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Evaluation of pain and anesthetic efficacy after topical application of microneedles: a randomized clinical trial

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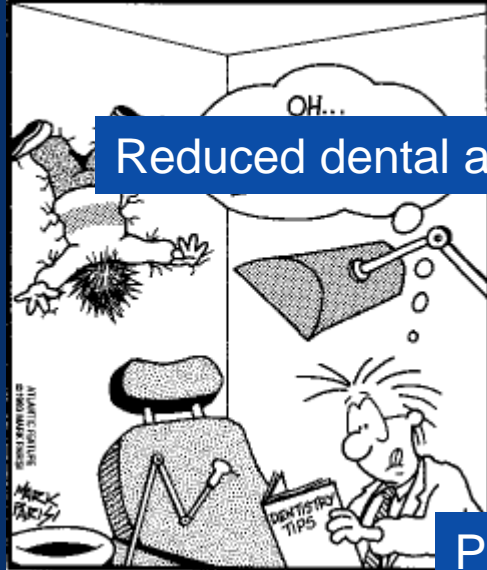
University of Campinas - UNICAMP

Piracicaba, SP, Brazil



Dental phobia

off the mark by Mark Parisi
www.offthemark.com



Reduced dental attendance

Poorer oral health

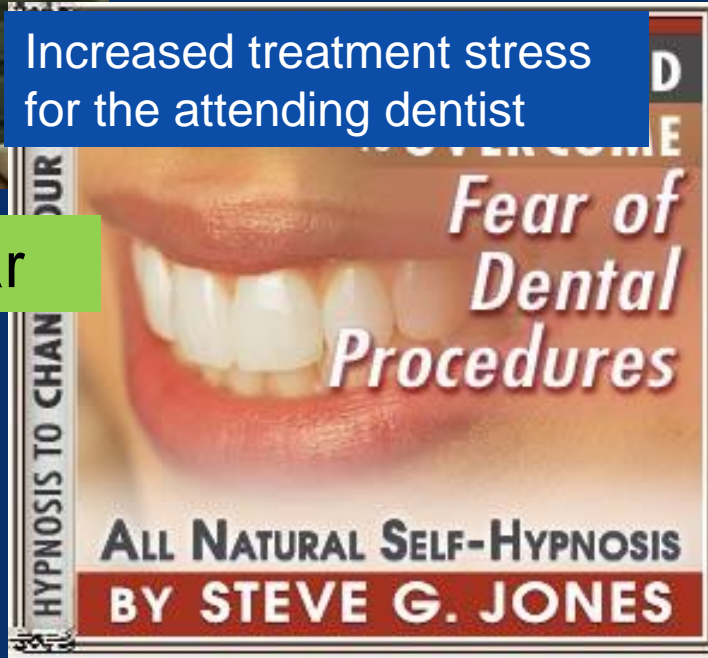
Pain

Anxiety



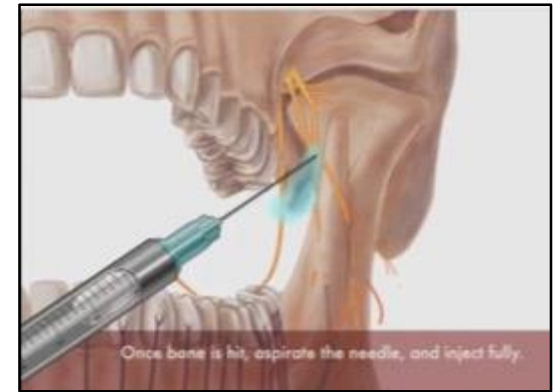
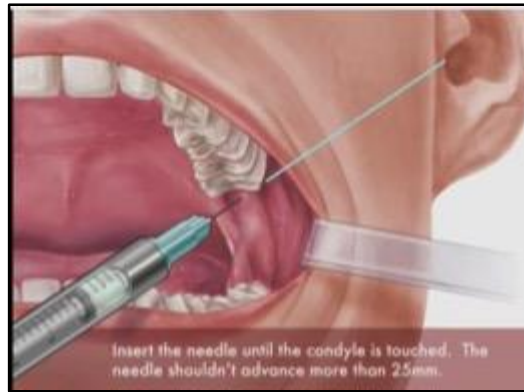
Increased treatment stress
for the attending dentist

Fear



How is dental anesthesia done?

A deep injection is required to numb the desired area or to block a nerve.



Topical anesthesia is used as a pre-injection step



- Poor drug penetration
- Often superficial numbness (1-2 mm) and deep injection can still be painful
- Dentists don't leave the drug long enough
- Palatal injections are quite painful

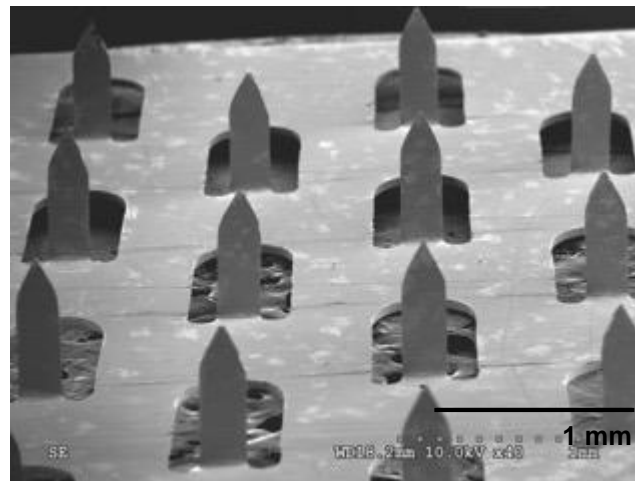
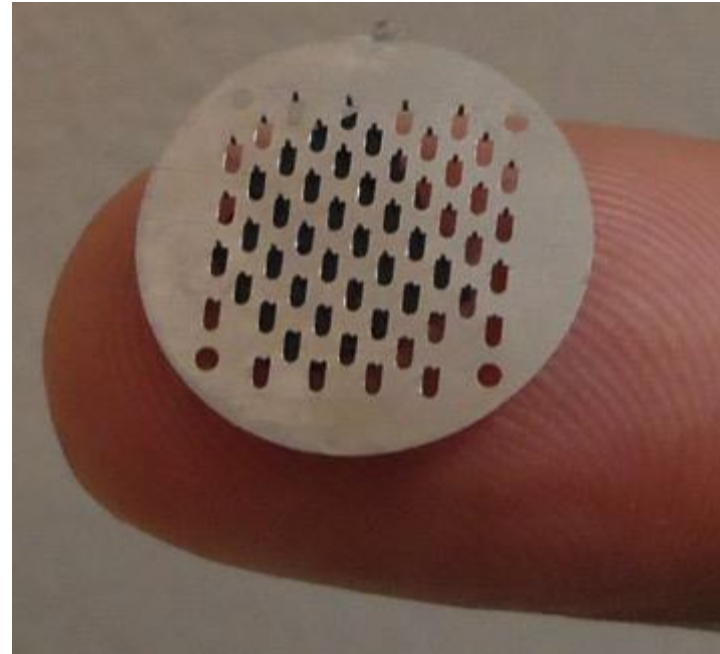
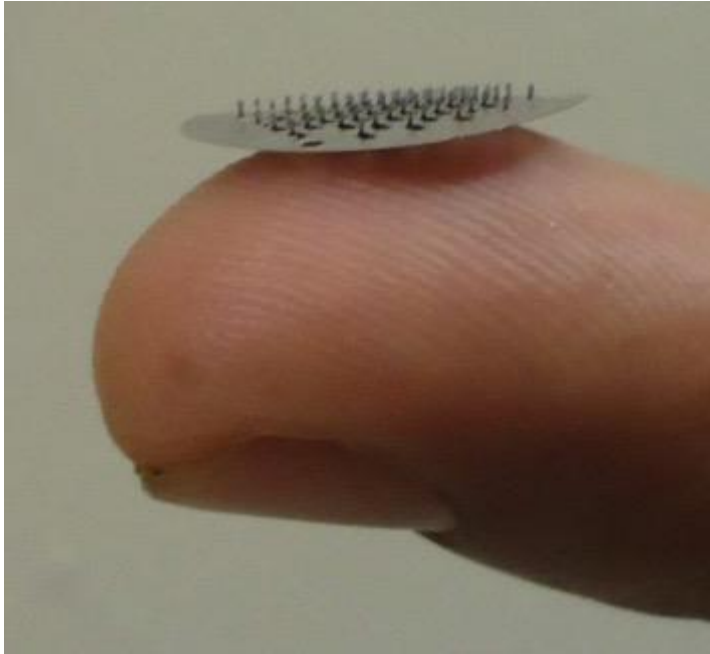
Can the topical anesthesia be improved to make deep injections less painful?

YES !!!

Topical anesthesia EMLA™ (eutectic mixture of 2.5% lidocaine and 2.5% prilocaine, Astra-Zeneca)

Can achieve anesthesia for palatal mucosa and even pulpal (deep) anesthesia after 10-30 min topical application

Microneedles

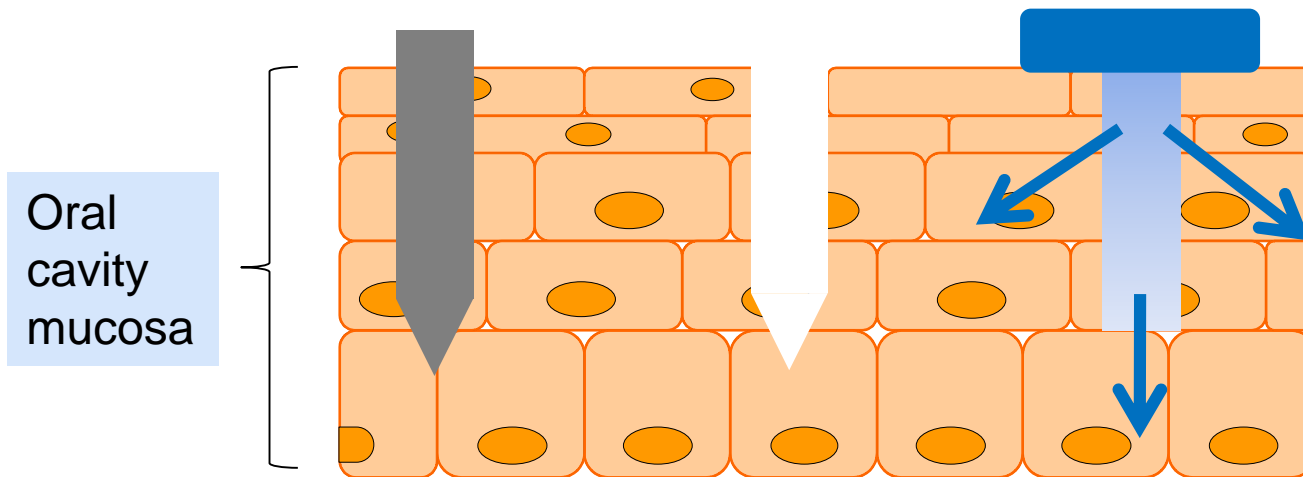


'Poke-n-patch' method

Step 1: Insert microneedle

Step 2: Remove microneedle

Step 3: Apply patch/film containing anesthetic



- Faster penetration
- Deeper delivery to achieve superior numbness

Aims of the project

- 1) Determine the pain associated with insertion of the microneedle device into different regions of the mouth in humans
- 2) Determine the efficacy from 'poke-n-patch' approach in increasing anesthesia effectiveness
 - Deep tissue (pulpal anesthesia with electrical pulp tester)
 - Soft tissue (pin prick)
 - Actual injection of lidocaine with a 30 gauge needle

Challenges

- Approval for human studies took > 1 year
- Shipping material to Brazil is a big challenge due to strict import control
- Microneedles sent month ago are still stuck at the airport in Brazil

Preliminary pain study in humans

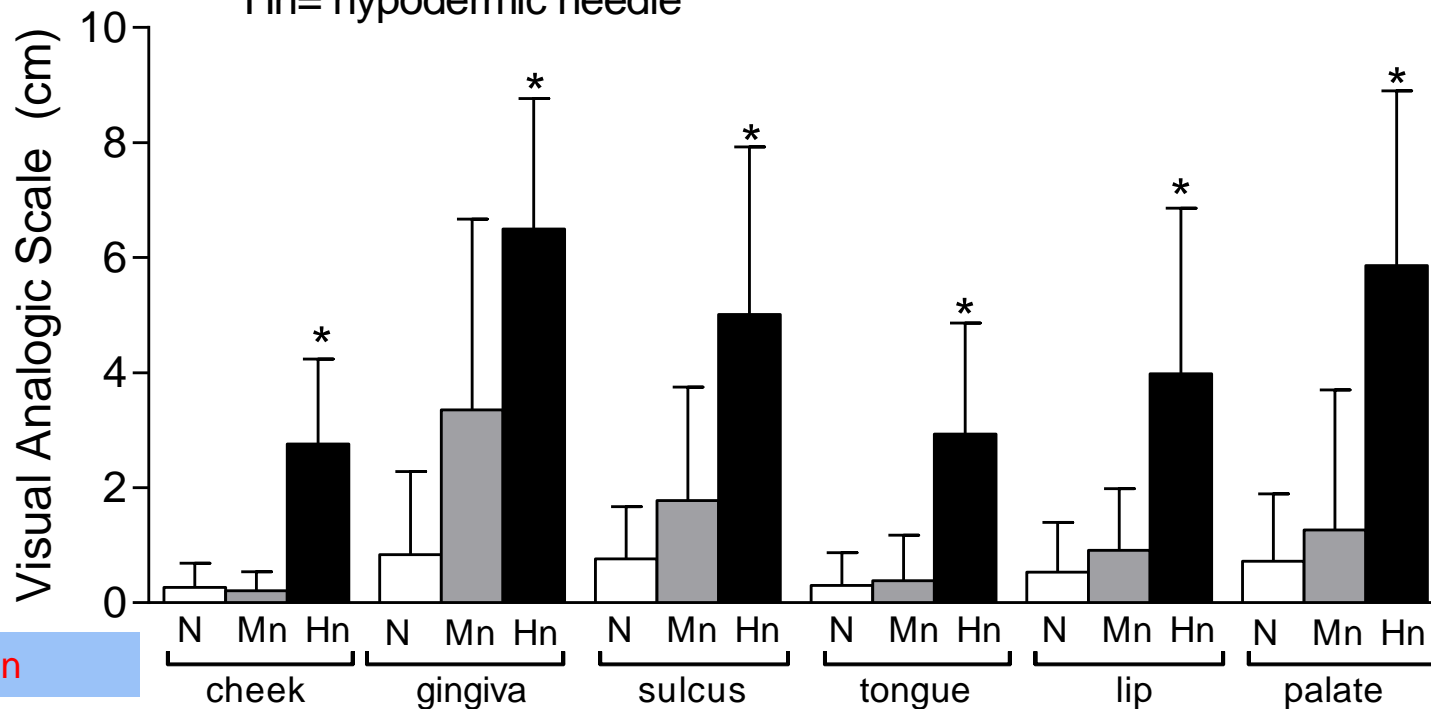
Extreme pain

N= negative control
Mn= Microneedles
Hn= hypodermic needle



Total 57 microneedles
on one patch

Each microneedle is
700 μm long



No pain

Acknowledgement

GRADUATE STUDENTS

1. Seth Boese
2. Pedro Gonzalez
3. Rohan Ingrole
4. Jasim Uddin
5. Raul Dominguez
6. Tatiana Colon

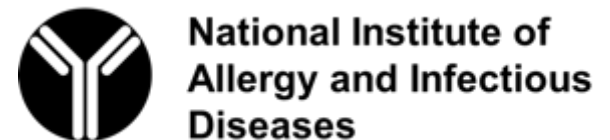
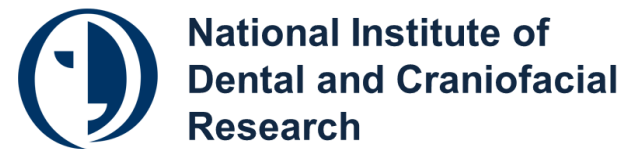
POSTDOCS

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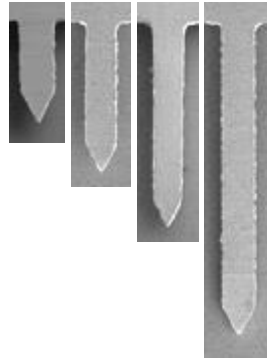


What is the level of pain induced by microneedles?

26-gage hypodermic needle

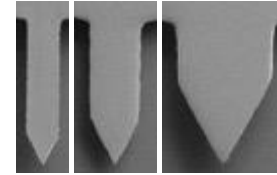
Length

500 μm to 1500 μm



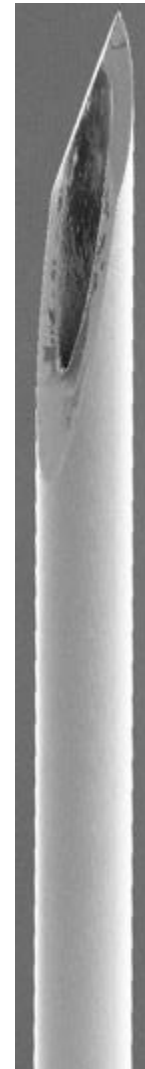
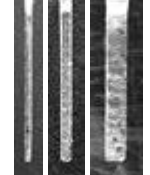
Width

160 μm to 465 μm



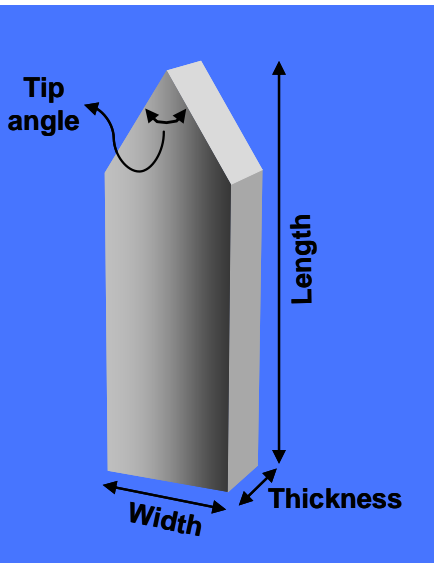
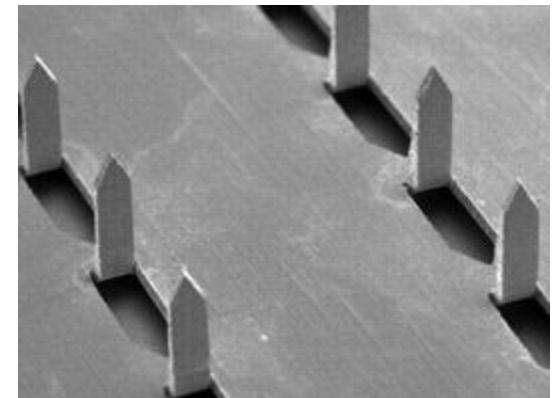
Thickness

30 μm to 100 μm



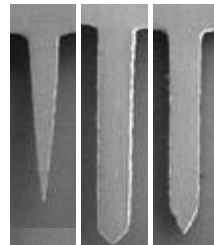
Array of microneedles

5 vs. 50

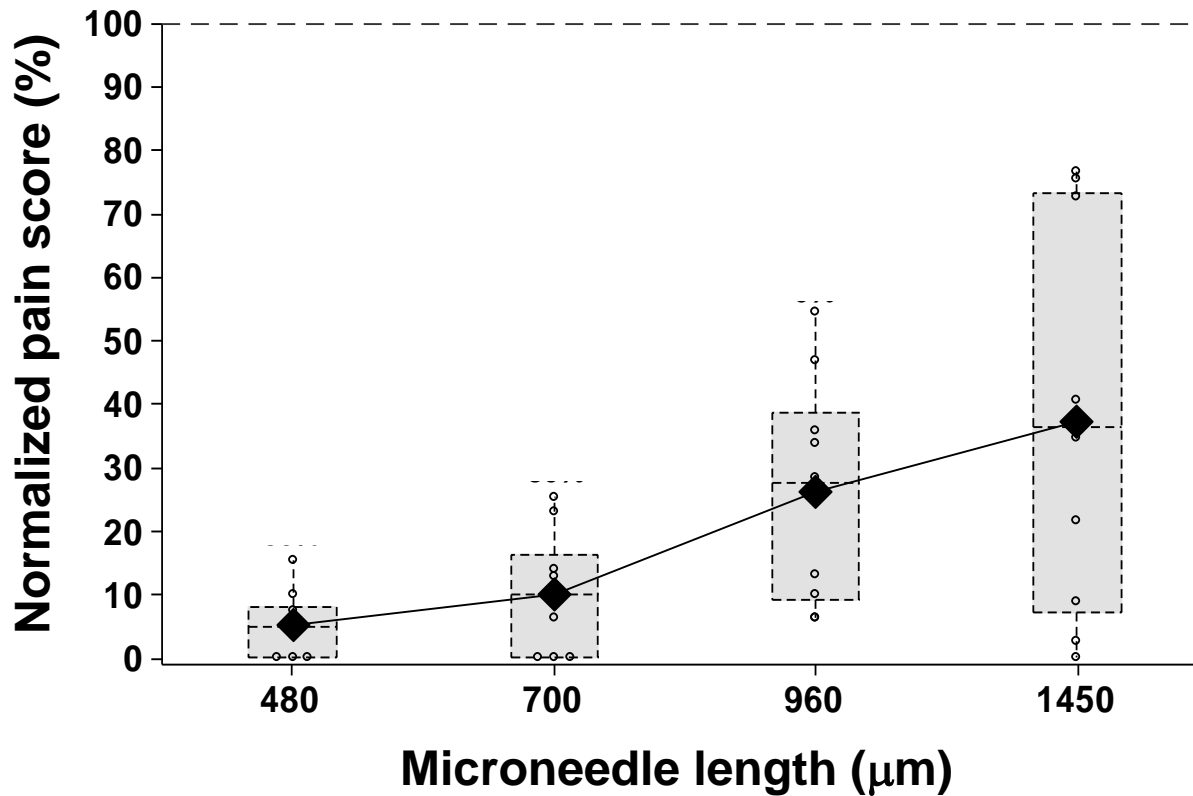


Tip angle

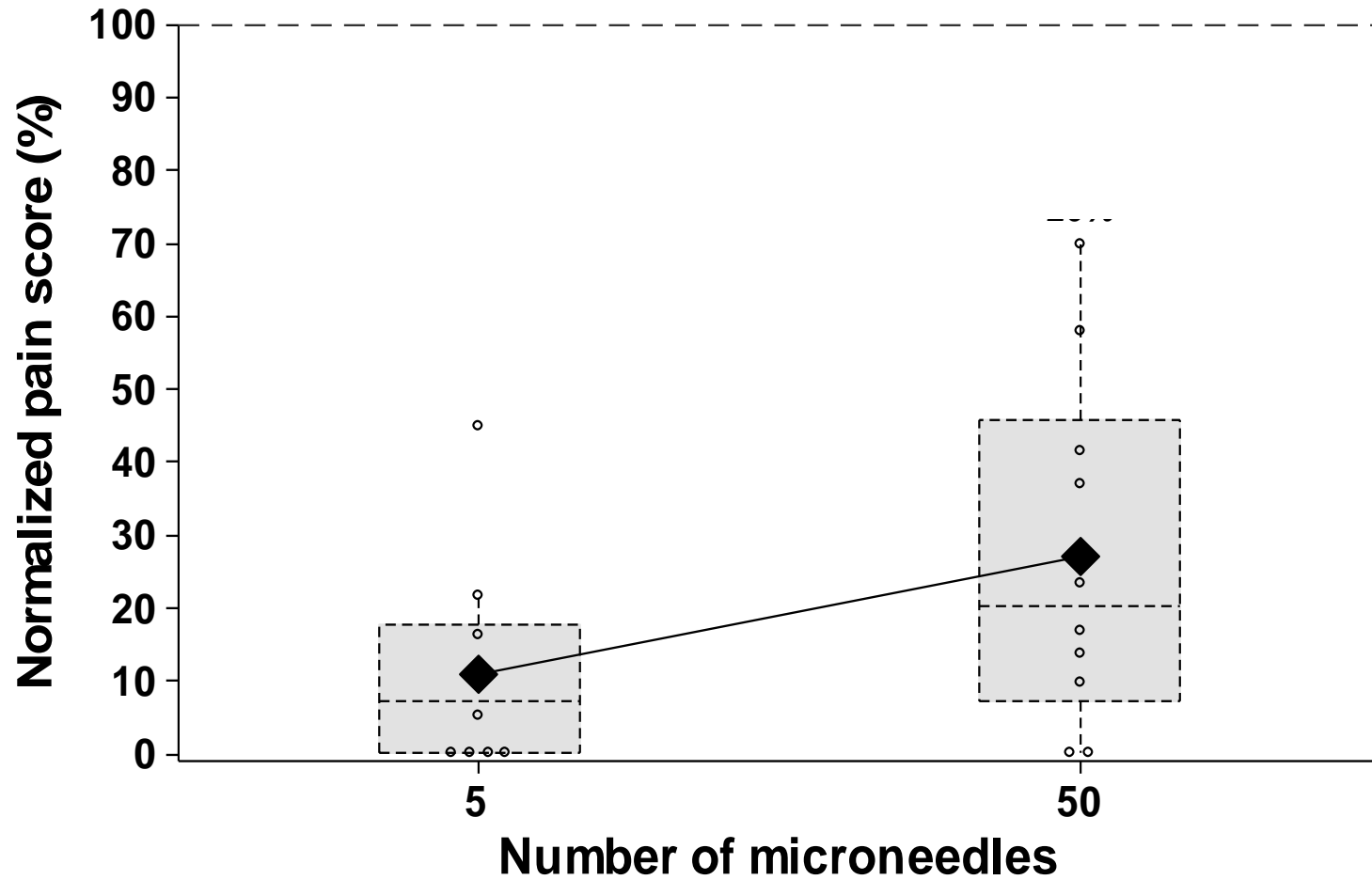
20° to 90°



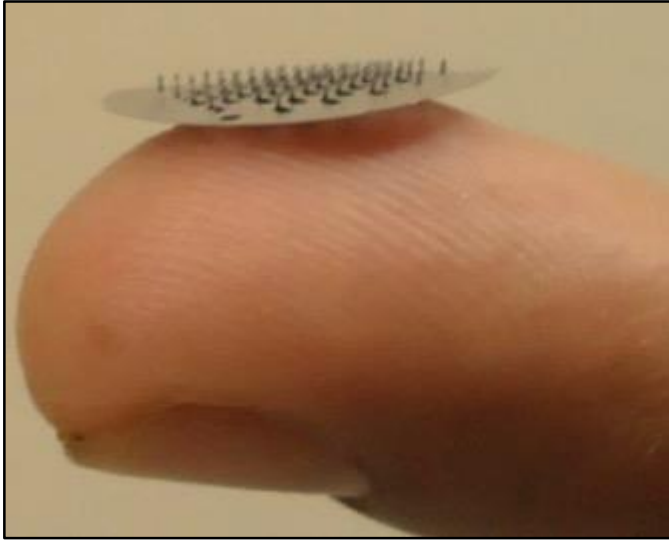
Effect of microneedle length



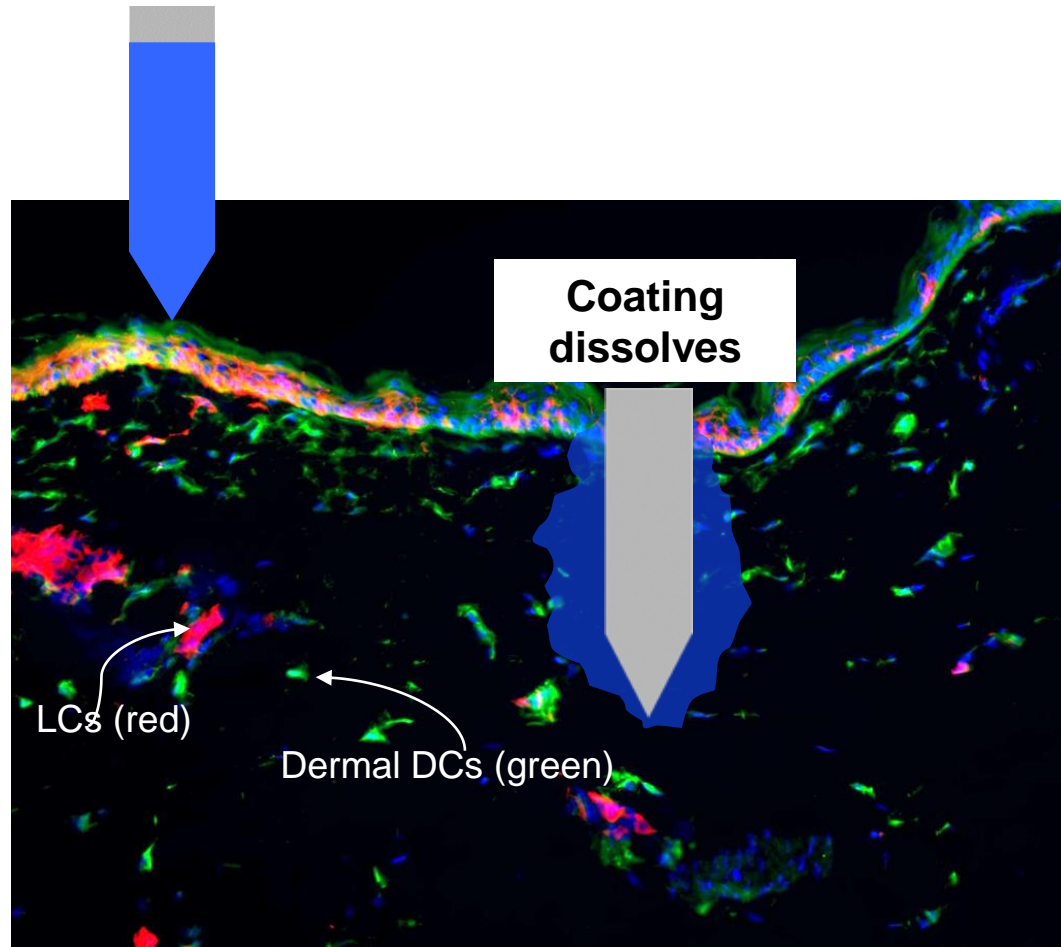
Effect of number of microneedles



Coated microneedles



Microneedle
coated with
allergen



LCs: red, CD1a
Dermal DCs: green, X111a

How is coating done?

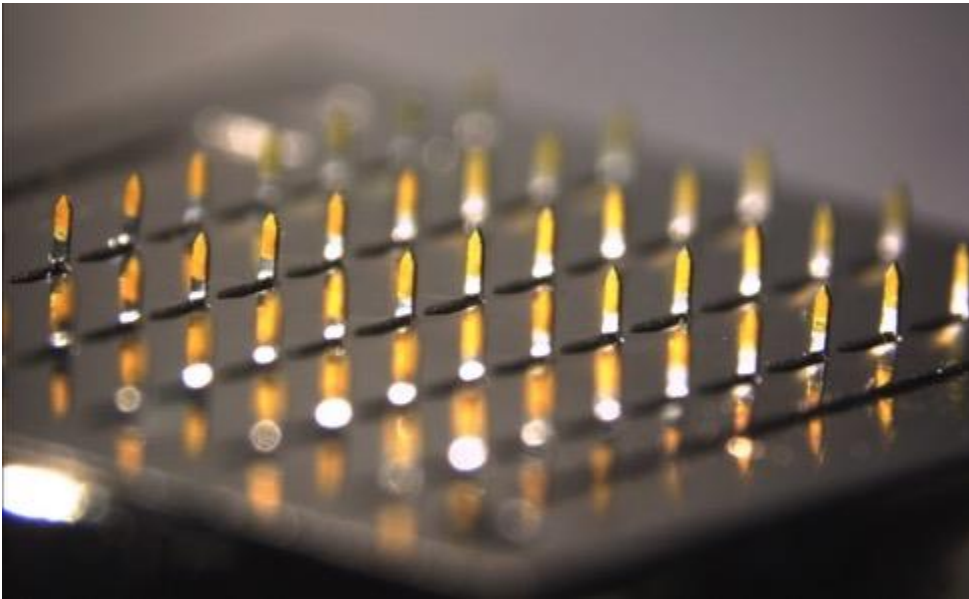
Coating solution comprises of FDA approved excipients:

- Carboxymethyl cellulose: *viscosity enhancer*
- Poly (ethylene oxide and propylene oxide): *surfactant*

Microprecision dip-coating

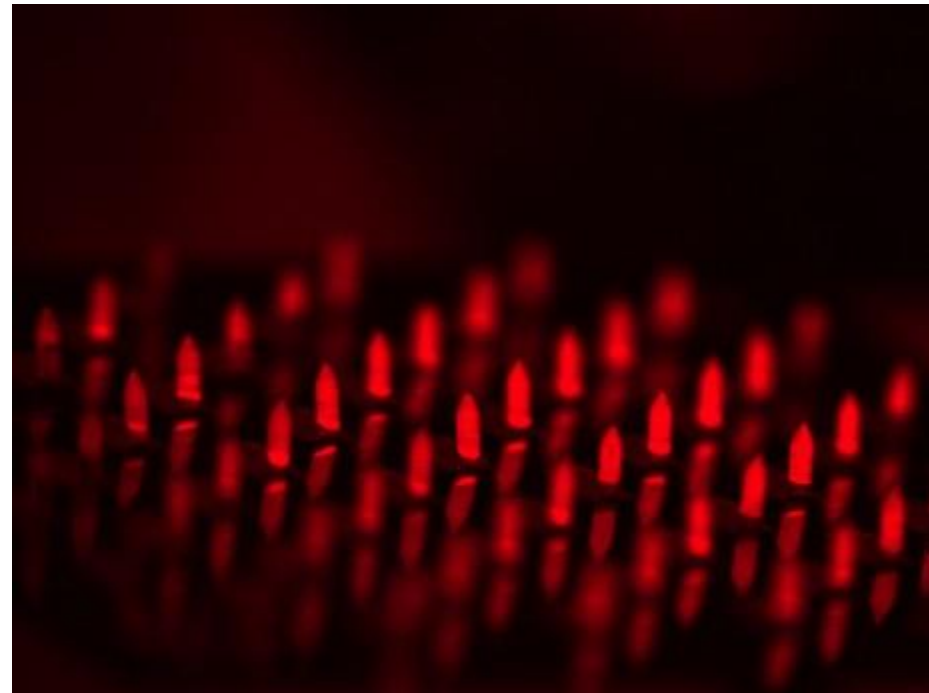
Coating
video

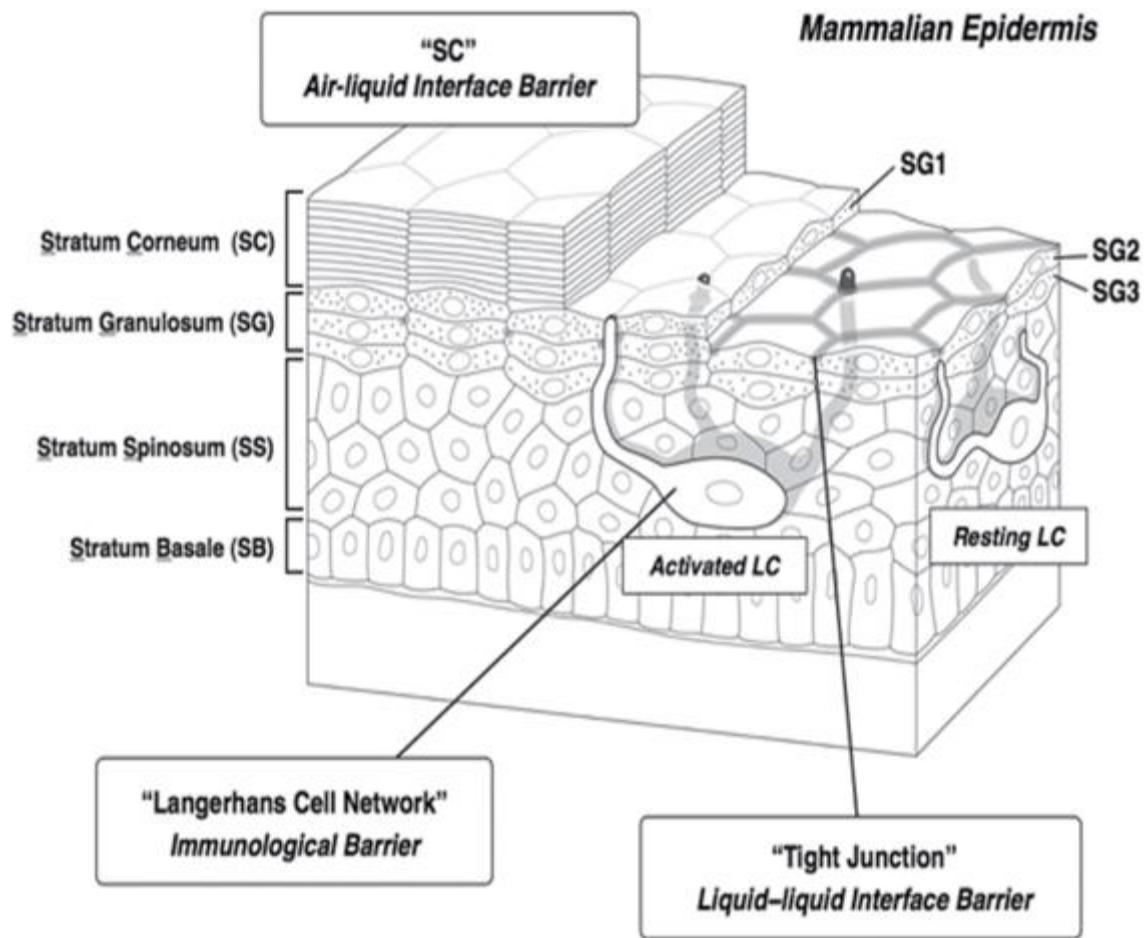
Microprecision coating of arrays



Small molecule coated

Microparticle coated

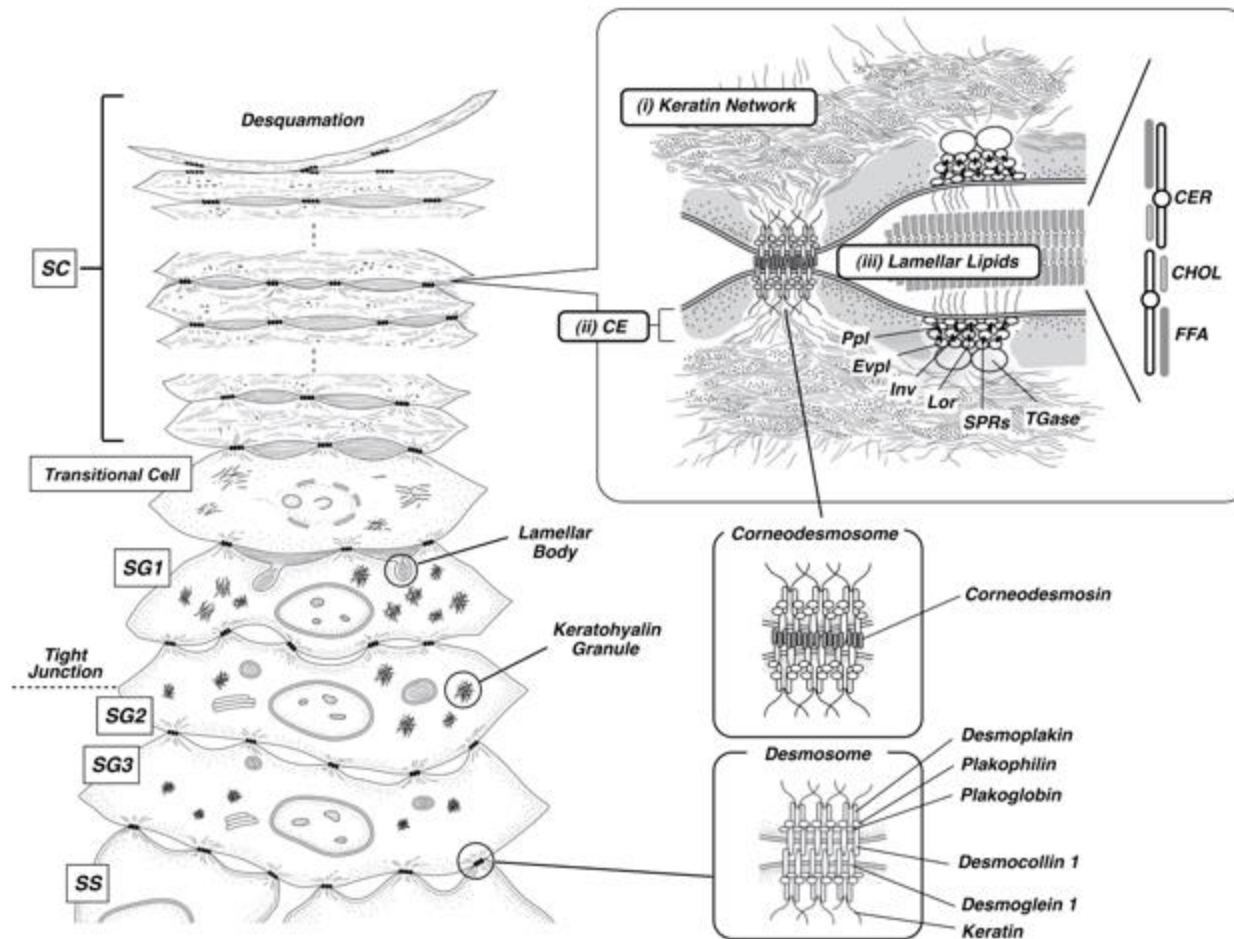




From: Dissecting the formation, structure and barrier function of the stratum corneum

Int Immunol. 2015;27(6):269-280. doi:10.1093/intimm/dxv013

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What is done to reduce dental pain?

