MTS (Microneedle Therapy System)

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TDDS (Transepidermal drug delivery system)
TDDS

Positive effects:
- low toxicity↓, GI trouble↓, bypass of hepatic metabolism

Limits:
- low concentration of delivered drug ( < 10mg/day)
- should be lipophilic↑, low molecular weight ↓

Several trials for enhancing TDDS:
- Occlusion, Stripping, Iontophoresis, Electroporation, Microneedle therapy system (MTS)

With normal creaming not more than 0.3% of liposomes can penetrate into the skin.

With the MTS up to 40 times of liposomes can be infiltrated through the stratum corneum.
New Needle Devices

Microfabricated Needle Patch
Microneedles Stamp
Micro Needle Roller

Micro-Channel photo
Introduction of Microneedle

- Body: Diameter(20mm) X Width(21.5mm)
- DISC: 9ea/ Angle: 14.5°
- A Disc: 25ea (Total needles: 200ea)
- Material: High-Quality Swedish Steel Rustproof
  - Special a method of construction 15% improvement of needle’s strength
- Process:
  Cutting, Grinder, Harden steel, Extremely low Temper.

- Body: Diameter(20mm) X Width(21.5mm)
- DISC: 8ea/ Angle: 15°
- A Disc: 24ea
  (Total needles: 192ea / 96ea)
- Material: High-Quality Swedish Steel
- Process:
  Cutting, Grinder, Harden steel, Extremely low Temper.

CR10: Needle Length 1.0mm
CR20: Needle Length 2.0mm
HF8: Needle Length 0.2mm
ME8: Needle Length 0.5mm
MD8: Needle Length 1.5mm
**TDDS by MTS – How to use?**

- **Control**: None applied
- **Non MTS**: simple apply
- **MTS(A)**: apply after MTS
- **MTS(B)**: apply -> MTS -> apply

- **Diffusion by microneedle**
- **Diffusion by microneedle**

- Rhodamine B base (Aldrich) 0.005M
- Applying condition: 100ul/cm² (nabulizing)
- Size of field: 10 x 10 mm (total 36 pieces)
- Tissue: Pig skin (dermal thickness 3.16mm)

- MTS apply: ↩️↑️↓️←️ repeat twice

- **Wait for 20 min**

<table>
<thead>
<tr>
<th>Non MTS</th>
<th>control</th>
</tr>
</thead>
<tbody>
<tr>
<td>MTS(A)</td>
<td>MTS(B)</td>
</tr>
</tbody>
</table>

*Diffusion by microneedle (16배)*

*Olympus CKX41*
Rhodamine B base – Pig skin

Non MTS

Control

MTS(A)

MTS(B)
Rhodamine B base – Pig skin
**Fluorescent image capture**

<table>
<thead>
<tr>
<th></th>
<th>Min</th>
<th>Max</th>
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</thead>
<tbody>
<tr>
<td>Reference</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Control</td>
<td>≈ 280um</td>
<td></td>
</tr>
<tr>
<td>MTS(A)</td>
<td>≈ 390um</td>
<td>≈ 980um</td>
</tr>
<tr>
<td>MTS(B)</td>
<td>≈ 940um</td>
<td>≈ 1470um</td>
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</table>

**Control**

![Control image](Image)

MTS(A)

![MTS(A) image](Image)

MTS(B)

![MTS(B) image](Image)
Drug delivery by MTS

Simple apply (1/2) -> MTS -> simple apply (1/2) : Best way

<table>
<thead>
<tr>
<th>Unit (µm)</th>
<th>0</th>
<th>400um</th>
<th>800um</th>
<th>1200um</th>
<th>1600um</th>
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<tbody>
<tr>
<td>Control</td>
<td>0</td>
<td>280</td>
<td>390</td>
<td>980</td>
<td>1470</td>
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<tr>
<td>Non MTS</td>
<td>261</td>
<td>261</td>
<td>261</td>
<td>261</td>
<td>261</td>
</tr>
<tr>
<td>MTS(A)</td>
<td>940</td>
<td>940</td>
<td>940</td>
<td>940</td>
<td>940</td>
</tr>
<tr>
<td>MTS(B)</td>
<td>940</td>
<td>940</td>
<td>940</td>
<td>940</td>
<td>940</td>
</tr>
</tbody>
</table>

Depth of penetration (µm)
TDDS by MTS – Time course

- Moticam 100(Image sensor) & Image analysis program for penetration depth
- Light source: 365nm (VL-4.LC)
- Rhodamine B base

Same condition with previous experiment
Penetration by MTS

Fluorescence image capture & analysis program

Rhodamine B base

react with 365nm wave light / emit 585nm light
TDDS by MTS – Time course
TDDS By MTS Using Ascorbic Acid

- Ascorbic acid : reacting with Sodium 2,6–dichloroindophenolate hydrate
- Bx : left forearm inner aspect (medial side)
- Control, non MTS(10 min), MTS(10min), MTS(30min),
- Ascorbic acid apply : 100ul/cm2
TDDS By MTS Using Ascorbic Acid
TDDS By MTS Using Ascorbic Acid

Control
Non MTS 10 min
MTS 10 min
MTS 30 min
Iontophoresis 10 min (sol X10)
MTS using Ascorbic Acid

- Iontophoresis: 10min, (X10, 1000μl / cm²)
TDDS By MTS Using Ascorbic Acid

MTS using Ascorbic Acid in human skin

- Control non MTS
- MTS 10 min
- IonP
- MTS 30 min

Depth of penetration (μm):
- 0 μm
- 345 μm
- 987.7 μm
- 1095.7 μm
- 1652.5 μm

unit(μm)
Further Studies

Conclusion

- TDDS : MTS > iontophoresis > simple application
- Time course : MTS >> simple application (steady at 30 min)

Ongoing & Future studies

- Hyperhidrosis, alopecia, gynoid lipodystrophy
Clinical Applications

Target Depth per Technology

- **PDL/IPL**
  - Depth ~ 500 µm

- **Fractional**
  - Depth ~ 400 - 800 µm

- **Deep Heating**
  - Depth ~ 1000 - 3000 µm
Photoaging & MTS??

Cross section of 50 year old skin

Epidermis

Photo aged skin:
~300 µm (dermis)

Healthy skin (dermis)

Cross section of 18 year old skin

Epidermis

Photo aged skin: minimal - none

Healthy skin (dermis)
Striae & MTS

MTS only

MTS + IPL 560
Striae & MTS

MTS only
(2 weeks later)

MTS + IPL 560
(2 weeks later)
Striae & MTS

Before

After
Striae & MTS

MTS + IPL 560

MTS only
Complications by IPL
Striae & MTS

IPL + XEO  MTS  4 weeks
Collagen fibers (MT stain)

Control Striae (Baseline)  67.3±0.7
Striae (Post-treatment 8 wk)  60.9±1.6

§P=0.063 By Wilcoxon signed rank test
Elastic fiber (VB stain)

Control Striae (Baseline) Striae (Post-treatment 8 wk)

15.7±0.3 11.5±0.7 14.4±0.2

§ P=0.063 By Wilcoxon signed rank test
Scar revision by MTS
Clinical application of MTS

For striae

1) MTS + IPL : hyperpigmentation (less pigmentation when combined with MTS? Scattering of target chromophores?)

2) MTS + Affirm ? : less effective d/t depth?

3) MTS + aramis/polaris : too long

4) MTS + thermage / fraxel : too expensive

5) MTS + Xeo / titan / non-ablative laser

Hyperhidrosis : MTS + botox?

Melasma : MTS + vitamin/transamic acid

Alopecia : MTS + hair growth factors?

DDS : transepidermal drug delivery system (ex… slim patches)