

---

# Nonablative Remodeling: A 14-Month Clinical Ultrasound Imaging and Profilometric Evaluation of a 1540 nm Er:Glass Laser

NATHALIE FOURNIER, MD,\* SERGE DAHAN, MD,<sup>†</sup> GILBERT BARNEON, MD,<sup>‡</sup> CÉLINE ROUVRAIS, MSc,<sup>§</sup> STÉPHANE DIRIDOLLOU, PhD,<sup>§</sup> JEAN MICHEL LAGARDE, PhD,<sup>§</sup> AND SERGE MORDON, PhD<sup>¶</sup>

\*Center Commercial La Croisée, Clapiers, France, <sup>†</sup>Dermatologie, Clinique St. Jean du Languedoc, Toulouse, France, <sup>‡</sup>Parc Euromédecine, Grabels, France, <sup>§</sup>Center Jean Louis Alibert, Institut de Recherche Pierre Fabre, Toulouse, France, and <sup>¶</sup>INSERM, Lille, France

---

**BACKGROUND.** Nonablative remodeling has been recently proposed as a new antiaging treatment with no downtime.

**OBJECTIVE.** To evaluate the efficacy and safety of nonablative skin remodeling with a 1540 nm Er:glass laser and contact cooling on perioral and periorbital rhytides at 14 months follow-up.

**METHODS.** Forty-two female patients (mean age 47 years), Fitzpatrick skin types I–IV were treated five times at 6-week intervals and checked 6 months after the last treatment. Patients were evaluated using clinical data, patient satisfaction (scale 1–4), digital pictures, ultrasound imaging, and profilometry data from silicone imprints in order to quantify the degree of improvement.

**RESULTS.** All subjects reported an improvement in the quality and visual aspect of their skin at 6 months (mean patient satisfaction

3.06/4) and at 14 months after enrollment (mean patient satisfaction 2.90/4). This was confirmed by a 43.41% reduction of anisotropy ( $P < 0.001$ ) 6 weeks after the fourth treatment, reaching 44.85% reduction 6 months after the fifth treatment ( $P < .001$ ). Ultrasound imaging demonstrated a 17% increase in dermal thickness ( $P < .001$ ) at 6 months and 11% 6 months after the last treatment ( $P < .05$ ). A lack of immediate or late adverse effects was noted at all stages of the procedure.

**CONCLUSION.** This study demonstrated that irradiation with a 1540 nm Er:glass laser emitting in a pulsed mode and coupled with an efficient cooling system increased dermal thickness, reduced the anisotropy of the skin, and improved clinical aspects. The lack of adverse effects within the 14 months confirmed that this procedure was safe. Overall the stability of the results many months after the treatment was remarkable.

N. FOURNIER MD, S. DAHAN, MD, G. BARNEON, MD, C. ROUVRAIS, MSc, S. DIRIDOLLOU, PhD, J. M. LAGARDE, PhD, AND S. MORDON, PhD HAVE INDICATED NO SIGNIFICANT INTEREST WITH COMMERCIAL SUPPORTERS.

---

A GROWING majority of patients are interested in the potential of nonablative therapy to smooth their wrinkles. Remodeling could be a new issue for them. This procedure induces controlled thermal dermal damage, leading to subsequent collagen remodeling while preserving the epidermis. Ross et al.<sup>1</sup> evaluated an Er:glass laser for nonablative skin remodeling, but the parameters used caused severe thermal damage which led to side effects and no remodeling. With this wavelength and different parameters, Mordon et al.<sup>2</sup> has demonstrated on rats that this laser could induce

collagen tightening and neocollagen synthesis without damaging the overlying epidermis. In 2001, Fournier et al.<sup>3</sup> published a preliminary clinical study with histology, profilometry, and ultrasound imaging involving 60 patients with a follow-up at 6 months.

The purpose of this study was to evaluate in a long-term study the efficacy and safety of nonablative skin remodeling on perioral and periorbital rhytides of this 1540 nm Er:glass laser at 14 months follow-up. Objective techniques such as ultrasound imaging and profilometry with silicone imprints were emphasized in this study.

## Materials and Methods

### Laser

The Er:Glass laser 1540 nm Aramis (Quantel Medical, Clermont-Ferrand, France) laser is a laser devoted to dermato-

---

Address correspondence and reprint requests to: Serge Mordon, PhD, UPRES EA 2689, INSERM IFR 114, Pavillon Vancostenobel, Lille University Hospital, 59037 Lille Cedex, France, or e-mail: mordon@lille.inserm.fr.

logical treatment (patent 5.897.549). The emitted wavelength (1.54  $\mu\text{m}$ ) is of particular interest because of the high water absorption. The wavelength is obtained from a specific co-doped Yb-Er:phosphate glass material, optimized for high-efficiency pumping absorption. The laser head is optimized to reduce pump radiation absorption by water and it is based on high-diffusion materials. The laser works in normal mode, delivering up to 5 J in 3 msec. It can work in either in single-shot mode or in a pulse-train mode with a repetition rate of up to 3 Hz. The beam is delivered by an optic fiber. An aiming beam is provided by a red laser diode. Internal cooling avoids a water connection and only a standard power outlet (10 A) is required. The system is compact, monitored by a microprocessor, and compliant with all medical standards.

For this study the laser was tuned at 8 J/cm<sup>2</sup>/pulse. The periorbital area was treated with three pulses (24 J/cm<sup>2</sup>) at a 2 Hz repetition rate and the perioral area was treated with five pulses (40 J/cm<sup>2</sup>). For both areas, a 4 mm spot handpiece was used, connected to a cooling system.

### Cooling System

The skin was cooled with a cryogen-sapphire tip handpiece (Constans Handpiece, Quantel Medical, Clermont-Ferrand, France) in direct contact with the skin. Cooling is obtained by purified tetrafluoroethane cryogen circulating in the tip. This handpiece has an 8 mm diameter viewing area and includes a real-time temperature monitor at the sapphire for immediate feedback. This handpiece is connected to an electronic unit producing a temperature stability within 1°C during treatment. For this clinical study, the cooling temperature was set at 5°C and contact was maintained for at least 2 seconds before firing the laser.

### Clinical Protocol

For each patient, age, sex, and phototype were recorded. Phototype was evaluated using Fitzpatrick's classification (I–VI). All perioral and periorbital areas involved in this protocol had no previous aesthetic treatments (lifting, filling injections, peeling, lasers, etc.). Contraindications to enrollment were the following: history of other laser procedures on the face, collagen-related diseases, treatment with isotretinoin within 2 years, keloids, pregnancy, peeling, dermabrasion, fillings, or antiaging treatments (creams, tablets).

Only perioral and periorbital rhytides were considered in this procedure. On each patient, four wrinkles were precisely located (A, B, C, and D) with ink, so they could be traced on a sketch accompanying each patient file and pictured easily. These rhytides were also noted on a tracing mask used for silicone imprint location and positioning of the ultrasound probe.

Unwanted effects were systematically noted before and after every treatment (1, none; 2, erythema; 3, edema; 4, blister; 5, hyperpigmentation; 6, hypopigmentation; 7, bruising; 8, skin whitening; 9, scarring). Pain was evaluated by the patient on a scale of 1–4 and recorded (1, none; 2, minimal; 3, bearable; 4, unbearable). Patient satisfaction was recorded according to the

improvement obtained, side effects, and discomfort observed on a scale 1–4 (1, not at all; 2, poorly satisfied; 3, satisfied; 4, very satisfied).

### Treatment

Patients did not use sun protection before or after the treatment, even in summer, since melanin absorption at 1.54  $\mu\text{m}$  is very low. No anesthesia was used. Along every wrinkle, 4 mm shots were juxtaposed (one shot consisting of three pulses for periorbital rhytides and of five pulses for perioral rhytides). Since there was no clinical end point visible with this technique, slight overlapping was accepted. The treatments were performed in two laser centers (Montpellier and Toulouse).

### Photographs

Digital photographs were taken at the first treatment—before, immediately after, 7 days after, and 6 weeks after—before and 6 weeks after for the next five treatments, and 6 months after the last treatment.

### Silicone Imprints

The silicone imprint process results in a “negative” replica of the surface of the skin using a silicone elastomer. Skin replicas of the periorbital and perioral areas were done, according to the technique described by Grove et al.<sup>4</sup> The technique used in this study was described in a previous article.<sup>3</sup> Anisotropy better reflected the improvement after treatment of the rhytides than the usual criteria of profilometry. Applications varied over a wide variety of systems, including actin networks and collagen networks.<sup>5</sup> Skin anisotropy is due to fiber alignment inside the skin, which results from prolonged exposure to a surrounding stress state. This anisotropy was believed to be caused by the preferential orientation of collagen fibers in the dermis.<sup>6</sup> In the case of skin remodeling, the extracellular matrix is changed over a period of months by dermal fibroblasts. The orientation of the initially deposited collagen is supposed to be a key in subsequent remodeling, setting a pattern which is then perpetuated.<sup>7</sup> The older the skin is, the more the anisotropy increased due to the disappearance of the arrangement of collagen networks. A value of 60–80 is usual for an 80-year-old patient, whereas a value of 15–20 is usual for a 20-year-old patient. The silicone imprints were performed at N0 (before treatment), N2 (6 weeks after the second treatment), N4 (6 weeks after the fourth treatment), and N5 (14 months after enrollment).

### Ultrasound Imaging

Ultrasound is a unique quantitative and qualitative tool for evaluating effects on the skin. With this technology it is possible to calculate changes in skin thickness and relate this to product performance. Ultrasound uses high-frequency sound waves to create an image of the skin and its immediate sub-

strate. A high-frequency signal is sent out from the emitting source into the skin. When the sound wave strikes a tissue it sends out an "echo," and for each tissue layer another echo is created. The size or amplitude of each of these echoes in conjunction with the difference in time it takes for the echoes to return to the emitting source provide the information needed to produce a two-dimensional representation of the skin. In this study, skin thickness was determined with a high-resolution B-mode real-time ultrasonic scanner (Derm-Cup 2020, MT, Toulouse, France). High resolution is obtained by means of a strongly focused, 20 MHz center frequency transducer with a 25 MHz bandwidth at  $-6$  dB. This system displays 10 frames/sec. The scanning field is 6 mm (laterally)  $\times$  5 mm (axially). The resolution is 0.2 mm (laterally) and 0.08 mm (axially).

Once the two-dimensional picture has been created, it is possible to see the structure of the skin as well as measure the thickness of the epidermis, the dermis, or subcutaneous fat. In measuring skin thickness the computer calculates the distance between two points and provides a measurement of this distance with an accuracy of 0.01 mm. Ultrasound imaging was performed at the Center Jean Louis Alibert, Toulouse. The recordings were done before treatment (T0), 3 months after the first treatment (T1), 1 week after the third treatment (T2), 1 month after the third treatment (T3), and 6 months after the fifth treatment (T4).

#### *Procedure and Follow-Up*

Patients were treated every 6 weeks, had five treatments, and had a control visit 6 months after the last treatment; the duration of the study was 14 months. For each session, digital pictures were taken before and after were taken and pain, secondary effects, and patient satisfaction were recorded. Silicon imprints were done before, at 12 weeks, at 24 weeks, and at 14 months. Ultrasound imaging was performed before the first treatment, 1 week after the third treatment, 3 weeks after the third treatment, and 14 months after enrollment.

#### *Data Analysis*

Data were analyzed by one author at INSERM (Lille, France), using digital pictures before and after treatments, quantitative analysis of silicone imprints, patient satisfaction index, and ultrasound images. Student's statistical tests were used to highlight the results.

## **Results**

### *Patients*

The enrollment consisted of 42 female patients, ranging in age from 34 to 67 years (mean age 47 years), with skin phototypes I-IV. All signed a consent form, which was approved by the local ethical committee.

Results were obtained at 6, 12, 18, 24, 30, and 54 weeks. Overall 210 treatment sessions were performed.

### *Side Effects*

For all 210 treatments, no side effects were reported, scored as 1 for all patients. When using this laser with the parameters given above, there was no immediate visible effect: no swelling, no erythema (except for a few seconds due to refreshment of the skin by the cooling device), and no bleaching. There were also no late visible side effects such as dyschromia, scabbing, or blisters. The treatment was almost imperceptible, with treated and untreated sites indistinguishable from each other, so the search of a visible clinical endpoint was not possible with this procedure.

### *Pain*

No pain (score 1) was reported in 210 sessions. Pain was scored 2 (minimal pain) for two sessions, probably because the cooling system was not applied long enough. When the laser and its cooling device are used properly and with the parameters of this study, patients experienced no discomfort, and only a very comfortable refreshing feeling due to the cooling device.

### *Patient Satisfaction*

Six weeks after the fourth treatment (6 months) patient satisfaction was scored at 3.06. At this time, 62% of patients scored their satisfaction as 3 (satisfied) or 4 (very satisfied). All appreciated particularly the lack of pain, discomfort, and downtime. Some patients had higher expectations than what they got, and were disappointed with their results. Some noticed that their improvement was slow (in months) and mild. They felt a sensation of a more elastic and more firm skin. Some were enthusiastic about their treatments. The majority of them wanted to go through further procedures. At 1 year patient satisfaction was scored at 2.9, despite the fact that the last treatment was performed 6 months before. This shows that the improvement lasted for months after the last treatment.

### *Photographs*

All patients had digital pictures taken as described previously. One can see a progressive and global mild improvement appearing around the third treatment and lasting at least 6 months after the last treatment. Some of the wrinkles became smoother and others nearly disappeared. None of the patients had full clearance of their wrinkles (Figure 1).



Figure 1. Left periorbital area A) before and B) 14 months later.

*Silicone Imprints*

Data came from 14 patients. Initially the anisotropy factor was 37.27. The improvement of anisotropy was 22.89% six weeks after the second treatment (anisotropy 28.74), 43.41% six weeks after the fourth treatment (anisotropy 21.09), and 44.85% at 14 months, including all treated sites (anisotropy 20.61). This improvement was more significant on periorbital areas (46.8% improvement) than on perioral areas (35.01%) at 6 months. It improved slightly at 14 months: 47.14% for the periorbital area and 38.64% for the perioral area (Figure 2). Statistical analysis showed a significant difference between N0 and N2 ( $P < .001$ ), N2 and N4 ( $P < .001$ ). The values of anisotropy decreased more and more as the number of treatments increased, mean-

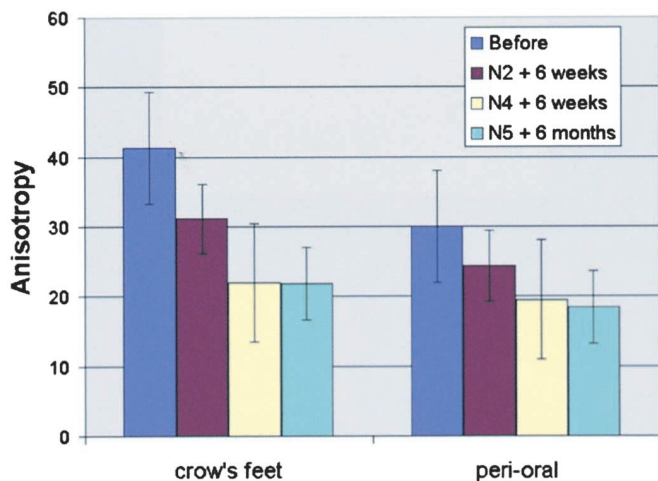


Figure 2. Improvement of anisotropy versus the number of treatments (crow's feet, nine patients; perioral, five patients).

ing that the microfurrows of the cutaneous microrelief progressively lost the preponderant direction given by the selected rhytide on every imprint (Figure 3). The three-dimensional images clearly reflected the softening of the wrinkle and the disappearance of the parallel microfurrows around this wrinkle, meaning that the skin slowly went back to the aspect it had before the rhytide put its mark on it. These results confirmed that the process of remodeling is long and that it improves with time.

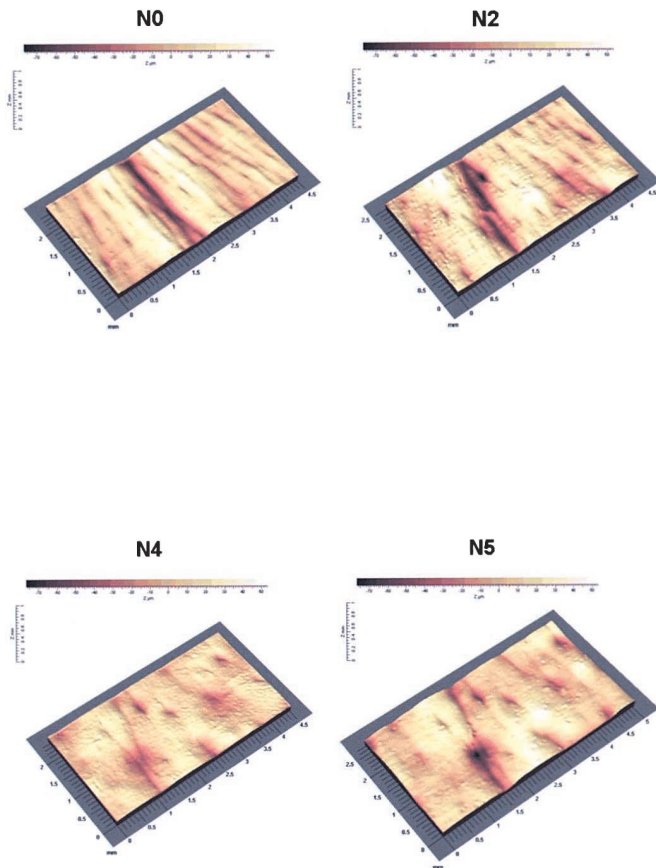
*Ultrasound Imaging*

Dermal thickness increased as a function of time. It was noted for four patients. Eighteen weeks after the first treatment (1 month after the third treatment), an increase of 17% in dermal thickness was obtained, and at 14 months an 11% increase was noted compared to the enrollment data (Figure 4).

**Discussion**

This study presented the follow-up at 14 months of another study previously published with results at 6 months.<sup>3</sup> At 6 months, including all treated sites, the results were the following: 40.2% reduction of anisotropy ( $P < .001$ ) 6 weeks and a 17% increase in dermal thickness ( $P < .005$ ). At 14 months, for the same sites, the results were the following: 44.85% reduction of anisotropy and 11% increase in dermal thickness ( $P < .005$ ).

Objective data obtained from silicone imprints and ultrasound imaging are not observer dependent and allowed comparison with other studies.<sup>8</sup> In this study and the previous one, our objective data are correlated

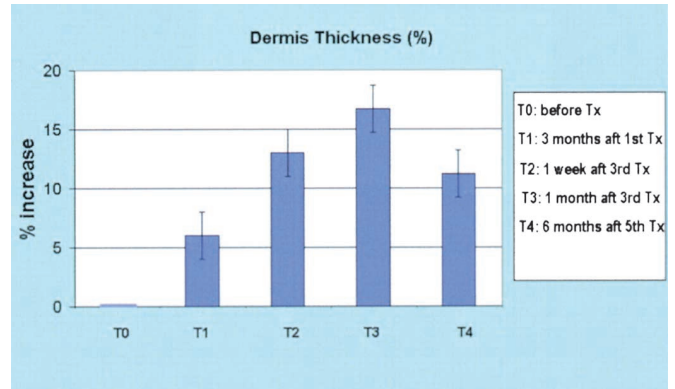


**Figure 3.** Example of a three-dimensional image after processing (periorbital area) (N0, before treatment; N2, 6 weeks after the second treatment; N4, 6 weeks after the fourth treatment; and N5, 14 months after enrollment).

to the clinical effects. Moreover, this type of evaluation is probably more reproducible than those based on evaluation of clinical pictures, which are too dependent on the quality of the pictures, the exposure, the eye of the observer, and the ability of the photographer.

With this long-term follow-up, average patient satisfaction was similar throughout the study, as it was 3.06 at 6 months and 2.90 at 14 months. This stability can be explained by the fact that patients felt comfortable with this treatment. And even if the wrinkles do not disappear totally, they are smoothed. Besides, the patients described improvements in the elasticity and quality of their skin: they felt they “looked well.”

The level of patient satisfaction was correlated to the clinical pictures. Silicone imprints have provided a study of the cutaneous microrelief. The fact that is remarkable in our study is that this criteria of level of anisotropy diminishes with time. So even if the wrinkles do not completely disappear, the overall skin surface is improved. Several articles mention optical profilometry. However, the data are usually missing and it is not possible to compare them with our study.<sup>9</sup>



**Figure 4.** Percentage increase in dermal thickness ( $n = 4$ ). The recordings were done before treatment (T0), 3 months after the first treatment (T1), 1 week after the third treatment (T2), 1 month after the third treatment (T3), and 6 months after the fifth treatment (T4).

Concerning the ultrasound imaging, the increase of the dermis thickness obtained at 18 weeks after the first treatment was 17% (1 month after the third treatment) and reached 11% six months after the fifth treatment. This slight reduction was expected since a horizontal rearrangement of the new collagen fibers is usually obtained as time passes.<sup>10–12</sup> Similarly there are no comparable data in the literature.

Finally, these excellent results were obtained with an absolute lack of side effects and for all the patients who were not practicing sun protection. This means that the risk of hypo- or hyperpigmentation is almost none with this wavelength and the parameters used in our study.

It must be emphasized that these results are not due to the wavelength alone, but also to a judicious choice of parameters. Ross et al.,<sup>13</sup> with a similar wavelength but a different machine, did not obtain remodeling, but a lot of unwanted effects such as scars, blisters, etc. It was done on the postauricular area, which is not a sun-damaged area. The fluences ranged from 16 to 146 J/cm<sup>2</sup>, 2–6 J/cm<sup>2</sup>/pulse, and the number of pulses ranged from 8 to 48. The skin was cooled at  $-10^{\circ}\text{C}$  and the spot size was 5 mm. The lack of remodeling after the procedure could be explained by two main facts. The delay between pulses inside the pulse train was too short: less than half of that used in Mordon et al.’s<sup>2</sup> study. The fluences were too high, as the critical efficacy threshold is around 60 J/cm<sup>2</sup>, otherwise the epidermis can be damaged. By emitting in a pulse-train mode, this laser allows adjustment of the depth where the thermal effect should be spatially induced. As demonstrated in the experimental study, it appears to be a much better solution than single-pulse emission.<sup>2</sup> It could be regulated, within limits, by adjusting the cooling temperature and the number of pulses

in the sequence. As we chose a fixed temperature of 5°C for all the treatments, and as the number of pulses increased, the deeper the thermal effect was. The fluence per pulse was also adapted so the intensity of the thermal effect induced by the total fluence could be controlled to avoid the critical temperature which leads to cell destruction. The aim was to stimulate the fibroblasts, not to destroy them. Increasing the fluences per pulse is tempting for physicians, since they can see a slight clinical end point. The thickness of preserved tissue is greater for the lowest temperature, and the depth of the damaged tissue depends on the number of pulses, corresponding to the total energy applied on the skin. According to this principle, different numbers of pulses were used in this study depending on the thickness of the skin area treated in order to obtain thermal damage to a determined depth corresponding to fibroelastosis zone.

Using the same laser and similar parameters, Lupton and Alster<sup>14</sup> performed remodeling on 24 patients who had discrete to moderate wrinkles on the perioral and periorbital areas. Fluences ranged from 30 to 40 J/cm<sup>2</sup>, 10 J/cm<sup>2</sup>/pulse. The number of pulses ranged from three to four. Patients had four treatments at 1-month intervals. Clinical evaluation and digital pictures were performed at 1, 3, and 6 months after the last treatment. Samples for histology were taken just after, at 1 month, and at 6 months after the first treatment. Progressive improvement of skin texture and of the wrinkles were obtained after each control. There was no unwanted effects except a brief erythema linked to the cooling. Biopsies of the last control showed a significant increase in collagen. These results are very close to the ones we obtained in our study. The authors emphasized the fact that the improvement is slow, over many months. This characteristic of remodeling must be clearly explained to the patient; if not, they will be disappointed and there is a high risk that they will give up before the end of the full procedure. In our study, the subjective and objective improvement occurred progressively, over months, and lasted 6 months after the last treatment.

## Conclusion

In this study, objective investigation processes led to indisputable data which are correlated to the clinical evaluation. The anisotropy data fitted well with the

patient satisfaction index. This 1540 nm laser emitting in a pulsed mode, coupled with this cooling system, is safe; there were no adverse effects and no downtime. To avoid patient disappointment, physicians should clearly explain that remodeling requires months to reach its goal. Long-term follow-up showed that the improvement continues after each treatment and lasted for months after the last session.

*Acknowledgments* The authors wish to thank Quantel Medical (France) for the loan of the laser, sponsoring of the silicone imprint evaluations, and ultrasound image processing.

## References

- Ross EV, Sajben FB, Miller CH, Barnette DJ, Hsia J. Non-ablative skin remodeling: selective dermal heating using an IR laser with surface cooling. *Lasers Surg Med* 1999;11(suppl):25-6.
- Mordon S, Capon A, Creusy C, et al. In vivo experimental evaluation of skin remodeling by using an Er:glass laser with contact cooling. *Lasers Surg Med* 2000;27:1-9.
- Fournier N, Dahan S, Barneon G, et al. Nonablative remodeling: clinical, histologic, ultrasound imaging, and profilometric evaluation of a 1540 nm Er:glass laser. *Dermatol Surg* 2001;27:799-806.
- Grove GL, Grove MJ, Leyden JJ. Optical profilometry: an objective method for quantification of facial wrinkles. *J Am Acad Dermatol* 1989;21:631-7.
- Olsen L, Maini PK, Sherratt JA, Dallon J. Mathematical modelling of anisotropy in fibrous connective tissue. *Math Biosci* 1999;158:145-70.
- Nickell S, Hermann M, Essenpreis M, Farrell TJ, Kramer U, Patterson MS. Anisotropy of light propagation in human skin. *Phys Med Biol* 2000;45:2873-86.
- Dallon J, Sherratt J, Maini P, Ferguson M. Biological implications of a discrete mathematical model for collagen deposition and alignment in dermal wound repair. *IMA J Math Appl Med Biol* 2000;17:379-93.
- Marks R, Edwards C. The measurement of photodamage. *Br J Dermatol* 1992;127(suppl 41):7-13.
- Goldberg DJ, Rogachefsky AS, Silapunt S. Non-ablative laser treatment of facial rhytides: a comparison of 1450nm diode laser treatment with dynamic cooling as opposed to treatment with dynamic cooling alone. *Lasers Surg Med* 2002;30:79-81.
- Dunn MG, Silver FH. Viscoelastic behavior of human connective tissues: relative contribution of viscous and elastic components. *Connect Tissue Res* 1983;12:59-70.
- Guidry C, Grinnell F. Studies on the mechanism of hydrated collagen gel reorganization by human skin fibroblasts. *J Cell Sci* 1985;79:67-81.
- Imayama S, Braverman IM. A hypothetical explanation for the aging of skin. Chronologic alteration of the three-dimensional arrangement of collagen and elastic fibers in connective tissue. *Am J Pathol* 1989;134:1019-25.
- Ross EV, Sajben FP, Hsia J, Barnette D, Miller CH, McKinlay JR. Nonablative skin remodeling: selective dermal heating with a mid-infrared laser and contact cooling combination. *Lasers Surg Med* 2000;26:186-95.
- Lupton JR, Alster TS. Nonablative cutaneous laser resurfacing using a 1.54µm erbium-doped phosphate glass laser: a clinical and histologic study. *Lasers Surg Med* 2001;13(suppl):46.