# Side-Opening Hollow Microneedles for Transdermal Drug Delivery

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## ABSTRACT SUMMARY

This study developed a novel microneedle design to inject drug and other solutions into the skin. Using a polymer core supported by an external metal coating for structural support, a laser was used to drill the hollow needle bore off center. This produced a hollow needle with a side opening that was strong enough to insert into skin.

## INTRODUCTION

Arrays of hollow microneedles have been proposed to achieve painless injection and infusion of drug solutions into the skin [1-3]. Using the tools of microfabrication, a variety of hollow microneedle designs have been developed and a limited number have been demonstrated to deliver drug into skin. Most hollow microneedles have been fabricated out of silicon, which is not yet known to be safe for human use. Some have been fabricated out of metal, which can provide strong needles made of FDA-approved materials.

In our previous work, we fabricated solid microneedles having a number of different designs, including polymer microneedles with extremely sharp tips (1 – 10 μm), as shown in Figure 1A [4]. We also fabricated hollow metal microneedles which have less sharp tips (30 – 80 μm) because the hollow bore opening is at the needle tip, as shown in Figure 1B [5] Although these blunt-tipped microneedles can insert into skin and deliver drug, hollow metal microneedles with sharp tips would be easier to insert and less prone to clogging.

This observation motivated the present study, which uses sharp-tipped, solid, polymer microneedles as a core structure that is coated with metal to provide added strength. By drilling the hollow needle bore off center, tip sharpness can be retained.

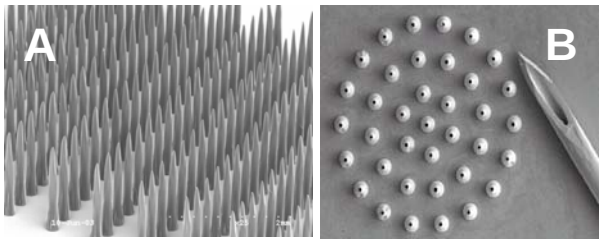


***Figure 1****. Previously fabricated microneedles. (A) An array of solid, polymer microneedles was fabricated by molding master structures fabricated using lithography [4]. (B) Hollow, metal microneedles were fabricated by electroplating laser-etched, polymer molds [5].*

## EXPERIMENTAL METHODS

### *Microneedle fabrication*

The needle fabrication process involved four steps. First, arrays of microneedles made of SU-8 epoxy photoresist were fabricated by patterning SU-8 onto glass substrates and defining needle shape by lithography. Then, the tips of the needles were sharpened using reactive ion etching.

The next step involved laser drilling holes through the microneedles and base substrate oriented off-center, but parallel to the microneedle axis. This created holes that serve as the microfluidic needle bores for injection or infusion, which terminate in side-opening holes along the needle shaft below the needle tip. Finally, the needle arrays were coated with nickel by electroplating to increase their mechanical strength.

### *In vitro skin insertion test*

To test the ability of side-opening, hollow microneedles to insert into skin, microneedle arrays were attached to a vertical micropositioner that pressed the microneedles against and into pig cadaver skin. The needles were left inserted within the skin for 10 min, after which they were removed and a solution of Trypan Blue was placed onto the insertion location to facilitate imaging needle penetration sites. After 5 min, the dye was washed off the skin surface and the skin was imaged using bright field microscopy.

## RESULTS and DISCUSSION

Using a novel microneedle design and fabrication method, we made hollow polymer microneedles with a metal coating and off-axis side openings, as shown in Figure 2. Each array contains 69 individual needles measuring 570 μm in height,

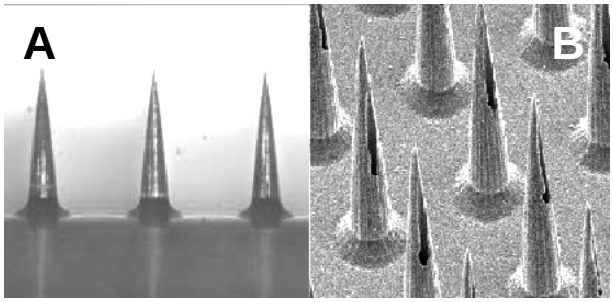


***Figure 2****. Scanning electron micrograph images of a section of a side-opening, hollow microneedle array. (A) Side view showing needle bores through needles and base substrate. (B) Top-side view showing side-opening holes on needles with sharp tips.*

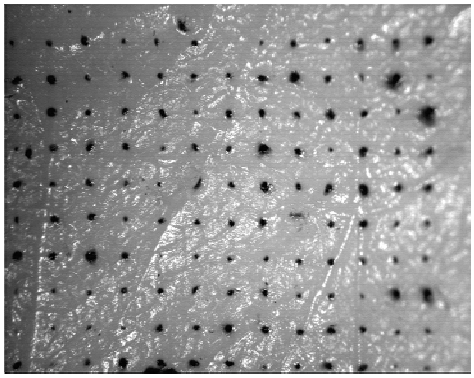

***Figure 3.*** *Surface of porcine skin after insertion and removal of microneedles in vitro followed by topical staining with a tissue-marking dye, as shown by light microscopy. Each stained spot corresponds to the site of microneedle penetration into the skin.*

120 µm in base diameter, and tapering to a sharp tip. The position of the side-opening hole could be moved to different heights along the needle shaft and the size of the hole could be varied by changing laser drilling parameters. The shape of the hole was an oblong oval shape, which was inherent to the microneedle fabrication method.

These microneedles were designed to have a polymer core with a metal coating that would provide mechanical strength. To determine if these microneedles were sufficiently strong, they were inserted into pig cadaver skin. After removing them, the microneedles were examined by brightfield microscopy and found to remain intact. The skin was also exposed to a blue dye, which stained sites of microneedle penetration after excess dye was wiped off the skin surface. Figure 3 provides an image of the skin surface, which indicates that essentially all microneedles were inserted into the skin to create pathways for transdermal penetration.

For drug delivery applications, microneedles need to be interfaced with a pump or syringe for injection or infusion. Figure 4 shows a 69-needle array of microneedles coupled with a liquid manifold and pump connection. This system could be used for transdermal drug delivery as well as other microfluidic applications.

## CONCLUSION

We microfabricated arrays of hollow microneedles with side openings using a hybrid design based on a polymer microneedle core and a metal coating for added mechanical strength. These needles were capable of inserting into porcine skin in vitro. Altogether these microneedle arrays have properties critical to successful hollow microneedles: sharp tips for easy insertion, sufficient mechanical strength to insert into skin, fluidic channels for active drug delivery, and side openings to prevent clogging.

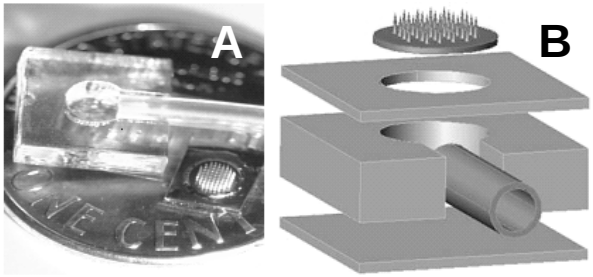


***Figure 4.*** *(A) Photomicrograph of a 69-needle microneedle array and its manifold pump connection shown next to a US penny. (B) Schematic design of the microneedle array with manifold pump connection.*

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