What is Tixel®?

• A fractional thermo-mechanical skin rejuvenation system.
• Tixel employs a hot metallic pyramidal Tip to transfer heat by conduction upon contact with tissue.
• Two handpieces are available:
  • Facial 81 (9x9) pyramids, 1cm²
  • Peri Orbital 24 (6x4) pyramids, 0.3cm²
Energy Transfer

- Tixel transfers thermal energy by brief contact of a hot tip with tissue
What is the source of the heat?

- An electrical ceramic heater is attached to the base of the Tip.
How does the energy transfer to the skin from the Tip?

- The Tip base temp is 400 deg. C.
- The pyramid edges are blunt.
- The Tip apexes touch the skin briefly and recede.
Does the tip protrude the skin physically?

No

The tip apexes push the skin to establish good thermal contact. They do not protrude the skin.
What are the properties of the Tip?

- Medical grade titanium
- Sterile at working temperature
- Biocompatible
- Durable and easy to clean
- Does not degrade
- Blunt pyramid apexes
- Can be used up to 250,000 pulses without changing
Which grade of Titanium is used?

The tip is made of identical alloys used in orthopedics and dental implants.

The mechanical properties of the titanium do not change at high temperature.
Why does the tip color change with time?

Upon heating titanium oxidizes to form a thin durable biocompatible oxide layer, TiO$_2$. The layer thickens with time. It’s color changes as it thickens.

<table>
<thead>
<tr>
<th>Layer Thickness (nm)</th>
<th>10-25</th>
<th>25-40</th>
<th>40-50</th>
<th>50-80</th>
<th>80-120</th>
<th>120-150</th>
<th>150-180</th>
<th>180-210</th>
</tr>
</thead>
<tbody>
<tr>
<td>Color</td>
<td>Golden</td>
<td>Purple</td>
<td>Deep Blue</td>
<td>Light Blue</td>
<td>Yellow</td>
<td>Orange</td>
<td>Purple</td>
<td>Green</td>
</tr>
</tbody>
</table>
Can it be cleaned?

The oxide layer, TiO2, is “non-stick” and can be easily cleaned by brushing with IPA (Isopropyl Alcohol). It has been validated and certified by the (BSI) British Standards Institute for cleanliness.
Can it be sterilized?

The system automatically sterilizes the tip by heat. The sterilization standard is called “Dry heat sterilization” ISO 20857. Due to the very high temperature the tip is always sterile during treatment.
What is the motion accuracy?

The mechanism has a tolerance of 30 microns. After each pulse the motion system is re-set to its “home” position. This maintains high accuracy and repeatability.
Why does Tixel use 400ºC

This is the temperature required to create thermal effects in the skin upon brief contact. CO₂ laser beams heat the skin to similar temperatures.

Reference
Thermographic and Histological Evaluation of Laser Skin Resurfacing Scans
Bernard Choi, Eric K. Chan, Jennifer K. Barton, Sharon L. Thomsen and Ashley J. Welch
IEEE JOURNAL OF SELECTED TOPICS IN QUANTUM ELECTRONICS, VOL. 5, NO. 4, 1999
CO₂ Laser Beam Vaporization Process

Thermal images of pulsed CO₂ Laser irradiation

Thermal camera range = -101°C to 398°C
What is the “chromophore” of Tixel?

Laser beam has a single wavelength that is absorbed by a specific component. Tixel applies heat which is uniformly absorbed by all tissue components.
What is the skin temperature profile in Tixel?

Heat Wave Model

Temp / scale

- 400 °C Surface
- 250 °C Upper Epidermis
- 50-60 °C 200-250 µ depth
Which Parameters are used to control heat transfer?

The handpiece controls:

- Contact Time (by speed) - "pulse duration in msec"
- Thermal matching (by distance) - “protrusion in µ”
- Number of pulses (either 1 or 2)

This provides control over thermal effect dimensions: Depth and Width.
Temperature Profile in Skin

Calculated by analytical model
How much energy does Tixel transfer to the skin?

0.2 millijoules per pyramid apex

<table>
<thead>
<tr>
<th>Tixel</th>
<th>RF</th>
<th>CO₂</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tixel’s Energy Transferred to skin (by a single pyramid) [mJ/pyramid]</td>
<td>Sharp Pin RF Energy per pin transferred to skin [mJ/pin]</td>
</tr>
<tr>
<td>Tixel Pulse duration [ms]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>0.13</td>
<td>4-62</td>
</tr>
<tr>
<td>10</td>
<td>0.19</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>0.24</td>
<td></td>
</tr>
</tbody>
</table>
Does Tixel Cause Pain?

Low Pain

With Tixel there is no charring, no smoke, no bleeding and relatively low pain. Analgesic creams are not required at low settings.
Why is Tixel less painful than laser?

Low energy is transferred evenly and gradually by stamping.
What is the difference between the way Tixel transfers energy compared to CO2 laser?

Ablative lasers transfer energy within less than 1 millisecond.

The process is associated with an explosion of water which absorbs the energy and heats up to very high temperatures.

Laser causes charring, smoke and pain.
Tixel transfers 0.2 mj/point within 6-16 milliseconds.
Tixel energy transfer is by stamping.
Pain sensors in skin

Pain nociceptors are located in the viable epidermis.
Nociceptors or free nerve endings, provide information about harmful or potentially harmful events that may cause loss of function
Types of Pain Nociceptors

Aδ fast transmission of short pulses

VS

C Fiber slow transmission of long pulses.

Pain - Laser Vs. Tixel

CO₂ laser applies very short pulses (µs) onto skin. Laser light is absorbed by water, resulting in high temperature and explosions. Delta fibers transmit signals to brain.

First Pain

Tixel applies long pulses (ms) onto skin. Heat is absorbed by water which vaporizes gradually. The result is a low pain sensation transmitted by C fibers.

Second Pain

Laser pulse in µs Tixel pulse in ms
# Pain Sensations per Pulse

<table>
<thead>
<tr>
<th>No. of Pain Sensations per pulse</th>
<th>Single</th>
<th>Multiple</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tixel - stamping</td>
<td>✔️</td>
<td></td>
</tr>
<tr>
<td>CO2 Laser - scanning</td>
<td>✔️</td>
<td>✔️</td>
</tr>
<tr>
<td>RF - electrode switching</td>
<td></td>
<td>✔️</td>
</tr>
</tbody>
</table>
Healing: GLP pre-clinical study

Tixel at Low – Med- Hi settings
Abdomen of 5 young pigs, 12 sites per animal, total 60 Treatment sites

Pathology Report
Conclusions

The Tixel device created a wedge shaped dermal area of collagen coagulation (acute thermal necrosis), which remained for three days and was cleared by mononuclear cells (lymphocytes, macrophages). By 3 days the epidermis was regenerated, but there were small superficial pustules or crusts observed in the lesion areas. By 14 days there was complete regeneration of the lesions. Rare foci of minimal superficial dermal fibrosis were observed at 14 days.
Safety – Facial Real World Evidence (RWE) and Peri Orbital (PO) Clinical Study

**RWE**
- 57 patients, 3-4 Facial treatments each, Medium settings (12ms/500-1000µ)
- No SAE
- 7 mild AE all resolved within max. 8 weeks (mild pigmentation)
- Crust spots 5-7 days

**PO Clinical Study**
- 72 patients, 3 Eye Lid treatments, Low settings (8ms/400µ)
- No SAE
- No AE
- Mild Erythema, 2-3 days.
Histopathology In Vivo Young Pig Tissue of Abdomen

Non Ablative Fractional Effect

<table>
<thead>
<tr>
<th></th>
<th>Low 6msec/400μ</th>
<th>Med 12msec/600μ</th>
<th>High 16msec/800μ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depth</td>
<td>197 μm</td>
<td>237 μm</td>
<td>251 μm</td>
</tr>
<tr>
<td>Width</td>
<td>325 μm</td>
<td>354 μm</td>
<td>493 μm</td>
</tr>
<tr>
<td>Coverage</td>
<td>10%</td>
<td>11%</td>
<td>15%</td>
</tr>
</tbody>
</table>

Pre-clinical study
30 min. after, X20 magnification, Single Pulse
How do thermal site dimensions relate to energy and healing?

<table>
<thead>
<tr>
<th>Days from biopsy</th>
<th>Device setting</th>
<th>Tixel [µm]</th>
<th>Depth ± SD</th>
<th>Width ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>acute</td>
<td>Low</td>
<td>197 ± 27</td>
<td>325 ± 116</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Low</td>
<td>129 ± 77</td>
<td>163 ± 38</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Low</td>
<td>54 ± 70</td>
<td>87 ± 129</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>Low</td>
<td>0 ± 0</td>
<td>0 ± 0</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Days after biopsy</th>
<th>Device setting</th>
<th>Tixel [µm]</th>
<th>Depth ± SD</th>
<th>Width ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>acute</td>
<td>Medium</td>
<td>237 ± 40</td>
<td>354 ± 67</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Medium</td>
<td>148 ± 54</td>
<td>245 ± 52</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Medium</td>
<td>122 ± 45</td>
<td>204 ± 47</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>Medium</td>
<td>0 ± 0</td>
<td>0 ± 0</td>
<td></td>
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<thead>
<tr>
<th>Days from Biopsy</th>
<th>Device setting</th>
<th>Tixel [µm]</th>
<th>Depth ± SD</th>
<th>Width ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>acute</td>
<td>High</td>
<td>251 ± 32</td>
<td>493 ± 117</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>High</td>
<td>271 ± 101</td>
<td>373 ± 135</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>High</td>
<td>168 ± 74</td>
<td>181 ± 117</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>High</td>
<td>51 ± 54</td>
<td>114 ± 128</td>
<td></td>
</tr>
</tbody>
</table>

Acute Depth SD is less than 20% ensuring safety on thin tissue such as eyelids (epidermis and dermis are 500µ thick) and supraclavicular area (E&D=700µ).
Wound healing at Maximum settings

Healing
Young Porcine Skin X10 magnification

High 16 msec

T=0 days

T=1 day

T=8 days
How does the volume of the thermal effect of Tixel compare to Micro needle RF?

**VOLUME OF THERMAL EFFECT**

- Due to the pyramidal shape of the tip apex, the greater the protrusion, the greater the volume of the thermal effect in the skin.
- In MN-RF the thermal effect is narrower.
At which settings are open channels optimal?

Based on our research the most effective micro-channels are created at 6/400.

What is the mechanism of permeation and absorption?

Tixel fractures the Stratum Corneum and evaporates water from the upper skin layers. Skin is dehydrated at these sites. Hydrophilic substances absorb through the micro-channels.
Drug Delivery via Superficial Open Micro-Channels

Histology after Tixel treatment 6/400

Fluorescence microscopy in 5ALA cream incubated skin after Tixel 6/400

Viable epidermis
Dermis

In vivo human skin

Publication Pending by M. Haedersdal

Superficial open channels are created in stratum corneum following Tixel treatment
Non treated skin

Histology (Control)

Fluorescence microscopy in 5ALA cream incubated skin without Tixel

Publication Pending by M. Haedersdal

In vivo human skin
Thank you

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