# An Algorithmic Approach to Hypertrophic Scars and Keloids: Maximizing Nonsurgical Options

**Shauna Kranendonk, MD; Suzan Obagi, MD**

Hypertrophic scars and keloids are very common concerns among dermatologic patients, whether from a medical or cosmetic standpoint. The treatment of these lesions is challenging and associated with variable response or recurrence. The authors of this study review the most current literature on the treatment of hypertrophic scars and keloids ranging from intralesional therapies to laser and surgical modalities. The authors describe a treatment algorithm employing combination therapies while aiming to limit the use of surgical intervention. Representative case reports are presented to illustrate the use of solo or combination therapy.

Hypertrophic scars and keloids are routinely encountered in the cosmetic dermatology setting. Patients either present with cosmetic concerns or have symptoms of pain and/or pruritus associated with these lesions. Occasionally, there may be a functional component if the scar interferes with movement of the involved area.

Intralesional corticosteroids have been a mainstay of treatment, but numerous alternative modalities are available. Proper sequential use of these modalities, particularly when used early in the course of disease, can impede the development of hypertrophic and keloidal scarring and result in superior cosmetic and functional outcomes.

This article will review factors contributing to hypertrophic scars and keloids and present an algorithmic approach for treatment of these lesions (Figure 1). The emphasis will be on maximizing nonsurgical intervention due to the risk of recurrence associated with excision of these lesions.

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## BACKGROUND

Hypertrophic scars differ clinically from keloids, in that hypertrophic scars do not grow beyond the boundaries of the original wound, while keloids grow horizontally beyond the margins of the original wound.[1] Hypertrophic scars are less likely to recur after treatment and show no racial predilection.[2] Hypertrophic scars and keloids occur more frequently on the face, neck, and chest, but can occur at any anatomic location.

Risk factors for development of hypertrophic scars or keloids include trauma, mechanical forces (namely increased wound tension or stretching), infection, inflammation, and foreign body reaction.[3] Genetic susceptibility also is a factor with increased incidence of keloids in Fitzpatrick skin types IV to VI.

Histologically, hypertrophic scars display a nonspecific dermal fibroblastic proliferation, thickened dermis, and epidermal atrophy. Hypertrophic scars are more cellular than keloids, which in contrast display characteristic hypocellular, glassy, hyalinised, eosinophilic collagen fibers.[4] It is possible that hypertrophic scars and keloids represent a continuum of the same fibroproliferative process.[5]

## PATIENT EVALUATION

In most instances, a history of recent surgery or trauma with clinical findings of flesh-colored to erythematous fibrotic plaques is sufficient to make a diagnosis, and a biopsy becomes unnecessary. Malignant tumors, including dermatofibromasarcoma protuberans,[6,7] and giant cell fibroblastoma,[8] along with infections and sarcoidosis should be considered in the differential diagnosis in the absence of supportive findings. Lobomycosis, or lacaziosis, is a granulomatous fungal infection caused by *Lacazia loboi* that presents with keloidlike scarring. *Lacazia loboi* is endemic in Central and South America, particularly the Amazon basin, and has been reported in dolphins.[9] Soil and vegetation are likely sources of infection.

Postprocedural impending scarring often presents as an area of erythema or induration. This is especially true in post–skin resurfacing patients. When intense or prolonged postprocedural erythema is seen, infection or contact dermatitis should be considered in the differential diagnosis. Bacterial skin infection is due most frequently to *Staphylococcus aureus* and may present with erythema, warmth, discharge, and/or pustules. Bacterial infections with gram-negative organisms, such as *Pseudomonas aeruginosa*, are less frequently encountered. Yeast infections due to *Candida* species may be seen, especially with prolonged use of petrolatum-based emollients or recent use of antibiotics. Herpes simplex infection also may be seen and presents with burning or tenderness along with vesicles, erosions, and/or crusting. Allergic contact dermatitis can develop to topical antibiotics or topical emollients used in the postoperative setting. Appropriate cultures for fungus, virus, and/or bacteria, along with history of topical applications, should be obtained. Treatment of the etiology behind the postprocedural erythema may halt progression of this area to an organized scar. However, should the area remain erythematous, aggressive management is required to minimize or prevent hypertrophic or keloidal scarring from occurring.

## TREATMENT APPROACHES

The key to successful treatment of hypertrophic scars or keloids is early intervention. Our approach to both types of scars is similar so we will refer to these lesions as hypertrophic scars/keloids (HTS/K). The first signs of impending HTS/K are erythema, pruritus, and tenderness, often manifesting as early as 1 to 2 weeks after the initiating event. Following skin resurfacing with peels, dermabrasion, or laser, impending scar formation may simply present with intense erythema (substantially more redness than typically encountered at the 1- to 2-week point) or an area of delayed wound healing. In most cases, tenderness or pruritus will accompany the intense erythema, helping to distinguish early HTS/K from normal postprocedural erythema. Once a diagnosis of HTS/K or impending HTS/K has been established, we follow a treatment algorithm beginning with pulsed dye laser (PDL)(Figure 1).

### Vascular Laser

The PDL is a mainstay for treatment of early HTS/K. The PDL treatment is beneficial in reducing erythema and helps prevent the development of HTS/K.[10] Through the concept of selective photothermolysis, the PDL is believed to damage the microvasculature of the impending scar.[11] Selective photothermolysis refers to the specific targeting of a structure or tissue through the use of a precise wavelength of light at the proper pulse width to heat the desired target while minimizing unnecessary heating of the normal surrounding tissue.

Studies of keloids show the 585-nm PDL decreases fibroblast proliferation and type III collagen deposition.[12] Pulsed dye laser treatment has been associated with downregulation of transforming growth factor-beta 1 (TGF-β1) expression. Transforming growth factor-β1 is thought to induce and regulate collagen formation.[13,14] Downregulation of TGF-β1 also has been linked to an increase in matrix metalloproteinase-13 (collagenase-3) function.[15]

The authors began treatment with a 595-nm PDL (Perfecta or VBeam, Candela Corporation), as early as 1 to 2 weeks postexcision or surgery, with settings of 10-mm spot, 1.5-millisecond pulse duration and fluences of 5.0 to 7.5 J/cm$^2$, cryogen 30/20 delay/duration in millisecond. While some physicians may use higher fluences when treating HTS/K, several studies using higher fluences have not shown notable differences in outcomes.[16-18] A more recent article suggested fluences used to treat HTS/K should range from 4.5 to 7.5 J/cm$^2$ with spot sizes of 5- to 10-mm (smaller spot size used higher fluences).[19] Patients with Fitzpatrick skin types V and VI should be approached with caution, using lower fluences and reduced cryogen cooling to prevent injury to the skin. Alternatively, Nd:YAG lasers can be used in these patients so as to minimize the competition of the laser

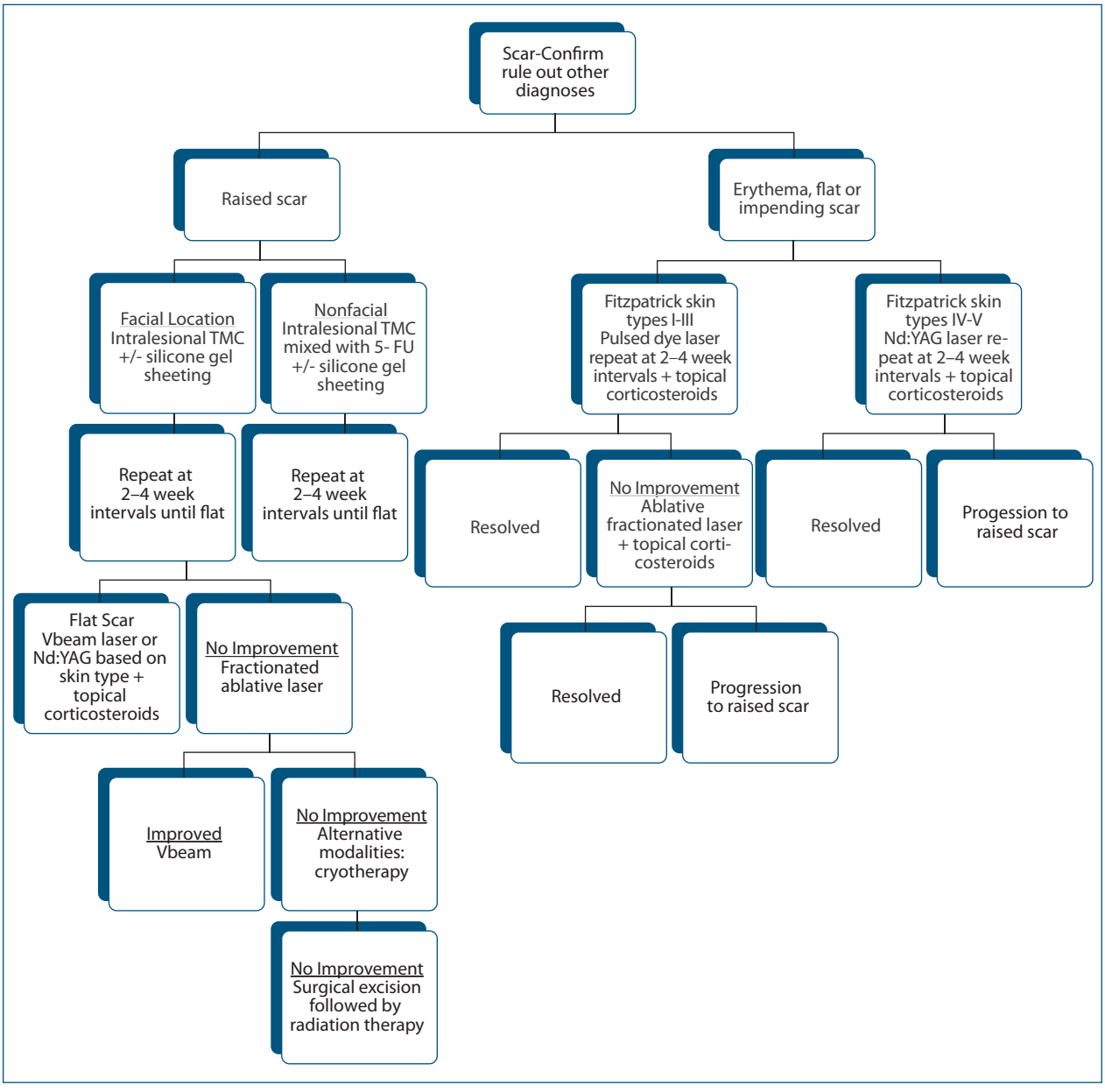


**Figure 1.** Algorithm to the approach and treatment of hypertrophic and keloidal scars. Abbreviation: TMC, triamcinolone acetonide.

beam with melanin.[20] Nd:YAG lasers are operated using vascular lesion settings but at slightly lower fluences.

Alternatively, newer Nd:YAG lasers can be operated in a new manner that is used for nonablative photorejuvenation. This new method allows the Nd:YAG lasers to be operated in high-fluence (12–18 J/cm$^2$) but short microsecond bursts (0.3 µs) modes at 5 to 8 Hz. The laser is waved over the skin surface from a distance of about 3 to 4 cm. A 1-cm area of scar is usually treated until about 200 to 500 pulses are delivered. It is imperative to stop and let the skin cool if the patient feels the heat sensation to be uncomfortable.

Patients are selected for vascular laser treatments based on the appearance of an impending scar (prolonged erythema, pruritus, or delayed healing) or if they have a slightly elevated, erythematous scar. Additionally, these patients are prescribed a mid- to high-potency topical steroid to be applied to the affected area 3 times per week. Patients are treated with vascular lasers at 2-week intervals until the erythema has resolved. Thus, this modality is best employed when the scar is just forming or is still relatively thin.

Practices that do not have access to a PDL or Nd:YAG laser can utilize broadband light devices with caution. Broadband light lasers usually have a larger spot size that may require protecting the normal tissue while only treating the involved area.

## Intralesional Therapy

Scars that progress to fibrotic raised plaques require the use of intralesional corticosteroids. While some studies have shown reduction in scar size with use of PDL,[21] the authors prefer the use of intralesional corticosteroids to reduce scar thickness. The results of intralesional steroids usually appear much faster than the results of PDL alone.

Intralesional corticosteroid monotherapy has been a mainstay of treatment for HTS/K.[22,23] The exact mechanism of action is not fully understood. Synthetic corticosteroids are believed to inhibit fibroblast proliferation, decrease the production of proinflammmatory cytokines, chemokines, adhesion molecules, lysosomal enzymes, and tissue inhibitor of metalloproteinase.[24] Systemic side effects of corticosteroids include menstrual dysfunction in women, adrenal cortical axis suppression, cushingoid features, hyperglycemia, the development of glaucoma or cataracts, and avascular necrosis. Local side effects include skin and subcutaneous tissue atrophy, telangiectasia, steroid acne, and hypopigmentation.[25] The lowest effective concentration of triamcinolone acetonide should be used to minimize side effects. As will be described below, concentrations are based on anatomic location and scar thickness with lower concentrations of triamcinolone acetonide used in areas of thin skin, such as the face, or in scars that are less raised.

## Facial HTS/K

The authors treat HTS/K on the face with triamcinolone acetonide intralesional injection. The authors begin with concentrations of 2.5 to 5 mg/mL of triamcinolone acetonide with maximum facial concentration of 20 mg/mL. Injections are performed using a 27-gauge needle. The use of a 27-gauge needle is important because smaller gauge needles do not allow adequate delivery of drug into the scar, and require greater pressure to inject. The needle should be placed into the center of the scar tissue, avoiding injecting into the subcutaneous tissue to reduce the risk for fat atrophy. Solution is injected until a slight blanch of the scar is seen.

The use of intralesional 5-fluorouracil (5-FU) on the face is avoided in patients with light complexions due to the occurrence of a transient dyschromia, which the patients may find objectionable. In patients with darker skin, 5-FU combined with triamcinolone acetonide can be used as the dyschromia may be less apparent. In fact, in darker skin types, the combination injection may be safer than the use of high dose intralesional triamcinolone acetonide alone, which may cause permanent depigmentation.

Injections are performed at 2- and 4-week intervals adjusting the triamcinolone acetonide concentration as needed to achieve flattening of the scar. In patients in whom the combination treatment is used, the authors use 2 to 10 mg/mL of triamcinolone acetonide mixed with 5-FU (50 mg/mL)(1.0 mL of triamcinolone acetonide 10 mg/mL mixed with 1.0 mL of 5-FU results in a 5 mg/mL concentration of 5-FU with triamcinolone acetonide). These injections can be alternated with biweekly vascular laser therapy.

## Nonfacial HTS/K

Hypertrophic scars and keloids on the trunk and extremities are frequently thicker than facial scars. Higher concentrations of triamcinolone acetonide (10–40 mg/mL) are often required when treating these lesions, but can result in significant skin and subcutaneous atrophy. In fact, we often see patients to address the steroid atrophy of the skin and/or subcutaneous tissue resulting from overly zealous cortisone injections (Figure 2). Once these complications occur, the only feasible option is surgical correction. It is for this reason that the authors recommend that any nonfacial HTS/K lesions be treated with a combination of triamcinolone acetonide and 5-FU.

5-Fluorouracil diluted with triamcinolone acetonide provides excellent reduction in scar thickness while limiting exposure to high concentrations of triamcinolone, thus minimizing the risk for steroid atrophy and telangiectasia formation. 5-Fluorouracil, a pyrimidine analog primarily used as a chemotherapeutic agent, has been shown to inhibit fibroblast proliferation in vitro[26] and in vivo.[27] It also has an inhibitory effect on type I collagen gene expression in human fibroblasts through inhibition of TGF-β signaling.[28] Numerous studies have demonstrated the effectiveness of 5-FU on HTS/K.[29-31] Adverse effects of 5-FU include skin ulceration, burning, pain, and hyperpigmentation.

Hyperpigmentation is limited to the injection site and typically resolves spontaneously after 3 months. For this reason, the authors limit use of 5-FU to nonvisible locations on the trunk and extremities, including use on the earlobes in fair-skinned patients.

Contraindications to 5-FU include pregnancy or breastfeeding and allergy to the medication. Patients with liver disease should be treated with caution.[32] The authors do not perform laboratory studies in patients receiving 5-FU injections.

The authors inject using concentrations of 2 to 20 mg/mL of triamcinolone acetonide mixed with 5-FU (50 mg/mL) and repeat injections every 2 to 4 weeks, adjusting the concentration of triamcinolone acetonide according to response. Extending injections beyond this timeframe can result in regrowth of scar tissue.

Once flattening of the HTS/K is achieved, patients are treated with vascular laser to treat residual erythema

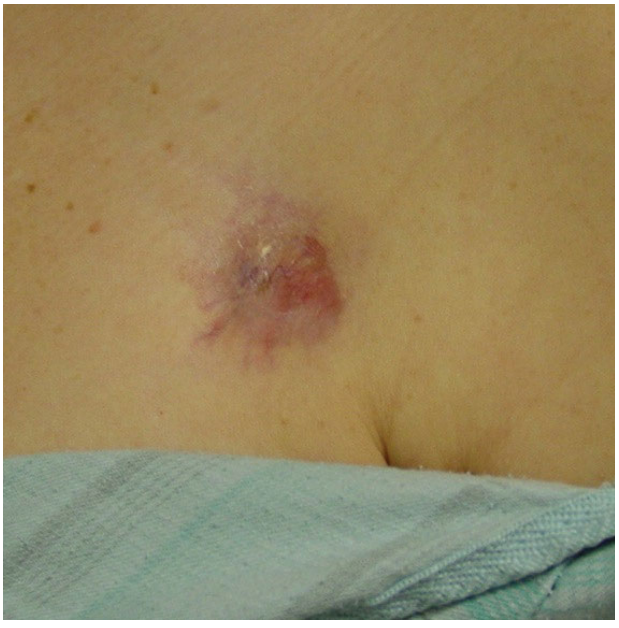

**Figure 2.** A keloid developed after nevus removal. Patient was treated with intralesional triamcinolone acetonide 40 mg/ml, which resulted in fat atrophy, skin atrophy, and telangiectasias at the time of presentation. She underwent surgical revision of this area.

or telangiectasias using the same laser parameters as described above. Vascular laser treatments are performed at 2-week intervals until the erythema has resolved. If, after vascular laser therapy, residual fibrosis is noted, fractionated laser therapy may be initiated as mentioned below. It may be prudent to wait to begin fractionated or ablative laser therapy until the scar has not shown signs of regrowth for approximately 6 months.

### Silicone Gel Sheeting

Silicone gel sheeting has been used as an adjunctive therapy for HTS/K, prophylactically and therapeutically. Silicone gel sheeting reduces tension on hypertrophic scars[33] which may contribute to its mechanism of action. Other possible mechanisms of action include increased collagenase activity and increased wound hydration.[34-36] A randomized controlled trial by Li-Tsang et al[37] showed that silicone gel sheeting reduced symptoms of itching, and tenderness, along with reducing the thickness of the hypertrophic scars. The authors instruct patients to apply silicone gel sheeting to the scar for 12 to 24 hours daily between intralesional injections.

### Fractional Laser Resurfacing

Fractional laser resurfacing is a newer modality employed by the authors in the treatment of HTS/K. Fractional resurfacing lasers create microscopic vertical columns of thermal damage, referred to as microthermal zones, or MTZs, in a gridlike pattern, leaving intervening normal skin untouched.[38,39] Nonablative infrared fractional lasers penetrate into the dermis to a depth of 400 to 1000 µm, leaving the epidermis intact. The resultant thermal injury stimulates a wound healing response through the generation of heat shock proteins, myofibroblasts, and increased collagen type III production.[38] Subsequent dermal remodeling is believed to contribute to the improved skin texture seen in the treatment of scars. Fractional nonablative 1540-nm laser resurfacing of thermal burn scars showed significant improvement in texture with thinner scars showing greater improvement.[40] This may be due to a greater depth of thermal injury needed to remodel thicker scars.

Thicker HTS/K unresponsive to intralesional therapy are treated with ablative fractional $CO_2$ laser resurfacing. Ablative fractional resurfacing penetrates to depths of 1500 to 2000 µm, vaporizing both epidermal and dermal tissue. This results in greater depth of penetration, and greater recovery time compared to nonablative resurfacing. Previous reports have demonstrated improvement in skin texture and pigmentation using fractional ablative resurfacing for burn scars.[41-43] Additional studies using ablative laser resurfacing in the treatment of HTS/K are needed to better understand the molecular mode of action and establish optimal treatment parameters.

## ALTERNATIVE THERAPIES

Numerous alternative therapies are available in the treatment of HTS/K, which are not included as part of our standard algorithm. Imiquimod is an immune response modifier FDA approved for use in basal cell carcinoma, actinic keratoses, and genital warts.[44] Imiquimod stimulates IFN-α and TNF-α, proinflammatory cytokines, which are antifibrotic.[45] An initial study by Berman and Kaufman[46] showed promising results with application of imiquimod cream 5% in preventing recurrence of keloids after surgical excision, while more recent studies have not shown effectiveness.[47,48] Based on this data, the authors do not utilize imiquimod for treatment of HTS/K at this time.

Cryotherapy is effective in flattening keloids in 51% to 74% after 2 or more sessions according to several studies.[49-51] Cryotherapy can be used alone or in combination with corticosteroid injections. According to Layton et al,[49] early, more vascular lesions respond better to cryotherapy than larger, more developed keloids. Disadvantages of cryotherapy include pain, prolonged healing, and hypopigmentation, which may be permanent. Because of these risks, smaller lesions in patients with Fitzpatrick skin types I to III are better suited for this treatment.

### Surgery

Surgical excision of hypertrophic scars is not advised, as these lesions tend to improve spontaneously over time or with intralesional injections. Keloids recalcitrant to treatment may be treated with surgical excision but only after all other therapies have failed. Complete surgical excision as monotherapy has been associated with an increase incidence of recurrence, often with keloids larger than the original lesion.[52-54] Keloid excision should therefore be combined with adjuvant therapy in the form of corticosteroid injections or radiation therapy. Corticosteroids can be injected into the wound bed postoperatively, but wound dehiscence due to inhibition of collagen formation is a potential concern. It has been recommended to leave sutures in an additional 3 to 5 days to reduce this risk.[55]

Excision with postoperative radiation is more effective than radiation alone[56] but results are still variable with objective response rates of 25% to 100% of patients.[57-59] Radiation may be administered in the immediate postoperative period with total doses of 20 Gy administered over several sessions.[60,61] The main concern with radiation therapy is the risk for malignant transformation. Radiation therapy is therefore limited to adults with care to avoid areas with greater malignant potential, including the breast and thyroid.[62]

Earlobe keloids are one exception in which surgical monotherapy is effective. Earlobe keloids are most frequently the result of ear piercing with contact allergy to nickel or other impurities often implicated as a cause.[63] Tangential shave removal with secondary intention healing, in the authors' experience, is highly effective for nodular keloids. Care is taken not to disturb normal skin during keloid removal and electrocautery is avoided or kept at a minimum so as to minimize keloid reformation.

Pressure earrings are widely used adjuvant therapy to prevent recurrence after earlobe keloid excision.[64-66] Tissue hypoxia with subsequent degradation of collagen and fibroblast degeneration or decrease in blood flow with an increase in collagenase-mediated collagen breakdown are possible explanations for the compression effect.[36] While few studies have been performed looking at the effects of pressure therapy alone after excision of earlobe keloids,[67] earlobe compression remains a conservative therapeutic option. A drawback to the use of pressure earrings is the potential for noncompliance which may result from the device being uncomfortable and/or cosmetically unacceptable.

## FUTURE THERAPIES

Interferon-α has been used locally in the treatment of hypertrophic scars and keloids with conflicting results. Interferon-α has antifibrotic and antiproliferative effects which are believed to be a result of interference with the TGF-β1 pathway.[68] Improvement in hypertrophic scars has been reported when injected with triamcinolone,[69] but studies using IFN-α as monotherapy for keloid prophylaxis have been ineffective.[70-72]

Topical tamoxifen has been shown to decrease expression of TGF-β and may be beneficial in the treatment of HTS/K.[73] Further studies investigating the effectiveness of tamoxifen on HTS/K are warranted.

Investigators in Europe are studying the effects of insulin injections on both preventing HTS/K and improving the appearance of older scars.[74] Scientists hypothesize that fibroblast activity is inhibited by the hormone and that insulin may also stimulate the production of fats and proteins to repair scar tissue. Other studies suggest a potential role for vitamin D supplementation in the prevention or early treatment of HTS/K.[75,76]

## CASE REPORTS

### Patient 1

An African-American male with keloids along the mandible presented. He is shown before and after (Figure 3) 12 monthly sessions of triamcinolone acetonide 10 mg/ml + 5-FU. This conservative approach yields improvement in scar height while not affecting skin color.

### Patient 2

A Caucasian female had undergone a facelift and developed keloidal scarring. The referring physician had already revised the area once with recurrence and has tried several intralesional triamcinolone acetonide injections with no improvement of the scars.

The patient is shown before and after (Figure 4A-B) 8 injections of triamcinolone acetonide 5 mg/ml + 5-FU with good response to the therapy. She developed a slight regrowth of the infralobular keloid 3 years later, which responded well to repeat injections.

### Patient 3

A patient suffered a dog bite injury with fibrotic, depressed scarring of the right buccal cheek, hypertrophic scarring along the right lid-cheek junction, and fibrotic scarring of the right nasal sidewall. She is shown at baseline (Figure 5A) and was treated with subcision to elevate the depressed areas and PDL to address erythema. She is shown after 3 subcisions and 2 PDL treatments (Figure 5B) with improvement in erythema and scar depth. Patient then underwent nonablative fractionated laser treatment (ablative fractionated lasers had not yet been developed) to address remaining

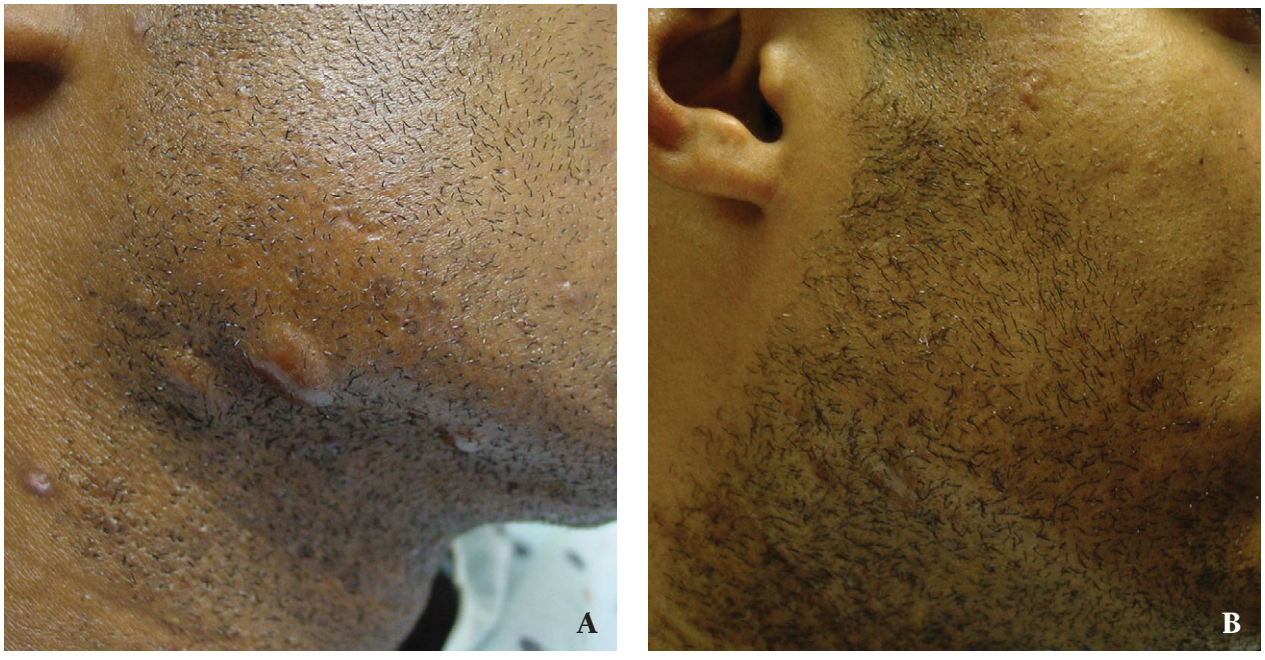


**Figure 3.** African American male with keloids along the mandible. He is shown before (A) and after (B) 12 monthly sessions of triamcinolone acetonide 10 mg/ml + 5-FU.

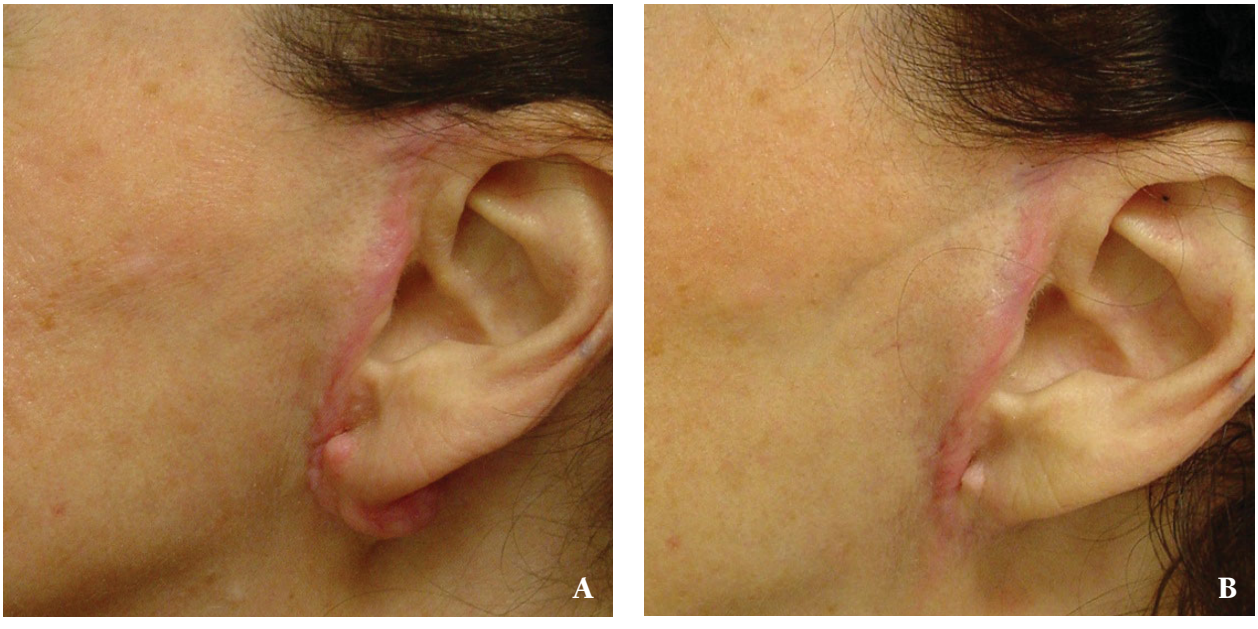


**Figure 4.** Patient is shown before (A) and after (B) 8 injections of triamcinolone acetonide 5 mg/ml + 5-FU. She developed a slight regrowth of the intralobular keloid 3 years later, which responded well to repeat injections.

fibrosis. She is shown after 6 nonablative fractionated laser treatments with nice improvement in the scar textures (Figure 5C).

## Patient 4

Patient was seen after being treated in the burn unit for widespread herpes zoster (Figure 6A). She had hypertrophic scarring and webbing of the neck and chest. Her range of motion was severely limited. She is shown 4 years after 10 injections of triamcinolone acetonide 5 mg/ml + 5-FU followed by 4 PDL sessions. The injections were used first to reduce scar height; then PDL was used to address erythema and texture.

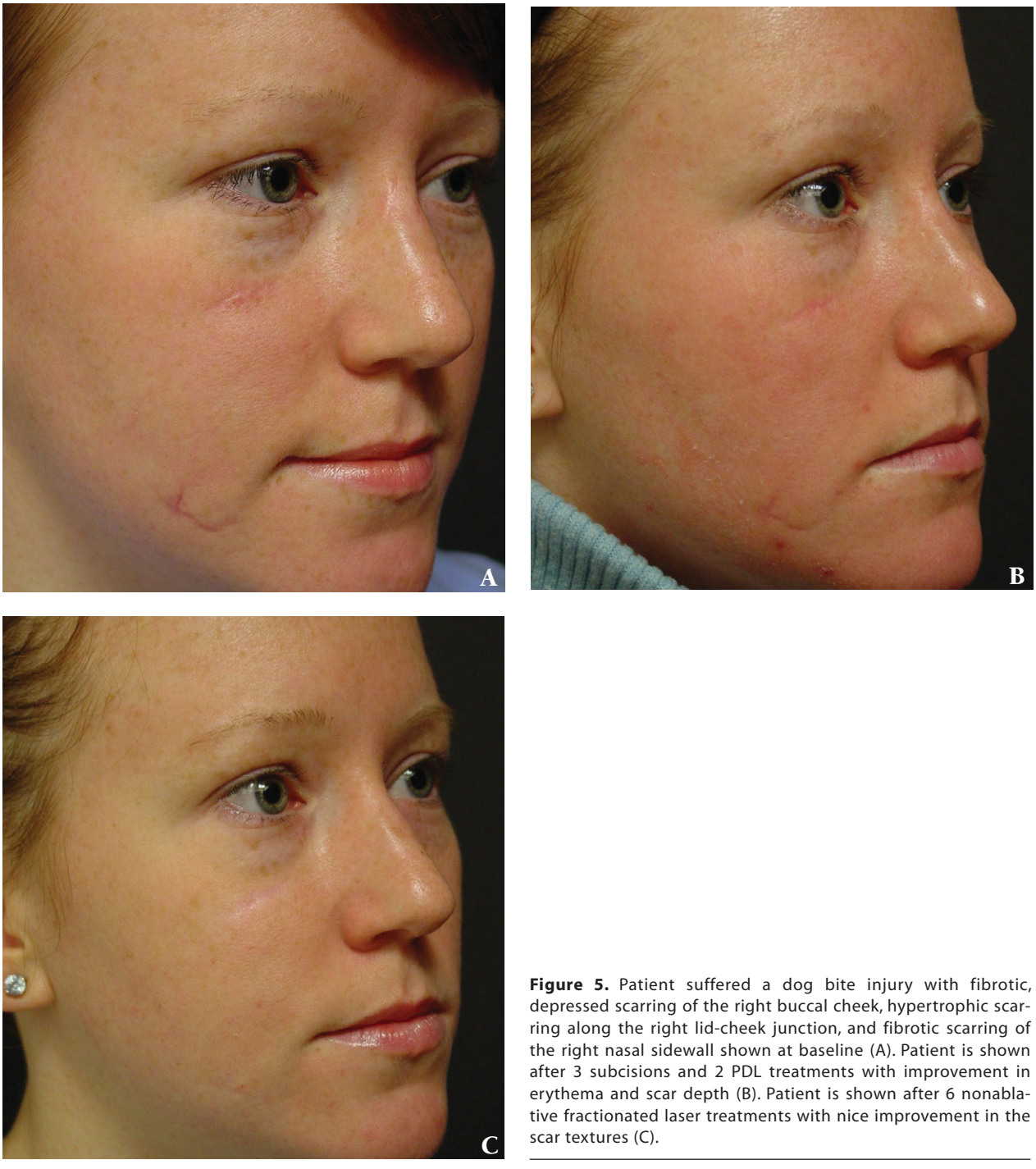


**Figure 5.** Patient suffered a dog bite injury with fibrotic, depressed scarring of the right buccal cheek, hypertrophic scarring along the right lid-cheek junction, and fibrotic scarring of the right nasal sidewall shown at baseline (A). Patient is shown after 3 subcisions and 2 PDL treatments with improvement in erythema and scar depth (B). Patient is shown after 6 nonablative fractionated laser treatments with nice improvement in the scar textures (C).

## Patients 5 and 6

Keloid scars of the ears of 2 different patients are shown before (Figures 7A and 8A) and after (Figures 7B and 8B) conservative tangential shave removals. Anatomic ear morphology is maintained.

## Patient 7

The patient was seen after developing hypertrophic scarring on the face (Figure 9A) from a chemical peel and on the arms from a brachioplasty (Figure 9B). She had decreased ability to open her mouth and decreased ability to abduct her arms.

Patient is shown after undergoing 2 triamcinolone acetonide injections to the face alternating with 9 PDL sessions (Figure 9C). She regained full ability to open her mouth. She is shown after undergoing 4 triamcinolone acetonide + 5-FU injections to the arms (Figure 9D), 9 PDL sessions, and

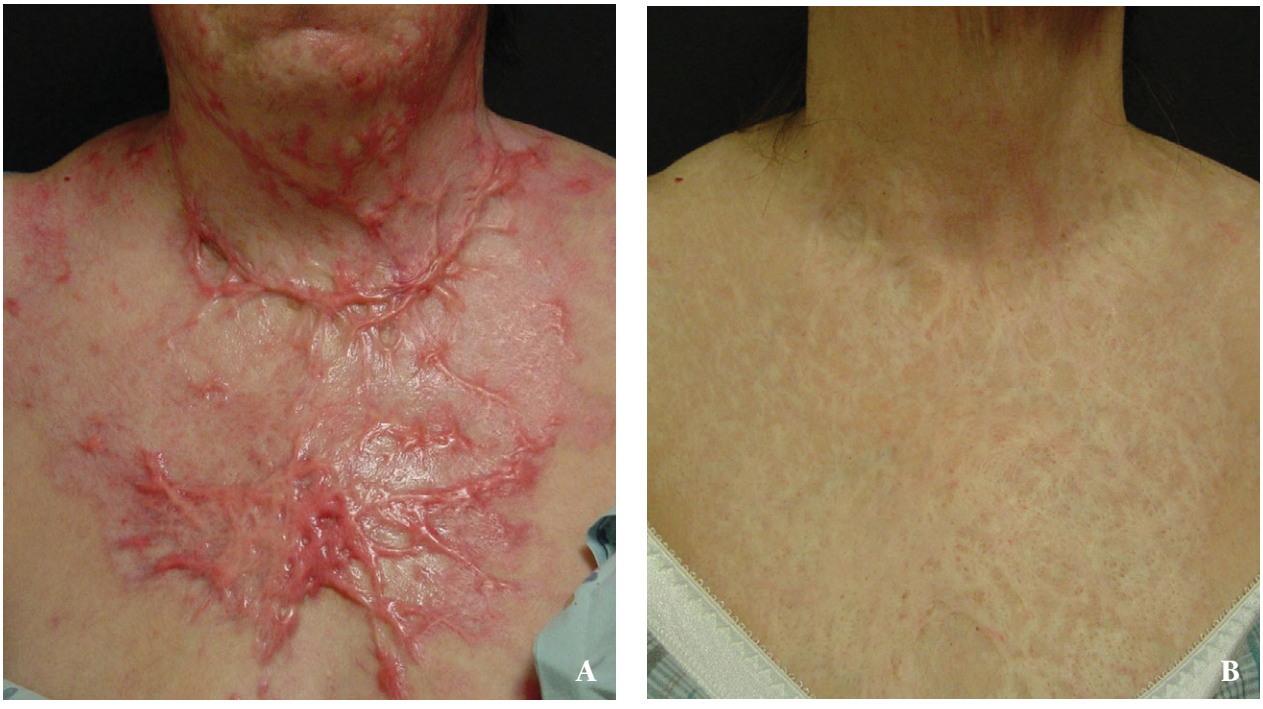


**Figure 6.** Hypertrophic scarring and webbing of the neck and chest (A). She is shown 4 years after 10 injections of triamcinolone acetonide 5 mg/ml + 5-FU followed by 4 PDL sessions (B). The injections were used first to reduce scar height then PDL was used to address erythema and texture.

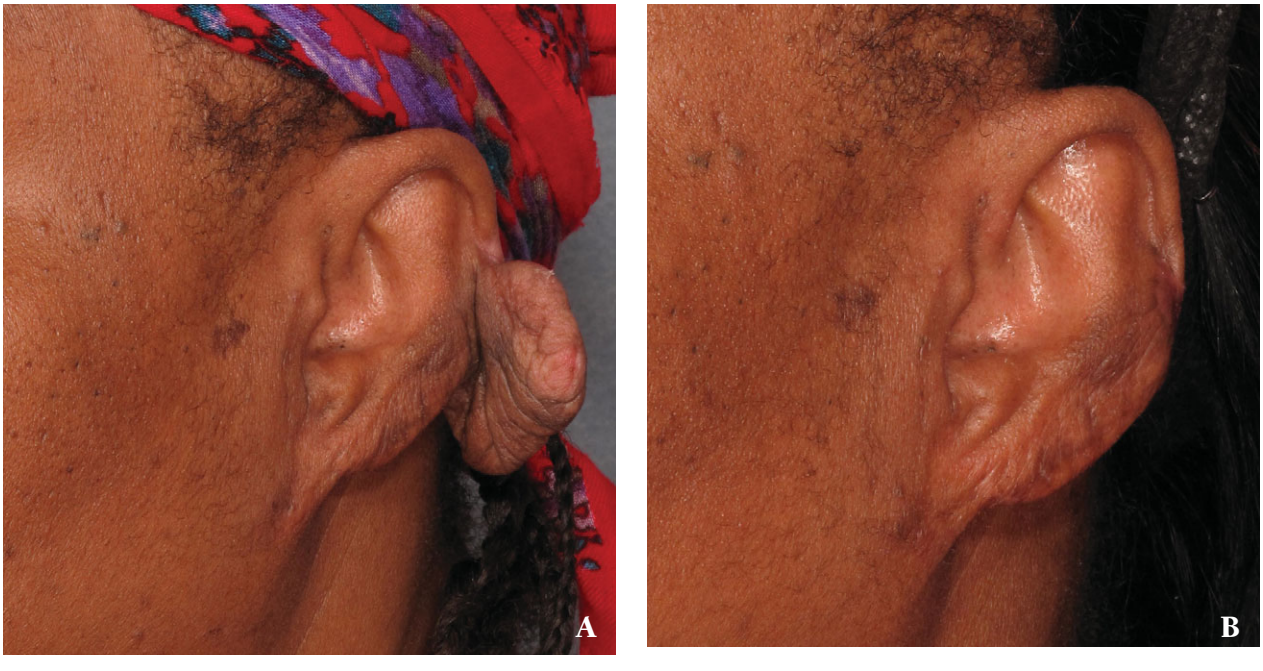


**Figure 7.** Keloid scars of the ears shown before (A) and after (B) conservative tangential shave removals. Anatomic ear morphology is maintained.

followed by 4 nonablative fractionated laser sessions. She now has ability to abduct her arms fully.

## CONCLUSION

Hypertrophic scaring/keloid prevention and management continues to be a challenge. Early intervention is imperative

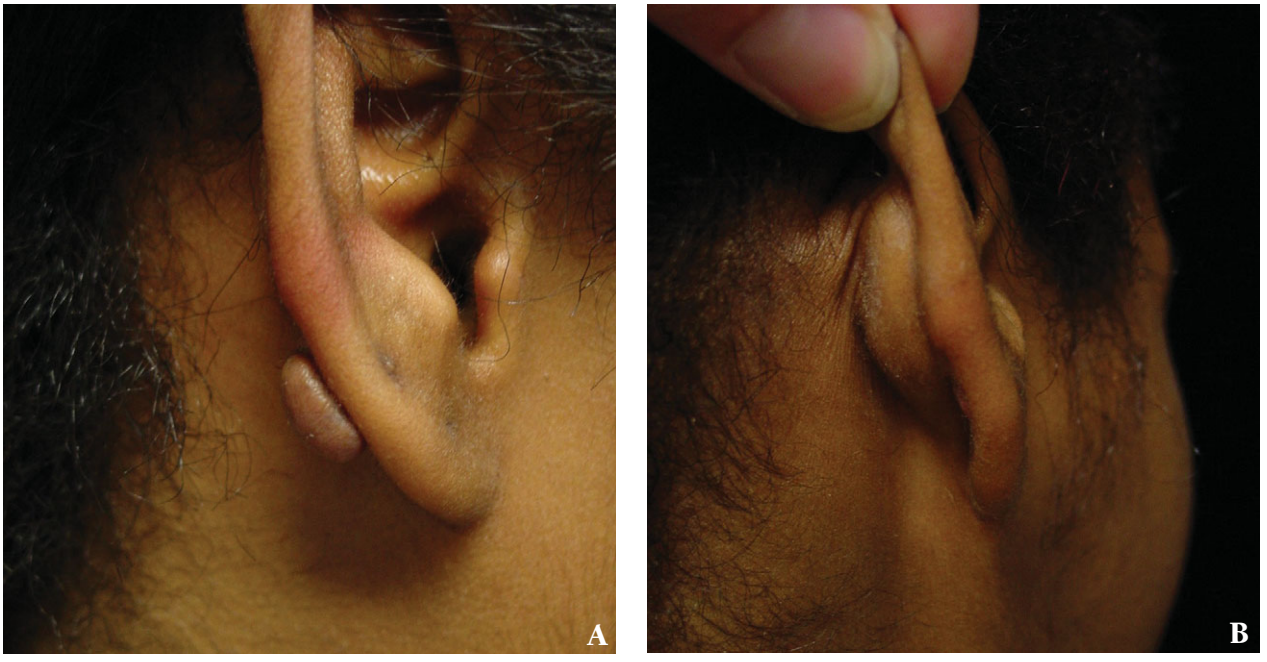


**Figure 8.** Keloid scars of the ears shown before (A) and after (B) conservative tangential shave removals. Anatomic ear morphology is maintained.

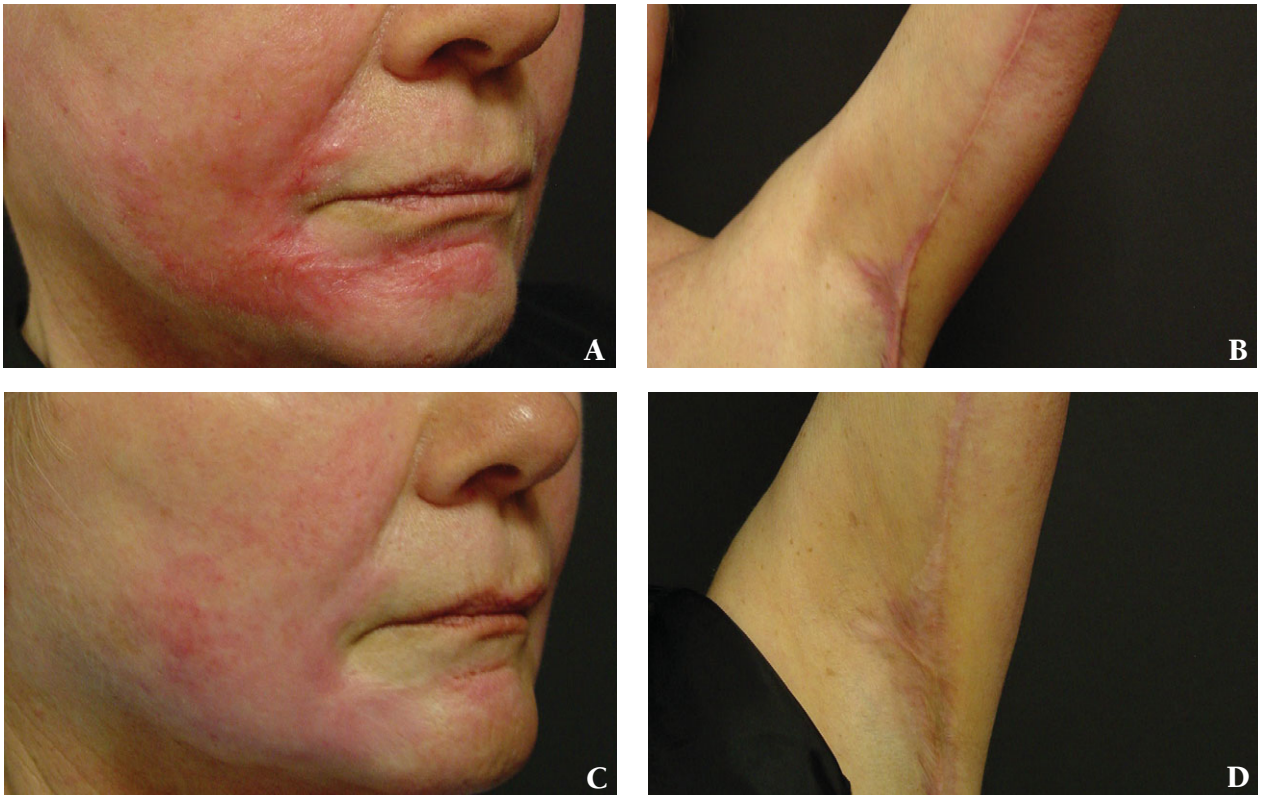


**Figure 9.** Hypertrophic scarring on the face from a chemical peel (A) and on the arms from a brachioplasty (B). Patient had decreased ability to open her mouth and decreased ability to abduct her arms. She is shown after undergoing 2 triamcinolone acetonide injections to the face alternating with 9 PDL sessions (C) has regained full ability to open her mouth. She is shown after undergoing 4 triamcinolone acetonide + 5-FU injections to the arms, 9 PDL sessions, and followed by 4 nonablative fractionated laser sessions. She now has ability to abduct her arms fully (D).

in managing these lesions. Greater understanding of the underlying pathophysiology may lead to new therapeutic modalities to expand our treatment options.

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