Carbon Nanotube-Polyimide Composite Microneedles for Rapid Transdermal Drug Delivery

Bradley Lyon, Adrianus Indrat Aria, Morteza Gharib.
Graduate Aeronautics Laboratories, California Institute of Technology, Pasadena, CA

Statement of Purpose: Carbon nanotubes (CNT) and other self-assembly nanomaterials allow for direct access to the nano and micro length scales for fabricating biomedical devices. Here, we demonstrate the use of CNT patterned into 100 um hollow microbundles as a scaffolding for making CNT-polyimide composite microneedles. Polyimide is wicked passively through the CNT microneedle to create a composite material that is strong enough to achieve skin penetration while retaining the shape of the CNT microbundles. Successful *in vitro* skin penetration in porcine is demonstrated. Potential drug delivery rates are characterized by experiment and model. Controllable flow rates can be achieved over a wide range from 0.01mL/s to 10mL/s

Methods: *Carbon nanotubes* are fabricated on a silicon wafer coated with 1 nm iron catalyst that is patterned into hollow rings (100 um outer dia., 25 um inner dia.) thru photolithography and electron beam evaporation. During chemical vapor deposition, ethylene and hydrogen gas interact with sintered catalyst nanoparticles to form vertically-aligned CNT with approximate diameter of 25nm.

Polyimide is spin coated onto the CNT to create a uniform composite of CNT and polymer while simultaneously creating a flexible base for the array (1a). For lightly viscous polyimide, such as Poly(3,3′,4,4′-benzophenonetetracarboxylic dianhydride-co-4,4′-oxydianiline/1,3-phenylenediamine), we demonstrate that curing can be done thermally without clogging the central cavity. Poor mechanical adhesion between polyimide and silicon allow the resulting device to be easily removed from the silicon mechanically with tweezers.

Fluid flow through the device is achieved by removing the device from its silicon substrate and transferring it onto a microfluidic port with an inner diameter of 4mm allowing for actuation of approximately 6-7 needles. The port was tested with two reservoirs: (1) a 20mL syringe to demonstrate steady flow and a (2) PDMS skin patch to demonstrate release of small therapeutic doses (~0.5mL).

In vitro skin penetration experiments are performed by placing the array into contact with constant force (1.5kg) into full thickness dorsal skin from Yucatan Miniature Swine. Microneedles are coated in dry methylene blue power prior to penetration which is reconstituted into a dye upon contact with interstitial fluid from the skin.

Results: *Fluid Delivery* is achieved for steady flow release. Despite the very small 25um cavity diameter per needle, the integrated area of the microneedle array allows for very low hydraulic resistance as seen by the roughly 1mL/s fluid release (1b). A Poiseuille flow model was used to characterize the achievable drug delivery rates given different needle sizes and number of total needles in the array. Flow rates as high as 10mL/s and as low as 0.01mL/s can be achieved (2). Generally, the same flow rate achieved with a standard hypodermic can be achieved with 100 microneedles over an order of magnitude smaller than the hypodermic.

In Vitro Skin Penetration is seen for 100um dia. polyimide needles. Height and uniformity of the microneedles which stems from the quality of the CVD growth process is key to achieving a positive result. Skin penetration is optimally achieved without damaging the microneedle at a needle height of about 200um (1c).

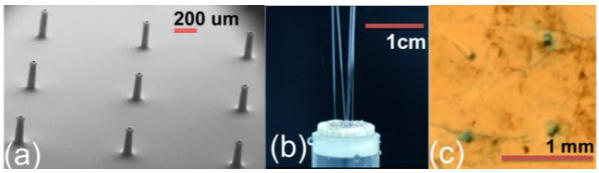

Figure 1. (a) CNT-polyimide microneedle array with 100um outer dia. (b) Steady flow delivery at 1mL/s. (c) *In vitro* pig skin penetration

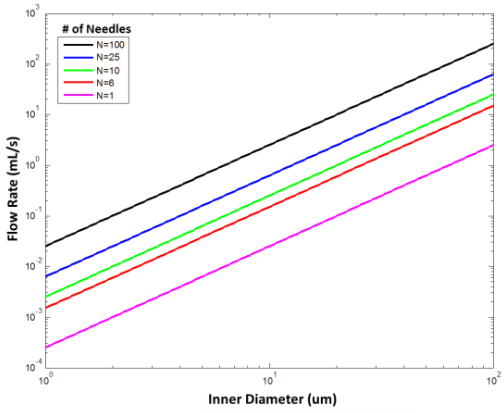

Figure 2 Analytic model for typical total flow rate given number of needles and diameter

Conclusions: The use of patterned CNT microbundles is demonstrated as a scaffolding for creating a CNT-polyimide composite microneedle. Polyimide conformally coats the CNT and creates a composite which is strong enough to achieve skin penetration. In principle, the fabrication technique is not polymer specific and can be generalized to a wide range of polymers. By using CNT scaffolding, we can tune the needle size to as low as 100nm as well as specify the number of needles and needle spacing to achieve optimal transdermal drug delivery.