Fractional treatment of aging skin with Tixel, a clinical and histological evaluation

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ABSTRACT
Objective: This study presents clinical results of Tixel, a new fractional skin resurfacing system based on thermo-mechanical ablation technology. Tixel employs a hot (400°C) metallic tip consisting of 81 pyramids. Treatment is performed by rapidly advancing the tip to the skin for a preset tip–skin contact duration. Thermal energy transfer to the skin creates micro-craters by evaporation. Methods: Treatment results with tip types, D and S, with high and low thermal conductivity, were evaluated. Twenty-six subjects received three facial treatments, with 4–5-week intervals between treatments, without analgesia or cooling. In addition, histopathologies of Tixel and CO₂ laser were performed. Results: Crater properties are related to contact duration and to thermal conductivity. The D tip created char-free ablative craters 100–320 μm wide with a thermal zone 100–170 μm deep. The S tip created non-ablative coagulation preserving the epidermis. Skin complexion improvement was achieved in all subjects; average treatment pain of 3.1/10, downtime of 0–1 days, and erythema clearance of 3.5 days. Subject's satisfaction was 75% and wrinkle attenuation was achieved in 75% of the cases. There was no incidence of bleeding, scarring, or post-inflammatory hyperpigmentation. Conclusions: Tixel may be used safely for ablative and non-ablative resurfacing with low pain, low downtime, and quick healing.

Introduction
Fractional laser resurfacing technologies are widely used in dermatology. Short-pulse CO₂ lasers are generally considered to be among the best modalities for high-precision ablation of thin tissue layers without bleeding and with minimal collateral damage (1). They are widely utilized in skin fractional skin resurfacing (2,3) for improved skin texture and fine wrinkles. Treatment is painful, requiring pre-application of analgesic creams and protective eyewear. Downtime is about 5 days. With a penetration depth of only 30–50 μm by the 10.6-μm wavelength laser beam into tissue, it is possible to vaporize crater arrays of skin down to the papillary dermis or deeper, and achieve excellent skin resurfacing results. With an array of ~100–250 μm 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. In the vaporization process, the temperature produced by a single-pass laser beam attains ~350–400°C in the crater (4).

Since thermal energy causes tissue vaporization, one may expect that by bringing a metallic element having high thermal conductivity, heated to a temperature of ~350–400°C, in contact with the skin for a duration of a few milliseconds and a depth of ~50–150 μm, an ablative effect which is clinically identical to the CO₂ laser effect will occur.

The objective of the current article is to present a novel thermo-mechanical ablation (TMA) technology and to show clinical and histopathology data using the Tixel device. A comparison to fractional CO₂ laser histology is also provided.

Materials and methods

The Tixel
The Tixel (Novoxel, Germany) is a thermo-mechanical system for fractional ablation. It applies a tip, made of metallic, gold-plated biocompatible materials (Figure 1A). The tip is fixated at the distal section of the Tixel’s handpiece which is equipped with a linear motor (Figure 1B). The tip’s active surface consists of an array of 81 (9 × 9) pyramids evenly spaced within...
a boundary area of $1 \times 1$ cm. The pyramids are 1.25 mm tall having a radius of about 100 microns at peak vertex. The back plane of the tip is flat and is connected to a coin-sized heater which is kept at a constant temperature of $400^\circ C$ during operation. When not in use, the tip is base-positioned at a distance of 20 mm from the skin's surface (home). The tip weighs 7 g and is re-usable. The system authenticates, inspects, monitors, sterilizes, and exchanges tips automatically. Tip cleaning after treatment is performed within 5 min at $540^\circ C$ using an accessory heater. Self-sterilization is performed within 5 min at $350^\circ C$. Tip cleaning, sterilization, and biocompatibility have been validated. The handpiece weighs 270 g. Two tip types have been used: D with high thermal conductivity and S with low thermal conductivity. When the user activates the handpiece, the linear motor rapidly advances the tip which comes in brief contact with the tissue. Thermal energy is transferred to the skin, creating micro-craters in it by evaporation. The tip recedes within a precisely controlled distance and time to its home position, away from the tissue (Figure 2). The duration of the pulse, that is, time of contact between tip and skin, can range from 6 ms to 18 ms. A double pulsing mode is enabled. The motor’s displacement accuracy is in the range of 1–8 μm and the pulse repetition rate is 1 Hz. A 14-ms pulse delivers a high-energy pulse of ~25 mJ/crater, while a 10-ms pulse delivers a medium-energy pulse of ~15 mJ/crater, and a 6-ms pulse delivers a low-energy pulse of ~10 mJ/crater. The theoretical and engineering foundations of the Tixel technology have previously been described in Lask et al. 2012 (5). The utilization of the Tixel does not require the use of protective eyewear or of a smoke evacuator.

**The thermal model**

The thermal effects of the Tixel tip on the skin were simulated (MATLAB, Version 8.5, Mathworks, USA) by a dynamic model which takes into account both the tip’s motion profile and thermal properties of skin and the tip materials. The initial temperature of the tip is $400^\circ C$ and it is assumed that during contact with the skin it evaporates the tissue's water content and cools down to $100^\circ C$. After reaching $100^\circ C$, it is assumed that only thermal damage occurs. At the first stage of simulation, the tissue evaporation is calculated. Each iteration of the model loop is built from 3 steps: calculation of the tissue volume that is vaporized by the thermal energy of the tip, propagation of the tip into the crater that is now vaporized, and calculation of the new temperature of the tip as well as collateral damage as described in reference 5.

**Treatment procedure and assessments**

Fractional resurfacing treatments by the Tixel device have been performed by two independent investigator-initiated groups.

Group 1 enrolled 10 female subjects for wrinkle reduction mainly on the periorbital and perioral regions. Eight completed the whole treatment procedure and 2 dropped for non-safety-related reasons. Subjects were between the ages of 42 and 65 years and with a Fitzpatrick Skin Type of II–IV. The treatment included 3 treatment sessions 35 days apart with 1–6 months follow-up after the third session. The full face ($n = 1$), periorbital area ($n = 6$), and/or perioral area ($n = 5$) were treated with the Tixel device using either the D tip (14-ms single pulse or 9-ms double pulse) or the S tip (9-ms single pulse). This prospective study was assessed by the investigator. Each treatment session and follow-up session included evaluation of the skin complexion, the Fitzpatrick’s wrinkle scoring, pain level of the treatment, downtime, and time to clearance of erythema. Face photography at $0^\circ$, $90^\circ$ right, and $90^\circ$ left was performed with a Nikon D7100 camera before and after each session. Subjects’ satisfaction was assessed after each session via questionnaire.

Group 2 enrolled 23 female subjects. 18 completed the whole treatment procedure and 5 dropped for non-safety-related reasons. Subjects were between the ages of 50 and 75 years and with a Fitzpatrick Skin Phototype of II–IV. Seventeen subjects presented mild-to-moderate photodamage. The treatment included 3 full-face treatment sessions 1–2 months apart with 2 follow-up visits at 1–2 months and 3–4 months after the third session. The full-face treatment ($n = 18$) was performed with...
a range of parameters. In addition, CO₂ laser was applied for histopathology comparison (YouLaser, Quanta, 24 W, 750 µs, 2 stacks, density: 100 spots/cm², 36 mJ/point and Lumenis 1080 s, CW, 30 W, 50 ms/Pulse combined with Alma fractional Pixel CO₂ Omnifit handpiece, 9 × 9 array in 11 × 11 mm treatment zone). Histologies were evaluated in a blinded manner by the histopathologist.

In addition, a female domestic swine (7 weeks old, Kibbutz Lahav, Israel) was in vivo submitted to triplicates of Tixel treatments at the dorsal flank. Skin biopsies were extracted immediately after treatment and 7 days after treatment. Histologies were analyzed by a blinded histopathologist. The study was approved by the ethical committee of the Pre-clinical Research unit of Assaf Harofeh Medical Center.

Results

Crater characterization

Fractional TMA of skin utilizes pre-heated tips to generate a matrix of craters in the skin surrounded by healthy tissue (Figure 3). The clean craters shown in the figure have a coagulated diameter of about 320 µm on the skin surface corresponding with an active area of roughly 10%.

Tixel vs. laser

Figure 4 presents histopathology of laser versus Tixel craters at typical treatment parameters of both devices. An ablative Tixel crater using the D tip, 9-ms double pulse is compared with a CO₂ laser crater. Fractional thermal ablation with Tixel created a lesion 160 µm in diameter (vs. 320 µm with laser) and a thermal damage with dermal coagulation of the papillary dermis (depth of 170 µm, same as laser). Although Tixel and CO₂ laser craters have a general similarity, in contrast to the laser crater, the Tixel crates are clean of necrotic tissue or charring.

Histopathology

Biopsies were taken from the forearms and upper arms of two male volunteers, immediately after treatment with Tixel at the Tixel device applying either the D tip or the S tip at 9–16-ms single pulse. This study was a review of records retrospectively assessed by the investigator. Each session included an evaluation of the pain level during treatment, downtime and time to clearance of erythema. Face images at frontal, right oblique, and left oblique positions were acquired via a Canfield Reveal Imager before and after each session. Subject satisfaction was assessed at the follow-up session.

All patients applied Biafine or Cicalfate lotions following treatments, and were allowed to use sunscreen cream (SPF 50) and unperfumed makeup once microcrusting appeared.

In all cases, pain level has been graded on a scale of 1–10 by the subject where 1 is no pain and 10 is very painful. Tixel treatments were performed without applying any sort of analgesic substances or cooling.

The average ± standard deviation of downtime, clearance of redness, and pain level were reported, for all sessions combined.

Histopathology

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Table 1. Summary of crater characteristics.

<table>
<thead>
<tr>
<th>Figure</th>
<th>Thermal damage</th>
<th>Thermal effect on</th>
<th>Tixel pulse duration</th>
<th>Tip type</th>
<th>Device</th>
</tr>
</thead>
<tbody>
<tr>
<td>4A</td>
<td>170 in depth, 330 in width</td>
<td>Coagulation of upper papillary dermis</td>
<td>Ablation Vaporized</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>5A</td>
<td>180 in depth, 380 in width</td>
<td>Coagulation of upper papillary dermis</td>
<td>Ablation Vaporized</td>
<td>14 ms double</td>
<td>D</td>
</tr>
<tr>
<td>5B</td>
<td>170 in depth, 160 in width</td>
<td>Coagulation of upper papillary dermis</td>
<td>Ablation Vaporized</td>
<td>9 ms single</td>
<td>D</td>
</tr>
<tr>
<td>5C</td>
<td>160 in depth, 200 in width</td>
<td>Coagulation of upper papillary dermis</td>
<td>Ablation Vaporized</td>
<td>9 ms single</td>
<td>D</td>
</tr>
<tr>
<td>5D</td>
<td>165 in depth, 210 in width</td>
<td>Coagulation of upper papillary dermis</td>
<td>Non-Ablation Coagulated Vacuolation</td>
<td>14 ms single</td>
<td>S</td>
</tr>
<tr>
<td>5E</td>
<td>170 in depth, 160 in width</td>
<td>Coagulation of upper papillary dermis</td>
<td>Non-Ablation Coagulated Vacuolation</td>
<td>9 ms double</td>
<td>S</td>
</tr>
<tr>
<td>5F</td>
<td>100 in depth, 100 in width</td>
<td>Normal</td>
<td>Non-Ablation Coagulated Vacuolation</td>
<td>9 ms single</td>
<td>S</td>
</tr>
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</table>

*Internal crater width measurement.

**Tixel crater variety**
Crater properties and extent of thermal damage with Tixel are closely related to the choice of the tip, the pulse duration, and the number of pulse repetitions. The D tip creates ablative craters (Figure 5A–C) while the S tip creates non-ablative thermal lesions (Figure 5D–F). Table 1 summarizes the main characteristics of craters at several Tixel pulse durations. Lesion dimensions are 100–380 μm wide and 100–180 μm deep. The histology shows no hemorrhage or edema.

The D tip generated clean epidermal evaporation and a dermal coagulation of maximum 180 μm in depth, which corresponds to the upper papillary dermis.

The S tip had a milder effect. The coagulated epidermis is preserved, forming an essentially dressed crater. The epidermis 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 cleft is formed between the damaged epidermis and dermis, as can be seen in Figure 5D and E, or a mild vacuolation in Figure 5F. In this later case, dermal coagulation at the upper papillary dermis is avoided due to the very brief pulse that has been applied.

The thermal model for ablation with Tixel shows the extent of the evaporation and thermal damage as a function of pulse duration, for both S tip and D tip (Figure 6). There is a profound difference between S and D tips in the extent of the ablative damage. The simulation predicts that the D tip ablates a considerable amount of tissue; while the S tip performs only minimal ablation. Simulation for a 9-ms single pulse is compatible with the histological results presented in Figure 5. The D tip that vaporized the whole epidermis (Figure 5C) presents a calculated 65-μm ablation (Figure 6 red triangle); the S tip that induced a non-ablative lesion (Figure 5F) presents a calculated 5-μm ablation (Figure 6 black triangle). This can be explained by the differences between their thermal diffusion coefficients. The D tip heat transfer rate to tissue is much faster than the S tip. For the 9-ms pulse duration, the model also predicts that ablation occurs in the first 0.25 ms for the D tip and in the first 0.01 ms for the S tip. Tissue ablation is thus a considerably rapid event when compared with the entire pulse length. Furthermore, the thermal damage that was calculated to be about 74 μm for both cases (Figure 6 circles) also matches the histologies. The coagulation damage, created during tip progression in the tissue, is determined by the thermal diffusivity of the tissue rather than the thermal diffusivity of the tip; and since both tips are in contact with tissue for a similar duration, a similar extent of tissue coagulation is expected.

**The healing process**
Histologies on the same day of Tixel treatment and after 7 days, on an in vivo porcine model, were examined (Figure 7). A Tixel crater 250 μm wide, 170 μm deep with focal necrosis of the epidermis and focal underlying dermal coagulation is presented (Figure 7A). Seven days after, epidermal regeneration is observed with a surface crust and a dermal epidermal cleft (150 × 50 μm) filled with new fibroblasts and macrophage cells (Figure 7D), indicating that healing occurs normally. This effect is associated with new collagen formation. A non-ablative pulse is also presented where the epidermis and stratum corneum are not ablated (Figure 7B). Rather they are compressed. A cleft is formed in the epidermal–dermal junction and minimal superficial necrosis is seen in the dermis. Seven days after (Figure 7E), there is complete epidermal regeneration with a focal crust on the stratum corneum and minimal dermoeipidermal cleft with focal collagen degeneration and macrophage infiltration. A low-energy non-ablative crator is associated with minimal epidermal damage with vacuolation at the epidermal–dermal junction and no dermal coagulation (Figure 7C). After Seven days, complete regeneration of the epidermis with minimal crust and underlying minimal collagen degeneration is observed (Figure 7F).

**Clinical results**
All subjects (100%) agreed or strongly agreed in both studies that no analgesics or pain relievers are necessary during the treatment.

![Figure 6. Theoretical thermal model of Tixel, with D tip and S tip, showing the extent of tissue ablation and tissue coagulation during various pulse durations.](image-url)
Discussion and conclusions

Tixel fractional treatment is a novel thermal resurfacing treatment which can generate ablative as well as non-ablative micro-craters in the skin. Superheating water molecules in the skin tissues with a high-conductivity metallic tip is effective in vaporizing the skin cells in a safe, precise, and predictable effect.

Tixel’s D tip creates ablative craters with similar properties to fractional CO₂ lasers. At the settings applied, Tixel’s S tip generates non-ablative “dressed” craters with underlying thermal damage extending down to the papillary dermis. The epidermal dressing of the crater enhances the healing providing rapid re-epithelialization and epidermal regeneration of the lesion. Moreover, the crater’s cover may act as a natural physiologic dressing protecting from post-treatment infection during the healing process.

This technology is safe and offers good resurfacing results, with nearly no downtime. Craters with diameters narrower than those of laser crater are associated with rapid healing. As treatment downtime is very short, additional treatments can be performed as compared with fractional ablative and non-ablative lasers for optimal outcome.
Treatment presents low discomfort for the patient. The device is operator-friendly as there is no smoke, no protective eyewear is required, and there is no risk of accidental harm by invisible laser radiation on the patient, physician, or personnel. Treatment pain is low, not requiring the application of analgesic creams. Contrary to lasers, which require analgesia and cooling to limit the patient’s pain, Tixel patients did not ask for any pain relief.

<table>
<thead>
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<th>Table 2. Clinical results, groups 1 &amp; 2.</th>
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<tr>
<td>Number of subjects</td>
</tr>
<tr>
<td>Treatment pain level&lt;sup&gt;a,b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Downtime&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Clearance of erythema&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Subject’s satisfaction</td>
</tr>
<tr>
<td>Wrinkle attenuation&lt;sup&gt;c&lt;/sup&gt;</td>
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</tbody>
</table>

<sup>a</sup>In a scale of 1 minimal to 10 maximum, without analgesia or pain relief.
<sup>b</sup>Mean score.
<sup>c</sup>Percent of subjects that present wrinkle improvement.

Figure 8. Full-face treatment. (A,C) Before and (B,D) after 4 months from the 3rd treatment session with D tip, 9–14-ms single-pulse one pass. Woman 58 years, phototype IV.

Figure 9. Full-face treatment. (A,C) Before and (B,D) after 4 months from the 3rd treatment session with D tip, 9–14-ms single-pulse one pass. Woman 58 years, phototype IV.

Figure 10. Periorbital treatment. (A,C) Before and (B,D) after 1 month from the 2nd treatment session with D tip, 14-ms single-pulse one pass. Woman 59 years, phototype II.

Figure 11. Periorbital treatment. (A) Immediately after treatment, (B) 5 days after treatment with D tip, 14-ms single pulse. Woman 59 years, phototype II.
relief during treatment or afterward. The low pain level experienced is probably the result of several factors: (a) smaller diameter craters in comparison to lasers; (b) while overall energy applied per crater is similar to laser, Tixel employs a fraction of the energy density; (c) The entire matrix of 81 Tixel craters is created in a single step lasting about 15 ms whereas a single laser beam having much higher energy density is applied within 0.5 ms repeatedly close to 100 times to generate 1-cm² treatment site. While further studies should be conducted to explore this new technology, this clinical evaluation was useful in providing both quantitative and qualitative understanding of Tixel's capabilities.

In conclusion, Tixel is a promising versatile fractional system for both ablative and non-ablative resurfacing.

**Note**

Some aspects of the TMA technology are patented and other aspects are patent pending.

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**Declaration of interest**

All authors state lack of conflict of interest. The authors may be compensated in the future with company options.

**References**