

Formation of Microchannels in Skin with a Hand-applied, Plastic Microneedle Array

Craig Moeckly, Kris Hansen, Jerome Gysbers, Daniel Duan, Kris Siebenaler, Alexei Demchouk 3M Drug Delivery Systems, 3M Center, St. Paul, MN 55144

Abstract

Purpose

3M has produced polymeric microneedle arrays that, when applied by hand, disrupt the stratum corneum and epidermis creating microchannels in the skin. The purpose of this work was to characterize the microchannels, test the durability of the microneedles, and demonstrate enhanced delivery of topically applied formulations of lidocaine hydrochloride.

Methods

3M's Microstructured Transdermal System (MTS) arrays were applied to domestic swine using controlled forces to demonstrate reliability of penetration, depth of penetration, and durability of the microstructures to repeat application under both normal and high force. Tissue levels of lidocaine and MPSS following topical application with and without microneedle pretreatment were determined by HPLC-MS analysis following digestion of biopsies. As an additional test of durability, arrays were applied to a rigid surface under extreme force to measure the effect on the microstructures.

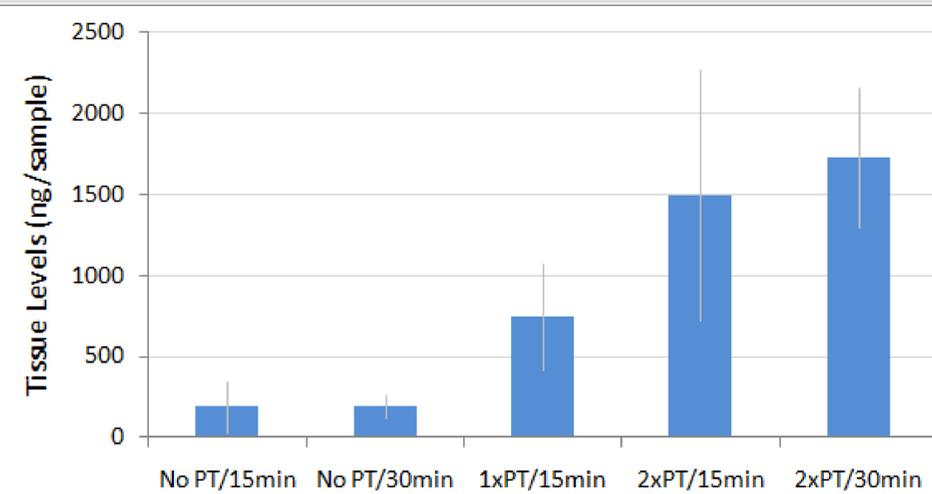
Results

Nearly all microneedles penetrated the stratum corneum upon hand force application. The depth of penetration varied from <100µm to nearly 150µm depending on the application force and the firmness of the underlying tissue. The arrays showed excellent durability to repeated in-vivo application, with less than 5% of the structures evidencing even minimal tip bending after 16 applications. Under extreme force against a rigid surface, the microneedles bent but did not break. A lidocaine hydrochloride formulation applied topically in-vivo showed ~340% increase in local tissue levels when the MTS arrays were used to twice pre-treat the skin prior to applying the drug. Local delivery of a topically applied formulation of MPSS was over one order of magnitude higher when the application site was twice pre-treated with the MTS array.

Conclusions

3M's MTS array (marketed as 3M™ Microchannel Skin System) provides repeatable and robust penetration of the stratum corneum and epidermis and enhances delivery of some formulations such as lidocaine hydrochloride.

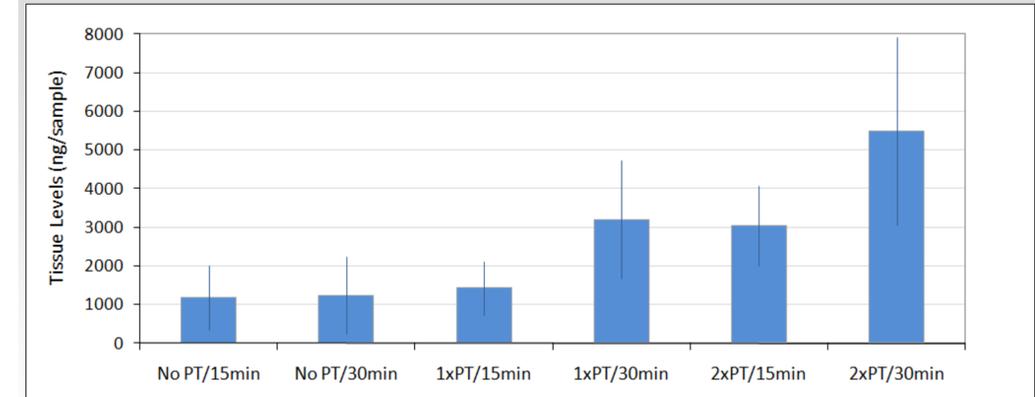
Results: Local tissue concentrations of methylprednisolone following application and pretreatment with the MSS



Tissue levels of methylprednisolone following formulation application on skin that was not pre-treated with an MTS array, pre-treated one time with an MTS array or pre-treated 2 times in succession with an MTS array.

Application time of the formulation, indicated on the graph, was either 15min or 30min.

Results: Local tissue concentrations of lidocaine following Application and pretreatment with the MSS



Tissue levels of lidocaine following formulation application on skin that was not pre-treated with an MTS array, pre-treated one time with an MTS array or pre-treated 2 times in succession with an MTS array. Application time of the formulation, indicated on the graph, was either 15min or 30min.

Materials: The Microchannel Skin System used in-vivo (swine, 20-35kg)



Methylene blue was used to stain swine skin (in-vivo) following hand application of the MSS device with < 2lbf. Each blue spot corresponds to a microchannel created in the stratum corneum.



Results: Completeness and Depth of Penetration, Hand application of the MSS

Percent staining (penetration) for square arrays vs application force to firm or soft tissue, n=3

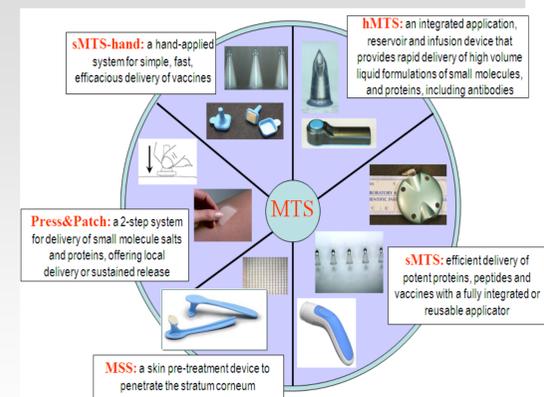
	1.2-1.4 lbf	3 lbf	5 lbf
Firm Tissue, Avg+/-SD	82+/-6%	95+/-4%	92+/-11%
Soft Tissue, Avg+/-SD	48+/-34%	84+/-7%	99+/-2%

Average in-vivo DOP for square arrays vs application force to firm tissue (rib area), n=3 applications with 66 measurements/application

Application Force	2 lbf	3 lbf	5 lbf
Average DOP (n=3)	85 µm	100 µm	138 µm
St Dev	4.6 µm	18.0 µm	12.7 µm
% RSD	5.4%	18.1%	9.3%

Conclusions

The MSS, the first microneedle product launched from 3M's MTS platform, demonstrates consistent penetration of the stratum corneum with as little as 1.3lbf, applied by hand. The depth of penetration varies from about 80-150µm depending upon the force of application and upon the firmness of the underlying tissue. Following pretreatment of the skin with the MSS device some drug formulations may be absorbed faster or to a greater extent than when they are applied to skin without microchannels.



Acknowledgments

The authors wish to thank Ryan Simmers, David Wirtanen, Ron Krienke, Jim Christensen, Joann Oesterich, Chris Webb, Mary Hopp and Tonya Grunwald.

