing, energy device treatments, and incisional and excisional procedures, in the setting of concurrent or recent isotretinoin use.

MATERIALS AND METHODS The American Society for Dermatologic Surgery authorized a task force of content experts to review the evidence and provide guidance. First, data were extracted from the literature. This was followed by a clinical question review, a consensus Delphi process, and validation of the results by peer review.

RESULTS The task force concluded that there is insufficient evidence to justify delaying treatment with superficial chemical peels and nonablative lasers, including hair removal lasers and lights, vascular lasers, and nonablative fractional devices for patients currently or recently exposed to isotretinoin. Superficial and focal dermabrasion may also be safe when performed by a well-trained clinician.

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ISSN: 1076-0512 • Dermatol Surg 2017;0:1–14 • DOI: 10.1097/DSS.0000000000001166

The purpose of this consensus document is to offer clinical recommendations based on the review of current evidence regarding the safety of skin procedures and surgery in patients receiving isotretinoin currently or within the past 6 months. This is the first consensus document, published by the American Society for Dermatologic Surgery which specifically addresses this topic.

Scope of the Consensus Statement

Published and unpublished descriptive, observational and randomized studies were reviewed for safety reports pertaining to the use of isotretinoin within 6 months of treatment with dermabrasion, lasers and other energy devices, chemical peels, or incisional and excisional surgery. Complications considered were enhanced risk of scarring or other adverse events. Not considered were the risks associated with skin procedures and surgeries in the context of treatment with other oral retinoids (e.g., acitretin) and topical retinoids. Similarly, the isotretinoin-associated impact on effectiveness of skin surgeries and cosmetic dermatologic procedures was not evaluated. Intended users of this guideline may include surgical specialists who routinely perform cutaneous procedures (e.g., dermatologists, plastic surgeons, otolaryngologists, and ophthalmologists) and also specialists who may commonly refer patients for these procedures, such as family physicians, internists, and pediatricians, as well as nurses and other medical professionals.

Methods

Search Strategy

The literature on the incidence of scarring associated with skin procedures and surgeries occurring less than 6 months after discontinuation of isotretinoin was reviewed. Electronic databases (MEDLINE, EMBASE, Cochrane library, and CINAHL) were searched for a 34-year period, 1982 to 2016, for English language articles. The search terms “isotretinoin,” “13-cis-retinoic acid,” or “Accutane” were used serially in conjunction with the following key words: “laser(s),” “dermabrasion,” “resurfacing,” “chemical peel,” “scarring,” “scar,” “surgery,”

“wound healing,” “keloid,” “skin fragility,” and “hypertrophic scar.” A total of 116 articles were identified after removal of duplicates and consensus review by 2 data extractors (M.A. and A.W.), and this number was reduced to 57 after abstract review. Manual review of the full text of these articles resulted in 36 selected source documents, which were distributed and reviewed by the members of the consensus guidelines task force.

In addition, public announcements were made of the intent to produce this consensus statement with the aim of obtaining additional information or feedback from physicians and patients. Specifically sought for review were unpublished works in preparation relevant to the topic, as well as the written opinions of relevant task-specific formal or ad hoc groups and committees comprising medical professionals.

Data Extraction

A systematic review of the source documents was performed by a specially constituted task force of content experts in dermatologic surgery (proposed by the executive director of the ASDS and ratified by the executive committee of the ASDS), and reviewed by additional members in pediatric dermatology and general dermatology; methodologists; physicians in other relevant specialties; and patient representatives. Assessment of the quality and strength of the evidence was performed using an expert consensus process. The process was initiated by making source materials available to each task force member, followed by discussion of the evidence during a series of face-to-face meetings and conference calls.

Clinical Questions and Review Process

To simplify the development of this consensus guideline, 4 questions were presented to the task force that comprised the expert panel.

- (1) Is there an increased risk of pathological scarring or developing other adverse effects when dermabrasion is performed within 6 months of isotretinoin use?
- (2) Is there an increased risk of scarring or other adverse effects when laser and energy device

procedures are performed within 6 months of isotretinoin use?

- (3) Is there an increased risk of scarring or other adverse effects when chemical peels are performed within 6 months of isotretinoin use?
- (4) Is there a risk of increased scarring or other adverse events when incisional and excisional skin surgical procedures are performed within 6 months of isotretinoin use?

Recommendations were formulated by expert consensus based on the Delphi method, and 2 rounds of Delphi process were performed. To address the primary clinical questions in a systematic manner, the following functional questions were also posed to the members of the task force:

- (1) Based on the available literature, would it be safe to consider cutaneous surgery and other non-surgical procedures within 6 months of isotretinoin use?
- (2) If yes to Question 1, which skin procedures could be considered safe within 6 months of isotretinoin?
- (3) What dosage of isotretinoin may be considered safe when administered within 6 months of cosmetic procedure or surgery?

Consensus Process

Adoption of final recommendations required unanimous agreement of all consensus guidelines task force members. In addition, individual task force members were asked to rate confidence in each of the final recommendations on the GRADE (Grading of Recommendations Assessment, Development and Evaluation) scale of A to D (A = high, B = moderate, C = low, D = very low) regarding their personal assessment of the quality and relevance of the supporting evidence.

Validation Process

Validation of this guideline before submission for publication was performed by internal and external peer review. Internal peer review included review by members of the ASDS guidelines committee not involved directly in the production of these guidelines.

External peer review was performed by content experts, both dermatologists and nondermatologists, identified by the ASDS Board of Directors.

Literature Summary

Background

Isotretinoin (13-cis-retinoic acid) is a retinoic acid and metabolite of vitamin A that has been FDA-approved since September, 1982, for the treatment of severe and nodulocystic acne. It is typically dosed at an upper limit of $1 \text{ mg}\cdot\text{kg}^{-1}\cdot\text{d}^{-1}$ for several months to reach an appropriate total cumulative dose. Isotretinoin has been shown to cause involution of the pilosebaceous unit, the site of stem cells required for repopulating epidermis and hair follicles after deep wounding.¹ For patients receiving isotretinoin, historical practice has been to recommend avoidance of dermatologic procedures such as chemical peels, dermabrasion, laser treatment of the skin and wax depilation during medication treatment and for at least 6 months after treatment because of potential risk of pathological scarring or irritation of the skin. Based mostly on the dermatologic surgery literature, surgeons in various other specialties have also adhered to these recommendations.^{2,3} Indeed, this warning is listed in the manufacturers' patient information leaflet for isotretinoin. This is in contradistinction to the observation that nodulocystic or severe inflammatory acne patients who have recently completed treatment with isotretinoin are among those most likely to benefit from treatment of their acne scars with modalities such as laser, dermabrasion, or chemical peels.

Basic Science and Animal Studies

Biology of Wound Healing

Wound healing occurs in 3 phases: inflammation, proliferation, and remodeling. Initial injury results in the activation of the clotting cascade and recruitment of neutrophils, with this inflammatory phase typically lasting up to 3 days. The proliferative phase is characterized by granulation tissue formation as a result of fibroblast proliferation and migration, angiogenesis, and the beginning of epithelialization. The proliferative phase starts on Day 3 and peaks on Day 7.

During the remodeling phase, extracellular matrix and collagen networks are reorganized, and wound contracture occurs due to myofibroblasts. Numerous cytokines are required for appropriate wound healing, including the platelet-derived growth factor, fibroblastic growth factor, epidermal growth factor (EGF) and transforming growth factor (TGF)- β .⁴

On a cellular level, hypertrophic scars or keloid scars are associated with an increase in collagen synthesis and in TGF- β . Collagenase (matrix metalloproteinase) activity is required for scar remodeling since non-cross-linked collagen synthesized during early wound healing is replaced with cross-linked collagen during remodeling.

Wound Healing in the Context of Isotretinoin

While there is extensive basic science and animal model literature examining the effects of various retinoids on scarring and the wound-healing process,⁵ in this review only the effects of isotretinoin were assessed. All literature related to other retinoids, including all-trans-retinoic acid, were excluded. In 1985, Abergel and colleagues⁶ determined that isotretinoin (13-cis-retinoic acid) reduced both collagen and collagenase activity and increased the activity of elastase in fibroblasts cultured from excised keloids after a 6-hour incubation with the drug. Isotretinoin has also been shown to inhibit TGF- β -mediated short-term growth in both embryonic and keloidal fibroblasts in culture.^{7,8}

In a study on beagle dogs from 1987, Dzubow and colleagues discovered that 13-cis-retinoic acid at a dose of $2.5 \text{ mg}\cdot\text{kg}^{-1}\cdot\text{d}^{-1}$ for 2 months did not significantly affect wound healing after full-thickness wounding by punch biopsy or dermabrasion when compared with controls. No alteration in the pilosebaceous unit was noted after treatment, and no keloids or hypertrophic scarring were observed.⁹ Frosch and colleagues treated diabetic rats already at risk for poor wound healing with doses of $1 \text{ mg}\cdot\text{kg}^{-1}\cdot\text{d}^{-1}$ for 5 days before performing deep 6 mm punch biopsies. There was no difference in wound surface area between isotretinoin-treated animals and controls after 14 days, but there was a delay in wound healing noted in

animals treated with acitretin. No excessive granulation tissue was observed at any time.¹⁰ Moy and colleagues, found no difference in wound healing or scar appearance in rabbits that were treated with 3 weeks of isotretinoin at a dose of $4 \text{ mg}\cdot\text{kg}^{-1}\cdot\text{d}^{-1}$. Additionally, no differences in the rate of collagen synthesis or in the expression of genetically distinct collagen genes, as determined by messenger RNA level measurements, could be noted in treated animals versus controls at 1, 2, and 3 weeks after injury.¹¹ Gencoglan and colleagues treated rats with 1 week of isotretinoin at $2 \text{ mg}\cdot\text{kg}^{-1}\cdot\text{d}^{-1}$ and found that although there was no difference in scar appearance at 1 week post-incision, mast cells were significantly increased in the treated group compared with the control. Mast cells are thought to influence extracellular matrix deposition and remodeling and are increased in many fibrotic conditions such as uterine fibroids, pulmonary fibrosis, and liver fibrosis.¹² Larson and colleagues compared partial- and full-thickness wound healing in pigs receiving isotretinoin ($2 \text{ mg}\cdot\text{kg}^{-1}\cdot\text{d}^{-1}$) to control pigs that did not receive the medication. The wounds were evaluated at 7, 14, and 28 days, and there was no statistical difference in scars clinically or histologically at any time point.¹³ It should be noted, however, that hypertrophic scarring and keloid formation often appear more than 4 weeks after wounding. Only 1 of the reviewed studies examined clinical effects more than 4 weeks after treatment, and as such this outcome cannot be adequately assessed.

The only in vitro or animal study to implicate isotretinoin in delayed wound healing was that of Arboleda and colleagues. Here the authors concluded that very high doses of isotretinoin ($10 \text{ mg}\cdot\text{kg}^{-1}\cdot\text{d}^{-1}$) for 4 weeks before and 2 weeks after wounding were a cause of delayed wound contracture in guinea pigs assessed 1 and 2 weeks postprocedure. This difference normalized after discontinuation of isotretinoin.¹⁴

Paradoxically, isotretinoin seems to have a stimulating effect on growth in bone and tooth models. Bergoli and colleagues in 2010 showed that isotretinoin at a high dose of $7.5 \text{ mg}\cdot\text{kg}^{-1}\cdot\text{d}^{-1}$ continued daily for 30 days before surgery in a rat model led to accelerated alveolar (tooth socket) repair.¹⁵ De Oliveira and colleagues¹⁶ reported a similar finding in rats treated with

7.5 mg·kg⁻¹·d⁻¹ of oral isotretinoin, demonstrating a nonstatistically significant trend toward accelerated calvarial bone formation compared with controls at 21 days after injury.

Keloids and Scarring After Dermabrasion and Isotretinoin

In 1985, Roenigk and colleagues presented a case series of 9 patients with acne treated with isotretinoin at doses ranging from 0.5 to 1 mg·kg⁻¹·d⁻¹ for 2 to 7 months who had full-face dermabrasion either during treatment or less than 6 months after medication cessation. Dermabrasion was performed using either wire brush and diamond fraise, or diamond fraise alone. When compared with historic controls who had undergone dermabrasion without any concurrent or recent isotretinoin exposure, there was no notable difference in scarring or other outcomes initially; however, an addendum to the article highlighted 2 additional patients who subsequently developed atypical keloids.¹⁷ In 1986, Rubenstein reported a case series of 6 patients who developed keloidal scarring after treatment with wire brush or diamond fraise full-face dermabrasion while on a course of isotretinoin at 0.5 to 1 mg·kg⁻¹·d⁻¹ for 4 to 14 months. Specifically, 3 of the patients received dermabrasion while still medicated with isotretinoin, and 3 had stopped treatment 2.5 to 6 months earlier. Keloids emerged 1 to 4 months after treatment. Of note, one of the patients was concurrently being treated with prednisone 10 mg daily and sulfasalazine for ulcerative colitis, and another was receiving isoniazid, pyridoxine, and rifampin for a positive tuberculin test.¹⁸ In 1988, Zachariae reported 2 cases of delayed wound healing and keloid formation after dermabrasion while receiving isotretinoin. In one case, a patient received 60 mg daily of isotretinoin for acne and dermabrasion for facial acne scarring and experienced a 3-month delay in wound healing with subsequent development of a keloid. The second patient was treated with dermabrasion of the nose for rhinophyma. Immediately after the procedure, he began a course of isotretinoin 60 mg daily for rosacea. This resulted in prolonged healing of 4 weeks and keloid formation on the right nose at 8 weeks.¹⁹ Alt and colleagues reported scarring after dermabrasion in 4 patients on

isotretinoin.²⁰ An additional case report by Katz and colleagues reported a female patient treated for acne scarring with diamond fraise full-face dermabrasion. She was started on isotretinoin to address an acne flare (dose not specified) 6 weeks after the procedure and developed hypertrophic scars at 14 weeks post-dermabrasion.²¹

Limited and Less-Invasive Dermabrasion Procedures and Scarring With Isotretinoin

More recent literature on the use of dermabrasion suggests that a less invasive and more focal procedure may be safe to perform while on isotretinoin, or in cases when the drug has recently been discontinued. In a prospective study, 7 patients on 10 to 40 mg daily of isotretinoin for 1 to 6 months underwent manual (without hand engine) diamond fraise dermabrasion to focal areas of preexisting scarring on the face. No procedure-associated scarring was noted at 180 days postprocedure. Wound-healing postprocedure was normal, with complete re-epithelization in all 7 cases.²² Picosse and colleagues presented a prospective study involving 10 patients with depressed facial scars and isotretinoin exposure within the previous 1 to 3 months treated with medium-depth chemical peel to the entire face and manual sandpaper dermabrasion to 1 cm² areas of focal scarring. At 6 months follow-up, complete re-epithelialization had occurred without hypertrophic scars or keloids. Depressed acne scars were improved, and only 1 patient of Fitzpatrick skin type V developed postinflammatory hyperpigmentation.²³

Scarring After Laser and Isotretinoin

Only 3 cases could be found in the literature of abnormal scarring occurring in the context of isotretinoin exposure less than 6 months before performing laser procedures. These cases involved, respectively, an argon laser, a fully ablative erbium: YAG laser, and a pulsed-dye laser. Zachariae reported a case of keloidal scarring emerging 12 weeks after treatment in a patient treated with an argon laser while concurrently on isotretinoin 60 mg daily for 1 month¹⁹ Bernstein reported keloid formation after treatment of a capillary malformation on the face and neck with a 585-nm pulsed-dye laser, 450 microsecond pulse

duration at a fluence of 6.0 J/cm² and a spot size of 5 mm in a patient who had started isotretinoin 2 weeks before laser. Keloids on the chest occurred 2 weeks after laser treatment.²⁴ Khatri described a 19-year old boy treated with 4 months of 80 mg/d isotretinoin who was treated focally with nonablative fractional laser (100 mJ/mB, 10-mm spot, 15 milliseconds, 3 passes using a diode 1,540-nm laser), ablative fractional laser (91 J/cm², rep rate of 30 Hz, 3 passes using an erbium:YAG 2,940-nm laser), and full ablative laser (2 J, 5-mm spot, 8 Hz, 8 passes using an erbium:YAG 2,940-nm laser). Only the fully ablative treatment seemed to elicit abnormal healing by clinical examination and biopsy after 6 months.²⁵

Fractional Ablative and Nonablative Laser With Isotretinoin

There are 2 randomized controlled trials in which patients on isotretinoin therapy were concomitantly treated with ablative or nonablative laser. In one such study, acne scar patients on isotretinoin (0.5 mg·kg⁻¹·d⁻¹) received no treatment (n = 55) versus treatment with fractional CO₂ laser (n = 25). No differences in scarring or side effects were noted between the groups.²⁶ In 2014, Yoon and colleagues, assessed the safety and the efficacy of nonablative fractional 1,550 nm Erbium-doped fiber laser treatment preceded by 1 month of low-dose isotretinoin (10 mg/d) for the treatment of acne and acne scarring in 35 patients, compared with 18 control patients randomized to receive isotretinoin only. There was no group-specific worsening of acne scars, or induction of hypertrophic scars or keloids.²⁷ Leal and colleagues described a case control study in which 60 acne scar patients treated with a 1,550 nm nonablative fractionated erbium:fiber laser received low-dose isotretinoin (20 mg/d) or no retinoid treatment. No difference in adverse outcomes including scarring, erythema, or hyperpigmentation was noted between the groups.²⁸

Case report data are consistent with these findings. As noted earlier, in a patient treated with isotretinoin and various fractional and ablative lasers, Khatri found that scarring developed only in the fully ablative laser site. Punch biopsies demonstrated flattened epidermis

and fully evolved dermal scar in the fully ablative laser site, with mild papillary dermal fibrosis in the ablative fractional laser treatment site, and only mild thickening of the papillary dermis in the nonablative fractional laser site.²⁵ A case report of successful, uncomplicated treatment with a fractionated CO₂ laser was published by Kingsley in 2012 (1 patient who completed isotretinoin therapy 4 months before laser treatment—dose unspecified).²⁹ An abstract from the American Society for Lasers in Medicine and Surgery (ASLMS) annual meeting in 2011 reported no hypertrophic scars or keloids in 35 patients with Fitzpatrick skin types II-V receiving low-dose isotretinoin (10 mg daily) for at least a month before treatment with a 1,550 nm nonablative fractional laser (Fraxel re:store).³⁰

Kim and colleagues reported normal re-epithelialization and no hypertrophic scars or keloids at 6 months in 20 patients treated with full-face fractional ablative CO₂ laser resurfacing for acne scarring during and/or within 1 to 3 months of discontinuing oral isotretinoin treatment (10–60 mg/d).³¹ Park and colleagues report a case of a patient successfully treated for multiple eccrine hidrocystomas of the face with oral isotretinoin 20 mg/d plus fully ablative pulsed CO₂ laser resurfacing. No scarring was observed at 6 months follow-up.³² Noh and colleagues similarly found no scarring or abnormal wound healing in a case of sebaceous hyperplasia treated with CO₂ laser resurfacing and concurrent isotretinoin 20 mg/d for 1 year and 10 mg/d for the following year (for a cumulative dose of 150 mg/kg).³³

Laser Hair Removal With Isotretinoin

No adverse events were noted in 6 female patients with acne with facial hirsutism and Fitzpatrick skin types II or III treated with isotretinoin at a daily dose of 0.5 to 1 mg/kg for 1 to 3 months before undergoing laser hair removal with an 810 nm diode laser. The isotretinoin dose was reduced to 0.3 to 0.5 mg·kg⁻¹·d⁻¹ during the course of the laser treatments, which were performed at approximately 2-month intervals, for a total of 4 to 9 treatments per patient.³⁴ Khatri and colleagues reported uncomplicated laser hair removal for patients on isotretinoin in several different case series. The first was in 2004, when 7 patients with Fitzpatrick skin

types II or III were treated with an 810-nm diode laser to the axilla, bikini, or chin area. At the time of the first laser treatment, patients had received isotretinoin 20 to 80 mg daily for 1 to 6 months.³⁵ In 2006, Khatri reported a series of 6 skin type II female patients treated with isotretinoin therapy for nodular acne for an average duration of 3 months (range: 2–6) with an average dose of 73 mg/d (range: 40–80 mg) before receiving concurrent hair removal treatments to the axilla, bikini, chin, or sideburn area using a long-pulse flash lamp system (LuxRS handpiece and a wavelength of 650–1,200 nm; [EsteLux; Palomar Medical, Cynosure, Westford, MA]) without developing scarring or delayed wound healing.³⁶

In a retrospective analysis of 11 patients with Fitzpatrick skin types III–V on isotretinoin therapy 20 to 60 mg/d for 4 to 12 months for acne vulgaris who received concurrent laser hair removal using a long-pulsed 1,064 nm Nd:YAG laser (fluence 30–55 J/cm², pulse duration 10–30 ms, spot size 10 mm, repetition rate 2 Hz; CoolGlideTM; Cutera, Brisbane, CA), there was no incidence of vesiculation, permanent pigmentary alterations, or scarring in any patient.³⁷ Of note, isotretinoin was held for 3 days before and after each laser treatment. In another study, acne scar patients on isotretinoin (0.5 mg·kg⁻¹·d⁻¹) were randomized to receive no treatment versus treatment with hair removal laser. No differences in scarring or side effects were noted between the 2 treatment groups.²⁶ Patwardhan and colleagues describe normal healing in laser hair removal patients on isotretinoin based on their single-center experience.^{38,39}

Other Lasers With Isotretinoin

Cumulatively, several abstracts report over 100 patients on isotretinoin treated with numerous devices, including Q-switched alexandrite and Nd:YAG lasers, without evidence of scarring or abnormal wound healing after up to 7 years of follow-up.^{30,38,39} Similarly, Moradi found that 148 patients receiving isotretinoin 1 mg·kg⁻¹·d⁻¹ for at least 4 months treated with 3 sessions of low-power pulsed-dye laser and 5 weekly sessions with an Er:YAG laser did not incur scarring or sequelae compared with age-matched controls.⁴⁰

Chemical Peels and Isotretinoin

Gerber reported a case of keloidal scarring after treatment with 70% glycolic acid peel after 10 weeks of treatment with 10 mg isotretinoin 3 times per week.⁴¹

In another study, 60 consecutive patients with moderate to severe facial acne were randomized to receive either oral isotretinoin 20 mg/d for 16 weeks or oral isotretinoin 20 mg/d along with 20% salicylic acid peels every 2 weeks for 16 weeks. Acne was more effectively treated in the isotretinoin and peel group, and there were no events of scarring or delayed wound healing in either treatment arm.⁴²

Incisional and Excisional Surgery and Isotretinoin

Performance of incisional and excisional surgical procedures while on isotretinoin therapy is controversial. Allen and colleagues reported 3 patients who presented with nasal tip deformities (bossa formation, asymmetry, and prominence of a composite graft) subsequent to the use of isotretinoin initiated within 2 years after rhinoplasty. The nasal tip deformities were first observed within 6 months after 6-month courses of isotretinoin were started.⁴³ Conversely, a case report by Yew and colleagues⁴⁴ found normal healing and resolution of genital warts when isotretinoin was used immediately after surgical debulking.

Systematic reviews on the safety of isotretinoin in incisional surgery do not support the need for cessation of isotretinoin within 6 months of cold-steel surgical procedures.^{2,3,45} In a review of isotretinoin in elective plastic surgical procedures, Ungarelli observed that although most plastic surgeries could be performed safely while on isotretinoin, there is a theoretical risk of necrosis in muscle flaps because of the associated increase in creatine phosphokinase and the potential for rhabdomyolysis in patients who are taking isotretinoin.³

Other Surgeries, Including Nonsurgical Procedures, and Isotretinoin

There are circumstances in which dermatologic surgeons may be consulted by other services regarding the

safety of continuing isotretinoin during, or before, surgery. Experts have suggested that isotretinoin is contraindicated within 6 months of LASIK procedures because of the potentially increased risk of dry eye.⁴⁶ Alternatively, administration of isotretinoin for 4 to 8 weeks after surgical repair of proliferative vitreoretinopathy seems to be safe and may in fact result in improved rates of retinal attachment, decreased macular pucker, and improved postoperative vision.^{47,48} In a retrospective cohort study of 26 patients having wisdom tooth extraction, 25 while on isotretinoin and 1 within a month of discontinuing the medication, Sharma detected higher rates of alveolar osteitis (3/26, 11.4%) than expected (3%–5%).⁴⁹ However, association with isotretinoin and alveolar osteitis could not be made because of limited sample size; thus, there is insufficient evidence at this time for deferring molar surgery during treatment with isotretinoin.

Other Dermatologic Procedures Not Listed Elsewhere, and Combination Procedures, With Isotretinoin

Chandrashekar reported a comparative, retrospective cohort study of 110 patients, 55 on oral isotretinoin and 55 not, treated for acne scars or hirsutism with various cosmetic dermatologic procedures (including dermaroller, microneedling, radiofrequency tightening, laser hair removal, and ablative CO₂ resurfacing). Patients with known keloidal tendencies, active acne, or active infection were excluded. The treatment group received 0.5 mg·kg⁻¹·d⁻¹ isotretinoin in addition to topical acne treatment while the historical control group received topical therapy only. Atypical scarring, delayed wound healing, keloids, or hypertrophic scars were not observed in any patient.²⁶

Dermatologic Procedures in the Context of Isotretinoin: Prospective Studies, Systematic Reviews, Meta-Analyses, Guidelines Documents, and Consensus Statements

Most studies assessing the impact of isotretinoin on wound healing and scar formation after cosmetic procedures have been case series and small cohort studies. One larger prospective study recently reported by Mahadevappa and colleagues⁵⁰ prospectively tracked adverse events in 183 patients

receiving 503 procedural interventions. The procedures performed included a wide range of cosmetic treatments, including laser, microdermabrasion, and incisional surgery, with 1-year follow-up revealing only 2 cases of keloid formation and sporadic instances of transient erythema and hyperpigmentation. This supports previous work that indicated a low rate of abnormal scarring in the context of isotretinoin and suggests a likelihood of significantly less than 1% per patient and per procedure.

A multidisciplinary group headed by Leah K. Spring, DO, and Andrew C. Krakowski, MD, recently convened a face-to-face consensus conference to discuss the timing of procedural interventions in the context of isotretinoin use. This important effort included representation from every subspecialty of clinical dermatology, including general medical dermatology, pediatric dermatology, and dermatologic surgery. Relevant literature identified through a comprehensive literature search was categorized by subtopic, with each topic reviewed by teams of 2 reviewers, including a procedural dermatologist and a pediatric dermatologist. The 6 topics reviewed were wound healing/animal models, dermabrasion, chemical peels, surgery, laser hair removal, and ablative/nonablative laser. Authors concluded that there is insufficient evidence to support delaying manual dermabrasion, superficial chemical peels, elective surgery, laser hair removal, and scar ameliorating procedures such as fractional ablative and nonablative laser for patients currently on, or having recently completed isotretinoin. Mechanical dermabrasion and fully ablative laser procedures are not recommended based on the available literature. The consensus article from this group was notable for its emphasis on process, including an exhaustive literature review and formal review of the identified literature by small, diverse dedicated teams, followed by group consensus.

Major Recommendations

The ASDS specific recommendations emerged from the 2 rounds of Delphi process and were then adopted unanimously (i.e., full consensus) by the members of the task force. The rating of the quality of evidence

TABLE 1. Level of Evidence and Study Characteristics

Study	No. of Subjects	Design	Level of Evidence	Intervention	Intervention Timing	Isotretinoin Dose	Findings
Yoon and colleagues ²⁷	35	RCT	1b	Erbium 1,550 nm laser	Concurrent	10 mg/d	Normal healing
Chang and colleagues ⁴⁸	35	RCT	1b	Surgical repair of proliferative vitreoretinopathy	<1 mo after	10 mg/d	Improved surgical outcomes, normal healing
Picosee and colleagues ²³	10	Cohort	2b	Dermabrasion + TCA 35% chemical peel	1–3 mo prior	Cumulative dose: 122–161 mg/kg	PIH in 2 patients, normal healing
Chandrashekar and colleagues ²⁶	110	Retrospective	4	CO2 laser, dermaroller, microneedling, Nd:Yag 1,064 nm, IPL or Diode 980 nm	Concurrent	0.5 mg·kg ⁻¹ ·d ⁻¹	Normal healing, 1 case of PIH
Fekrat and colleagues ⁴⁷	20	Cohort	2b	Surgical repair of proliferative vitreoretinopathy	<1 mo after	40 mg BID	Improved surgical outcomes, normal healing
Kar and colleagues ⁴²	60	Cohort	2b	Salicylic acid 20%	Concurrent	20 mg/d	Normal healing and improved resolution of acne scars with addition of chemical peel
Sharma and colleagues ⁴⁹	26	Retrospective	4	Wisdom tooth extraction	Concurrent, 1 mo prior	Not specified	Increased rate of alveolar osteitis (1.4%) compared to cited rates (3%–5%)
Leal and colleagues ²⁸	60	Case-Control	3b	Fractionated Erbium	Concurrent, >6 mo prior	20 mg/d	Normal healing
Systematic Review Spring and colleagues, 2017		Systematic review	2a		na	na	Large surface dermabrasion is contraindicated, there is no evidence to support waiting 6 mo before treating with laser hair removal, nonablative lasers, surgery or chemical peels.
Abdelmalek and colleagues ⁴⁵		Systematic Review	2a		na	na	Recommend not delaying surgery if patient is on systemic retinoid, little evidence available to support waiting 6 mo before treating with cosmetic intervention

TABLE 1. (Continued)

	No. of Subjects	Design	Level of Evidence	Intervention	Intervention Timing	Isotretinoin Dose	Findings
Ungarelli and colleagues ³		Systematic review	3a		na	na	Based on pharmacokinetics, 30 days should be sufficient to avoid any possible complications from isotretinoin
Wootton and colleagues ²	1	Systematic review, case report	2a	Shoulder arthroscopy	6 mo prior	20 mg/d	Normal healing, no consistent evidence of side effects from using isotretinoin within 6 mo of procedure
Case Series/Reports							
Roenigk and colleagues ¹⁷	11	Case series	4	Dermabrasion	Concurrent, 1–3 mo prior	0.5–1 mg·kg ⁻¹ ·d ⁻¹	Milia 1/11, 2 subsequent patients reported with unusual keloids
Rubenstein and colleagues ¹⁸	6	Case series	4	Dermabrasion	Concurrent, 2–6 mo prior	0.5–1 mg·kg ⁻¹ ·d ⁻¹	Atypical keloids 6/6 with complete or partial resolution
Zachariae ¹⁹	3	Case series	4	Dermabrasion and argon laser	Concurrent	60 mg/d	Atypical keloids 3/3
Katz and colleagues ²¹	1	Case report	4	Dermabrasion	2 mo after	Not specified	Keloidal scarring
Bagatin and colleagues ²²	7	Case series	4	Dermabrasion	Concurrent	10–40 mg/d	Hypertrophic scarring in 1/7 patients
Bernstein and colleagues ²⁴	1	Case report	4	PDL 585 nm laser	Concurrent	Not specified	Keloidal scarring
Khatri and colleagues ³⁷	11	Case series	4	Nd:YAG 1,064 nm laser	Concurrent	0.5 mg·kg ⁻¹ ·d ⁻¹	Normal healing
Khatri and colleagues ³⁵	7	Case series	4	Diode 810 nm laser	Concurrent	20–80 mg/d	Normal healing
Cassano and colleagues ³⁴	6	Case series	4	Diode 810 nm laser	Concurrent	0.5–1 mg·kg ⁻¹ ·d ⁻¹ reduced to 0.3–0.5 mg·kg ⁻¹ ·d ⁻¹	Normal healing
Khatri and colleagues ³⁶	6	Case series	4	Long-pulse flash lamp	Concurrent	40–80 mg/d	Normal healing
Park and colleagues ³²	1	Case Report	4	Ultrapulse CO2	<1 mo prior	20 g/d × 6 wk	Normal healing and resolution of hydrocystomas
Kim and colleagues ³¹	20	Case series	4	CO2 fractional or ablative	Concurrent, 1 mo prior	10–40 mg/d	Normal healing
Noh and colleagues ³³	1	Case report	4	Fractional CO2	<1 mo after	150 mg/kg	Normal healing

TABLE 1. (Continued)

	No. of Subjects	Design	Level of Evidence	Intervention	Intervention Timing	Isotretinoin Dose	Findings
Khatri and colleagues ²⁵	1	Case report	4	Scar split and treated with: nonablative fractional 1,540 nm, ablative fractional erbium:YAG 2,940 nm, ablative Erbium:YAG 2,940 nm	Concurrent	80 mg/d	Normal healing and biopsy with nonablative and ablative fractional laser, clinical and biopsy scar with full ablative laser
Gerber and colleagues ⁴¹	1	Case report	4	Glycolic acid 70%	Concurrent	10 mg/d TIW	Significant erythema and hyperpigmentation
Larson and colleagues ¹³	1	Case report	4	Hidradenitis suppurative excision	4 mo prior	not specified	Normal healing
Allen and colleagues ⁴³	3	case series	4	Rhinoplasty	7–24 mo after	not specified	Nasal tip and soft tissue deformities in 3/3 patients
Yew and colleagues ⁴⁴	1	Case report	4	Surgical debulking of genital warts	<1 mo after	20 mg/d tapered over 8 mo	Normal healing with resolution of warts
Abstracts							
Kingsley and colleagues ²⁹	1	Abstract case report	na	Fractionated CO2	4 mo prior	6 month course, dose not specified	Normal healing
Alissa and colleagues ³⁰	100	Abstract, case series	na	Erbium, vascular, Q-switched alexandrite and Q-switched 532 nm double frequency, Q-switched Nd:YAG, nonablative fractional lasers	Concurrent	not specified	Normal healing
Hann and colleagues ³⁰	35	Abstract	na	Infrared fractional laser (1,550 nm)	Concurrent	10 mg/d	Acneiform eruption in 1 case, otherwise, normal healing
Moradi and colleagues ⁴⁰	148	Abstract, RCT	na	Nlite and Er:YAG 3	Concurrent, 4 mo prior	1 mg·kg ⁻¹ ·d ⁻¹	Similar rates of hyperpigmentation in both groups, no increase in hypertrophic/keloidal scarring
Opinion							
Coleman and colleagues ²⁰		Opinion	5	Dermabrasion	na	na	Wait 1 yr after cessation and start isotretinoin >6 mo
Patwardhan and colleagues ³⁸		Opinion/single clinic experience	5	Alexandrite, Nd:YAG, Erbium	Concurrent		Normal healing in laser hair patients on isotretinoin

PIH, postinflammatory hyperpigmentation; RCT, randomized controlled trial; TIW, three times per week.

TABLE 2. GRADE Quality of Evidence Associated With Each Recommendation

<i>Recommendation</i>	<i>GRADE Score</i>
Dermabrasion	
Focal or superficial manual dermabrasion to treat localized areas of the face while on isotretinoin or within 6 months after isotretinoin cessation is not associated with increased risk of scar or delay in wound healing, and there is no evidence in the literature that supports a need to delay treatment.	B
Full-face dermabrasion and mechanical dermabrasion with rotary devices is not recommended within 6 months of isotretinoin use, as it may be associated with increased risk of adverse events in selected patients.	B
Lasers/energy devices	
There is no evidence to justify delaying treatment with hair removal lasers and lights, vascular lasers, nonablative fractional devices, and ablative fractional devices in patients who are receiving isotretinoin or have received isotretinoin within the past 6 months.	B
Fully ablative (i.e., non-fractional) treatment of the entire face or nonfacial regions should generally be avoided until 6 months after completion of isotretinoin treatment because of the likely elevated risk of avoidable adverse events.	C
Chemical peels	
Superficial chemical peels can be safely administered to patients taking isotretinoin or within 6 months after isotretinoin therapy.	B
Insufficient data on the use of medium or deep chemical peels while on isotretinoin to preclude a recommendation in this case.	D
Other surgeries, including incisional and excisional surgery and nondermatologic procedures	
Isotretinoin should be stopped before LASIK surgery because of the risk of dry eyes.	D
The data for incisional and excisional cutaneous surgery on isotretinoin is insufficient to make any recommendations. In particular cases, incisional or excisional surgery may be medically necessary in patients receiving isotretinoin.	D
GRADE, Grading of Recommendations Assessment, Development and Evaluation.	

associated with each recommendation follows in parentheses.

- (1) Focal or superficial manual dermabrasion to treat localized areas of the face while on isotretinoin or within 6 months after isotretinoin cessation is not associated with increased risk of scar or delay in wound healing, and there is no evidence in the literature that supports a need to delay treatment (B). Full-face dermabrasion and mechanical dermabrasion with rotary devices is not recommended within 6 months of isotretinoin use, as it may be associated with increased risk of adverse events in selected patients (B). Significantly, the expert panel noted that large area dermabrasion is seldom used today and the relevant recommendations are therefore of primarily historical interest.
- (2) There is no evidence to justify delaying treatment with hair removal lasers and lights, vascular lasers, nonablative fractional devices, and ablative fractional devices in patients who are receiving isotretinoin or have received isotretinoin within the past 6 months (B). Fully ablative (i.e., nonfractional) treatment of the entire face or nonfacial regions should generally be avoided until 6 months after completion of isotretinoin treatment because of the likely elevated risk of avoidable adverse events (C).
- (3) Superficial chemical peels can be safely administered to patients taking isotretinoin or within 6 months after isotretinoin therapy (B). Insufficient data on the use of medium or deep chemical peels while on isotretinoin to preclude a recommendation in this case (D).
- (4) Isotretinoin should be stopped before LASIK surgery because of risk of dry eyes (D). The data for incisional and excisional cutaneous surgery on isotretinoin are insufficient to make any recommendations (D). In particular cases, incisional or excisional cutaneous surgery may be medically necessary in patients receiving isotretinoin.

The phrase “in a clinically appropriate manner” is used to denote usual and customary practice, as the precise method of performing cosmetic or surgical procedures is not the subject of this guideline.

Rating Scheme for the Strength of the Recommendations

Grading of the level of evidence and strength of recommendations in this clinical consensus statement was performed using the Oxford method (Table 1) and the GRADE system (Table 2), respectively.

Most of the consensus recommendations are founded on a substantial volume of case series and cohort study data, not on the results of randomized control trials, which are generally impractical and not likely forthcoming in this setting. In addition, the task force determined that the benefits of the recommendations to provide skin procedures in the context of isotretinoin in particular clinical scenarios outweighed the potential risks and burdens, which were generally deemed to be low. When insufficient evidence to offer a recommendation is noted in the recommendations, the task force intended that this not be construed as either implicit confirmation of safety or of risk.

Potential Benefits

Potential benefits of this guideline include early access to scar treatments for many patients who are at the highest risk for scarring, and thereby, potentially improved patient quality of life.

Potential Harms, Contraindications, and Qualifying Statements

The potential harms, including scarring, hyperpigmentation, or other sequelae of cosmetic procedures, have been reported in case reports and case series only. These risks were generally rated low to very low by the task force, except in the instances of insufficient evidence and full-face ablative resurfacing or dermabrasion. Although there are no significant data in the literature to support delaying a range of skin procedures in patients being treated with isotretinoin or those who have recently undergone such treatment, in selected cases it may be appropriate to provide patients with counseling regarding the relevant benefits and risks.

The task force issued the following qualifying statement: when procedures were performed in the setting of isotretinoin, the drug dosage ranged from 10 to

80 mg (0.25–1 mg/kg) daily. Although it is not clear that higher doses of isotretinoin are more harmful than lower doses when performing procedures, it may be prudent to treat with lower dose isotretinoin (e.g. 20–40 mg; 0.25–0.5 mg/kg) (C).

Implications Regarding Treatment of Acne and Acne Scarring

Severe acne is a common and disfiguring condition that may be treated with oral isotretinoin but may nonetheless leave affected patients with scarred skin. Prompt treatment of the associated scarring can relieve the significant psychosocial impact on affected patients. The data reviewed in the preceding analysis suggest that procedural interventions during or soon after isotretinoin treatment can safely and effectively address acne scarring and similar disorders, thus providing relief to patients without the need for protracted waiting.

Consensus Statement Approval

This consensus statement was approved by the ASDS Guidelines Task Force and was adopted as amended by the ASDS Board of Directors on November 9, 2016, whereupon it was immediately in effect.

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