Clinical Evaluation of Enhanced Nonablative Skin Rejuvenation Using a Combination of a 532 and a 1,064 nm Laser

Mei-Heng Tan,[1] Jeffrey S. Dover, MD,[1,2,3]* Te-Shao Hsu,[1] Kenneth A. Arndt,[1,2,3,4] and Brigitte Stewart[1]
[1]*Skincare Physicians, Chestnut Hill, Massachusetts*
[2]*Department of Dermatology, Yale University School of Medicine, New Haven, Connecticut*
[3]*Department of Medicine (Dermatology), Dartmouth Medical School, Hanover, New Hampshire*
[4]*Department of Dermatology, Harvard Medical School, Boston, Massachusetts*

Background and Objectives: Improvements in the physical signs of photoaging can be achieved by non-invasive laser resurfacing procedures. To evaluate the effectiveness and safety of the Nd:YAG 1,064 nm and KTP 532 nm lasers for non-invasive skin rejuvenation.
Study Design/Patients and Methods: Subjects requesting non-invasive skin rejuvenation underwent two treatments with the 532 nm laser to one side of the face and with both lasers to the other side, followed by three treatments with the 1,064 nm laser to both sides. Skin characteristics were evaluated before, during, and up to 4 months after treatment.
Results: A >25% improvement in overall skin condition was observed for >30% of subjects at the 1 month follow-up and >40% of subjects at the 4 month follow-up. The greatest improvements were observed for visual dryness, roughness, and uneven pigmentation. No adverse events were reported. There was a trend for greater improvement in patients who received more 1,064 nm treatments but this was not statistically significant.
Conclusions: The 532 nm KTP and 1,064 nm Nd: YAG lasers can be effectively and safely used for non-invasive skin rejuvenation. Lasers Surg. Med. 34:439–445, 2004.

Key words: non-ablative; rejuvenation; 532 nm laser; 1,064 nm laser

INTRODUCTION

Minimally invasive dermatological procedures have become very popular in the United States in the past few years [1]. The most commonly used lasers for skin resurfacing procedures are the carbon dioxide (CO_2) laser and the erbium:yittrium-aluminum-garnet (Er:YAG) laser [2–5]. These lasers utilize an ablative technique to remove the epidermis and upper dermal layers in order to promote re-epithelialization of a new epidermal layer and re-configuration of collagen structural proteins in the upper dermis. The treatment initiates growth of new collagen fibers that replace the elastotic, disorganized collagen/elastin connective tissue matrix associated with wrinkled or photodamaged skin, thus promoting a tightening of the skin and elimination of fine wrinkles.

The CO_2 and Er:YAG lasers have generally shown good results in diminishing and removing wrinkles. However, since the wavelengths used with these lasers target water as the major chromophore, these treatments ablate the full epidermis before reaching the target papillary dermis. Post-procedure, the epidermis has to heal requiring substantial care and regular changing of facial dressings for up to 14 days [6]. As the surface of the skin heals, the transparent epidermis appears pinkish-red in color for up to 3–6 months, during which time the patient must avoid exposure to direct sunlight [7]. Additional side effects may include hyperpigmentation, hypopigmentation, hypertrophic scarring, an inability of the skin to tan normally, and infection [6,8,9].

By selectively targeting chromophores in the dermis it may be possible to replicate the heat damage to the dermis produced by the CO_2 and Er:YAG lasers without damaging the epidermis. Improvements in skin conditions resulting from sun exposure, such as erythema, telangiectasia, and pigmentary changes can be achieved by targeting natural chromophores such as epidermal melanin and hemoglobin in blood vessels [10]. 532 nm laser light is highly absorbed by both melanin and hemoglobin [11] and is effective in treating both red and brown discoloration associated with sun damage [12]. Many wavelengths of light have been demonstrated to stimulate new collagen production in the papillary dermis [13–16]. 1,064 nm light is not well absorbed by melanin in the epidermis, but penetrates deep into the skin [17]. Unlike shorter wavelengths it has the potential for collagen rejuvenation of both the papillary and reticular dermis, with minimal epidermal damage [18–20]. Thus, a combination of these two laser treatments (532 and

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*Correspondence to: Jeffrey S. Dover, MD, Skincare Physicians of Chestnut Hill, 1244 Boylston Street, Suite 302, Chestnut Hill, MA 02467. E-mail: jdover@skincarephysicians.net
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1,064 nm) could potentially improve signs of chronic photodamage and also stimulate collagen production with minimal damage to the epidermis.

The objective of this study was evaluate the effectiveness of the long pulsed Nd:YAG 1,064 nm laser in conjunction with the KTP 532 nm laser for non-invasive skin rejuvenation.

PATIENTS AND METHODS

Subject Selection

Subjects who requested non-invasive treatment of facial wrinkles or skin rejuvenation were enrolled by convenience sampling. The study was conducted at one study site between October 2002 and July 2003. The study protocol, informed consent form, and advertisements for subject recruitment were approved by the Western Institutional Review Board prior to study initiation. Male and female subjects, at least 18-years-old, with a Fitzpatrick skin classification of I, II, III, or IV and either mild to moderate rhytids around the eyes and on the upper lip, or facial lentigines, erythema, or telangiectasia, were eligible for inclusion in the study. Subjects were excluded if they had undergone a previous laser treatment on the intended treatment sites within 6 months; had an active localized or systemic infection; were immunocompromised; had any coagulation disorder or photosensitivity to laser or collimated light; were pregnant or nursing; had psoriasis, vitiligo, active herpes simplex, or a history of keloid formation; or were using topical medications such as antibiotics, benzoyl peroxide, tretinoin, alpha-hydroxy preparation with concentrations greater than 8%, corticosteroids, or dihroxy acetone-containing products. No form of anesthesia was used. All subjects read and signed an informed consent form prior to the initiation of any treatment.

Device Descriptions

Two laser systems were used in this study: the "Lyra" Nd:YAG 1,064 nm laser system with extended duration pulse (EDP) and the "Aura" KTP 532 nm laser with StarPulse modality (Laserscope, San Jose, CA). The 1,064 nm Nd:YAG laser was used with a 10 mm hand piece with active cooling. The KTP 532 nm laser was used with 2 and 4 mm hand pieces with the Cool Spot cooling module. Both lasers are approved by the FDA for general dermatological applications.

Treatments and Evaluations

Each subject underwent five treatments at approximately 4-week intervals. For the first two treatments, one side of the face (selected at random prior to treatment) was treated with the 532 nm laser only, and the other side was treated with a combination of both the 532 and 1,064 nm lasers. For the last three treatments, both sides of the face were treated with the 1,064 nm laser only. All treatments were given at two pulses per second.

Treatments 1 and 2. The 532 nm KTP laser was first used to treat individual lentigines and telangiectasia over the entire face using a 2 mm beam diameter at 16 J/cm^2 and 18 milliseconds pulse duration. Each individual lentigo was treated with individual 2 mm spots laid down directly on the lentigo, one abutting the other to be sure that each lentigo was completely treated. The endpoint was slight graying of the lentigo. Individual telangiectasia were the traced from one end to the other. The endpoint of treatment was the vessel disappeared entirely. The 532 nm KTP laser was then used to treat the entirety of one side of the face using a 4 mm beam diameter, fluence of 9 J/cm^2 and a 30 milliseconds pulse duration. The treatment was performed applying the hand piece to the skin and moving it across the face with individual pulses applied one next to the other. A first pass was performed moving the hand piece across the face in a horizontal pattern then a second pass was performed moving the hand piece in a vertical pattern (Treatment A). The opposite side of the face was first treated with the same two passes described above followed by two passes using the 1,064 nm Nd:YAG laser with a 10 mm beam diameter, at 40 J/cm^2 and 65 milliseconds pulse duration for the lower face, and at 24 J/cm^2 with 30 milliseconds pulse duration to periorbital areas avoiding skin inside the orbital rim. The treatment was performed applying the hand piece to the skin and moving it across the face with individual pulses applied one next to the other. A first pass was performed moving the hand piece across the face in a horizontal pattern then a second pass was performed moving the hand piece in a vertical pattern (Treatment B). Cool gel was applied to all sites prior to treatment. Each laser hand piece has a chilled (1.5°C) sapphire tip aligned coaxial with the laser beam which when applied firmly and evenly to the skin insures adequate skin cooling. This limits unwanted epidermal damage and provides pain relief. All patients wore external eye shields. Gauze was placed inside the patients mouth overlying the teeth to protect them when treating with the 1,064 nm Nd:YAG laser.

Treatments 3, 4, and 5. Both sides of the face were treated with only the 1,064 nm Nd:YAG laser but not the 532 nm laser using the same parameters described above.

Subjects' assessments of skin characteristics (fine wrinkles, coarse wrinkles, visual dryness, roughness, uneven pigmentation, skin laxity, and overall appearance: where "fine wrinkles" was defined as shallow wrinkles that can be seen on close inspection in the mirror; "coarse wrinkles": deeper wrinkles that can be felt with fingertips and are easily noticeable; "visual dryness": dryness that can be seen as well as felt; "roughness": a rough texture that can be felt with your fingertips; "uneven pigmentation": including "sunspots" and unwanted freckles; "skin laxity": unwanted looseness of the skin; and "overall": how evaluators felt about their overall facial skin appearance and texture) were evaluated before treatment and 1 month after the final treatment on a scale from 0 (no problem) to 9 (severe problem). Subjects' evaluation of percentage improvement in these skin characteristics were assessed at 1, 2, and 4 months after the fifth treatment on a scale using 0–10%, 10–25%, 25–50%, 50–75%, 75–100% increments. Subjects' overall satisfaction and investigators' satisfaction

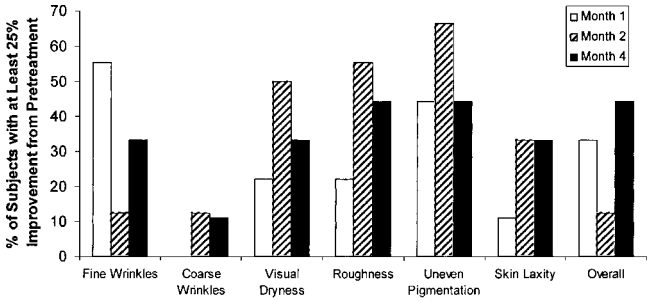

Fig. 1. Percentage of subjects with at least 25% improvement in specific skin conditions based on subjects own assessments, at 1 month (open bars; n = 9), 2 months (hatched bars; n = 8 or 9), and 4 months (solid bars; n = 9) after the end of treatment. Results are for overall improvement of all treated areas.

with treatment for the right and left sides of the face at 1, 2, and 4 months after the final treatment were assessed on a scale reflecting improvement using <29%, 30–39%, 40–49%, 50–59%, 60–69%, 70–79%, 80–89%, and 90–100% increments.

Standardized digital photographs were taken before each treatment, and at each follow-up visit. Pre-treatment and follow-up images were evaluated by a blinded panel of five dermatologic surgeons uninvolved in the treatments. Photographs were evaluated for the same skin characteristics on a scale from 0 (unapparent) to 9 (severe) 1 month following the final treatment.

Average improvement for each treatment was calculated using the mid-point of each scale increment. Paired tests were used for statistical comparisons of the two treatment methods.

Adverse events, such as blanching, crusting, pin-point bleeding, erythema, edema, itching, oozing, and blistering were also recorded immediately following each treatment and at each follow-up visit.

RESULTS

Ten subjects were enrolled in the study, but one subject discontinued after the second treatment due to inability to meet visit requirements and was not included in the evaluations. All nine subjects who completed the study were female. Five were Fitzpatrick skin type II and four type III. For the Fitzpatrick classification of facial wrinkling, one subject was class I (mild), five were class II

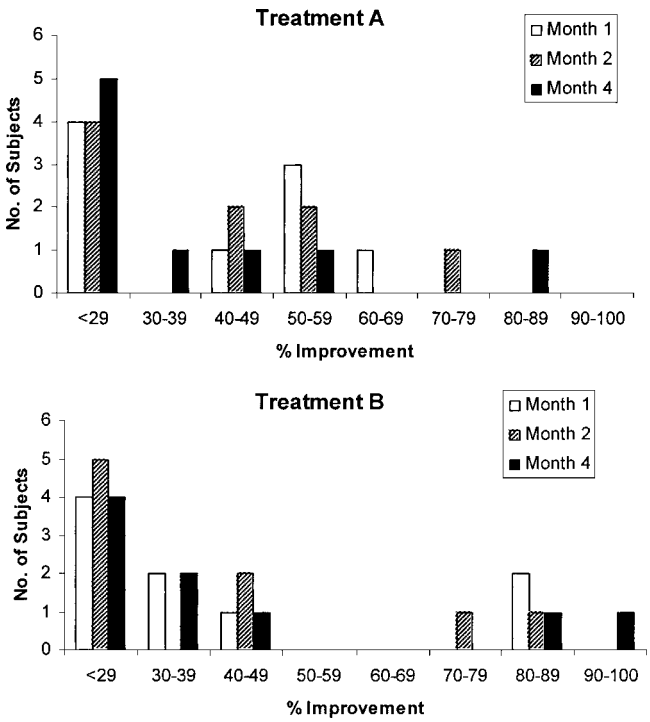

Fig. 2. Subject overall satisfaction with treatment at 1 month (open bars), 2 months (hatched bars), and 4 months (solid bars) after the end of treatment for Treatment **A** (**upper panel**) and Treatment **B** (**lower panel**). Treatment A: KTP (532 nm laser) only for two treatments followed by Nd:YAG (1,064 nm) laser for three treatments. Treatment B: KTP plus Nd:YAG lasers for two treatments followed by Nd:YAG laser only for three treatments (n = 9 for each treatment).

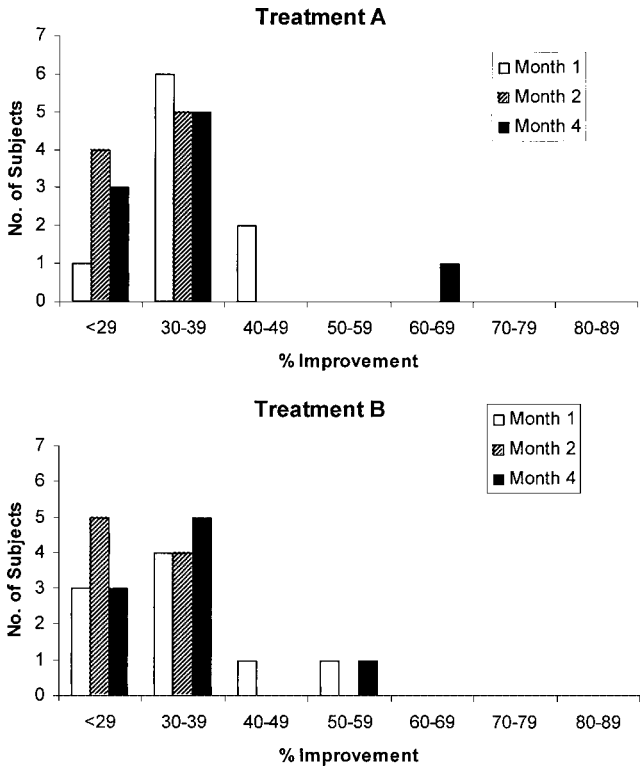

Fig. 3. Investigator overall satisfaction with treatment at 1 month (open bars), 2 months (hatched bars), and 4 months (solid bars) after the end of treatment for Treatment **A** (**upper panel**) and Treatment **B** (**lower panel**). Treatment A: KTP (532 nm laser) only for two treatments followed by Nd:YAG (1,064 nm) laser for three treatments. Treatment B: KTP plus Nd:YAG lasers for two treatments followed by Nd:YAG laser only for three treatments (n = 9 for each treatment).

(moderate), and three were class III (severe). All subjects found the procedure tolerable with minimal discomfort in spite of the absence of any form of anesthesia.

Improvements in Individual Skin Characteristics

Based on the subjects' assessments, the most notable improvements in individual skin characteristics were observed for visual dryness, roughness, and uneven pigmentation. At the 2 month follow-up, over 50% of subjects had at least a 25% improvement in these three conditions and 66% of subjects had a 50–75% improvement in uneven pigmentation (redness, telangiectasia, and solar lentigines). At the 4 month follow-up, over 30% of subjects had at least a 25% improvement in all skin characteristics including skin texture and fine to moderate wrinkling except for coarse wrinkles. An improvement of at least 25% in overall skin condition was noted by over 30% of subjects at the 1 month follow-up and by over 40% of subjects at the 4 month follow-up (Fig. 1).

Treatment Comparison

At the 1 month follow-up, five subjects reported at least a 30% improvement in overall satisfaction for each treatment. At least 50% improvement was reported for four subjects with Treatment A (two 532 nm laser treatments and three 1,064 nm laser treatments) and an 80–89% improvement was noted for two subjects with Treatment B (two 532 nm laser treatments and five 1,064 nm laser treatments). At the 4 month follow-up, at least 30% improvement was observed for four subjects with Treatment A and five subjects with Treatment B. Two subjects had at least 50% improvement with Treatment A and two subjects had at least 80% improvement with Treatment B (Fig. 2). Two subjects felt a significantly greater overall satisfaction with Treatment B compared to Treatment A, two subjects were slightly more satisfied with Treatment A than Treatment B, and five subjects were equally satisfied with both treatment regimens. The average overall improvement based on the subjects' assessments at the 4 month follow-up was 32.3% for Treatment A and 38.9% for Treatment B.

At the 1 month follow-up, a majority of subjects (8/9 for Treatment A and 6/9 for Treatment B) were considered by the investigators to have an overall improvement of at least 30%. One subject had an improvement of 50–59% with Treatment B. At the 4 month follow-up, six subjects for each

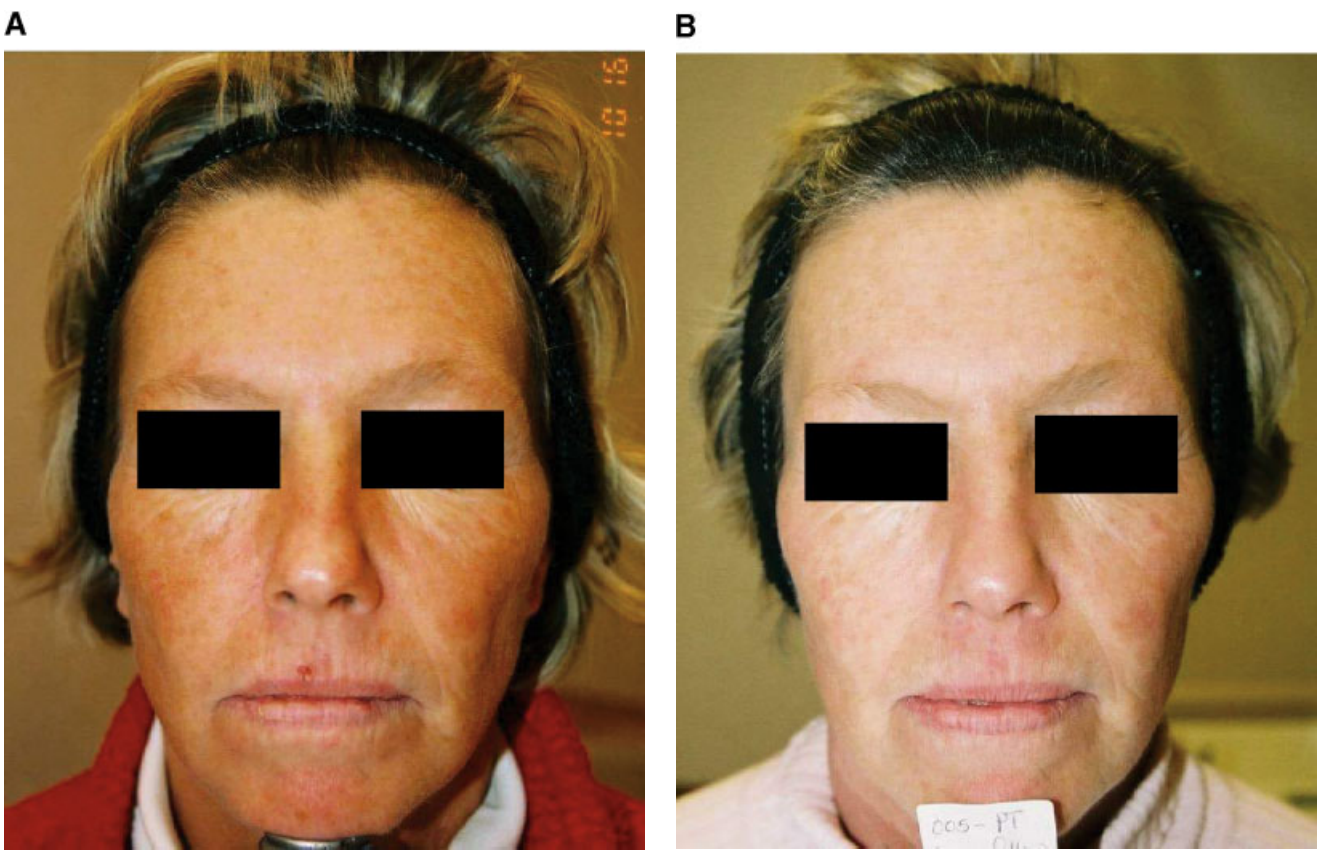

Fig. 4. **A**: Study subject before treatment. **B**: One month after five treatments. Right side, treatment B-532 and 1,064 nm; left side, treatment A-532 nm only for first two treatments. Subject overall satisfaction right and left sides 50–59%. Investigator overall satisfaction right side <29%, left side 30–39%. [Figure can be viewed in color online via www.interscience.wiley.com.]

treatment had at least a 30% improvement and one subject with each treatment had at least a 50% improvement (Fig. 3). There were no statistically significant differences between the two treatments for the investigator assessment of overall improvement. The average overall improvement based on the investigators assessment at the 4 month follow-up was 31.2% for Treatment A and 30.1% for Treatment B.

Blinded Investigator Assessment

Blinded investigator analysis performed 1 month after the last treatment revealed that all subjects had an overall improvement. This analysis showed improvement in fine wrinkles in two-thirds of subjects and a slight improvement in coarse wrinkles in five of nine patients. There were significant improvements in solar lentigines for all subjects and in erythema and telangiectasia for two-thirds of subjects (Figs. 4 and 5). Blinded investigator analysis did not find significant improvements in skin laxity, overall skin appearance or tone. Whilst there was a trend for the sides that received more 1,064 nm laser treatments to show a greater degree of textural improvement, this was also not significant.

Adverse Events

No subject reported any incidents of blistering, bruising, crusting, itching, edema, oozing, bleeding, or swelling during or immediately following any of the treatments.

DISCUSSION

The goals for rejuvenation of photoaged skin are to decrease dyspigmentation, telangiectasia, and erythema, and to improve rhytids, skin texture, and tone. The results of this study show that the combination of the 532 nm KTP and 1,064 nm Nd:YAG lasers can be effectively used to treat some of the signs of photodamage. The 532 nm laser selectively targets epidermal melanin and hemoglobin in blood vessels to achieve improvements in skin pigmentation and stimulates new collagen production in the papillary dermis [11,21,22]. 1,064 nm light penetrates to greater depth in the skin to stimulate collagen rejuvenation of both the papillary and reticular dermis [18–20], without the ablative epidermal effects of CO_2 and Er:YAG lasers. It is so poorly absorbed by hemoglobin and melanin to be relatively ineffective in the doses selected to improve either skin redness, telangiectasia, or dyspigmentation. The combination of the two lasers resulted in notable improvements in

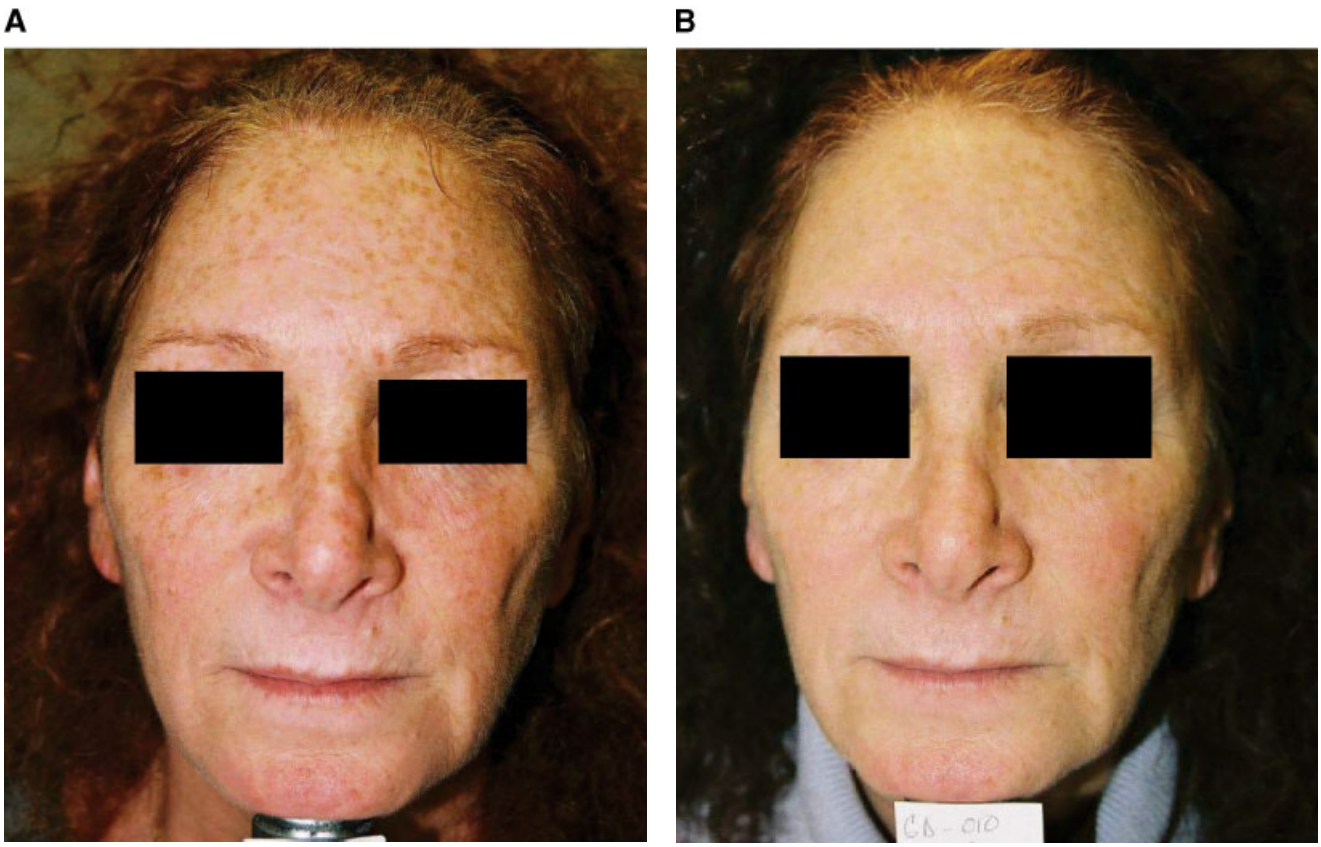

Fig. 5. **A**: Study subject before treatment. **B**: One month after five treatments. Right side, treatment B-532 and 1,064 nm; left side, treatment A-532 nm only for first two treatments. Subject overall satisfaction right side 80–89%, left side 50–59%. Investigator overall satisfaction right and left sides 30–39%. [Figure can be viewed in color online via www.interscience.wiley.com.]

sun-induced uneven pigmentation (lentigines, erythema, and telangiectasia) and fine solar-induced rhytids. In addition, improvements in skin texture and some improvement in skin laxity were observed.

While not statistically significant, the sides of the face treated with five 1,064 nm treatments showed greater clinical improvement in skin texture both based upon patient's own and by the blinded panelists observations than the side of the face treated with only three 1,064 nm treatments. There was a high patient satisfaction with the treatment protocol.

Unlike ablative laser skin resurfacing techniques, these treatments were not associated with any adverse side effects. There were no reports of any blistering, bruising, crusting, itching, edema, oozing, bleeding, or swelling with any of the treatments.

Carniol et al. [21] discussed the potential for non ablative facial skin rejuvenation using the long pulsed 532 nm diode laser. Lee [22] performed a comprehensive clinical and histological study on 150 patients who received between three and six treatments of either the 532 nm KTP laser, the 1,064 Nd:YAG laser or both lasers to the entire face. As expected, based on the reasoning above, the 532 nm KTP laser produced greater skin tightening and improvement in tone, texture and rhytids and far superior improvement in pigmentation and redness compared to the 1,064 nm Nd:YAG laser. Combination treatment with both lasers was found to be slightly superior to either alone.

The design of our study makes it difficult to directly compare with Lee's [22] study. We evaluated two different treatment regimens using the combinations of both lasers and found that two initial treatments using both the 532 nm KTP laser and 1,064 nm Nd: YAG followed by a further three treatments with the 1,064 nm Nd: YAG laser was slightly superior in addressing skin texture than two treatments using the 532 nm KTP alone followed by three treatments with the 1,064 nm Nd: YAG. More treatments with the 1,064 nm Nd: YAG results in a trend to greater improvement in texture.

A number of factors have limited the results of this study. The small number of subjects makes statistical significance difficult to achieve. Our data does not significantly support the statement that the side that recieved all five Nd:YAG laser treatments was better. There was no statistically significant difference noted and the number of subject is too small to draw any conclusions about the differences between the two sides. The lack of difference is probably due to the small number of subjects and the close similarity of treatments. The most visible response would occur from the KTP laser which was applied to both sides. The mild effects of the Nd:YAG laser on fine lines and texture was probably drowned in the KTP effect and there was not a sufficient difference between three and five treatments to be noticeable.

The study was conducted between October 2002 and July 2003, with the treatment phase spanning from October 2002 to March 2003, the majority of treatments in fall and winter. It is possible that seasonal variations may have affected the study outcomes as subjects' pigmentation may naturally lessen during the fall and winter seasons without the benefit of pigment laser treatments. Conducting the study during winter may have also influenced by worsening the skin parameters of dryness, roughness and fine lines.

Although these treatment regimens do not overcome one of the drawbacks of non-invasive skin rejuvenation—the need for multiple treatments–the overall skin improvements seen in our study were notable and were achieved without any adverse side effects. Thus, the combination of the 532 nm KTP laser and the 1,064 nm Nd:YAG laser can be effectively used to improve multiple signs of photoaging.

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