CLINICAL EVALUATION REPORT ON THE EFFICACY AND SAFETY OF THE CORE SYSTEM FOR FACIAL ENHANCEMENT TREATMENTS

BACKGROUND

Efforts to improve fractional ablative laser systems have led to the development of the traditional fractional CO2 lasers which can penetrate deeper than the mid-infrared lasers and therefore are predicted to result in better clinical results. High-energy CO_2 lasers removes the skin in a precisely controlled manner by creating thermally ablated areas which are subsequently repopulated by fibroblast activity and epidermal keratinocytes reproduction.

Syneron's fraction CO_2 laser (CORE) offers a fractional ablative treatment utilizing a CO_2 laser equivalent to traditional fractional CO_2 ablative treatments. The CORE system is designed to deliver a concentrated energy in a small focal spot in order to vaporize tissue.

The CORE system is intended for the performance of dermatological procedures requiring the excision, incision, ablation, coagulation, and resurfacing of soft tissue in dermatology and plastic surgery. The treatment is made-up of deep microscopic ablated zones surrounded by undamaged tissue, further allowing the control of depth and the level of heating around the small spot columns.

This clinical evaluation report summarizes the clinical performance and the safety of using the CORE system for treating facial skin laxity rhytides, pigmentation scarring and textural irregularities.

STUDY DESIGN

This is a prospective multi center study in which patients received up to 3 treatments (each on at least two facial areas) every 4-6 (±1) weeks, and returned for follow-up visits 4-7 days and 4-6 weeks and 12 weeks following the last treatment. Evaluation of improvement in wrinkling/elastosis was performed by investigator and the patients. Adverse event and the course of wound healing were monitored throughout the study. Patients comfort, social downtime and patients' satisfaction were recorded.
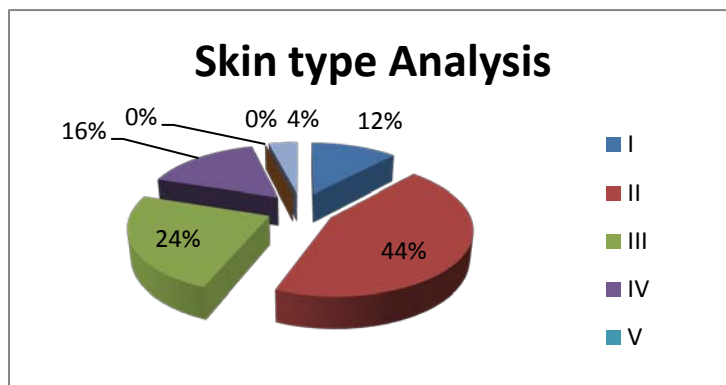
DATA ANALYSIS

Analysis was performed using the Statistix 9.0 Software and included the following: Descriptive analysis, two-sample t-test, paired t-test, one way ANOVA and Pearson correlation.
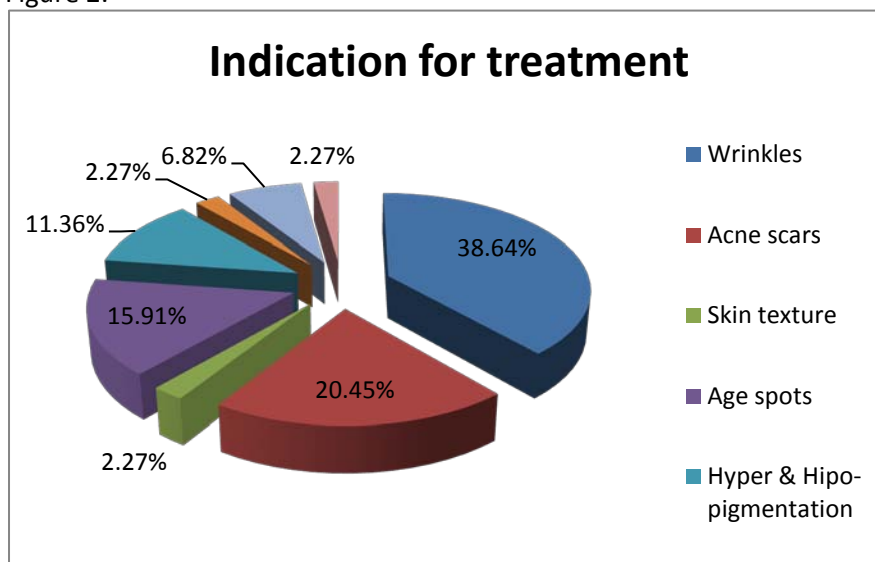
RESULTS

Patients from 3 beta sites in the US: Dr. Ross, Dr. Zelickson and Dr. Afsahi were evaluated here including 23 females and 2 males [aged 34-67] of whom 96% were Caucasians and 4% Hispanic; 44% were with skin type II, 24% had skin type III, 16% had skin type IV and only few patients were with skin type I (Figure 1). Patients' baseline degree of elastosis varied from 3-9 (most patients had a score between 5-7).

Figure 1

Skin type Analysis

16% 0% 0% 4% 12%

24% 44%

Legend: I, II, III, IV, V

All patients except for two received full face treatment, one patient received treatment to the entire face except for the peri-orbital region and another patient received treatment only at the cheeks and the forehead. The main indication for treatment was wrinkles (39%) followed by pigmented lesions (1/3) and acne scarring (20%). Almost 2/3 of the patients had more than one indication for treatment and the most common combination was wrinkling and pigmentation occurring in a total of 1/3 of the patients (Figure 2).

Figure 2.

Indication for treatment

2.27% 6.82% 2.27%

11.36%

15.91% 38.64%

2.27% 20.45%

Legend: Wrinkles, Acne scars, Skin texture, Age spots, Hyper & Hipo-pigmentation

Treatment parameters were 30-90mj/spot in modes Lite, Mid, Deep and Fusion. Two third of the patients were treated with a combination of different modes. Most treatments were done using energy in the range of 50-75mJ/spot. Interestingly, a higher energy level was used in older patients (Pearson correlation, r= 0.66, P = 0.001, most probably because their baseline skin condition was poor compared to younger patients. Different patterns were used including large/mid hexagon or square. Treatments were performed under 5-30% of topical anesthetic creams including 5% Lidocaine (by itself) in 17% of the patients or with the adjuvant of cooled air in 34% of the patients. In 8% of the patients a booster of Lidocaine block was added to the infra-orbital region. Other anesthetic formulations were either topical 30% Lidocaine/Tetracaine (used in 25% of the patients) or topical Lidocaine/ Prilocaine given to 17% of the patients. As expected, the type of anesthesia used was dependent on treatment parameters and energy level (Pearson r=0.46, P= 0.02) and the investigators' own preferences. Of note, all patients

needed to have some kind of anesthetic formulation applied. Out of 25 patients, ~ 1/3 received a second treatment and only one patient had a third treatment as well. Overall this analysis includes 44 treatments with the CORE system.

The wound healing response was followed up by the physicians at 4-7 days post the first treatment and was evaluated with regard to its completion, scab appearance and disappearance, associated complications, the overall degree of response and patients' social down time. Commonly, the immediate response was characterized by the appearance of edema, erythema, whitening and/or bleeding. Less common, the response was limited to erythema and edema. The overall degree of response was moderate in 90% of the patients and only one patient suffered from a severe response. Nevertheless, almost all treatments completed the healing response without any complications with scabs appearance at 1-2 days post the treatment and shedding off following additional 4 days. Thus complete reepithelializtion was obtained in3-6 days post treatments. The only exceptions were 1 patient having a 2 mm healing response and another patient with HSV on her lower lip that required a prophylactic regimen administration. The average patients' social downtime was 5 days (range2 -14 days). As expected, the use of higher energy setting resulted in longer patients' downtime (Pearson $r = 0.47$, $P = 0.03$). Also, older patients tend to have a slightly longer recovery period. Having a second treatment to the same area had no effect on the healing response in terms of period, severity and/or complications.

Efficacy evaluation was performed by both the physicians and the patients. This evaluation was performed at the first FU visit (4-6 weeks post treatment) and at the second FU visit at 3 month post the treatment. Those patients who received additional 1-2 treatments received an additional evaluation 4-6 weeks post the first treatment at the same visit in which their second/third treatment was applied. At the time of preparation of this report, only 4 patients completed the 3 mo FU visits, this data will not be included here.

The physicians graded the degree of elastosis as well as the improvement in patients' fine lines, folds, pores, pigmented lesions skin texture and coloration. The improvement was graded on a 4 scale system from level 0 (no improvement) to level 4 (significant improvement). The following table presents the average improvement in grades for each one of the above parameters as per physicians' assessment at the first FU.

Variable	N	Mean	SE Mean	Minimum	Maximum
Fine Lines	21	2.3810	0.3123	0.0000	4.0000
Pores	21	1.8095	0.4001	0.0000	4.0000
Folds	21	1.4762	0.2978	0.0000	3.0000
Pigmentation	15	1.6667	0.3034	0.0000	4.0000
Colrotaion	21	2.0476	0.2533	0.0000	4.0000
Texture	21	2.3810	0.3551	0.0000	4.0000

As can be seen, the most significant improvement was in fine lines and skin texture (an average improvement of 60% with 50-100% improvement found in at least half of the patients) followed by skin coloration (an average improvement of 50% with 50-100% improvement observed in at least half of the patients) and the appearance of pores (45% improvement with 50-100% improvement in 43% of the patients). Nevertheless, an improvement greater than 37% in at least half of the patients was noted in all other parameters: pigmentation and folds and the average Fitzpatrick elastosis grade was significantly improved from baseline to the first FU visit performed 1 month post the last treatment (Paired T test, $P = 0.0009$). Interestingly, a high correlation was found between the degrees of improvement in the different skin parameters (Pearson correlation for the different parameters $r = 0.89$-0.97, $P < 0.0001$)

Variable	N	Mean	SE Mean	Minimum	Maximum
Elastosis baseline	20	6.0500	0.3662	3.0000	9.0000
Elastosis 1 m FU	21	5.0476	0.3872	1.0000	8.0000

In a sub group of the patients (n=9 individuals) a second treatment was given 4-6 weeks post the first treatment. Prior to the second treatment the physicians graded their elastosis level according to the Fitzpatrick Elastosis grading system and also assessed their degree of improvement in regards to the appearance in fine lines, pores, folds, texture, pigmentation and skin coloration. In this group of patients it can be seen clearly (the following table) that there was a significant gradual decrease in their degree of elastosis from baseline (an average grade of 5.8) to the second treatment (an average grade of 5.2, statistically not significant) and an additional significant improvement at the 1 month post second treatment FU visits (an average grade of 4.4, Paired T test from the difference of the second treatment evaluation to the 1 month post second treatment visit, P = 0.008). Consistent with these results, physicians' assessment for improvement (on a 0-4 scale) in the different skin parameters post the first treatment was as follows.

Variable	N	Mean	SE Mean	Minimum	Maximum
Fine Lines Tx1	5	1.4000	0.2449	1.0000	2.0000
Pores Tx1	8	1.6250	0.3750	1.0000	4.0000
Folds Tx1	5	1.0000	0.0000	1.0000	1.0000
Texture Tx1	8	1.6250	0.3750	1.0000	4.0000
Pigmentation Tx1	7	1.4286	0.2020	1.0000	2.0000
Coloration Tx1	8	1.3750	0.3239	0.0000	3.0000

As can be seen, in this group of patients the percent of improvement post the first treatment was relatively low (an average improvement between 35-40% in ~1/3 of the patients) and therefore a second treatment was required. This second treatment resulted in much better results (up to an average of 50% improvement in 40% of the patients) as is it shown in the following table:

Descriptive Statistics

Variable	N	Mean	SE Mean	Minimum	Maximum
Fine Lines Tx2	7	2.0000	0.4880	1.0000	4.0000
Folds Tx2	7	1.0000	0.4364	0.0000	3.0000
Pores Tx2	7	1.2857	0.7143	0.0000	4.0000
Pigmentation Tx2	6	1.3333	0.4216	0.0000	3.0000
Texture Tx2	7	2.0000	0.6172	0.0000	4.0000
Coloration Tx2	7	1.5714	0.4286	0.0000	3.0000

In this group, because the first treatment had no significant effect, there was a need for a second treatment which eventually resulted in a lower level of elastosis as compared to the level of the group of patients that received only one treatment. This may suggest that a second treatment should be considered in all patients in order to gain even better results.

Variable	N	Mean	SE Mean	Minimum	Maximum
Elastosis baseline	7	5.8571	0.5948	3.0000	8.0000
Elastosis post 1Tx	9	5.2222	0.6827	2.0000	8.0000
Elastosis post 2Tx	7	4.4286	0.7825	1.0000	7.0000

In a similar manner to physicians'' assessment, the subjects rated their degree of improvement in all the different skin parameters as well as their overall improvement, and degree of satisfaction from the results. The following table describes the results of this analysis where the same scale (0-4) was used for the evaluation of subjects' improvement and satisfaction.

Variable	N	Mean	SE Mean	Minimum	Maximum
Overall 1FU	21	3.3810	0.1887	1.0000	4.0000
Laxity 1FU	21	3.0952	0.2172	0.0000	4.0000
Fine lines 1FU	21	3.2381	0.2381	0.0000	4.0000
Texture 1FU	21	3.3333	0.2218	1.0000	4.0000
Coloration 1FU	20	2.6500	0.2209	0.0000	4.0000
Pores 1FU	21	3.0000	0.3086	0.0000	4.0000
Satisfaction 1FU	21	3.4762	0.2026	0.0000	4.0000

It is clear that the patients were extremely satisfied from the results (87.5%) and rated their overall improvement as much as 85%mostly due to improvement in skin texture (83% improvement), fine line/wrinkles (81% improvement) and skin laxity (77% improvement).

As expected, a high degree of correlation was found between physicians' assessments and the corresponding assessments of the patients (Pearson correlation $r = 0.68$, $P = 0.008$ for skin texture; $r = 0.62$, $P = 0.003$ for skin coloration and $r = 0.58$, $P = 0.007$ for pores).

Baseline   4-7 days post Tx.1   4-6 wk Follow-up

Patient #1 is a 46.5 year old female with moderately wrinkles. Her first treatment was CO2RE lite, mid and fusion with 30-50% coverage. She received a total of 2 treatments at 6 week intervals. The second treatment was CO2RE lite and mid with 30-50% coverage. She did not experience any complications from the treatments. The improvement in the tone, texture and appearance of the wrinkles areas was scored as "Slightly" (1-25%).

Baseline	4-7 days post Tx.1	4-6 wk Follow-up

Patient #2 is a 53 year old female with moderately wrinkles and age spots. Her first treatment was CO2RE mid and fusion with 30-40% coverage. She received a total of 1 treatment. She did not experience any complications from the treatments. The improvement in the tone, texture and appearance of the wrinkles areas was scored as "Moderately" (25-50%).

Baseline	4-7 days post Tx.1	4-6 wk Follow-up

Patient #3 is a 60 year old female with moderately wrinkles, hyper-pigmentation and lantigos. Her first treatment was CO2RE lite with 35% coverage. She received a total of 2 treatments at 6 week intervals. The second treatment was CO2RE lite with 35% coverage. She did not experience any complications from the treatments. The improvement in the tone, texture and appearance of the wrinkles areas was scored as "Improved" (50-75%).

DISCUSSION

We report on a multicenter clinical study in which 25 patients (Fitzpatrick skin types I-IV between the ages of 34-67 years) received each one a single full face treatment with the CORE system for rhytides, sun-damaged skin, acne scarring and skin laxity at setting of 30-90 mJ/pulse, 2-40% coverage. Efficacy assessment revealed moderate or better overall improvement (50-100%) in at least half of the patients. With a significant decrease in elastosis score at 4-6 weeks post treatment. The average improvements in indices of skin texture and tightening (on a quartile scale) were: 2.38 for rhytides, 2.38 for texture, 2.0 for coloration, 1.8 for pores, 1.66 for pigmentation and 1.57 for folds.

In 9 patients a second treatment was performed 4-6 weeks post the first treatment. A very good improvement could be achieved with regard to skin texture, sallow complexion tactile roughness. Conversely, fine lines and mottled pigmentation, have demonstrated relatively minor improvement but could be further improved with the performance of a second treatment.

With regards to safety, treatments were tolerated well and the side effects experienced were limited to erythema/edema, whitening/mild bleeding and mild crusting with no incidence of scarring or delayed onset hypopigmentation even with the higher fluencies. Following full-face resurfacing with the CORE system, complete reepithelization was usually seen between 4-6 days and the average healing period for all patients lasted 5 days. A 2 mm crust healing response was noticed in one patient and another patient suffered from HSV on her lower lip that required a prophylactic regimen administration. This is in stark contrast to the 2-3 weeks of recovery following full-face resurfacing with the traditional CO_2 lasers.

CONCLUSION

Fractional ablative CO_2 laser resurfacing using this prototype for treatment of photo damaged facial skin is safe and efficient. Data suggest that in a sub set of patient a second treatment may be needed.

LIMITATIONS

At the time to this report preparation most patients have not completed their 3 month evaluations and therefore this data is missing.