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

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Dental phobia

- Pain
- Anxiety
- Fear
- Reduced dental attendance
- Poorer oral health
- Increased treatment stress for the attending dentist
How is dental anesthesia done?

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

- 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

Topical anesthesia is used as a pre-injection step
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

Oral cavity mucosa
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**

- Total 57 microneedles on one patch
- Each microneedle is 700 μm long

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**Visual Analogic Scale (cm)**

- N = negative control
- Mn = Microneedles
- Hn = hypodermic needle

- N Mn Hn
  - cheek
  - gingiva
  - sulcus
  - tongue
  - lip
  - palate

**Extreme pain**

- No pain
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What is the level of pain induced by microneedles?

- **Array of microneedles**
  - **Length**: 500 µm to 1500 µm
  - **Width**: 160 µm to 465 µm
  - **Thickness**: 30 µm to 100 µm

- **26-gage hypodermic needle**
  - **Length**: 500 µm to 1500 µm
  - **Width**: 160 µm to 465 µm
  - **Thickness**: 30 µm to 100 µm

- **Tip angle**: 20° to 90°

Gill et. al, Clin J Pain Volume 24, Number 7, Sept 2008
Effect of microneedle length

Gill et al., Clin J Pain Volume 24, Number 7, Sept 2008
Effect of number of microneedles

Gill et al., Clin J Pain Volume 24, Number 7, Sept 2008
Coated microneedles

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
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What is done to reduce dental pain?

http://aemstatic-ww2.azureedge.net/content/dam/rdh/print-articles/Volume%2034/Issue%206/1406flog01.gif