Nonablative Skin Tightening: A Review of the Literature

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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/cm^2.[7] Although fair results were observed in most patients, the authors deemed the

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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/cm^2 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/cm^2) to the Nd:YAG laser (Fluence: 100–130 J/cm^2) 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/cm^2. 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/cm^2 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/cm^2) and the 532-nm potassium titanyl phosphate (KTP) laser (Fluence: 6–15 J/cm^2) 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 telengiectasia 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/cm^2), the 1320-nm (Fluence: 22 J/cm^2) and 595-nm pulsed dye laser (Fluence: 12 J/cm^2).[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/cm^2) and 1064-nm (Fluence: 2.5 J/cm^2) 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-m 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/cm^2) versus 1064-nm Nd:YAG laser (Fluence: 50 J/cm^2).[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/cm^2) versus the 1064-nm Nd:YAG laser (Fluence: 73–79 J/cm^2).[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.

1320-nm Nd:YAG Laser

The 1320-nm laser system is one of the nonablative modalities being studied for skin tightening.[16] The primary chromophore of the 1320 wavelength is dermal water, it is very well scattered horizontally and vertically, thus allowing for maximal dermal injury.[18] The laser is coupled with a cryogen cooling system which serves to protect the epidermis.[19]

The first study combining cryogen cooling and ND:YAG 1320 was in 1997 by Nelson and his colleagues.[16] The study which was conducted on both humans and pigs proved that cryogen cooling prevented epidermal blistering and subsequent necrosis.

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/cm^2) 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/cm^2).[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/cm^2).[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.

Study (Ref. #)	N*	Study type	Parameter	Indication	Outcome	Side effects
5	11	Prospective clinical trial	5 treatments ST: I–II F: 5.5 J/cm^2 5-mm spot size 30% overlap 1–3 passes	Class I–II Perioral/ periorbital rhytids	Nine of eleven patients showed at least slight clinical improvements	Erythema Pinpoint bleeding
6	61	Randomized multicenter clinical trial	3 treatments ST: I–II F: 2.5 J/cm^2 7-mm spot size Carbon suspension	Class I–II hand and facial rhytids	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	Posttreatment: 60% Erythema 0.4% Pinpoint bleeding 2% Purpura 8-Weeks Posttreatment: 54% Erythema 0.9% Pinpoint bleeding 0.4% Pigmentation change
7	8	Prospective clinical trial	3 treatments ST: II–IV F: 7 J/cm^2 2 passes 3-mm spot size Endpoint of petechiae	Class I–III periorbital and Perioral rhytids	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	Posttreatment: 75% Petechiae 38% Pinpoint bleeding 24-Hours Posttreatment: 75% No paint 35% Mild pain
8	6	Blinded histological trial	3 treatments ST: II–IV F: 7 J/cm^2 2 passes 3-mm spot size 10%–20% overlap Endpoint of petechiae	Infra-auricular sun-damaged skin	3 months post-treatment: 4/6 showed mild fibrosis with histologic improvement 2/6 showed no changes	N/A
9	15	Controlled clinical study	3–5 treatments ST: II–III 3 passes F: 1064-nm: 100–130 J/cm^2 IPL 590-nm/755-nm: 40–70 J/cm^2	Perioral rhytids	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.	1064-nm: 0% Erythema 6% Blisters 590-nm: 53% Erythema 53% Blisters

						755-nm: 13% Erythema 53% Blisters
10	51**	Blinded pilot clinical study	7 treatments ST: I–V F: 22 J/cm^2 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
11	150	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/cm^2 4-mm handpiece 2–4 passes 1064-nm laser: F: 24–30 J/cm^2 10-mm handpiece	Facial sun damaged skin	6-Months Posttreatment: Investigator assessment: 34%, 19.6%, and 42.6% is the improvement in skin tightening in group 1,2 and 3 respectively 29.2%, 12.4% and 40.2% is the improvement in rhytides in group 1, 2 and 3 respectively Patients assessment: 35%, 14.6%, and 47% is the improvement in skin tightening in group 1,2 and 3 respectively 30.2%, 16% and 40.6% is the improvement in rhytides in group 1, 2 and 3 respectively Observer assessment: 35%, 16%, and 44.8% is the improvement in skin tightening in group 1,2 and 3 respectively 27%, 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 Group 3 92% Erythema 76% Swelling 10% hyper-pigmentation 4% Blisters
14	7	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 1. (*Continued*)

Study (Ref. #)	N*	Study type	Parameter	Indication	Outcome	Side effects
			1064-nm: F: 50 J/cm^2 10-mm spot size RF: F: 73.5 J/cm^2 1 cm^2 tip		RF Treatment: 15% median improvement in wrinkles 30% median improvement in skin laxity	
15	12	Blinded split-face study	Single treatment ST: I–II 3 passes 1064-nm: F:40 J/cm^2 for cheek 20–30 J/cm^2 for forehead 10 mm spot size RF: F: 73–79 J/cm^2 1 cm^2 tip Several passes	Mild to moderate skin laxity	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	1064-nm: Momentary discomfort

*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/cm^2) on 10 patients.[21] 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/cm^2.[22] 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/cm^2).[23] 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.[24] The system delivers RF energy and optical energy accompanied by thermoelectric cooling to protect the epidermis.[24] The optical energy creates a high temperature in the treatment zone which lowers the impedance for the RF current passing through the dermis.[25] 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.[25] The temperature of the tissue is continuously measured throughout the duration of the pulse to prevent overheating and improve safety.[27] ELOS technology comes as a combination of RF and IPL energy sources[26] or RF and infrared energy.[28]

In 2005, Doshi and Alster conducted one of the first studies using the aforementioned technology (Fluences: RF: 50–85 J/cm^2, Optical Energy: 32–40 J/cm^2) applying a series of 3 treatments in 20 female subjects.[24] 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/cm^2, Optical Energy: 15 J/cm^2).[25] 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.

Study (Ref. #)	N*	Study type	Parameters	Indication	Results	Side effects
17	35	Multicentre prospective clinical study	3 treatments F: 28–36 J/cm^2 1–2 passes 5-mm spot size	Periorbital rhytides	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.	5.6% Blisters-hyper pigmentation 2.8% Pinpoint scars
18	10	Prospective pilot clinical and histological study	3 treatments F: 32 J/cm^2 5 mm spot size 30% overlap 4-mm post-auricular biopsies	Periocular and postauricular rhytides	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%	100% Erythema 30% Blistering-Pitted scars 40% Hyper-pigmentation Mild—moderate pain 100% Mild burning
19	10	Prospective clinical and histological study	4 treatments ST: I–II F: 28–38 J/cm^2 1–2 passes 5-mm spot size 3-mm post auricular biopsies Endpoint of erythema	Periorbital , Class I–III perioral and cheek rhytides	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	100% Erythema
20	10	Prospective clinical and histological study	5 treatments ST: I–II F: 30–40 J/cm^2 1–3 passes 5-mm spot size 3-mm post auricular biopsies 30% overlap Endpoint of erythema	Class I–II facial rhytids	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	100% Erythema

21	10	Prospective clinical and histological study	8 treatments ST: I–V F: 30–35 J/cm^2 5 mm spot size 10% overlap 1-mm periauricular biopsies	full-face periocular, perioral, periauricular rhytides	2-Weeks Posttreatment: 20% Significant improvement 30% significant to fair improvement 30% fair improvement 20% no or very little improvement <u>Biopsy results:</u> Neocollagenisis in all patients Patient Satisfaction: 20% satisfied with results	10% periocular blister 40% severe pain 40% mild pain 20% no pain 90% immediate erythema
22	13	Prospective clinical and histological study	2 treatments ST: I–III F: 36–39 J/cm^2 1-mm biopsies	Periorbital rhytides	2-Months Posttreatment: <u>Physician assessment:</u> 4/13 good improvement Patient Satisfaction: 12/13 poor satisfaction <u>Profilometry study:</u> 4/13 marked improvement 7/13 fair improvement 1/13 deterioration	100% Erythema 23% swelling 8% crusting 8% pitted scars
23	10	Controlled short-term histological study	Single treatment F: 26–32 J/cm^2 1–3 passes	Periauricular rhytides	1-hour Posttreatment: <u>3 Passes</u>: Intraepidermal edema with acantholysis in all patients <u>2 Passes</u>: milder changes <u>1 Pass:</u> very minimal changes in one specimen only 3-days Posttreatment: <u>3 Passes</u>: Microthrombosis, widened vessels, sclerosis of the vessel walls and neurophilic granulocytes in all specimens <u>2 Passes</u>: milder changes (some specimens) <u>1 Pass:</u> no changes Clinical results observed after 2–3 passes only	Immediate Erythema Mild to moderate discomfort

*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/cm^2, Optical Energy: 30–45 J/cm^2) with an aggressive protocol of 5 treatments using the RF/IPL combination.[26] 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/cm^2 Optical Energy: 26–30 J/cm^2).[27] 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/cm^2 Optical Energy: 30–50 J/cm^2) with 3 treatments on 23 patients in two different centers.[28] 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/cm^2 Optical Energy: 10 J/cm^2) applying 3 treatments to 19 female Asian patients.[29] 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 susggested 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.[30] Pre-cooling, intra-treatment cooling, and post-cooling is delivered to assure epidermal protection throughout the procedure.[30] Lower fluences and a longer heating process are two elements of treatment with this infrared device.[32] This device has been approved by the FDA for dermal heating.[33]

In 2006, Ruiz-Esparaza conducted a study using one to three treatments on 25 patients utilizing this novel infrared device (Fluence: 70–120 J/cm^2).[30] 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/cm^2 and a high number of pulses. Patients treated at 30 J/cm^2 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.[31] Collagen fibril alteration was

Table 3. A review of trials using the ELOS technology.

Study (Ref. #)	N*	Study type	Parameters	Indication	Result	Side effects
24	20	Prospective blinded clinical study	3 treatments ST: I–III 3–4 passes RF energy 50–85 J/cm^2 Optical energy 32–40 J/cm^2	Mild to moderate facial and/or neck rhytids	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, periocular, 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, periocular, 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, periocular, 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, periocular, perioral and cheek rhytids respectively.	Transient erythema 80% mild pain 10% moderate pain 10% no pain 80% Edema 10% Vesiculation
25	15	Prospective blinded clinical study	3 treatments RF energy: 50–100 J/cm^2 Optical energy: 15 J/cm^2	Fine to deep wrinkles Facial rhytids	Average Reduction in facial wrinkling by: Investigator: 30% 3 Assessors: 14%, 25%, 32%	Edema Painful Hyperemia
26	108	Prospective blinded clinical study	5 treatments ST: I–V 1 full-face pass 2–7 sub-segmental passes RF energy up to 20 J/cm^2 Optical energy 30–45 J/cm^2	Rosacea, diffuse telangiectasia, dyschromia, hyper-pigmentation, class I–III wrinkles, and skin laxity	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	8.3% Swelling 4.6% Blistering 3.7% Hyperpigmentation or hypo pigmentation 16.7% Epidermal crusting 0.9% Scarring

(*Continued*)

Table 3. (*Continued*)

Study (Ref. #)	N*	Study type	Parameters	Indication	Result	Side effects
27	24	Prospective blinded clinical study	6 treatments ST: II–III 2 passes RF energy 70–90 J/cm^2 Optical energy 26–30 J/cm^2 PD: up to 200 ms	class I–III wrinkles and periorbital/ perioral rhytides	3-Months Post- treatment: Independent physicians Assessment: 25.8% no improvement 53.3% medium improvement 19.2% good improvement 0.8% excellent improvement Patients Assessment: 41.7% no improvement 41.7% medium improvement 16.7% good improvement	8.3% Erythema 4.2% Oedema 4.2% Dysaesthesia 45.8% No pain 50% Minimal pain 4.2% Slight pain
28	23	Prospective double centre clinical and histological study	3 treatments ST: II– IV 1 full-face pass 3 passes over wrinkles RF 80–100 J/cm^2 Optical energy 30–50 J/cm^2 Endpoint of erythema	Facial and neck wrinkles	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 Patient Assessment: 9% had 75%–100% improvement 22% had 50%–75% improvement 35% had 25%–49% improvement 35% had 0%–25% improvement Software Assessment: 50% had 50%–75% improvement 20% had 25%–49% improvement 30% had 0%–25% improvement Biopsy Results: Increase in epidermal thickness and more compact collagen fibers throughout the dermis	54% Mild erythema 23% Mild swelling 8% Superficial blister 80% Mild discomfort
29	19	Prospective blinded clinical study	3 treatments ST: III–V 2 passes wrinkle	Class I-III wrinkles, skin laxity and periorbital rhytides	3-Months Post-treatment: Masked Assessors Assessment: 52.6%–73.8% no improvement	5.3% No pain 78.9% Mild Pain 15.8% Moderate Pain

Score RF energy:	21.1%–36.8% mild improvement	100% Erythema
70–120 J/cm^2	5.3%–10.5% moderate improvement	15.8% Edema
Optical energy:	Patients Assessment:	7% Superficial crusting
10 J/cm^2 50%	5.3%–10.5% no improvement	
overlap	5.3%–21.1% mild improvement	
Endpoint of Edema	36.8%–47.4% moderate improvement	
	42.1%–52.6% significant improvement	

*Number of patients
Abbreviations: ST; Skin type, F; Fluence.

seen best with higher fluences and at the 1 to 2 mm depths. Marginal results were observed at the shallower depths and lower fluencies, likely due to the effect of contact cooling. Again, this reiterates the delicate balance between achieving sufficient clinical efficacy while minimizing side effects. It should be noted that skin tightening does not always correlate with immediate positive histological findings. This is explained by the fact that full clinical effect may take weeks or months to be demonstrated.

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/cm^2).[32] 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 complimentary therapies yields better results. There was a general consensus that the optimal treatment parameters were using a fluence range of 30–40 J/cm^2, 2–3 treatments, 1–2 passes and extra passes on areas that need immediate contraction or along vector lines. Complications were limited to minor erythema, but blisters were observed in areas that were overtreated. Clinical outcome ranged from mild to moderate in most patients. In 2007, Bunin and Carniol conducted a study using the infrared device, applying one to two treatments on 19 patients.[33] Although significant improvements were reported for all patients, details on parameters and results were not available.

Another study in 2007 conducted by Goldberg and his colleagues showed positive results in 11 of 12 patients each receiving two treatments (Fluence: 30–36 J/cm^2).[34] The best results were observed in patients who had draping skin. Mild to moderate results were observed in sagging skin that remained firmly associated with the subcutaneous tissue. No improvements were noticed in the jowls. Although all nonablative laser modalities currently target collagen, the presence of sagging may indicate compromise of the dermal-subcuteaneous junction, a condition that may not be easily addressed in the absence of more traditional surgery.

Later the same year, Chua and colleagues conducted a study to assess the efficacy of the infrared device (Fluence: 32–40 J/cm^2) with 3 treatments on 21 Asian patients.[35] They observed that 86% of

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

Study (Ref. #)	N*	Study type	Parameters	Indication	Results	Side effects
30	25	Blinded prospective clinical study	1–3 treatments ST: I–V F: 20–40 J/cm^2 PD: 5.3 s–6.1 s Spot area 1.5 cm^2	Eye brow drooping Lower face and neck skin laxity	Objective assessment: Eyebrow Lifting: 75% had improvements Cheek and neck flaccidity: 82% had improvements Significance of results: 54% excellent results 13% moderate results 25% minimal results 13% no results Skin contraction up to 12-months	12% Superficial 2nd degree burns Low to moderate pain
31	1	Blinded controlled histological cadaver and human study	Human PD: 3 s–6 s F:30, 45, 65 J/cm^2 4 passes Cadaver PD: 5s–10s F:50,100 J/cm^2	Assess ultra structural changes	Discontinuous distribution of collagen changes through the dermis In humans: Collagen alteration at 0–1 mm and 1–2 mm In cadaver: Collagen alteration at 1–2 mm	N/A
32	42	Multi-center clinical study	2–3 treatments F: 34–36 J/cm^2 2 passes 2 full passes 4–8 vector passes	Facial and neck skin laxity	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	Swelling Erythema Blisters
33	19	Prospective clinical study	1–2 treatments Several passes	Lower face and neck laxity	100% significant improvement 100% patient satisfaction	Erythema
34	13	Prospective Blinded clinical study	2 treatments F: 30–36 J/cm^2 3 passes Spot area 1.5 cm^2	Soft tissue ptosis of the lower face and skin	92% had clinical improvements	Erythema

35	21	Prospective clinical study	3 treatments ST: IV–V F: 32–40 J/cm^2 3 passes Spot area 1.5 cm^2	Facial and neck skin laxity	3-Months Post-treatment: Patient assessment: 5% no improvement 38% mild improvement 33% moderate improvement 24% good improvement 6-Months Post-treatment: Patient assessment: 19% mild improvement 38% moderate improvement 43% good improvement Patient satisfaction: 75% Satisfied 20% Little satisfaction 5% Not satisfied Physician's assessment: 86% mild to excellent lifting 14% no lifting	11% Blistering Minimal to no pain Edema
36	13	Prospective split-face single-linded clinical study	2 treatments ST: III–IV F: 36–46 J/cm^2 3 passes Spot area 1.5 cm^2	Forehead, cheek and submental laxity	1-Month Post-treatment: Blinded assessment: 56% no change 27% moderate improvement 18% significant improvement Blinded assessors reported inferior results at 3-months post-treatment Patients Assessment: 7.7% no change 7.7% mild improvement 46% moderate improvement 42% significant improvement Patients reported better results at 3-months post-treatment	0.8% Blisters

*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/cm^2) 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.

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