

Fractional Treatment of Aging Skin with Tixel[®], a Clinical Evaluation

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ABSTRACT

Background: Short pulse duration CO₂ lasers are generally considered excellent tools for the vaporization of thin layers of tissue with minimal collateral thermal damage. While being operated with an energy density above ~5 Joules/cm² and a pulse duration below a few milliseconds, shallow craters can be vaporized without bleeding and with a residual necrotic zone of only ~100-150 microns. Short pulse CO₂ lasers are widely used in fractional skin resurfacing in the form of arrays of focused beams with good results. Pain associated with fractional skin resurfacing is reduced by the application of analgesic cream prior to treatment.

Objectives: To establish a clinical overview of a novel ablative fractional skin resurfacing system, Tixel[®], based on thermo-mechanical ablation technology (TMA), with comparison to fractional CO₂ lasers in terms of treatment safety, efficacy and histopathology.

Materials and Methods: Tixel (Novoxel[®], Israel) employs a thermal tip containing an array of 81 biocompatible, heated metallic pyramids, which evaporate small diameter (100-300 micron) craters upon brief contact with the skin (4-18 milliseconds). Tip temperature is 400 °C; tip active area is 1 cm². Two tip array types are utilized: D for ablative craters (CO₂ laser equivalent) and S for non-ablative heat transfer to the papillary dermis.

Data pertaining to treatments performed on thirty-two patients with Tixel was reviewed. The patients consisted of 29 females and 3 males aged 35-65 years with skin phototypes I-V. Analgesic cream was not applied. In two cases, fractional CO₂ lasers (Quanta, YouLaser and Lumenis 40C) were used for comparison. Up to three treatments were performed in 4 to 5-week intervals. Post-treatment histopathology cross sections were taken with both Tixel and laser-treated skin. Before and after photographs were taken for documentation of the healing progress as well as for comparative improvements in skin texture and fine wrinkles. Pain level was also compared.

Results: Histopathology: Ablative Tixel and CO₂ laser histology cross sections are parameter-dependent and generally similar, except that there is no evidence of necrotic tissue in Tixel specimens. Non-ablative Tixel provides heating of the epidermis down to the papillary dermis with micro-channels formation and stratum corneum preservation (skin crushing).

Clearance of redness and healing: Ablative tip: average 3 days with Tixel vs. 4-5 days with laser. Non-ablative: 1-2 days with Tixel. Downtime: Ablative – 1 day with Tixel vs. 2 days with laser; Non-ablative - no downtime.

Clinical results: Similar to CO₂ laser (fine wrinkles, skin texture). Good results with treatment of pigmentation.

Pain level: Considerably better than laser. 1-3/10 with Tixel; 7-8/10 with laser.

Side effects: None

Conclusions: In ablative mode, Tixel is significantly less painful than laser with comparable efficacy and safety. Skin pigmentation can also be treated. Healing is faster with Tixel.

In non-ablative mode, Tixel demonstrated improved skin texture results with no downtime and quicker healing than in ablative mode.

1. INTRODUCTION

Short pulse CO₂ lasers are generally considered among the best tools for high precision ablation of thin layers of tissue without bleeding and with minimal collateral damage (1). They are widely utilized in skin resurfacing procedures, including fractional skin resurfacing (2,3). By operating a 10.6 micron CO₂ laser with an energy density above a threshold of ~5 Joules/cm² and a pulse duration below a few milliseconds (0.1–5 ms), the vaporization rate is faster than thermal diffusion into tissue, and collateral thermal necrosis is ~100-150 microns. With only a 30-50 micron penetration of the 10.6 micron wavelength laser beam into tissue, it is possible to vaporize craters arrays of skin down to or deeper than the papillary dermis and achieve excellent skin resurfacing results. With an array of ~100-250 micron focused beam spots, fractional resurfacing of ~12-20% of the skin surface ensures fast healing. The energy responsible for vaporization of tissue with a CO₂ laser is purely thermal. The tissue parameters which quantitatively dictate the threshold energy for vaporization with only 100-150 micron collateral damage are the vaporization energy of tissue which is ~3000 J/cm³ (4) and the beam penetration in tissue (30-50 micron). In the vaporization process, temperature craters produced by a single pass laser beam attain ~350-400 °C (5).

Since thermal energy is responsible for tissue vaporization, we may expect that by bringing a metallic element with a temperature of ~350-400 °C in contact with the skin for a duration of less than ~0.1-5 ms and a depth of ~50-150 microns, a clinical ablative effect which is identical to the CO₂ laser effect will occur. However, such an extremely fast and accurate thermo-mechanical procedure with a 350 °C array enclosed in a small ergonomic handpiece requires very specific geometrical, mechanical and thermal design. The objective of the current article is to present a new thermo-mechanical ablation (TMA) technology and compare it to CO₂ and erbium laser fractional skin resurfacing.

2. MATERIALS AND METHODS

Treatment results with a Tixel (Novoxel, Israel) unit as reported by two medical centers were analyzed. A parametric analysis of histopathology on human skin in-vivo of Tixel vs. laser was also performed.

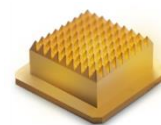


Figure 1: D and S types of Tixel pyramidal tip array

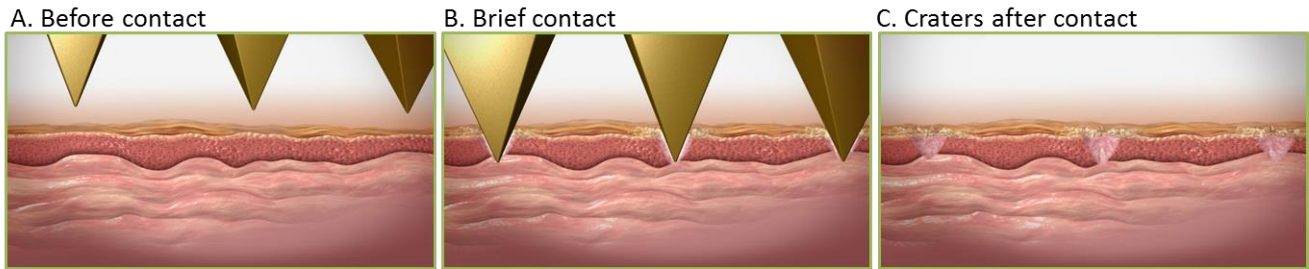


Figure 2: Schematic presentation of the process of vaporization of craters array with high temperature pyramidal tips. **A** – Fast advance toward tissue; **B** – Brief contact on skin surface and transfer of thermal energy to tissue; **C** – Vaporized craters after tips retraction. Temperature of 400 °C and short contact duration are identical to CO₂ lasers parameters, and ensure a tissue interaction which is very similar to CO₂ (or erbium) lasers.

2.1 Tixel handpiece

The Tixel handpiece is small and lightweight (approximately 250 grams), comprising of a miniature heater and a biocompatible material array of 9x9 tiny pyramidal tips (1 cm² treatment area), which are heated to a temperature of 400 °C. The tip array is shown in Figure 1. Tip height is about 2 mm and the distance between the pyramids is roughly 1 mm. Biocompatibility is preserved at temperatures of operation. A highly accurate linear motor generates an extremely fast oscillatory motion causing the high temperature tip array to vaporize tiny craters upon brief contact (4-18 ms) on the skin surface (Figure 2). The motor displacement accuracy is in the range of 1-8 microns, leading to a highly controlled vaporization depth in the range of 20–150 microns, regardless of tissue stiffness. There are two types of Tixel Tip arrays: an ablative type for deeper craters (type D) and a non-ablative type for shallow craters (type S). Maximal treatment speed is 1 m/sec. Tixel settings are: high energy pulse (~25 mJ/crater), medium energy pulse (~15 mJ/crater) and low energy pulse (~10 mJ/crater). The theoretical and engineering foundations of the Tixel technology are described in reference (6). The utilization of the Tixel did not require the use of protective eyewear or a smoke evacuator. In contrast to the common practice with CO₂ laser, Tixel treatments did not necessitate the application of analgesic creams (such as EMLA) prior to treatments.

2.2 Patients & treated areas

The total number of treated patients was 32. Study participants included 29 female and 3 male patients ranging in age from 35 to 65 years, with phototypes I-V.

The following skin areas were treated: Full-face - 28 patients, Periorbital only- 3 patients, Decollete - 10 patients, Hands - 15 patients. A few patients received treatment on more than one area.

In two of the cases, improvement comparisons between Tixel and CO₂ laser were made after 2 treatments of Tixel on one periorbital area and CO₂ laser on the contralateral side.

All patients were requested to apply Biafine or Cicalfate lotion twice a day for 4 days following treatment, and were allowed to use sun blocking (SP 50) makeup cream if desired.

2.3 Histopathology

Biopsies were taken from the forearms and upper arms of two patients on four separate occasions for histopathology comparison between CO₂ lasers (YouLaser, Quanta, 24 W, 750 μsec, 2 stacks, density 100, 36 mJ/point; Lumenis 40C, CW 30 W, 50 ms/scan, Alma Pixel scanner) and Tixel at both ablative mode and non-ablative mode.

2.4 Healing time

Healing progress was monitored and recorded using standardized photography, with attention to the duration of erythema and crusting of craters, as well as for comparison with CO₂ laser healing.

2.5 Results analysis

Standardized photographs were taken before and immediately after each treatment session. In several cases, photographs were taken more frequently after the first treatment to more closely follow-up healing. Each patient underwent a maximum of 3 treatment sessions, spaced 4-5 weeks apart.

2.6 Pain level

All patients were requested to grade their pain level (scale 1-10) with Tixel, and three patients with laser. Analgesic cream was not applied in both cases.

3. HISTOPATHOLOGY

Fractional Thermo-Mechanical Ablation of skin utilizes pre-heated tips to generate a matrix of tiny craters in the skin surrounded by healthy tissue (Figure 3). The clean craters shown in the figure have a diameter of about 160 microns.

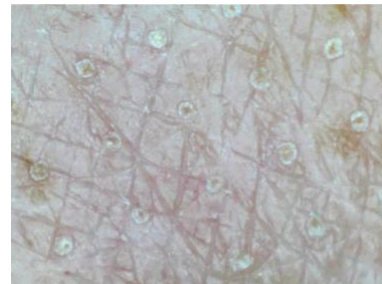


Figure 3: Microscope view of human skin immediately after treatment in which the array of coagulation points can be detected. Parameters: D tip, 9 ms double pulse.

3.1 Tixel vs. laser

Multiple biopsies from the upper arms of a 61-year-old male were taken immediately after laser treatment (Quanta, YouLaser) using typical treatment parameters (24 W, 36 mJ/crater), and after Tixel treatments using S and D Tips and a variety of treatment settings including varying pulse duration and number of pulse repetitions on the same treatment spot.

Figure 4 illustrates laser vs. Tixel craters at typical treatment parameters of both devices. The crater obtained with Tixel (D Tip, 9 ms double pulse) has similar characteristics as the laser crater. Fractional thermal ablation with Tixel induced a tiny lesion having an epidermal diameter of 160 μm (vs. 320 μm with laser) and a papillary dermal depth of 170 μm (same as laser). In contrast to the laser crater, the Tixel crater had no

epidermal necrotic tissue. The similarity between the depth of the laser crater and Tixel crater should result in similar dermal regeneration processes. Epidermal crusting is expected to be quicker due to the smaller diameter of the lesion.

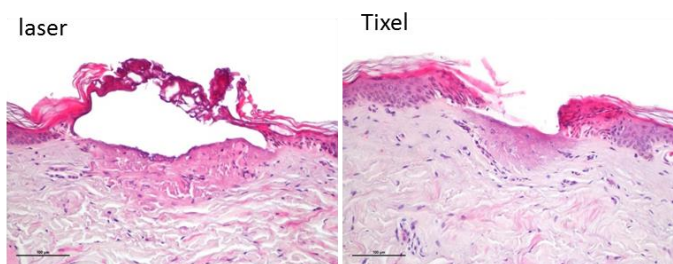


Figure 4: Histopathology of laser and Tixel immediately after treatment of human skin. Both craters present epidermal evaporation and dermal coagulation of the papillary dermis. Laser (Quanta, YouLaser, 24 W, 36 mJ/crater), Tixel (D Tip, 9 ms double pulse).

3.2 Tixel versatility

The extent of thermal damage is closely related to the choice of the tip, the pulse duration and the number of pulse repetitions. By adjusting treatment parameters, Tixel can create either ablative (Figure 5 A-C) or non-ablative (Figure 5 D-F) tiny thermal lesions (see Table 1). Lesion dimensions are 100-380 μm wide and 100-180 μm deep. The histologies show no hemorrhage and no edema.

Pain levels with all the settings used were low and did not require the use of analgesic creams except for those employed in case A (14 ms double pulse), which induced pain similar to the laser. This setting was taken as an extreme test parameter for comparative purposes, and demonstrates the ablative power of the Tixel technology.

In ablative mode, Tixel generated clean epidermal evaporation and a dermal coagulation of maximum 180 μm in depth, which corresponds to the upper papillary dermis.

In non-ablative mode, using the S tip, the coagulated epidermis is preserved and not evaporated. The tissue is compressed by the Tip contact and the extracellular space between the cells is increased due to cell shrinkage. A process of vacuolation takes place and a blister is formed between the damaged epidermis and dermis, as can be seen in Figure 5D & 5E, or a mild vacuolation in Figure 5F. Dermal coagulation at the upper papillary dermis is avoided in this case due to the very brief pulse that has been applied. Table 1 summarizes the main characteristics of craters at several Tixel settings.

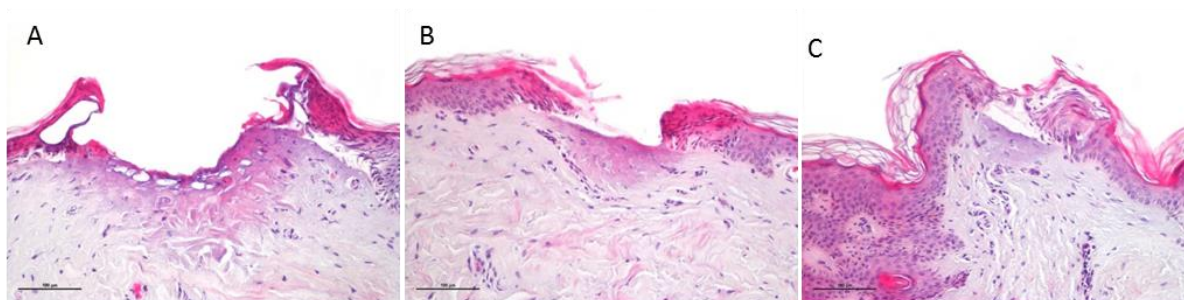
3.3 Histopathology of healing process

The epidermal dressing of the crater allows for a rapid re-epithelialization and epidermal regeneration of the lesion. This is demonstrated in Figure 6, which presents histology on the same day of treatment (A) and after 7 days treatment (B) with Tixel in non-ablative mode on porcine skin in vivo applying the same treatment parameters in both cases. As can be seen in (A), a blister has formed in the epidermal-dermal junction on the treatment day. The healing process 7 days after is demonstrated in (B). The blister has filled with fluids that contain growth factors and cytokines that have stimulatory effects on wound healing. Fibroblasts and macrophages migrate and proliferate in the cleft that has remained from the earlier blister.

The histopathology cross sections presented in Figures 4-6 lead to the following observations:

- Tixel's D tip vaporizes craters that have similar properties to CO_2 laser craters however without charring or tissue necrosis (clean craters).
- Tixel's S tip generates non-ablative "dressed" craters with thermal damage extending down to the papillary dermis. The epidermis is preserved and acts as a natural physiologic dressing for protection from post-treatment infection during the healing process.

Ablative mode



Non-ablative mode

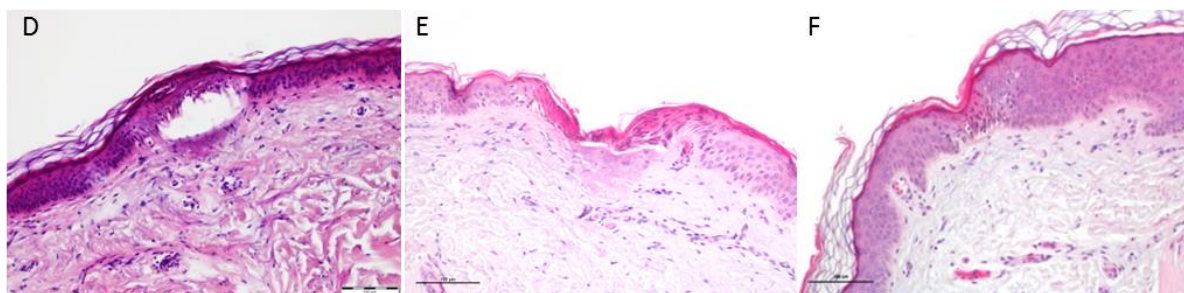


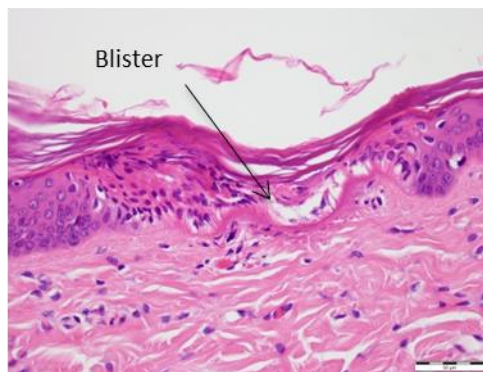
Figure 5: Histopathologies of Tixel treatments, at different settings, immediately after treatment of human skin. (A) D Tip, 14 ms double pulse. (B) D Tip, 9 ms double pulse. (C) D Tip, 9 ms single pulse. (D) S Tip, 14 ms single pulse. (E) S Tip, 9 ms double pulse. (F) S Tip, 9 ms single pulse.

Table1: Summary of crater characteristics

Device	Tip type	Pulse parameters	Thermal effect on		Thermal damage		Healing time	Figure
			Epidermis	Dermis	Width μm	Depth μm		
Laser CO ₂	-	-	Ablation Vaporized	Coagulation of upper papillary dermis	330	170	5 days	4A
Tixel	D	14 ms double	Ablation Vaporized	Coagulation of upper papillary dermis	380	180	5 days	5A
Tixel	D	9 ms double	Ablation Vaporized	Coagulation of upper papillary dermis	160	170	3 days	5B
Tixel	D	9 ms single	Ablation Vaporized	Coagulation of upper papillary dermis	200	160	3 days	5C
Tixel	S	14 ms single	Non-Ablation Coagulated Vacuolation r	Coagulation of upper papillary dermis	210	165	2 days	5D
Tixel	S	9 ms double	Non-Ablation Coagulated Vacuolation	Coagulation of upper papillary dermis	160*	170	2 days	5E
Tixel	S	9 ms single	Non-Ablation Coagulated Vacuolation	Normal	100	100	1 day	5F

* Internal crater width measurement

A. Immediately after



B. 7 days after

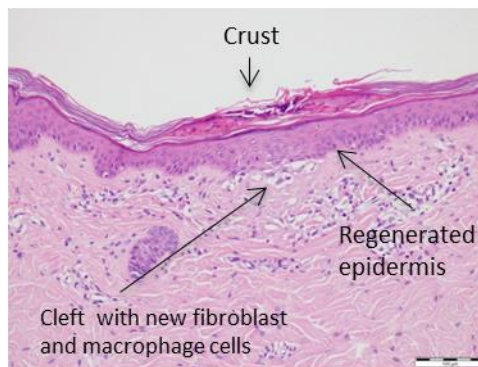


Figure 6: 2 Tixel histologies with S Tip, at same treatment parameters on day of treatment (A) and 7 days after treatment (B) on porcine skin in vivo. Epidermis is regenerated with a crust in the stratum corneum. The cleft that was formed in the dermis is filled with fibroblasts and macrophages.

4. CLINICAL RESULTS & HEALING DURATION

4.1 Ablative mode

Two patients had been treated on the left periorbital side with Tixel (D Tip, 9 ms double pulse) and on the right periorbital side with CO₂ laser (Lumenis 40C, Alma laser Pixel scanner, 30 W, 0.7 ms/crater, 50 ms full area scan duration) for split-face comparison. Patients were photographed daily for one week after treatment, and erythema as well as the craters' micro-crusting were evaluated. Figures 7A-D show a comparison of the post-treatment healing progress between the Tixel- and laser-treated periorbital sides of a 65-year-old male patient with skin type III. As evident from figures 7A-D, the skin healing process is similar in both cases.

Figures 8A-B and Figures 9A-B show photographs of before and 4 months after 2 treatments in the same patient. As can be seen in these image sets, the clinical results of ablative CO₂ laser and Tixel are also similar. This is expected due to the fact that identical thermal energies are delivered in both

technologies, also witnessed in the characteristics of the comparative histopathology cross sections.

4.2 Non-ablative mode

Figures 10A-B show the periorbital region of a 45-year-old female patient with skin type II, before and 3 months after 3 Tixel treatments. Treatments were performed with an S type non-ablative tip. There was no downtime and the erythema disappeared within one day.

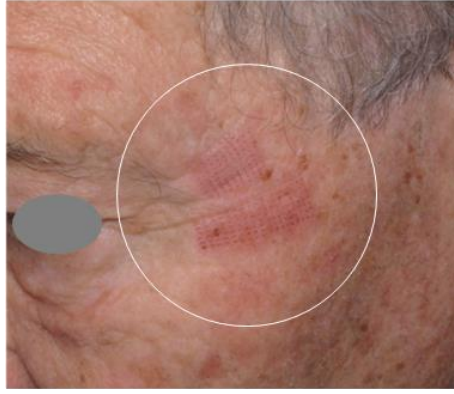
4.3 Ablative mode, skin pigmentation

Three patients were treated for skin pigmentation with an ablative D Tip. Preliminary results show pigmentation reduction in all patients after the first treatment. Figures 11A-B show photographs of a female patient before and 18 days after the first treatment. Skin redness lasted 3 days. Downtime was 1 day.

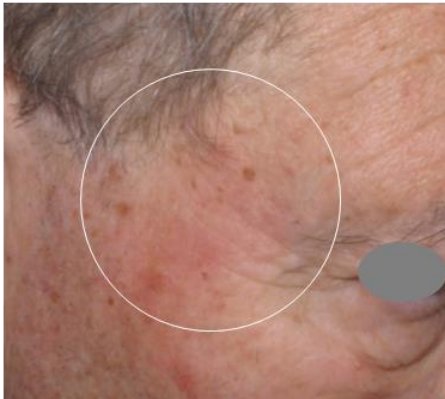
A. laser 2 days after



B. Tixel 2 days after



C. laser 1 week after



D. Tixel 1 week after

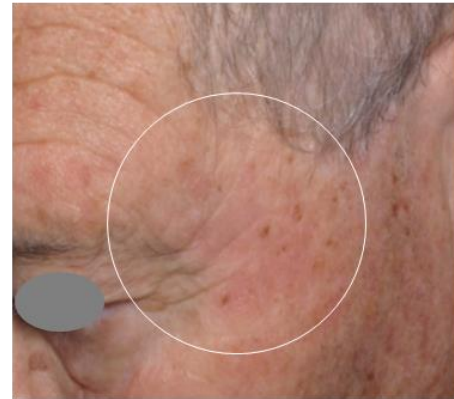
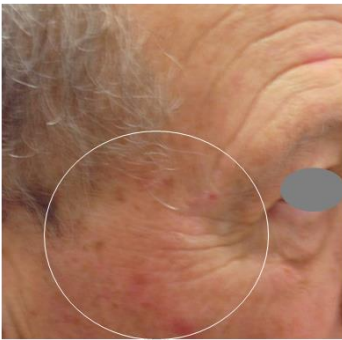


Figure 7: Tixel and laser healing 2 days and 1 week after treatment, (A&C) Laser (Lumenis, 40C; 30 W), (B&D) Tixel (D Tip, 9 ms double pulse)

A. Before



B. laser 4 months after

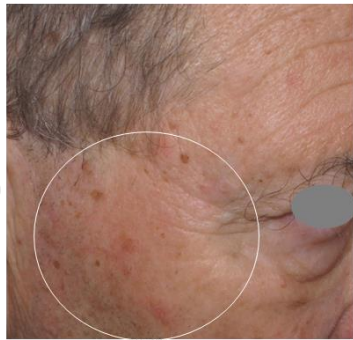
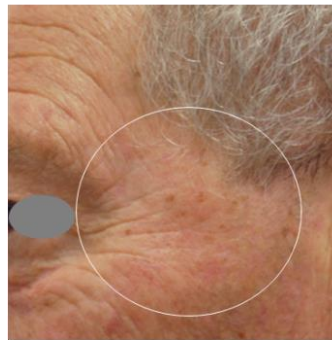


Figure 8: Wrinkle improvement after 4 months and 2 laser treatments (Lumenis, 40C; 30 W)

A. Before



B. Tixel 4 months after

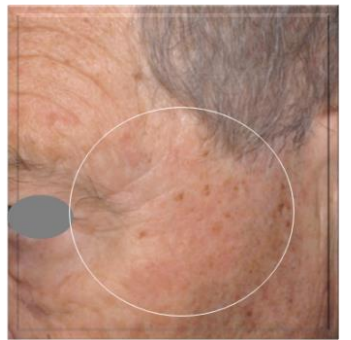
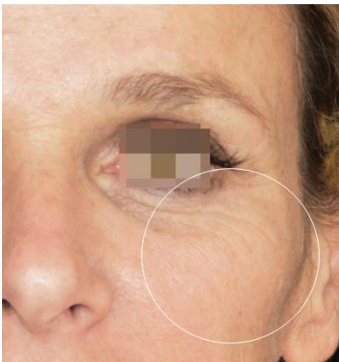


Figure 9: Wrinkle improvement after 4 months and 2 Tixel treatments, D Tip, 9 ms double pulse

A. Before



B. Tixel 3 months after

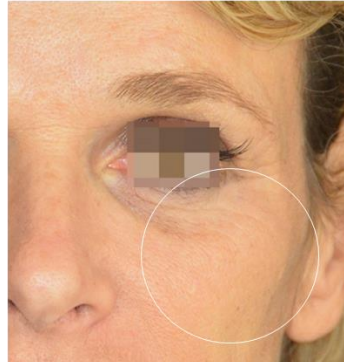


Figure 10: Texture and fine wrinkle improvement 3 months after 3 Tixel non-ablative treatments with S Tip.

A. Before



B. After



Figure 11: Pigmentation improvement after 18 days of a single Tixel treatment, S Tip, 9 ms double pulse.

4.4 Patient satisfaction from results

All patients responded well to the Tixel treatment and expressed satisfaction from textural improvement in the skin as well as localized reduction of wrinkles. All patients were also satisfied with the minimal downtime associated with treatment, which was no downtime following non-ablative treatment and up to one day downtime following ablative treatment. The erythema disappeared mostly within 2-3 days, and in few cases with more aggressive ablative treatment (i.e. D Tip type, 16 ms) within 4-6 days. The utilization of makeup is allowed.

4.5 Pain level comparison

All patients scored the pain level of Tixel treatment in the range of 1-3/10 (1-10 pain scale). Analgesic cream was not used. In stark contrast, all patients scored the pain level of laser treatment in the range 7-9/10 without analgesic cream.

5. DISCUSSION AND CONCLUSIONS

The similarity of the clinical effects of Tixel in its ablative mode and CO₂ lasers is not surprising in view of the identical thermal energy delivered to the tissues within similar time duration and similar depth, as well as crater diameters. The similar energy parameters of CO₂ laser and Tixel in ablative mode not only result in very similar histopathologies but also strikingly similar clinical outcomes, as witnessed in this clinical trial. However, Tixel ablative mode has two central advantages: it is essentially painless, thus not requiring the application of analgesic cream prior to treatment, and is easier to use, i.e., there is no smoke, protective eyewear is not required, and there is no risk of accidental application of invisible laser radiation for the patient, physician or personnel. In addition, by applying shorter pulse durations, tissue effects that are closer to erbium laser effects are achievable.

Regarding the non-ablative Tixel mode whereby skin crushing is achieved, we see two major advantages unattainable with lasers. Using this mode, it is possible to cause thermal heating of the epidermis down to the papillary dermis, without vaporizing the stratum corneum. As a result, a natural physiologic dressing against infection may be present. The stratum corneum in this mode is not expelled by cellular explosion as with lasers, due to the sealing effect of the tip when less energy is applied. However, beneath the epidermis, the temperature increases to the tip temperature of 400 °C

leading to vaporization and damage to cells. Micro-channels are formed between the cells (as seen in Figure 5F), which are later filled with fibroblasts (Figure 6) that produce new collagen. We attribute the clinical efficacy of the non-ablative mode to this micro-channeling effect.

In addition, as will be reported in a separate scientific article, the preliminary results of a study looking at skin permeability to Verapamil hydrochloride, a hydrophilic drug that does not penetrate skin, show significant permeability of the drug following Tixel non-ablative treatment.

In conclusion, Tixel technology is as efficient as CO₂ lasers while being painless, safer, as well as more compact and much simpler to use. It provides a high versatility and in many senses is more than a combination of CO₂ and erbium laser.

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Note: The Tixel technology is patent pending