Scar prevention and remodeling: a review of the medical, surgical, topical and light treatment approaches

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Abstract
Cosmetic, functional, and structural sequelae of scarring are innumerable, and measures exist to optimize and ultimately minimize these sequelae. To evaluate the innumerable methods available to decrease the cosmetic, functional, and structural repercussions of scarring, PubMed search of the English literature with key words scar, scar revision, scar prevention, scar treatment, scar remodeling, cicatrix, cicatrix treatment, and cicatrix remodeling was done. Original articles and reviews were examined and included. Seventy-nine manuscripts were reviewed. Techniques, comparisons, and results were reviewed and tabulated. Overall, though topical modalities are easier to use and are usually more attractive to the patient, the surgical approaches still prove to be superior and more reliable. However, advances in topical medications for scar modification are on the rise and a change towards medical treatment of scars may emerge as the next best approach.

Comparison studies of the innumerable specific modalities for scar revision and prevention are impossible. Standardization of techniques is lacking. Scarring, the body’s natural response to a wound, can create many adverse effects. At this point, the practice of sound, surgical fundamentals still trump the most advanced preventative methods and revision techniques. Advances in medical approaches are available, however, to assist the scarring process, which even the most advanced surgical fundamentals will ultimately lead to. Whether through newer topical therapies, light treatment, or classical surgical intervention, our treatment armamentarium of scars has expanded and will allow us to maximize scar prevention and to minimize scar morbidity.

Introduction
Ideas of wound healing, regeneration, and scarring have been the subject of intensive studies within the last 20 years. It is still somehow ironic that humans, the most evolved species on Earth, heal their wounds with scars while amphibians, such as salamanders, are able to regenerate a whole limb after being cut.¹ While scientific research has led to the discovery of the Murphy Roths Large (MRL) mice that heal with no scarring,² it still has not revealed the pathway for scarless injuries in humans.

Scars can create significant cosmetic, functional, and structural problems.³ Scar formation can result in adverse cosmesis, loss of function of a joint, or hindrance of growth in a child.⁴ Scars also have a dramatic impact on a patient’s psychological quality of life and have been associated with anxiety, social avoidance, and depression.⁴

While the three predictable and overlapping phases (inflammatory, proliferative, and remodeling) of wound healing remain the same, an alteration of these phases may result in greater or lesser scarring.⁵ Nature’s examples of these opposite ends of scarring in humans range from hypertrophic or keloidal scars at one end of the spectrum to fetal-like scars at the other end.

The fact that scars can be remodeled has led to several recent trials of medical and surgical interventions. The objective of this paper is to thoroughly review these findings and update the reader on the newer modalities of scar remodeling.

Pathogenesis of scar remodeling
The end result of scar formation is the replacement of a normal appearing skin of normal texture, elasticity, and resilience with a lesser functional and textural substitute. This lesser substitute will ultimately consist of an epidermis with flat rete ridges, a dermis that has thickened containing parallel-oriented, collagen fibers with perpendicularly oriented capillaries, diminished hyaluronic
acid content, and nearly none to very sparse elastic fibers.6

The change in collagen from collagen III in early wounds to collagen I in mature wounds is an important player in scar formation and appearance. While collagen III fibers accommodate the expansion and contraction of tissues, such as blood vessels and viscera, collagen I fibers barely accommodate stretch and are more rigid in nature.7–9 The finding that fetal cutaneous wounds, particularly in the first six months of gestation, heal without scar formation has revolutionized much of the wound literature.9 Despite having multiple structural differences between fetal wound healing and adult wound healing, the most notable one still relates to collagen I and III fibers: fetal skin has a higher ratio of type III to type I collagen (1:1) compared to adult skin (1:4).4

Scar remodeling works primarily at modifying the above factors through two main pathways: mechanical and chemical. The mechanical pathway of remodeling consists of either mechanical forces or mechanical stimuli (Figs. 3–6).

Mechanical forces, including stretching, tension, shear force, scratch, compression, as well as hydrostatic and osmotic pressures, can be perceived by cellular mechanoceptors and nerve fiber receptors as a stimulus to accelerate cell proliferation, angiogenesis, and epithelialization through various mechanotransduction pathways.9 One such mechanotransduction pathway modulates levels of transforming growth factor (TGF)-β. A discussion of the functions and effects of TGF-β on scars is detailed below.

Mechanical stimuli are also received by mechanosensitive nociceptors, and signals are transmitted to dorsal root ganglia that contain neuronal cell bodies in the afferent spinal nerves.9 Activation of these mechanosensitive nociceptors results in increased production of neuropeptides that modulate skin and immune cell functions. Noteworthy examples are substance P, calcitonin gene-related peptide, neuropeptide A, vasoactive intestinal peptide, and somatostatin.9 These proinflammatory responses are termed neurogenic inflammation.9

The chemical pathway of remodeling consists of several players but most notoriously TGF-β, matrix metalloproteinase (MMP), and tissue inhibitor of metalloproteinase (TIMP), as well as hyaluronic acid-stimulating activity (HASA). TGF-β is secreted by most cells involved in wound healing, including neutrophils, lymphocytes, macrophages, keratinocytes, and fibroblasts.4 It is a potent chemoattractant of macrophages, neutrophils, and fibroblasts, and stimulates extracellular matrix synthesis and prevents its degradation.4 Three highly homologous TGF-β genes in mammals, designated TGF-β1, -β2, and -β3, have been identified. TGF-β1 and -β2, from platelets and macrophages, increase epidermal cell motility and proliferation, chemotaxis of macrophages and fibroblasts, extracellular matrix synthesis, and remodeling.10 Shah et al.11 showed that the exogenous addition of a neutralizing antibody to TGF-β1 resulted in a reduction in the inflammatory and angiogenic responses, as well as a marginal reduction in cutaneous scarring. When they added neutralizing antibodies to TGF-β2 alone, it had little effect on inflammatory or angiogenic responses and no effect on the resultant scar. However, when neutralizing antibodies to TGF-β1 and TGF-β2 were administered together, the synergistic effect resulted in a dramatic amelioration of scar formation.12 Exogenous addition of TGF-β3 to cutaneous wounds in adult rodents also produces the same effects.12 In addition, treating adult mice wounds with interleukin (IL)-10 decreases production of IL-6 and IL-8, thereby reducing inflammation and the release of TGF-β, resulting in scarless healing.4 Similarly, human fetal wounds have higher ratios of TGF-β3 to TGF-β1 and TGF-β2 along with a less inflammatory infiltrate, thus favoring less scar formation.13

HASA, a glycoprotein, is found in fetal skin and is absent from adult wounds.4 Hyaluronic acid (HA) allows proliferating cells to avoid inhibitory contact. HA synthesis precedes mitosis and dissociates the dividing cell from its substratum, permitting cell movement.4 Fetal fibroblasts have more surface receptors for HA than adult fibroblasts, enhancing fibroblast migration and speeding wound healing.4 High levels of HA may also contribute to decreased inflammation of fetal wounds.4

Additionally, scarless wounds in human fetuses have a higher ratio of MMP to TIMP, favoring remodeling and less accumulation of collagen. This may be due to decreased expression of TGF-β1 and -β2 that consequently decreases MMP and increases TIMP expression.4

Scar prevention and remodeling

Scar treatment strategies can be categorized into two broad groups: prevention and remodeling. Historically, scar remodeling has been the mainstay, while recent advances have increasingly targeted scar prevention. The surgical fundamentals of proper patient selection, preoperative planning and preparation, intraoperative technique, and diligent aftercare still trump the most advanced preventative methods and revision techniques.

Scar prevention

In this section, a review of the studies pertaining to scar prevention with topical therapies, light treatment, and surgical intervention is considered (Tables 1–3).

Topical therapies

Moist exposed burn ointment. Moist exposed burn ointment (MEBO®; MEBO Company, Arcadia, CA, USA) is a
Table 1 Scar prevention: topical therapies

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Participants, n</th>
<th>Scar type and location</th>
<th>Study design</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atiyeh</td>
<td>2002</td>
<td>60 scars</td>
<td>Post-treatment of facial wounds; surgical and traumatic</td>
<td>MEBO vs. antibiotic ointment vs. adhesive tape</td>
<td>Marked prevention of unfavorable scars with improved cosmetic results with MEBO therapy</td>
</tr>
<tr>
<td>Atiyeh</td>
<td>2003</td>
<td>13 patients; 20 donor sites</td>
<td>Split-thickness skin graft donor sites</td>
<td>Tegaderm vs. MEBO</td>
<td>Faster healing with better scar quality, function, and appearance with MEBO</td>
</tr>
<tr>
<td>Gold</td>
<td>2001</td>
<td>96 patients</td>
<td>Skin sites NOS</td>
<td>Polymyxin B sulfate-bacitracin zinc vs. silicone gel</td>
<td>Topical silicone gel sheeting decreased hypertrophic scars and keloids after scar revision procedures in patients prone to abnormal scarring but not in low-risk patients</td>
</tr>
<tr>
<td>Chan</td>
<td>2005</td>
<td>50 patients; 100 wounds</td>
<td>Median sternotomy wounds divided into half for the two treatment groups</td>
<td>Control gel (water, glycerin, propylene glycol and hydroxyethyl cellulose) vs. silicone gel</td>
<td>Silicone gel-treated group had better scores for pigmentation, vascularity, pliability, height, pain, and itching</td>
</tr>
<tr>
<td>Rhee</td>
<td>2010</td>
<td>40 patients</td>
<td>Scar or mass excision on exposed areas</td>
<td>No treatment vs. silicone gel sheet</td>
<td>Improvement in pigmentation, vascularity, and height in the silicone gel group</td>
</tr>
<tr>
<td>Ho</td>
<td>2006</td>
<td>120 patients with 144 blue-black tattoos</td>
<td>Sites of blue-black tattoos</td>
<td>Laser treatment with the QS 1064 nm Nd:YAG laser followed by application of Contractubex gel BID between treatments vs. no intervention</td>
<td>Patients in the Contractubex gel group illustrated half as much scar development, and the risk of permanent hypopigmentation and transient hyperpigmentation was lower</td>
</tr>
<tr>
<td>Baumann</td>
<td>1999</td>
<td>15 patients</td>
<td>Sites of skin cancer removal surgery</td>
<td>Each scar was divided into part A and part B, one part was treated with Aquaphor and the other part with Aquaphor plus vitamin E</td>
<td>Topical vitamin E did not help in improving the cosmetic appearance of scars and led to a high incidence of contact dermatitis</td>
</tr>
<tr>
<td>van der Veer</td>
<td>2009</td>
<td>30 female patients</td>
<td>Bilateral reduction mammoplasty scars</td>
<td>Breast scars were divided into 4 sections, left lateral and medial and right lateral and medial; 2 sections were treated with calcipotriol and 2 sections were treated with vehicle only</td>
<td>No difference between the prevalence of hypertrophic scars or scar thickness</td>
</tr>
<tr>
<td>Chung</td>
<td>2006</td>
<td>24 patients</td>
<td>New surgical wounds at least 4 cm in length</td>
<td>Wounds were divided into 2 equal parts, and one part was treated with onion extract gel (Mederma) and the other with petrolatum</td>
<td>Mederma did not improve scar cosmesis or symptomatology when compared to petrolatum-based ointment</td>
</tr>
</tbody>
</table>

MEBO, moist exposed burn ointment; NOS, not otherwise specified.

burn ointment with a 1995 US-patented formulation. It contains six herbal extracts, including \( \beta \)-sitosterol as the active ingredient and sesame oil as an inactive ingredient.\(^\text{14}\) The main ingredient of MEBO, \( \beta \)-sitosterol, has been shown to have anti-inflammatory effects.\(^\text{15}\) Berberine, a secondary ingredient to MEBO, has been found to have antimicrobial effects.\(^\text{14}\) It is believed to act by increasing tissue moisture, resulting in decreased vascular activity and, therefore, preventing vascular overgrowth and scar hypertrophy.\(^\text{5}\) In a recent prospective study, Atiyeh et al. compared MEBO, an antibiotic ointment, and no topical therapy in patients with traumatic and surgical facial wounds. MEBO was found to produce significantly better results at follow-up after 1, 3, and 6 months.\(^\text{16}\) Other prospective studies of partial-thickness skin graft donor sites have compared MEBO with conventional wound care and with Tegaderm\(^\text{26}\) (3M Health Care, St. Paul, MN, USA). MEBO was superior to conventional wound care, with faster healing and less hyperemia and pigmentation. MEBO also exhibited faster healing and better improvement in scar quality than Tegaderm (see Fig. 1).\(^\text{17,18}\)

**Silicone gel sheeting.** Topical silicone gel sheeting has been an effective treatment for scars and keloids. It is believed to increase occlusion and hydration of wounds and decrease capillary activity, hyperemia, and collagen deposition, with resultant improvement in scar appearance.\(^\text{5}\) A randomized controlled trial (RCT) by Gold et al.\(^\text{19}\) compared routine postoperative care consisting of
antibiotic ointments and bandages with topical silicone gel sheeting after surgical procedures. Topical silicone gel sheeting decreased hypertrophic scars and keloids after scar revision procedures in patients prone to abnormal scarring but not those patients without any history of abnormal scarring. Another RCT by Chan et al. also compared silicone gel with a control gel in preventing hypertrophic scars in median sternotomy wounds. Although the majority of patients treated with the silicone gel developed hypertrophic scars, the silicone gel-treated group had significantly better scores on the Vancouver Scar Scale for all parameters, including pigmentation, vascularity, pliability, height, pain, and itching. A third RCT by Rhee et al. in Korean patients studied the effect of silicone gel sheeting on normal surgical scars and showed improvement in pigmentation, vascularity, and height in the silicone gel group at the 3-month endpoint.

Table 2 Scar prevention: light

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Participants, n</th>
<th>Scar type and location</th>
<th>Study design</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>McCraw35</td>
<td>1999</td>
<td>106 patients</td>
<td>171 anatomic sites</td>
<td>585 nm PDL laser at initially low energy followed by standard-fluency starting 2 weeks after surgery or 1-2 weeks after suture removal for 3-6 sessions every 3-4 weeks</td>
<td>Hypertrophic scar prevention with PDL</td>
</tr>
<tr>
<td>Nouri36</td>
<td>2003</td>
<td>11 patients</td>
<td>Postoperative linear scars</td>
<td>Half of scar was treated with 3-monthly 585 nm PDL treatments while other half was not treated</td>
<td>Treated side scored better in all parameters and cosmetic appearance. It was deemed safe and effective</td>
</tr>
<tr>
<td>Choe40</td>
<td>2009</td>
<td>27 patients</td>
<td>Total thyroidectomy scars</td>
<td>4-monthly treatments with the 1550 nm fractional Er:glass laser vs. the untreated surgical scars of a control group</td>
<td>The average Vancouver Scar Scale score was lower and better cosmetic outcomes were seen in the treated group</td>
</tr>
<tr>
<td>Capon43</td>
<td>2010</td>
<td>30 patients</td>
<td>Surgical scars</td>
<td>Immediately after surgery patients received either a high dose (80-130 J/cm²) or low dose (&lt;80 J/cm²) treatment with the 810 nm diode laser to half the scar; the other half of the scar was left untreated</td>
<td>810 nm laser-treated group showed improved appearance of surgical scar vs. control. Within the laser-treated group, the high-energy-treated group showed greater improvement</td>
</tr>
<tr>
<td>Barolet80</td>
<td>2010</td>
<td>3 patients</td>
<td>Hypertrophic scars or keloids secondary to acne or surgery</td>
<td>Post scar revision by surgery or CO₂ laser ablation on bilateral areas, one scar was treated daily by the patient at home with non-thermal, non-ablative NIR light-emitting diode (805 nm at 30 mW/cm²) for 30 days</td>
<td>Significant improvements on the NIR-treated vs. the control scar were seen in all measures. No significant adverse effects were reported</td>
</tr>
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</table>

NIR, near-infrared; PDL, pulsed dye laser.

Table 3 Scar prevention: Botulinum toxin type A

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Participants, n</th>
<th>Scar type and location</th>
<th>Study design</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ziade45</td>
<td>2013</td>
<td>30 patients</td>
<td>Facial wounds in patients presenting to the emergency room</td>
<td>Patients randomly assigned to “toxin; or “control” group. Those injected were injected within 72 h following suture of the facial wound into muscles directly or indirectly involved in scarring</td>
<td>1-year follow-up scars showed no statistically significant differences in the Patient Scar Assessment Scale scale, independent evaluator using the Observer Scar Assessment Scale and the Vancouver Scar Scale; however, they did show a statistically significant difference by the VAS with standardized photographs</td>
</tr>
<tr>
<td>Gassner46</td>
<td>2006</td>
<td>31 patients</td>
<td>Patients with traumatic forehead lacerations or undergoing elective excision of forehead masses</td>
<td>BTA injections into the musculature adjacent to a forehead wound or elective excision (15 U of BTA (Botox, Allergan, Irvine, CA, USA) per 2 cm intraoperative length) within 24 h after wound closure</td>
<td>Overall median VAS score for the BTA-treated group was 8.9 compared with 7.2 for the placebo group (P = 0.003), indicating enhanced healing and improved cosmesis of the experimentally immobilized scars</td>
</tr>
</tbody>
</table>

BTA, botulinum toxin type A; VAS, visual analogue scale.
Massage therapy. Massage therapy, regularly utilized for the treatment of burns and scars, is a simple regimen with minimal, if any, potential downside. A 1999 study performed in children with hypertrophic burn scars failed to illustrate any advantage of massage plus pressure therapy on vascularity, pliability, and height compared to pressure garments alone. Contractubex gel. Contractubex\textsuperscript{a} gel (Merz Pharma, Frankfurt, Germany) is a mixture of 10% onion extract, 50 U heparin per gram, and 1% allantoin.\textsuperscript{24} Sahin et al. performed skin biopsies in rats and divided them into four groups: group 1 received no therapy; group 2 had Contractubex application; group 3 had heparin gel application; and group 4 received allantoin application. They compared the outcomes 30 days following skin biopsies. The Contractubex group was found histologically to show mild immunoreactivities of laminin, fibronectin, and TGF-\beta as well as produce less histological evidence of scarring compared to the heparin gel or the allantoin gel groups, and all showed better results than the control group.\textsuperscript{24} A 2009 study comparing silicone gel (Scarfade), silicone gel sheet (Epi-Derm), and topical onion extract, including heparin and allantoin (Contractubex) for the treatment of postburn hypertrophic scars, concluded that silicone products, either in gel or sheet, are superior to Contractubex in the treatment of the hypertrophic scar.\textsuperscript{25} An RCT done by Ho et al. studied Chinese patients receiving Contractubex gel compared to control gel following laser tattoo removal. In the group receiving the Contractubex gel, only half as many developed scarring, and the risk of permanent hypopigmentation and transient hyperpigmentation was also significantly lower.\textsuperscript{26}

Topical vitamin E. A double-blind study in Mohs surgery patients compared Aquaphor\textsuperscript{b}, a standard emollient, with topical vitamin E mixed with Aquaphor. No biopsies were performed to measure the depth, density of fibroblasts, or other parameters of the scar, but both the physician’s evaluation and the patient’s evaluation of the scar did not show any benefit between the two groups. Additionally, one-third of patients treated with vitamin E developed contact dermatitis.\textsuperscript{27}

Topical calcipotriol. An RCT by van der Veer et al. evaluated topical calcipotriol in preventing hypertrophic scars after bilateral reduction mammoplasty. The study found no difference between the prevalence of hypertrophic scars or scar thickness.\textsuperscript{28}

Topical tretinoin. Otley et al. utilized a porcine model to evaluate perioperative topical 0.1% tretinoin on the healing of high-tension excisional wounds and survival of full-thickness skin grafts. At the excisional sites, topical tretinoin had neither positive nor negative effects on wound healing or final scar appearance.\textsuperscript{29}

Imiquimod. Topical 5% imiquimod has been utilized for the treatment of hypertrophic scars and keloids. It is believed to act via the induction of interferons, which leads to collagen breakdown.\textsuperscript{30} A 2005 randomized, double-blinded, placebo-controlled study of the prevention of hypertrophic scarring after breast surgery reported scar improvement with imiquimod compared to petrolatum alone or no therapy.\textsuperscript{31}

Mederma. Mederma\textsuperscript{a} (Merz Pharmaceuticals, Greensboro, NC, USA) is a mixture of avobenzone 3%, octocrylene 10%, oxybenzone 6%, water and allium cepa (onion) bulb extract. A split-scar study compared Mederma cream with petrolatum ointment in patients undergoing Mohs or excisional surgery. The results did not demonstrate any advantages of Mederma over petrolatum in improving scar appearance or symptoms.\textsuperscript{32} A 2007 study by Hosnuter et al.\textsuperscript{33} demonstrated that topical onion extract as a gel was not statistically significant for improving scar height and itching, and it was ineffective in reducing scar discoloration.
Light

Pulsed dye laser. The 585 nm and 595 nm pulsed dye laser (PDL) selectively targets oxyhemoglobin, which may reduce the local microcirculation, which in turn impairs the proliferation of fibroblasts, resulting in a decrease in hypertrophic scar formation. PDL has been shown to reduce the expression of TGF-β1, as well as reduce fibroblast proliferation and collagen deposition. Initial uncontrolled studies showed hypertrophic scar prevention with PDL treatment starting at two weeks post-operation and with repeat treatments every 3–4 weeks for a total of three to six sessions. A split-scar study by Nouri et al. confirmed these results by showing improvement in the treated side after three monthly treatments starting on the date of suture removal. Biopsies showed greater elastin and normal appearing collagen organization in the treated side. Further studies defined the ideal PDL parameters for scar prevention to be: 585 nm wavelength; 10 mm spot size; 3.5–5.5 J/cm² fluence; 450 μs–1.5 ms pulse duration; and two to three treatment sessions.

Non-ablative fractional Er:Glass. In 2009, Choe et al. demonstrated the use of the 1550 nm Er:glass laser in South Korean post-thyroidectomy patients. These patients received four treatments with a 1550 nm non-ablative Er:glass laser at monthly intervals beginning at suture removal. At six months post-surgery, the treatment group had an average Vancouver Scar Scale score of 1.52, while the control group had a score of 3.00. While the treatment group showed impressive improvement, the study was limited by its short follow-up period and lack of a split-scar design.

Diode. Capon et al. developed a novel 810 nm diode laser for use in the immediate postoperative period. This laser demonstrated that dermal heating in the postoperative period induces elevation of heat shock protein 70 for up to seven days after the photoirradiation. This prolonged elevation in heat shock protein 70 is also generally accompanied by a reduction in the synthesis of other proteins, causing a temporary cessation of cell proliferation. Immediately after closure, patients received a single treatment of either high energy or low energy along half of the surgical site. The other half served as an internal control. Patients who received a high-energy treatment showed a greater scar improvement rate at 1-year follow-up.

Avotermin

Avotermin is a human recombinant TGF-β3 medication designed for scar reduction. A phase II, double-blind, within-patient, placebo-controlled, randomized trial in which lateral portions of a scar received either intralional Avotermin or intralional placebo was performed. The central limb was untreated. Injections were done on post-operation day 0 and 1, and the resultant scar was compared at one year post-procedure to the original scar. Avotermin-treated scars had a smaller surface area, and histology showed architecture similar to normal skin with rete ridges, dermal papillae, and a normal-appearing papillary dermis.

Botulinum toxin type A

Ziade and colleagues demonstrated 30 patients with facial wounds randomized to receive injection of botulinum toxin type A (BTA) 72 hours postoperatively or a control. Results were mixed, only showing a statistically significant difference by the visual analogue scale with standardized photographs and not by other scoring modalities. By inducing temporary muscular paralysis and relieving tension on wound edges, it is hypothesized that reducing the tension may reduce wound widening, hypertrophy, and hyperpigmentation.

A 2006 study by Gassner and colleagues demonstrated enhanced wound healing and less noticeable scars compared with a placebo group in patients injected with BTA.

Scar revision

In this section, a review of the literature pertaining to topical therapies, light treatment, and surgical intervention to scar revision or modification is entertained (see Tables 4–7).

Surgical

Beak-plasty. A Z-plasty converts the direction of the scar from vertical to parallel to the relaxed skin tension lines (RSTL), thereby reducing the risk of hypertrophic change. However, the lateral limbs of the Z flap form a steep angle against the RSTL, which makes them susceptible to hypertrophic change. When mechanical forces work on a straight scar, the scar is strained and fibroblasts in the scar are stimulated. With a beak-plasty, Z-like-shaped flaps composed only of lazy-S lines are designed. Beak-plasty scars composed of multiple lazy-S-shaped scars are less likely to develop hypertrophy than straight scars (Fig. 2).

“W-plasty” and geometric broken line closure. A W-plasty is used to break up a linear scar, create irregularity, and align along RSTL, better hiding the scar. GBLC is a scar irregularization technique that uses a mixture of squares, rectangles, triangles, and other shapes to create a random sequence that interdigitates on either side (Fig. 3). V-Y and Y-V advancement flaps can be used to alter the length of scars and/or elevate or

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depress a free margin. V-Y can lengthen a contracted scar by making a V-shaped incision along the length of the scar. After extensive undermining, the V-shaped flap can be pushed away, lengthening the incision. A Y-V repair similarly shortens an area of excessive laxity (Fig. 4).

Table 4  Scar revision: Surgical

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Participants, n</th>
<th>Scar type and location</th>
<th>Study design</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nagasao</td>
<td>2007</td>
<td>21 patients</td>
<td>Face, upper extremities, lower extremities, abdomen</td>
<td>See Fig. 2. Z-like shaped flaps composed only of lazy-S lines designed to reduce the effect of mechanical forces</td>
<td>No wound dehiscence, wound infection, or flap necrosis. The lateral limbs did not become hypertrophic in any patient at a minimum of 9 months postoperative follow-up, and patients were pleased with the results</td>
</tr>
<tr>
<td>Mallucci</td>
<td>2009</td>
<td>35 patients</td>
<td>Revision of tethered, sunken skin: breast, lower limb, upper limb, chest wall, laparotomy, tracheotomy scars</td>
<td>An ellipse is marked around the scar with the perimeter of the ellipse drawn so that it lies upon the point at which the scar depression starts. The ellipse is de-epithelialized, and an incision through dermis, around the perimeter of the de-epithelialized ellipse, is made. The incised dermal edges are approximated using a continuous 4/0 Monocryl suture, and a “dermal tube” is formed</td>
<td>A simple, consistent, and reproducible method by which sunken and tethered scars can be improved. All patients reported improvement and no complications</td>
</tr>
</tbody>
</table>

Table 5  Scar revision: Antimitotic drugs

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Participants, n</th>
<th>Scar type and location</th>
<th>Study design</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yosipovitch</td>
<td>2001</td>
<td>10 patients, at least 28 keloids</td>
<td>Keloids on various areas</td>
<td>Keloids received either corticosteroid injections of triamcinolone 40 mg/mL at volumes corresponding to size (0.1 mL/cm²), or corticosteroids plus cryotherapy (either before or after the injection), or cryotherapy sprayed to center of lesion continuously at a distance of 1 cm from the skin</td>
<td>Keloid thickness responded significantly better to cryotherapy and triamcinolone vs. triamcinolone alone or cryotherapy alone. Combined treatment and intralesional corticosteroid alone both improved pruritus. No significant side effects were noted with any treatments, and no recurrence of keloids was noted with the combined therapy</td>
</tr>
<tr>
<td>Asilian</td>
<td>2006</td>
<td>69 patients</td>
<td>Keloids and hypertrophic scars</td>
<td>3 random groups were assigned. In group 1, intralesional TAC (10 mg/mL) was injected at weekly intervals for 8 weeks. In group 2, 0.1 mL of 40 mg/mL TAC was added to 0.9 mL of 5-FU, 50 mg/mL, and injected weekly for 8 weeks. In group 3, in addition to weekly TAC + 5-FU injection for 8 weeks, lesions were irradiated by 585 nm PDL, 5–7.5 J/cm², at the 1st, 4th, and 8th weeks</td>
<td>Efficacy of TAC + 5-FU was comparable with TAC + 5-FU + PDL, but the TAC + 5-FU + PDL combination was more acceptable to the patients and produced better results. The TAC + 5-FU + PDL combination appeared to be the best approach for treatment of keloid and hypertrophic scars</td>
</tr>
<tr>
<td>Naeini</td>
<td>2006</td>
<td>45 patients</td>
<td>Keloids or hypertrophic scars</td>
<td>Monthly, for 4 months, group A was treated with bleomycin and group B with cryotherapy and intralesional triamcinolone injection</td>
<td>Bleomycin may be more effective than cryotherapy combined with intralesional triamcinolone injection in the treatment of larger keloids and hypertrophic scars (size &gt; 100 mm²)</td>
</tr>
</tbody>
</table>

5-FU, 5-fluorouracil; PDL, pulsed dye laser; TCA, triamcinolone acetonide.
Dermal tube. Dermal tube is an innovative technique to revise tethered scars. The dermal tube alters the aesthetic outcome through the creation of volume, subsequently converting scar concavity into scar convexity. This process involves creating an ellipse around the line of depression. After de-epithelializing the ellipse, an incision is made and a tube is created to allow tissue to grow into the defect, thus improving the appearance of the scar.

Table 6 Scar revision: light

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Participants, n</th>
<th>Scar type and location</th>
<th>Study design</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alster</td>
<td>2003</td>
<td>22 patients</td>
<td>Bilateral hypertrophic inframmary scars in 22 females</td>
<td>Scars were randomly assigned to receive two treatments of either PDL alone or PDL followed immediately by 10-20 mg triamcinolone. Fluences ranging 4.5-5.5 J/cm² (average of 5.0 J/cm²) were used. Evaluation was done before each of the two treatment sessions and 6 weeks after the final treatment</td>
<td>Treatment with 585 nm PDL irradiation alone had substantial clinical and histologic improvement. The additional use of intralesional corticosteroids did not significantly enhance clinical outcome except in those scars that were the most symptomatic</td>
</tr>
<tr>
<td>Cassuto</td>
<td>2003</td>
<td>23 mature scars in 22 patients</td>
<td>Various mature scars</td>
<td>A long-pulsed frequency doubled Nd: YAG laser was used an average of 2.4 treatments. An endpoint of vessel disappearance for vascular scars or darkening or graying of pigmented scars was used. Energy density ranged from 17 J/cm² for pigmentation and 22 J/cm² for vascularity with the laser automatically selecting pulse duration</td>
<td>Treatment of persistent scar erythema can be achieved with 2-3 treatments at 17-22 J/cm² at 5 mm spot size or 65-90 J/cm² at 2 mm spot size. Facial scars showed a 94% clearance of erythema, while inframammary scars were the most difficult with only a 46% average clearance</td>
</tr>
<tr>
<td>Kwon</td>
<td>2000</td>
<td>36 patients</td>
<td>Scars from scratching, knife injury, laceration, car accident, simple excision, focal burn, and focal inflammation. scars varied from hypertrophic to depressed to burns</td>
<td>Pulsed Er:YAG laser at 500-1200 mJ/pulse at 3.5-9 W was used. Two to five passes were performed. Results were assessed 6-12 months after treatment</td>
<td>Er:YAG was effective in 9 of 12 hypertrophic scars, 17 of 20 depressed scars and 2 of 4 burn scars with improvement greater than 50%</td>
</tr>
<tr>
<td>Pham</td>
<td>2011</td>
<td>13 patients</td>
<td>Fitzpatrick skin types I-III and facial surgical scars present for at least 6 months after surgery but less than 5 years. All scars had not been previously treated within the past 6 months</td>
<td>Treatment once every 4 weeks for a total of 4 treatments. Initial settings for the 1550 nm NAFL laser at energy level 40 mJ and treatment level 4 and subsequently increased on each visit according to the patients' tolerance level</td>
<td>Statistically significant improvement in the patient's assessment of the color, stiffness, thickness, and irregularity of the scar but not for pain or itching. Observers noted a statistically significant improvement in pigmentation, thickness, relief, and pliability but not vascularity</td>
</tr>
<tr>
<td>Tierney</td>
<td>2009</td>
<td>15 scars in 12 patients</td>
<td>Scars from Mohs surgery for non-melanoma skin cancer on the face, neck, chest, and back. Patients were a minimum of 2 months out from Mohs surgery</td>
<td>Split-scar trial with treatment of one-half of the scar with 1550 nm NAFL erbium-doped fiber laser and the other half with the 595 nm V-beam PDL. Four treatments were performed at 2 week intervals with final assessment 1 month post-treatment</td>
<td>Both lasers showed improvement over baseline, however, the NAFL showed greater improvement than PDL in pigmentation, hypopigmentation, thickness, texture, overall cosmesis. Patients did cite greater pain with NAFL but still preferred it over the PDL</td>
</tr>
<tr>
<td>Ruiz-Esparza</td>
<td>2003</td>
<td>22 patients</td>
<td>Moderate to severe cystic acne scars on the face</td>
<td>A non-ablative radiofrequency unit, which delivers a concomitant spray of cryogen, was used. One session was done in 20 patients and 2 sessions in 2 patients. Average fluence per energy delivery was 72 J/cm². Follow-up ranged from 1 to 8 months</td>
<td>Patients were evaluated by questionnaires and active acne lesion counts. Excellent response (75% or greater diminution in active acne counts) was seen in 82% of the patients, moderate response in 9%, and no response in 9% of patients</td>
</tr>
</tbody>
</table>

NAFL, non-ablative fractional laser; PDL, pulsed dye laser.
made around the de-epithelialized area, and the dermal edges are approximated, forming a tube. Finally, closure is performed over this new tube.

Dermabrasion. Dermabrasion, best performed 6–8 weeks post wounding, removes the superficial skin layers, allowing re-epithelialization from underlying adnexal structures and surrounding epithelium. Dermabrasion is used primarily for improving contour and color match between the surgery site or the scar and that of the normal surrounding skin. A 2012 review article states that although dermabrasion is used less often with the advent of newer laser resurfacing, which is now available, dermabrasion remains as a viable option, especially for those with atrophic scars. A 2012 split-scar study compared fractionated CO₂ laser and diamond fraise dermabrasion on post-surgical scars of the face. Results revealed less erythema and bleeding at day 0, less erythema and edema at one week, and a trend toward less erythema at one month with fractionated CO₂.

Table 7 Scar revision: Other

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Participants, n</th>
<th>Scar type and location</th>
<th>Study design</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Klingerg⁷⁵</td>
<td>2008</td>
<td>3 patients</td>
<td>Hemifacial hypertrophic scars and keloids resulting from severe burns 2-13 years previously</td>
<td>2 injections of adipose tissue, with a 13-month interval, harvested from abdominal subcutaneous fat</td>
<td>Clinical appearance and subjective patient evaluation suggests considerable improvement in skin texture and skin thickness. Histology showed evidence of collagen deposition, local hypervascularity, and hyperplasia</td>
</tr>
<tr>
<td>Costal⁷⁶</td>
<td>1999</td>
<td>9 patients</td>
<td>Active hypertrophic scars of various locations, all post burn injuries ranging from 3 to 11 months of age</td>
<td>Elastic bandages that forced a pressure of 24 mmHg over the scar</td>
<td>Pressure treated histology samples vs. controls illustrated the presence of fibrillin and elastin more similar to normal skin</td>
</tr>
<tr>
<td>Kasper⁷⁷</td>
<td>2008</td>
<td>4 patients</td>
<td>Depressed Mohs surgical scars from basal cell carcinoma removal</td>
<td>Treated with hyaluronic acid and calcium hydroxylapatite filler agents 5-6 months after Mohs procedure</td>
<td>All patients reported “extremely satisfied aesthetic improvement”, and one patient reported a reduction in pain in the scar area</td>
</tr>
<tr>
<td>Zhibo⁷⁹</td>
<td>2009</td>
<td>12 patients</td>
<td>Established keloids</td>
<td>BTA was injected into the lesions at 3-month intervals for a maximum of 9 months at a concentration of 35 units/ml. Total doses ranged from 70 to 140 units per session</td>
<td>At 1-year follow-up, three of the included 12 patients demonstrated excellent, five good, and four fair results</td>
</tr>
</tbody>
</table>

Figure 2 Design process of the beaky-plasty. Each of the straight line limbs in conventional Z-plasty is modified into a lazy-S-curved line. Initially a Z is designed (a). Each limb of the initial Z is divided into two (b) and then further divided into two with perpendicular lines (c). Arches are drawn with the ends of the segments as centers and the arch passing through the center dots (d,e,f). Flaps are raised, rotated, and sutured (g,h). From Nagasao et al.⁴⁷
demonstrated in Campbell and Eisen’s 2010 article, is a method similar to dermabrasion utilizing electrosurgical instruments, which have the potential of lower cost, ease of use, and less bleeding. Sculpting dermabrasion, described by Snow et al. in 1994, is another similar technique to dermabrasion utilizing a no. 15 scalpel blade to microshave and feather the skin. This technique is rapid and safe, and no special surgical suits, face shields, or equipment are needed, and optimal cosmetic results can be obtained (Figs. 5 and 6).

Antimitotic drugs. Blocking any phase of mitosis results in cessation of cell proliferation and initiation of apoptosis. The current antimitotic medications, which are used for hypertrophic scars, include corticosteroids, 5-fluorouracil (5-FU), bleomycin, and mitomycin C. Corticosteroids, working through reduction of fibroblast proliferation and collagen synthesis, as well as by the suppression of inflammatory mediators, have long been used for hypertrophic scars and keloids. Corticosteroids were found to be more effective on hypertrophic scars when combined with cryotherapy, but hypopigmentation was more common in this group. Intralesional bleomycin, injected monthly into keloids that had previously failed at least three injections of intralesional triamcinolone, showed favorable results with regard to scar height, erythema, and pliability. Bleomycin acts by binding to both double- and single-stranded DNA, leading to breaks.
In large keloids and hypertrophic scars (those measuring greater than 100 mm²), bleomycin can have up to an 88% success rate with a series of three to five intralesional treatments. Fluorouracil, an analog of pyrimidine, has been shown to target rapidly proliferating fibroblasts. A 2006 study by Asilian et al. compared treatment of hypertrophic scar treatment with intralesional triamcinolone acetonide (TAC; 10 mg/ml) versus TAC + 5-FU (0.1 ml of 40 mg/ml TAC added to 0.9 ml of 5-FU [50 mg/ml]) versus TAC + 5-FU followed by 585 nm PDL laser irradiation at the first, fourth, and eighth weeks. 5-FU proved most effective when combined with corticosteroids and PDL. Mitomycin C, when applied for 3–4 minutes to the wound bed, can prevent...
keloid recurrence after resection. However, other studies did not confirm the same result.\(^\text{64}\)

**Light**

**Pulsed dye laser.** The 585 nm PDL can provide long-standing improvement of hypertrophic scars and keloids, as evidenced by reduction of scar erythema, height, symptoms, and rigidity.\(^\text{63}\) Hypertrophic scars and keloids can be treated with comparable settings to the ones used for scar prevention mentioned above. Fluences ranging from 6.0 to 7.5 J/cm\(^2\) (5 or 7 mm spot size) and 4.5 to 5.5 J/cm\(^2\) (10 mm spot size) and pulse durations from 0.45 to 1.5 ms have demonstrated improvement. Laser treatments are typically repeated at 6–8 week time intervals. After PDL, histology demonstrated a decrease in the number of fibroblasts, and the collagen fibers appeared looser and less coarse.\(^\text{66}\) Intraleisional injections of corticosteroids decreased pruritus; however, it did not significantly enhance the clinical outcome.\(^\text{66}\) PDL has also successfully been used to treat an atrophic facial scar in at least one patient.\(^\text{67}\)

**Frequency doubled Nd:YAG.** The long pulsed frequency doubled Nd:YAG laser produces laser energy at 332 nm wavelength, which is selective for oxyhemoglobin.\(^\text{68}\) Cassuto and Emanuelli demonstrated in 2003 that treatment of persistent erythema in mature scars more than two years old could be achieved with two to three treatments at 17–22 J/cm\(^2\) at a 5 mm spot size or 65–90 J/cm\(^2\) at a 2 mm spot size. Facial scars showed a 94% clearance of erythema.\(^\text{68}\)

**Er:YAG laser.** The Er:YAG has a 2940 nm wavelength with high water absorption and therefore almost total absorption by the epidermis.\(^\text{69}\) The Er:YAG has been effectively used to revise hypertrophic, depressed, and burn scars with the greatest improvement in depressed scars.\(^\text{69}\) Settings used were 500–1200 mJ/pulse and 3.5–9 W with a 2 mm handpiece.\(^\text{69}\)

**Non-ablative fractional laser.** Fraxel\(^\text{6}\) (Fraxel SR1500 RE:Store; Solta Medical, Hayward, CA, USA) is a 1550 nm erbium-doped fiber laser that creates non-ablative dermal microthermal injury zones. Facial surgical scars between six months and five years were treated every four weeks for four treatments at 40 mJ/cm\(^2\) energy and treatment level 4, covering 11% of the treated area.\(^\text{70}\)

Observers rated significant improvement in scar pigmentation, thickness, relief, and pliability but not vascularization. Younger scars tended to respond better to treatment.\(^\text{70}\)

Another split-scar study by Lin et al. showed efficacy from a 1550 nm erbium-doped non-ablative fractional laser (NAFL) for scars. Regardless of energy level, treatment density with 14% coverage was as efficacious as 26% coverage.\(^\text{71}\) Scar improvement was greater at three months than at one month, implying induction of long-term scar remodeling.

A split-scar study by Tierney et al. of scars older than two months after Mohs, compared 1550 erbium-doped NAFL and 595 nm PDL. Four treatments were performed at 2-week intervals, and a blinded physician scored the scar characteristics before and after each treatment and one month after the final treatment.\(^\text{72}\) Both lasers showed improvement over baseline. NAFL showed greater improvement than PDL in the following characteristics: pigmentation variation, hypopigmentation, thickness, texture, and overall cosmesis.\(^\text{72}\) However, patients reported greater pain with NAFL but ultimately still preferred it to the PDL.\(^\text{72}\)

**Fractionated carbon dioxide.** A 2012 split-scar study by Jared Christophel et al. compared fractionated CO\(_2\) laser and diamond fraise dermabrasion on postsurgical scars of the face.\(^\text{56}\) Results revealed less erythema and bleeding at day 0, less erythema and edema at one week, and a trend toward less erythema at one month with fractionated CO\(_2\).\(^\text{56}\)

**Radiofrequency.** Radiofrequency (RF) current is formed when charged particles flow through a closed circuit. As the energy meets resistance in the tissue, heat is produced.\(^\text{73}\) As RF energy is not dependent on any specific chromophore, it has the advantage of being useful for all skin types as epidermal atrophy is not at risk of destruction.\(^\text{73}\) Twenty-two patients with acne scars received one to three treatments with a non-ablative RF unit at an average fluence of 72 J/cm\(^2\).\(^\text{74}\) An excellent response (75% or greater diminution in acne scars) was seen in 82% of the patients, moderate response in 9%, and no response in 9% of patients.\(^\text{74}\)

**Other**

**Fat injection.** Three patients with hemifacial hypertrophic burn scars were treated with autologous fat transfer and followed for six months.\(^\text{75}\) Clinical appearance and patient satisfaction at follow-up showed improvement in skin texture and thickness.\(^\text{75}\) Histologic examination showed patterns of new collagen deposition, local hyper-vascularity, and dermal hyperplasia.\(^\text{75}\)

**Pressure.** Nine patients with active hypertrophic scars aged 3–11 months were treated with elastic bandages that created a pressure of 24 mmHg. Biopsies of pressure-treated and control scars were evaluated for collagen organization, epidermal thickness, and the presence of elastin, fibrillin, tenascin, and z-smooth muscle actin.\(^\text{76}\) Pressure-treated samples showed presence of fibrillin and elastin that was more similar to normal skin. In addition,
low levels of $\alpha$-smooth muscle actin, similar to that in normal skin, were observed.\textsuperscript{76}

**Fillers.** Four patients with depressed Mohs surgical scars were successfully treated with HA and calcium hydroxyapatite filler agents.\textsuperscript{77} Results showed only minimal downtime and high patient satisfaction and tolerance; however, correction only lasted nine months or less.\textsuperscript{77}

**Botulinum toxin.** Xiao and Qu, in a 2012 study, demonstrated *in vitro* that using BTA to inhibit hypertrophic scars was effective in the rabbit model, and the application of BTA may be useful for inhibiting hypertrophic scars.\textsuperscript{78}

Intralesional BTA for the treatment of established keloids in a prospective, uncontrolled 2009 study demonstrated some improvement in all patients at 1-year follow-up.\textsuperscript{79}

**Conclusion**

Scarring, the body’s natural response to a wound, can create many adverse cosmetic, functional, and structural effects. Scars can have a dramatic impact on a patient’s quality of life and have been associated with anxiety, social avoidance, and depression.\textsuperscript{4} While any disruption or prolongation of the wound healing process can result in greater scarring, so too can alteration in the healing process potentially result in a more favorable outcome.

Initial employment of sound surgical fundamentals prefaced by adequate explanation of realistic expectations still trump the most advanced preventative methods and revisional techniques. If the results should be less than satisfactory, numerous interventions currently exist, and research is ongoing to optimize outcomes. While scar revision as such has been the historical mainstay of therapy, more recent advances have increasingly targeted scar prevention. Whether through topical therapies, light treatment, or surgical intervention, treatments exist to allow the maximization of scar prevention and minimization of scar morbidity. While true scarless surgery may not yet be clinically obtainable, scar minimizing surgery and techniques currently exist to enhance outcomes.

**References**


