

Introduction to Microneedles

Microneedles (MNs) are miniaturized needles allowing painless delivery and sampling to and from the dermal layer. While they have traditionally been used for the delivery of drugs and vaccines, their simple manufacturing process and ease-of-use has generated interest in their potential diagnostic applications.

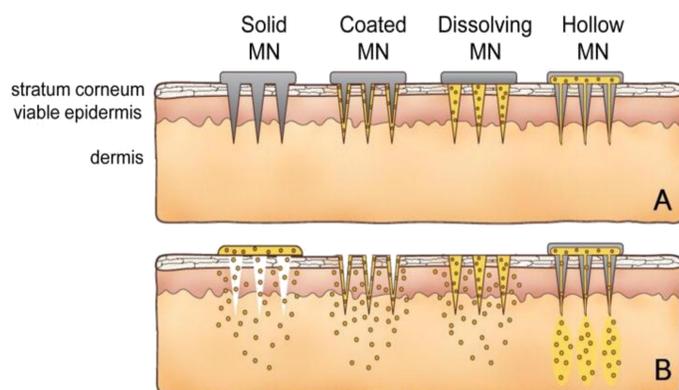


Fig 1. Most microneedles fit into 4 categories i) Solid MNs, ii) Coated MNs, iii) Dissolving MNs, iv) Hollow MNs.¹

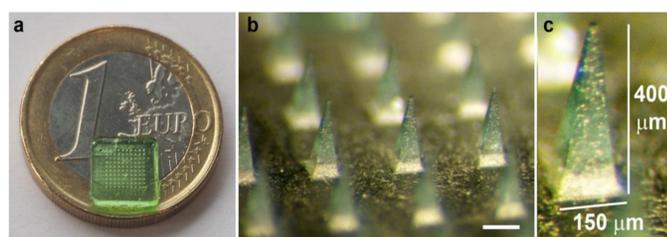


Fig 2. MNs are very small relative to hypodermic needles, with typical lengths < 0.5 mm.²

Diagnostic Applications

MN patches can be used to deliver diagnostic agents and sensors. Delivery of two sensors could allow ratiometric detection.

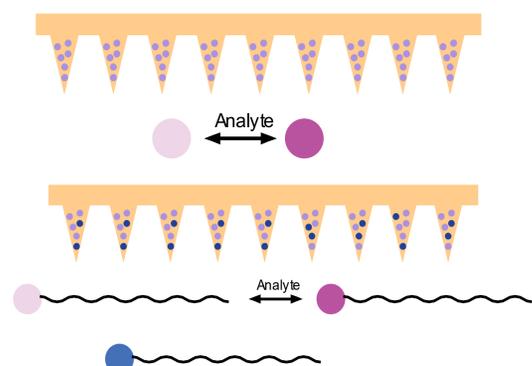


Fig 3. Co-delivery of a sensor and a reference dye serves to correct for the amount of dye delivered.

References

- Kim Y.-C.; Park J.-H.; Prausnitz M. Microneedles for drug and vaccine delivery. *Adv. Drug Deliv. Rev.* **2012**, *64* (14), 1547-1568.
- Brambilla D.; Proulx S.T.; Marschalkova P.; Detmar M.; Leroux J.-C. Microneedles for noninvasive structural and functional assessment of dermal lymphatic vessels. *Small.* **2016**, *12* (8), 1053-1061.

Hypothesis

MNs could be used for the delivery of specifically designed diagnostic agents to the dermal layer, to allow real-time monitoring of various health parameters.

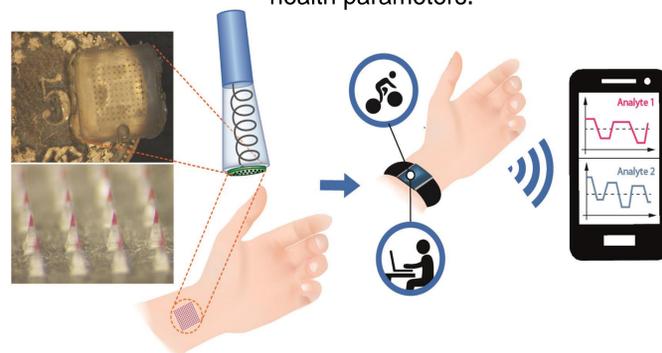


Fig 4. A fluorescent imaging agent, paired with a wearable device, could allow at-home monitoring of bodily analytes.²

Materials and Methods

Through a simple casting process, dissolving polymeric MNs can be manufactured with a diagnostic agent localized in the tips.

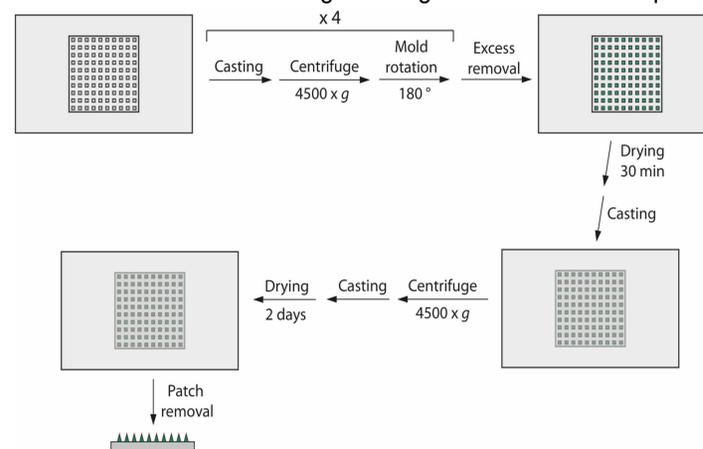


Fig 5. Diagram outlining casting process and highlighting easy fabrication of MNs.

MNs for ROS Sensing

MNs could be loaded with a tailored redox-sensitive fluorescent dye, to allow quantification of reactive oxygen species (ROS) in the skin.

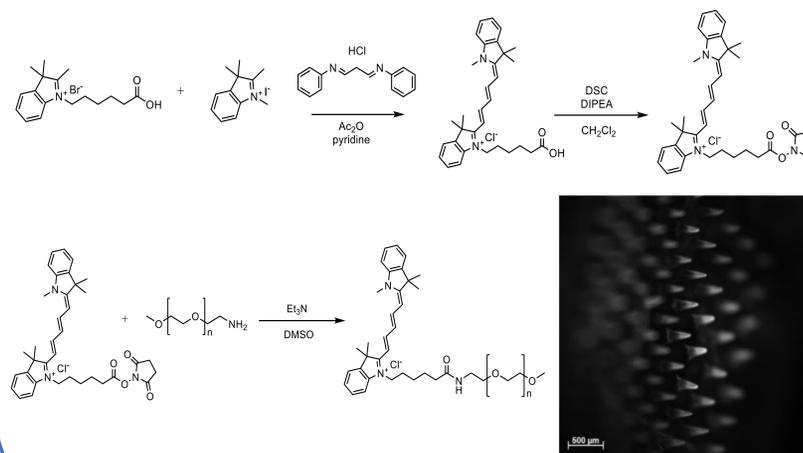


Fig 6. A simple synthesis of the ROS-sensitive fluorescent dye, Cyanine-5. This dye can be conjugated to PEG and loaded into MN tips for delivery to the skin.

Results

The fluorescent dye Cy5 and its ROS sensing counterpart H-Cy5, along with a PEGylated form, were synthesized and found to have promising ROS-sensing properties when incorporated into MNs.

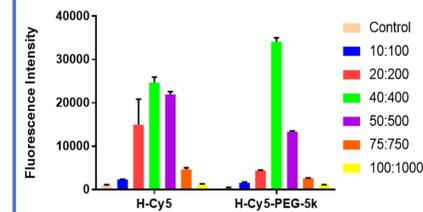


Fig 7. Following reduction, Cy5 and its PEGylated conjugate regain fluorescence in the presence of ROS.

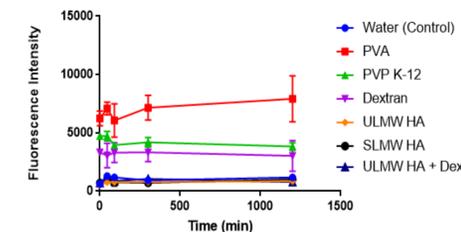


Fig 8. Various MN polymers were investigated, to determine optimal materials for MN stability.

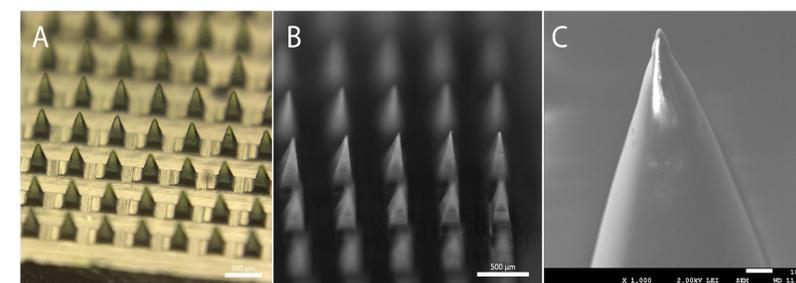


Fig 9. Microscopic images of a MN array, and the functional tattoo generated in rat skin. Left = Cy3; Middle = Cy5; Right = Overlay of both dyes.

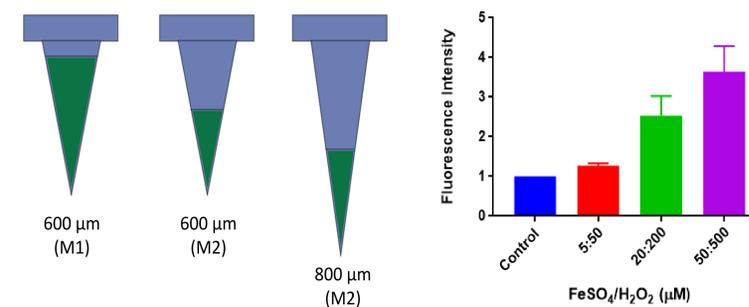


Fig 10. SEM image of a MN tip.

Fig 11. Fluorescence of H-Cy5-PEG in response to ROS in skin-simulating gels.

Outlook

- These results are being validated. Fluorescent sensors for other physiological analytes will be synthesized and optimized for MNs.
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