Nonablative Skin Tightening: A Review of the Literature

Shadi M. Alhalabi and Basil M. Hantash
Elixir Institute of Regenerative Medicine, San Jose, CA.

Abstract: Rhytides, wrinkles and other signs of photoaging are gaining in prevalence due to increased sun exposure, phototoxic drugs and demographic changes. Cosmeceutical products, lasers, and surgery have all been used to reverse the signs of aging. However, these treatment modalities have suffered from either limited efficacy or a high incidence of side effects and prolonged downtime. In order to overcome these limitations, physicians have turned their attention to nonablative modalities, in hopes of achieving a balance between efficacy and safety. Recent advances suggest that nonablative lasers may be effective treatment options for wrinkles by inducing skin tightening. The goal of this review is to shed light on the technical aspects and clinical outcomes of the most promising nonablative lasers currently being used to achieve skin tightening.

Introduction

A number of techniques have been employed to reduce the appearance of rhytides and skin laxity, including dermabrasion, chemical peels, and surgical reconstruction. Over a decade ago, resurfacing lasers emerged as and remain the gold standard for facial skin tightening. Despite their appreciable clinical benefit, ablative lasers remain plagued by significant downtime with an increased incidence of adverse effects such as prolonged erythema and edema, hyperpigmentation, permanent hypopigmentation, scarring and infection.1–3 Patients are now demanding procedures with both reduced downtime and sufficient clinical improvements. This has led to the development of a number of nonablative laser technologies with a more favorable risk-reward profile. Unlike ablative lasers, nonablative lasers induce a dermal thermal injury without epidermal vaporization. Often times, this epidermal protection is achieved through the adjunctive use of a surface cooling mechanism. The goal of this review is to shed light on the technical aspects and clinical outcomes of the most promising nonablative lasers currently being used to achieve skin tightening.

1064-nm Q-Switched Neodymium: Yttrium-Aluminum-Garnet Laser

The 1064-nm Q-switched neodymium:yttrium-aluminum-garnet (Nd:YAG) laser was the first nonablative tool used for skin rejuvenation.4 This system performs deep dermal heating while sparing the epidermis. The chromophores for the 1064-nm irradiation in decreasing order are melanin, hemoglobin and water.5 In 1997, Goldberg and Whitworth investigated the rhytid improvement capabilities of the Q-switched Nd:YAG laser.5 Pinpoint bleeding was sought as an endpoint for the treatment. Nine of 11 patients showed improvements but only 3 were observed to have improvements equal to that achieved with the carbon dioxide lasers. The same 3 patients exhibited erythema at 1 month post-treatment. Although modest efficacy was demonstrated, this device did not appear to deliver the ideal balance between safety and efficacy.

In 1999, Goldberg and Metzler studied the efficacy of topical carbon suspension-assisted low fluence Q-switched Nd:YAG laser treatment.6 The carbon served as an artificial chromophore and exhibited high absorption of the 1064-nm laser beam. Lower fluences were used and the majority of adverse effects were limited to mild erythema rather than pinpoint bleeding. Thus, it seems that the carbon suspension is a useful tool in reducing the adverse effects of the treatment.

In 2000, Goldberg and Silapunt treated 8 patients with perioral and periorbital rhytides using the Q-switched Nd:YAG laser, a less aggressive treatment protocol was used with only 3 treatments and a fluence of 2.5 J/cm².7 Although fair results were observed in most patients, the authors deemed the
laser system less ideal due to post-treatment petechiae in most patients. The authors suggested further investigation of optimal fluences, number of laser passes, and intervals between treatments to provide more optimal results. A year later the same authors conducted a histological study using the Q-switched Nd:YAG, fluence was raised to 7 J/cm² and an endpoint of petechiae was sought.8 Biopsy specimens revealed mild fibrosis, improvement in skin elastosis, and improved organization of collagen fibrils. However, results were only evident in 4 of 6 patients and were less impressive than those achieved with carbon dioxide laser resurfacing.

Subsequently, Goldberg and Samady conducted a clinical trial comparing the intense pulsed light (IPL) (Fluences: 40–70 J/cm²) to the Nd:YAG laser (Fluence: 100–130 J/cm²) in treating facial rhytids applying 3–5 treatments.9 Mild-to-moderate improvements were seen using both systems. A similar contact cooling system was used in both modalities. This new cooling approach allowed for fluences in the 1064-nm laser to be raised up to 130 J/cm². Although clinical improvements were similar, the 1064-nm laser was associated with better patient tolerance and less side effects.

In 2003, Dayan and colleagues performed a blinded clinical study using the 1064-nm Nd:YAG laser applying 7 treatment using a fluence of 22 J/cm² and a large 10-mm handpiece.10 The study pointed out that the better clinical improvements were evident in those patients with more severe photodamage prior to treatment. They also conceded that to recognize subtle improvements by nonablative modalities, multiple full-face treatments are necessary. Finally, the authors suggested that thorough patient education must be assured due to the strong correlation between patient satisfaction and patient’s having realistic expectations of the treatment outcomes.

Later the same year, Lee conducted a first of its kind study combining the 1064-nm Nd:YAG laser (Fluence: 24–30 J/cm²) and the 532-nm potassium titanyl phosphate (KTP) laser (Fluence: 6–15 J/cm²) applying 3–6 treatments.11 The advantage of this combination lies in the ability to address not only wrinkles but also other complications of photodamage such as telangiectasia and dyschromia. Greater collagen stimulation was observed due to the synergistic effect of both lasers. Results achieved with the KTP laser were superior to those achieved via the 1064-nm laser. Yet, the combination of both lasers resulted in outcomes superior to either lasers alone which was explained by the KTP laser targeting superficial vessels and the 1064-nm laser targeting deeper layers. Side effects were also more severe when combining both lasers while treatment with the 1064-nm laser alone produced the least side effects. The KTP laser is very well absorbed by melanin, therefore patients with darker skin were not treated to avoid complications. Clinical regression was noted at around 9 months which is believed to be the threshold for the treatment process. Patients with frequent sun exposure and rosacea are at a higher risk for recurrence of problems. The authors supported the full-face treatments concluding that the overall collagen remodeling will yield better results in localized regions.

In 2005, Dang and colleagues conducted a study comparing the biophysical properties of skin in the KM mice before and after treatment with the Q-switched 1064-nm (Fluence: 2.5 J/cm²), the 1320-nm (Fluence: 22 J/cm²) and 595-nm pulsed dye laser (Fluence: 12 J/cm²).12 The greatest skin elasticity improvements were seen in the 1064-nm laser treatment. The authors suggested that this is due to greater amounts of thermal damage caused by this modality. Marked erythema was also most evident in the 1064-nm laser compared with other modalities but this is explained by absence of a cooling system with the 1064-nm laser.

A few months later, another study compared the histologic, biochemical and mechanical properties of murine skin after treatment with the 1320-nm (Fluence: 22 J/cm²) and 1064-nm (Fluence: 2.5 J/cm²) laser systems.13 The 1064-nm system proved to be more effective than the 1320-nm system. Compared to the 1320-nm laser system, the 1064-nm laser induced 25% greater improvement in skin elasticity, 6% increased dermal thickness and 11% higher synthesis of hydroxyproline, a major component of collagen. Greater collagen III synthesis was observed in 1064-nm treatments while 1320-nm treatments mainly produced collagen I. This was assumed to be the result of different types of reactions, with the 1064-nm a photo-mechanical reaction and the 1320-nm laser a photo-thermal reaction. The importance of hydroxyproline lies in the fact that it’s a major component of collagen fibrils and rarely found elsewhere. There was also an increasing trend in dermal thickness up to 2 months. While exciting, there remains a lack of histological studies that...
assess the durability of collagen formation in the long-term.

In December, 2005, Taylor and Prokopenko conducted a first of its kind study to compare single-treatment with the radiofrequency (RF) system (Fluence: 73.5 J/cm²) versus 1064-nm Nd:YAG laser (Fluence: 50 J/cm²).14 Better overall results were evident on the laser treated sides in regards to wrinkles and skin laxity. Both systems showed similar results for texture, pores and pigmentation. Although the study was conducted on a small number of patients with only modest improvements noted in both modalities, the 1064-nm laser had the upper hand as assessed by blinded observers.

In 2007, Key conducted a split-face study comparing single-treatment with the RF system (Fluence: 40 J/cm²) versus the 1064-nm Nd:YAG laser (Fluence: 73–79 J/cm²).15 Better overall facial improvements were apparent on the laser treated sides. The 1064-nm laser also resulted in greater improvements on the lower face, while upper face improvements were the same with both modalities. This clinical trial should be credited for its strong study design which allows for better objective assessment of treatment modalities.

The 1064-nm laser system has proved to be an outstanding tool in nonablative skin tightening. Although only mild to moderate results are achieved, the use of concomitant cooling has kept adverse effects to a minimum. One advantage lies in the ability to treat all skin types, in addition to the technical ease of performing the procedure. Further prospective studies with a greater number of patients and different laser combinations are needed. Table 1 summarizes clinical trials using the 1064-nm laser.

In 1999, Kelly and his colleagues conducted a study on 35 patients with facial rhytides receiving 3 treatments using the ND:YAG 1320 (Fluence: 28–36 J/cm²) in combination with cryogen cooling.17 Mild improvements were seen at 3 months post-treatment in mild, moderate and severe rhytides. At 6 months post-treatment, statistically significant results were only seen in patients with severe rhytides. The explanation for this discrepancy is that severe rhytides have the greatest potential for improvement. The authors also determined that blistering is more likely to occur when the skin surface temperature exceeds 50 °C post-treatment, thus they recommend surface temperature to be kept between 42 °C–46 °C after each laser treatment.

The same year, Menaker and his colleagues conducted a study on 10 patients applying 3 treatments using the ND:YAG laser 1320-nm system (Fluence: 32 J/cm²).18 Pre-study testing showed that lower fluences were ineffective and higher fluences caused blisters. Thus, a balance between side effects and efficacy was necessary, but this resulted in modest clinical outcomes as only 40% of patients showed subtle improvements. Blistering was noted in 40% of patients and only seen in the periocular treatment sites. The authors postulated that this could be due to the reduced skin thickness. Therefore, certain precautions such as lower fluences must be used when treating areas of thinner skin in order to minimize side effects. In most patients who showed clinical improvements, an increase in dermal collagen was also observed histologically.

In 1999 and 2000, Goldberg conducted two studies using a newer prototype 1320-nm Nd:YAG laser (Fluence: 28–40 J/cm²).19,20 After 4 to 5 treatments, 80% to 100% of patients reported at least some improvement in the quality of their skin. Objective assessment showed that 60% to 80% of patients had skin improvements which were mostly subtle. Evidence of new collagen formation was noted in all subjects but this did not always correlate with clinical rhytid improvement. The new prototype used in this study contained a thermal sensor in its handpiece thus allowing accurate monitoring of the skin temperature during procedure. Goldberg emphasized that since each patient starts treatment with different skin temperatures, treatment parameters should be adjusted differently to each patient. Immediate erythema was the only side effect of this study.
Table 1. Review of clinical trials using the 1064-nm Q-switched Nd:YAG laser system.

<table>
<thead>
<tr>
<th>Study (Ref. #)</th>
<th>N*</th>
<th>Study type</th>
<th>Parameter</th>
<th>Indication</th>
<th>Outcome</th>
<th>Side effects</th>
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<tr>
<td>5</td>
<td>11</td>
<td>Prospective clinical trial</td>
<td>5 treatments&lt;br&gt;ST: I–II&lt;br&gt;F: 5.5 J/cm²&lt;br&gt;5-mm spot size&lt;br&gt;30% overlap&lt;br&gt;1–3 passes</td>
<td>Class I–II Perioral/ periorbital rhytids</td>
<td>Nine of eleven patients showed at least slight clinical improvements</td>
<td>Erythema&lt;br&gt;Pinpoint bleeding</td>
</tr>
<tr>
<td>6</td>
<td>61</td>
<td>Randomized multicenter clinical trial</td>
<td>3 treatments&lt;br&gt;ST: I–II&lt;br&gt;F: 2.5 J/cm²&lt;br&gt;7-mm spot size&lt;br&gt;Carbon suspension</td>
<td>Class I–II hand and facial rhytids</td>
<td>8-Month Posttreatment: Investigator Assessment: Class I rhytides: 97% showed at least slight improvement Class II rhytides: 86% showed at least slight improvement Patients Assessment: Class I rhytides: 86% showed at least slight improvement Class II rhytides: 68% showed at least slight improvement</td>
<td>Posttreatment: 60% Erythema 0.4% Pinpoint bleeding 2% Purpura 8-Weeks Posttreatment: 54% Erythema 0.9% Pinpoint bleeding 0.4% Pigmentation change</td>
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<tr>
<td>7</td>
<td>8</td>
<td>Prospective clinical trial</td>
<td>3 treatments&lt;br&gt;ST: II–IV&lt;br&gt;F: 7 J/cm²&lt;br&gt;2 passes&lt;br&gt;3-mm spot size&lt;br&gt;Endpoint of petechiae</td>
<td>Class I–III periorbital and Perioral rhytids</td>
<td>3 months post-treatment: Investigator Assessment: 75% had fair outcome 25% had poor outcome Patient Assessment: 75% had fair to good outcome 25% had poor outcome</td>
<td>Posttreatment: 75% Petechiae 38% Pinpoint bleeding 24-Hours Posttreatment: 75% No pain 35% Mild pain</td>
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<tr>
<td>8</td>
<td>6</td>
<td>Blinded histological trial</td>
<td>3 treatments&lt;br&gt;ST: II–IV&lt;br&gt;F: 7 J/cm²&lt;br&gt;2 passes&lt;br&gt;3-mm spot size&lt;br&gt;10%–20% overlap&lt;br&gt;Endpoint of petechiae</td>
<td>Infra-auricular sun-damaged skin</td>
<td>3 months post-treatment: 4/6 showed mild fibrosis with histologic improvement 2/6 showed no changes</td>
<td>N/A</td>
</tr>
<tr>
<td>9</td>
<td>15</td>
<td>Controlled clinical study</td>
<td>3–5 treatments&lt;br&gt;ST: II–III&lt;br&gt;3 passes&lt;br&gt;F: 1064-nm: 100–130 J/cm²&lt;br&gt;IPL 590-nm/755-nm: 40–70 J/cm²</td>
<td>Perioral rhytids</td>
<td>Investigator Assessment: All modalities showed mild to moderate improvement Patient Satisfaction: Higher patient satisfaction with 1064-nm laser at 2,4,8 and 24 weeks posttreatment.</td>
<td>1064-nm: 0% Erythema 6% Blisters 590-nm: 53% Erythema 53% Blisters</td>
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Nonablative laser skin tightening

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755-nm:
- 13% Erythema
- 53% Blisters
- Transient mild erythema
- Minimal to no discomfort

**Blinded pilot clinical study**
- 7 treatments
  - ST: I–V
  - F: 22 J/cm²
  - 3 passes
  - 10-mm handpiece
- Facial sun damaged skin
- Post 7th treatment:
  - Patient Assessment:
    - 42.5% reduction in fine wrinkles
    - 32% reduction in coarse wrinkles
    - 45.8 improvement in skin laxity
  - Masked Physician Assessment:
    - 10.7% reduction in fine wrinkles
    - 11.9% reduction in coarse wrinkles
    - 17.3% improvement in skin laxity
- Transient mild erythema
- Minimal to no discomfort

**Prospective clinical histological study**
- 3–6 treatments
  - ST: I–V
  - Group 1: 532-nm laser
  - Group 2: 1064-nm laser
  - Group 3: 532-nm + 1064-nm lasers
  - 532-nm laser:
    - F: 6–15 J/cm²
    - 4-mm handpiece
    - 2–4 passes
    - 1064-nm laser:
    - F: 24–30 J/cm²
    - 10-mm handpiece
- Facial sun damaged skin
- 6-Months Posttreatment:
  - Investigator assessment:
    - Group 1: 34%, 39.6%, and 42.6% is the improvement in skin tightening in group 1,2 and 3 respectively
    - Group 2: 12.4% and 40.2% is the improvement in rhytides in group 1, 2 and 3 respectively
  - Patient assessment:
    - Group 1: 35%, 14.6%, and 47% is the improvement in skin tightening in group 1,2 and 3 respectively
    - Group 2: 16% and 40.6% is the improvement in rhytides in group 1, 2 and 3 respectively
  - Observer assessment:
    - Group 1: 35%, 16%, and 44.8% is the improvement in skin tightening in group 1,2 and 3 respectively
    - Group 2: 13.6% and 37.6% is the improvement in rhytides in group 1, 2 and 3 respectively
- Histological Results:
  - New collagen formation in all patients, most evident in 3rd group

**Group 1**
- 90% Erythema
- 90% Swelling
- 12% Hyper-pigmentation
- 2% Blisters

**Group 2**
- 68% Erythema
- 40% Swelling
- 2% Blisters

**Group 3**
- 92% Erythema
- 76% Swelling
- 10% hyper-pigmentation
- 4% Blisters

**Blinded split-face study**
- Single treatment
  - ST: II–IV
  - 3 passes
- Mild to moderate sagging skin
- 1064-nm Treatment:
  - 30% median improvement in wrinkles
  - 30% median improvement in skin laxity
- None

(Continued)
<table>
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<tr>
<th>Study (Ref. #)</th>
<th>N*</th>
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<th>Indication</th>
<th>Outcome</th>
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</tr>
</thead>
<tbody>
<tr>
<td>15 12</td>
<td>Blinded split-face study</td>
<td>Single treatment</td>
<td>ST: I–II 3 passes 1064-nm: F:40 J/cm² for cheek 20–30 J/cm² for forehead 10 mm spot size RF: F: 73–79 J/cm² 1 cm² tip Several passes</td>
<td>Mild to moderate skin laxity</td>
<td>2–4 Months Posttreatment: Blinded panel Assessment: 1064-nm Laser: 47.5% overall improvement 30.2% upper face improvement 35.7% lower face improvement RF modality: 29.8% overall improvement 31.3% upper face improvement 23.8% lower face improvement Patient Assessment: 58.3% stated greater improvement on laser treated sides</td>
<td>1064-nm: Momentary discomfort</td>
</tr>
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</table>

*Number of patients.
**Only 34 patients completed the study.

**Abbreviations:** ST, Skin type; F, Fluence.
In 2001, Trelles and his colleagues tested a more aggressive protocol of 8 treatments using the 1320-nm laser system (Fluence: 30–35 J/cm²) on 10 patients. Improvements were similar to past studies, with only two patients reported satisfaction with the procedure. Mild to severe pain was associated with this treatment protocol. In order to achieve higher patient satisfaction, Trelles suggested that careful patient selection and realistic patients’ expectations are very important factors. It was also suggested that combining laser treatment with parallel epidermal treatment will yield better results.

The same year of 2001, Levy, Trelles and their colleagues treated periorbital rhytides on 13 patients with a conservative protocol of 2 treatments and a fluence of 36–39 J/cm². Silicon printing and profilometric assessment were part of the evaluation. Objective assessment showed modest changes and patient satisfaction was poor. Crusting and pitted scars were also among the side effects.

In 2002, Fatemi and his colleagues studied the short-term histological findings associated with the use of the 1320-nm laser (Fluence: 26–32 J/cm²). The best clinical results were achieved using 3 passes and a target temperature of 45 °C to 48 °C. The aforementioned parameters also induced maximal acantholysis and spongiosis, edema, neutrophil recruitment, microthrombosis, and multiple vascular changes. The study noted that subclinical epidermal injury is also an important factor in skin tightening due to the cytokines released that may contribute to the ingress of fibroblasts and their activation to synthesize new collagen.

The 1320-nm is a nonablative tool which has evolved through the years. The clinical improvements associated with the use of this device are subtle. Patients with severe rhytides seem to benefit the most, similar to the findings observed with the ND:YAG laser treatments. Side effects such as hyperpigmentation and blisters were observed. The pain experienced during treatment ranged from mild to severe. An important advancement in the system was the addition of a thermal sensor which allowed for accurate monitoring of skin temperature. The 1320-nm has also proved to induce neocollagenesis, although this did not always correlate with clinical results. Further patient trials are required in order to find the optimal parameters for the treatment of rhytides using this laser modality.

Table 2 summarizes clinical trials using the 1320-nm laser.

**ELOS Technology**

As the demand for nonablative remodeling is on the rise, a relatively new system combined the RF and diode laser energies [termed ELOS] in an attempt to treat mild to moderate facial rhytides and skin laxity. This system delivers RF energy and optical energy accompanied by thermoelectric cooling to protect the epidermis. The optical energy creates a high temperature in the treatment zone which lowers the impedance for the RF current passing through the dermis. This technology appears to be an ideal option for darker skin types due to the fact that optical energy has weak absorption of melanin and RF energy does not depend on chromophores for its effects. The temperature of the tissue is continuously measured throughout the duration of the pulse to prevent overheating and improve safety. ELOS technology comes as a combination of RF and IPL energy sources or RF and infrared energy.

In 2005, Doshi and Alster conducted one of the first studies using the aforementioned technology (Fluences: RF: 50–85 J/cm², Optical Energy: 32–40 J/cm²) applying a series of 3 treatments in 20 female subjects. Immediate erythema and edema were sought as an endpoint for each treatment. Energy was increased with each subsequent session based on the patient’s pain tolerance and clinical response. At 3 months, modest improvements were seen in all patients as assessed by the investigator and the patients. At 6 months, clinical improvements were slightly reduced as assessed by the investigator and the patients. The authors concluded that further studies are needed for better understanding of this technology and in order to reach optimal treatment parameters.

Later the same year, Kulick conducted a study on 15 patients applying a 3-treatment protocol using the ELOS technology (Fluences: RF: 50–100 J/cm², Optical Energy: 15 J/cm²). Four patients did not complete the study due to pain and other unspecified reasons. Energy settings were based on the depth of the wrinkles, and Fitzpatrick wrinkles classification was used to assess improvements. Reduction in wrinkles varied from 14% to 32%. Although patients were treated before treatment with oral diazepam or codeine, all patients felt the treatment was painful. Pain was also
Table 2. A review of trials using the 1320-nm laser.

<table>
<thead>
<tr>
<th>Study (Ref. #)</th>
<th>N*</th>
<th>Study type</th>
<th>Parameters</th>
<th>Indication</th>
<th>Results</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>17</td>
<td>35</td>
<td>Multicentre prospective clinical study</td>
<td>3 treatments F: 28–36 J/cm² 1–2 passes 5-mm spot size</td>
<td>Periorbital rhytides</td>
<td>3-Months Posttreatment: Significant improvements were noted in the mild, moderate and severe rhytide group. 6-Months Posttreatment: Significant improvements were only noted in the severe rhytide group.</td>
<td>5.6% Blisters-hyperpigmentation 2.8% Pinpoint scars</td>
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<tr>
<td>18</td>
<td>10</td>
<td>Prospective pilot clinical and histological study</td>
<td>3 treatments F: 32 J/cm² 5 mm spot size 30% overlap 4-mm post-auricular biopsies</td>
<td>Periocular and postauricular rhytides</td>
<td>1-Month Posttreatment: Minimal improvement in rhytide severity 40% Increase in collagen 40% Decrease in collagen 10% 50% had minimal homogenization of collagen 3-Months Posttreatment: Minimal improvement in rhytide severity 40% Histological assessment: Increase in collagen 30% Decrease in collagen 10%</td>
<td>100% Erythema 30% Blistering-Pitted scars 40% Hyper-pigmentation Mild—moderate pain 100% Mild burning</td>
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<tr>
<td>19</td>
<td>10</td>
<td>Prospective clinical and histological study</td>
<td>4 treatments ST: I–II F: 28–38 J/cm² 1–2 passes 5-mm spot size 3-mm post auricular biopsies Endpoint of erythema</td>
<td>Periorbital , Class I–III perioral and cheek rhytides</td>
<td>6-Months Posttreatment: Physician assessment: 20% Substantial improvement 60% some improvement 20% no improvement Patient Assessment: 80% at least some improvement Biopsy Results: Collagen formation evident in all patients</td>
<td>100% Erythema</td>
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<tr>
<td>20</td>
<td>10</td>
<td>Prospective clinical and histological study</td>
<td>5 treatments ST: I–II F: 30–40 J/cm² 1–3 passes 5-mm spot size 3-mm post auricular biopsies 30% overlap Endpoint of erythema</td>
<td>Class I–II facial rhytids</td>
<td>6-Months post treatment: Physician assessment: 0% total improvement 20% substantial improvement 40% some improvement 40% no improvement Patient assessment: 100% at least some improvement Biopsy results: Collagen formation in all patients</td>
<td>100% Erythema</td>
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<td>Page</td>
<td>Prospective Clinical and Histological Study</td>
<td>Patients</td>
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<td>Fluence</td>
<td>Biopsy</td>
<td>Posttreatment &amp; Results</td>
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<tr>
<td>21</td>
<td>8 treatments ST: I–V F: 30–35 J/cm² 5 mm spot size 10% overlap 1-mm periauricular biopsies</td>
<td>21</td>
<td>2-Weeks: 20% significant improvement 30% significant to fair improvement 30% fair improvement 20% no or very little improvement</td>
<td>full-face pericocular, perioral, periauricular rhytides</td>
<td>10% periocular blister 40% severe pain 40% mild pain 20% no pain</td>
<td>90% immediate erythema</td>
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<tr>
<td>22</td>
<td>2 treatments ST: I–II F: 36–39 J/cm² 1-mm biopsies</td>
<td>22</td>
<td>2-Months: 4/13 good improvement</td>
<td>Periorbital rhytides</td>
<td>100% Erythema</td>
<td>23% swelling 8% crusting 8% pitted scars</td>
</tr>
<tr>
<td>23</td>
<td>Single treatment F: 26–32 J/cm² 1–3 passes</td>
<td>23</td>
<td>1-hour: 3 Passes: Intraepidermal edema with acantholysis in all patients 2 Passes: milder changes 1 Pass: very minimal changes in one specimen only</td>
<td>Periauricular rhytides</td>
<td>Immediate Erythema</td>
<td>Mild to moderate discomfort</td>
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*Number of patients.

**Abbreviations:** ST, Skin type; F, Fluence.
directly proportional to the amount of RF energy and discomfort was greater for areas with less subcutaneous fat. Since pain appears to be the most prominent concern of all patients, RF energy settings should be driven by each patient’s pain tolerance with special attention paid to areas over bony prominences. Patient assessments were not included in the study, and this represented a weakness of the study.

In 2005, Sadick and colleagues also conducted a study using the ELOS technology (Fluences: RF: up to 20 J/cm², Optical Energy: 30–45 J/cm²) with an aggressive protocol of 5 treatments using the RF/IPL combination. The study was conducted at two different centers. Modest improvements in skin laxity and wrinkles were reported based on subjective patient assessment scores. The best improvements were seen in class I wrinkles compared to class II and III wrinkles. The study did not include blinded physician assessments. Side effects were minimal but some were serious such as scarring and crusting.

August 2005, Hammes and his colleagues treated 24 patients with the ELOS modality (Fluences: RF: 70–79 J/cm² Optical Energy: 26–30 J/cm²). Wrinkle improvement and pain data were collected using a numerical analogue scale. Improvements were seen in 58.3% and 74.2% of patients as measured by patients and independent physicians, respectively. Some patients had better responses than others; this discrepancy was not fully understood but could be related to age. This study further demonstrates the need for careful patient selection and appropriate study design since the findings suggested and previous studies confirm that younger patients tend to fair more favorably with laser treatments due to a more vibrant wound healing response.

In another study, Sadick and Trelles tested the ELOS technology (Fluences: RF: 80–100 J/cm² Optical Energy: 30–50 J/cm²) with 3 treatments on 23 patients in two different centers. Side effects were mostly limited to erythema and swelling and results varied from mild to moderate as assessed by the physicians. Patient assessments were less favorable; the authors concluded this was due to very high expectations of the patients enrolled in the study. Computer based assessment was also less favorable.

Yu and colleagues used the combination of RF and infrared energy (Fluences: RF: 70–120 J/cm² Optical Energy: 10 J/cm²) applying 3 treatments to 19 female Asian patients. Objective assessment showed that mild to moderate improvements were seen in 26.2% to 47.4% of areas treated. Subjective assessment showed mild to moderate improvement in 89.5% to 100% of areas treated. The study suggested that lower optical energy could be used yielding clinical improvements with higher patient safety. This study suggested that this laser combination is able to treat Asian skin with minimal side effects.

The ELOS technology with both combinations has proven to be a tool which could be used for nonablative skin tightening. Most results were assessed to be mild to moderate. Erythema was universal to all of the clinical trials. Minimal pain and blisters were also associated with this laser system. Further clinical and histological studies are needed to reach parameters that optimize the clinical benefit and minimize side effects. Table 3 reviews clinical trial conducted utilizing the ELOS technology.

### 1100 nm–1800 nm Spectrum

A novel infrared device using selectively filtered infrared lights combined with simultaneous cooling emerged as a nonablative rejuvenating tool. Infrared rays target water as a chromophore; the rays are selectively filtered in order to achieve thorough but gradual heating of the dermis. Pre-cooling, intra-treatment cooling, and post-cooling is delivered to assure epidermal protection throughout the procedure. Lower fluences and a longer heating process are two elements of treatment with this infrared device. This device has been approved by the FDA for dermal heating.

In 2006, Ruiz-Esparaza conducted a study using one to three treatments on 25 patients utilizing this novel infrared device (Fluence: 70–120 J/cm²). Most patients showed improvements ranging from minimal to excellent with immediate contraction in 22 of the 25 patients. Three patients showed no improvement. The best results were achieved when using a combination of 30 J/cm² and a high number of pulses. Patients treated at 30 J/cm² expressed no pain during the procedure. High patient satisfaction was observed as immediate results were present and minimal pain was associated with the procedure.

The same year of 2006, Zelickson and his colleagues conducted a study to assess the ultrastructural changes in cadaver and human skin post-treatment. Collagen fibril alteration was
Table 3. A review of trials using the ELOS technology.

<table>
<thead>
<tr>
<th>Study (Ref. #)</th>
<th>N*</th>
<th>Study type</th>
<th>Parameters</th>
<th>Indication</th>
<th>Result</th>
<th>Side effects</th>
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<tbody>
<tr>
<td>24</td>
<td>20</td>
<td>Prospective blinded clinical study</td>
<td>3 treatments ST: I–III 3–4 passes RF energy 50–85 J/cm² Optical energy 32–40 J/cm²</td>
<td>Mild to moderate facial and/or neck rhytids</td>
<td>3-Months Post-treatment: Blinded investigator assessment: Mean clinical improvement score is 2/4, 1.62/4, 1.38/4, and 1.85/4 in nasolabial, periorcular, perioral and cheek rhytids respectively. Patient assessment: Mean clinical improvement score is 1.77/4, 1.77/4, 1.31/4, and 1.46/4 in nasolabial, periorcular, perioral and cheek rhytids respectively. 6-Months Post-treatment: Blinded investigator assessment: Mean clinical improvement score is 1.63/4, 1.33/4, 1.27/4, and 2/4 in nasolabial, periorcular, perioral and cheek rhytids respectively. Patient assessment: Mean clinical improvement score is 1.63/4, 1.8/4, 1.1/4, and 1.36/4 in nasolabial, periorcular, perioral and cheek rhytids respectively.</td>
<td>Transient erythema 80% mild pain 10% moderate pain 10% no pain</td>
</tr>
<tr>
<td>25</td>
<td>15</td>
<td>Prospective blinded clinical study</td>
<td>3 treatments RF energy: 50–100 J/cm² Optical energy: 15 J/cm²</td>
<td>Fine to deep wrinkles Facial rhytids</td>
<td>Average Reduction in facial wrinkling by: Investigator: 30% 3 Assessors: 14%, 25%, 32%</td>
<td>Edema Painful Hyperemia</td>
</tr>
<tr>
<td>26</td>
<td>108</td>
<td>Prospective blinded clinical study</td>
<td>5 treatments ST: I–V 1 full-face pass 2–7 sub-segmental passes RF energy up to 20 J/cm² Optical energy 30–45 J/cm²</td>
<td>Rosacea, diffuse telangiectasia, dyschromia, hyper-pigmentation, class I–III wrinkles, and skin laxity</td>
<td>Physician Assessment: 40.5% overall wrinkle improvement Patient Assessment: 75.3% overall skin improvement 41.2% overall wrinkle improvement 64.7% class I wrinkles improvement 38.6% class II wrinkles improvement 20.4% class III wrinkles improvement 62.9% overall skin laxity improvement 92% overall patient satisfaction</td>
<td>8.3% Swelling 4.6% Blistering 3.7% Hyperpigmentation or hypo pigmentation 16.7% Epidermal crusting 0.9% Scarring</td>
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(Continued)
Table 3. (Continued)

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<th>Study (Ref. #)</th>
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<tbody>
<tr>
<td>27</td>
<td>24</td>
<td>Prospective blinded clinical study</td>
<td>6 treatments ST: II–III 2 passes RF energy 70–90 J/cm² Optical energy 26–30 J/cm² PD: up to 200 ms</td>
<td>class I–III wrinkles and periorbital/ perioral rhytides</td>
<td>3-Months Post-treatment: Independent physicians Assessment: 25.8% no improvement 53.3% medium improvement 19.2% good improvement 0.8% excellent improvement</td>
<td>8.3% Erythema 4.2% Oedema 4.2% Dysaesthesia</td>
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<tr>
<td>28</td>
<td>23</td>
<td>Prospective double centre clinical and histological study</td>
<td>3 treatments ST: II–IV 1 full-face pass 3 passes over wrinkles RF 80–100 J/cm² Optical energy 30–50 J/cm² Endpoint of erythema</td>
<td>Facial and neck wrinkles</td>
<td>3-Months Post-treatment: First Physician Assessment: 17% had 75%–100% improvement 43% had 50%–75% improvement 26% had 25%–49% improvement 13% had 0%–25% improvement Second Physician Assessment: 7% had 75%–100% improvement 48% had 50%–75% improvement 35% had 25%–49% improvement 9% had 0%–25% improvement</td>
<td>54% Mild erythema 23% Mild swelling 8% Superficial blister 80% Mild discomfort</td>
</tr>
<tr>
<td>29</td>
<td>19</td>
<td>Prospective blinded clinical study</td>
<td>3 treatments ST: III–V 2 passes wrinkle</td>
<td>Class I–III wrinkles, skin laxity and periorbital rhytides</td>
<td>3-Months Post-treatment: Masked Assessors Assessment: 52.6%–73.8% no improvement</td>
<td>5.3% No pain 78.9% Mild Pain 15.8% Moderate Pain</td>
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Nonablative laser skin tightening

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<tr>
<th>Score RF energy:</th>
<th>70–120 J/cm²</th>
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<tr>
<td>Optical energy:</td>
<td>10 J/cm² 50%</td>
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<th>Endpoint of Edema</th>
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<tr>
<td>21.1%–36.8% mild improvement</td>
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<td>5.3%–10.5% moderate improvement</td>
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<tr>
<td>100% Erythema</td>
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<td>5.3%–21.1% mild improvement</td>
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<td>36.8%–47.4% moderate improvement</td>
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<td>42.1%–52.6% significant improvement</td>
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Nonablative laser skin tightening

seen best with higher fluences and at the 1 to 2 mm
depths. Marginal results were observed at the shallow
derg. Contact cooling may contribute to the ef
fect of contact cooling. Again, this results in
the delicate balance between achieving sufficient
clinical efficacy while minimizing side effects.

In 2006, a multi-center investigator study
reported their longer-term (12–18 mo post-treatment)
follow-up results using the infrared device
(Fluence: 34–36 J/cm²). The authors noted that
skin laxity due to sagging responds better than
laxity due to voluminous subcutaneous fat volume.
Results were both immediate and sometimes
delayed up to 6 months. The authors suggested
combining the infrared treatment with other com-
plementary therapies yields better results. There
was a general consensus that the optimal treat-
ment parameters were using a
fluence range of
30–40 J/cm², 2–3 treatments, 1–2 passes and extra
passes on areas that need immediate contraction
or along vector lines. Complications were limited
to minor edema, but blisters were observed in
areas that were overtreated. Clinical outcome
was reported for 19 patients. Although significant improve-
ments were not available, another study in 2007 conducted by
Goldberg and his colleagues showed positive results in 11
patients who had draping skin. Mild
mild-to-moderate results were observed in sagging skin
that remained firmly associated with the subcuta-
neous tissue. No improvements were observed in patients who had draping skin.

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Table 4. A review of trials using the 1100–1800-nm spectrum.

<table>
<thead>
<tr>
<th>Study (Ref. #)</th>
<th>N*</th>
<th>Study type</th>
<th>Parameters</th>
<th>Indication</th>
<th>Results</th>
<th>Side effects</th>
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<tbody>
<tr>
<td>30</td>
<td>25</td>
<td>Blinded prospective clinical study</td>
<td>1–3 treatments ST: I–V</td>
<td>Eye brow drooping Lower face and neck skin laxity</td>
<td>Objective assessment: &lt;br&gt; Eyebrow Lifting: &lt;br&gt; 75% had improvements &lt;br&gt; Cheek and neck flaccidity: 82% had improvements &lt;br&gt; Significance of results: &lt;br&gt; 54% excellent results &lt;br&gt; 13% moderate results &lt;br&gt; 25% minimal results &lt;br&gt; 13% no results &lt;br&gt; Skin contraction up to 12-months</td>
<td>12% Superficial 2nd degree burns</td>
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<td></td>
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<td>F: 20–40 J/cm² PD: 5.3 s–6.1 s</td>
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<td>Low to moderate pain</td>
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<td>Spot area 1.5 cm²</td>
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<tr>
<td>31</td>
<td>1</td>
<td>Blinded controlled histological cadaver and human study</td>
<td>Human PD: 3 s–6 s F:30, 45, 65 J/cm² 4 passes</td>
<td>Assess ultrastructural changes</td>
<td>Discontinuous distribution of collagen changes through the dermis &lt;br&gt; In humans: Collagen alteration at 0–1 mm and 1–2 mm &lt;br&gt; In cadaver: Collagen alteration at 1–2 mm</td>
<td>N/A</td>
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<td>32</td>
<td>42</td>
<td>Multi-center clinical study</td>
<td>2–3 treatments F: 34–36 J/cm² 2 passes 2 full passes 4–8 vector passes</td>
<td>Facial and neck skin laxity</td>
<td>3-Months Post-treatment: 90% visible improvement 3% outstanding 40% moderate 46% mild 14% not visible Improvements after 2nd treatment: 2.3% Outstanding 33.3% Moderate 38% Mild 9.5% None</td>
<td>Swelling</td>
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<td>Erythema</td>
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<td>Blisters</td>
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<tr>
<td>33</td>
<td>19</td>
<td>Prospective clinical study</td>
<td>1–2 treatments Several passes</td>
<td>Lower face and neck laxity</td>
<td>100% significant improvement 100% patient satisfaction</td>
<td>Erythema</td>
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<tr>
<td>34</td>
<td>13</td>
<td>Prospective Blinded clinical study</td>
<td>2 treatments F: 30–36 J/cm² 3 passes Spot area 1.5 cm²</td>
<td>Soft tissue ptosis of the lower face and skin</td>
<td>92% had clinical improvements</td>
<td>Erythema</td>
</tr>
<tr>
<td>Study Type</td>
<td>Treatments</td>
<td>Parameters</td>
<td>End Point 1</td>
<td>End Point 2</td>
<td>Side Effects</td>
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<tr>
<td>Prospective clinical study</td>
<td>3 treatments</td>
<td>3 passes, ST: IV–V, F: 32–40 J/cm², Spot area 1.5 cm²</td>
<td>3-Months Post-treatment: Patient assessment: 5% no improvement, 38% mild improvement, 33% moderate improvement, 24% good improvement</td>
<td>Minimal to no pain, Edema</td>
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<td>6-Months Post-treatment: Patient assessment: 19% mild improvement, 38% moderate improvement, 43% good improvement</td>
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<td>Patient satisfaction: 75% Satisfied, 20% Little satisfaction, 5% Not satisfied</td>
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<td></td>
<td>2 treatments</td>
<td>3 passes, ST: III–IV, F: 36–46 J/cm², Spot area 1.5 cm²</td>
<td>1-Month Post-treatment: Blinded assessment: 56% no change, 27% moderate improvement, 18% significant improvement</td>
<td>0.8% Blisters</td>
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<td></td>
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<td>Blinded assessors reported inferior results at 3-months post-treatment</td>
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<td></td>
<td>Patients Assessment: 7.7% no change, 7.7% mild improvement, 46% moderate improvement, 42% significant improvement</td>
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<td></td>
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<td></td>
<td>Patients reported better results at 3-months post-treatment</td>
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</table>

*Number of patients.

**Abbreviations:** ST, Skin type; F, Fluence; PD, Pulse Duration.
patients showed improvements and 95% expressed overall satisfaction with the procedure. This study suggested that the device was capable of safely treating darker skin types.

In 2008, Chan and his colleagues conducted a split-face study using the infrared technology (Fluence: 36–46 J/cm²) with 2 treatments on 13 Asian patients.36 The authors observed that 27% of patients showed moderate improvement as assessed by blinded investigators. Approximately 46% of patients graded their improvements as moderate. One patient experienced a blister which was the only complication observed in the study. The authors believe that this may be due to overheating when overlapping passes or due to poor contact cooling.

This novel infrared device has been shown to be a useful tool for nonablative skin tightening. The multiple pass, low fluence approach may offer the optimal combination of safety and efficacy. Ultrastructural changes associated with the infrared light have also been confirmed. Improvements are mostly mild to moderate and in some cases excellent. The treatment is highly tolerated by patients due to the minimal pain associated with this procedure. Blistering is the most common side effect associated. This device offers another treatment option for skin tightening, although additional studies are needed to further prove its efficacy. Table 4 summarizes the clinical trials conducted using the aforementioned nonablative modality.

Conclusion
Today’s patients are more sophisticated with a preference for nonablative treatments due to concerns regarding untoward side effects, cost and prolonged downtime associated with traditional ablative laser therapy and surgical procedures. Nonablative skin tightening has emerged as a potential solution for this concern. Although nonablative skin tightening devices reduce the risk of side effects, this often appears to come at the cost of reducing efficacy. Thus far, only mild to moderate results have been achieved with nonablative modalities, and the hunt for the ideal treatment modality remains ongoing. Future studies must focus on refinement of this technology and treatment protocols if the nonablative laser modalities are to replace the historical golden standard for facial skin tightening.

**Abbreviations**
ELOS, electro-optical synergy; ER:YAG, erbium: yttrium-aluminum-garnet; IPL, intense pulsed light; KTP, potassium titanyl phosphate, Nd:YAG, neodymium:yttrium-aluminum-garnet; RF, radio-frequency.

**Disclosure**
The authors report no conflicts of interest.

**References**


