Development of 3D-Printed Hollow-Core Microneedles for Drug Delivery and Therapeutics in Mice Models

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Enhancing drug delivery is a key obstacle in numerous biomedical applications. Pursuing the ability for on-demand and precise control over where therapeutics and remedies are delivered to the patient, drastic improvements in the efficacy and repeatability of many treatments may be realized. Through the various pathways of drug delivery, including oral intake, transdermal, or inhalation, injection-based methods offer the most rapid relief for many aliments in the bloodstream.[1] The use of a hypodermic needle or IV in these applications often results in discomfort to the patient due to the needles penetrating down to the veins, past nerve endings in the dermis layer.[2] Microneedles (MNs) avoid this by penetrating less than 1 mm into the epidermis and dermis layers, avoiding nearly all pain receptors.[3] The 3D-printed MNs developed in this work aim to administer therapeutic solutions directly to sarcoma tumors under the skin or to inflamed muscles and joints in psoriasis-ridden mice via injection. Fabrication of the MNs described here takes advantage of a hollow-core to administer solutions to these sites without relying on coatings or diffusion-limited techniques.[4] These MNs were printed via stereolithography (SLA) using high-temperature liquid (HTL) resin from Boston Micro Fabrication at a resolution of 20 µm. MN patches, shown in *Figure 1,* were comprised of 25 individual needles on a 5x5 mm hollow block. These needles were designed with a five-plane lancet tip, where additional bevels were added on the front side to improve ease of injection and provide minimal resistance during penetration of the skin.[5] MN dimensions were customizable based on the application with most instances using a 1 mm tall needle with a 250 µm opening. The needle period across the patch was set at 1 mm to allow the skin to have some elasticity during penetration and to concentrate pressure at the needle tips. In testing the MN patches on mice with sarcoma tumors underneath the epithelium layer, it was observed that the MNs were able to deliver AAV6-GFP vectors into the tumor cells without directly penetrating through the tumor *(Figure 2*). This pathway also highlighted greater delivery efficiency, based on GFP concentration, than intra tumor injection of a similar volume via hypodermic needle.

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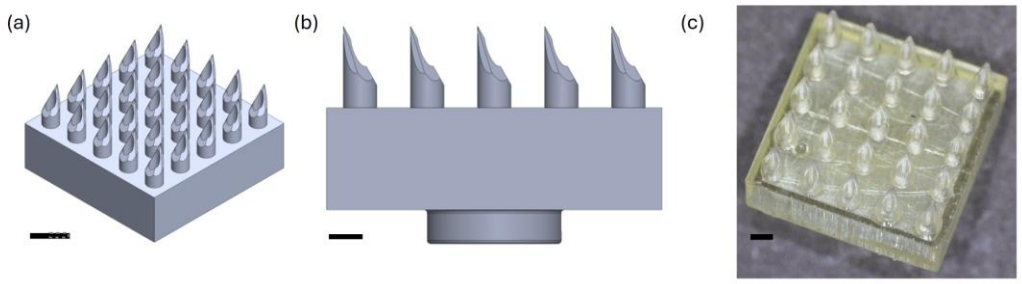

Figure 1: 3D Rendering of MN Patch shown in (a) isometric view and (b) side profile (Scale Bar: 1 mm). (c) Image of 3D-printed MN patch using HTL on an SLA printer (Scale Bar: 500 µm).

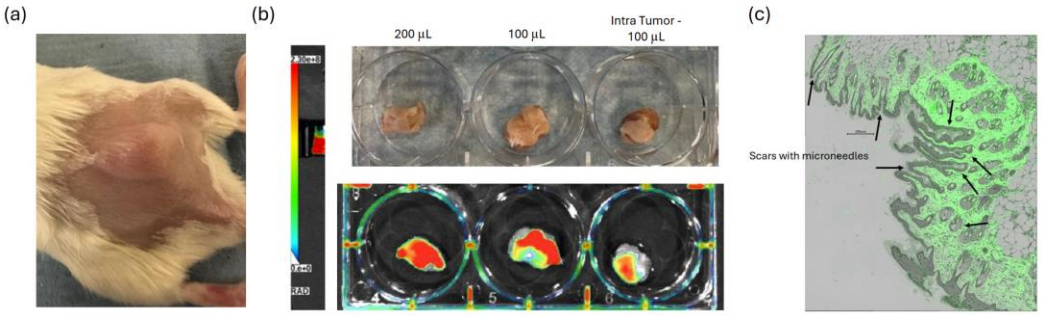

Figure 2: (a) Mouse lower back with sarcoma tumor following microneedle injection. (b) Loading of GFP into sarcoma tumors at various injection volumes compared to intra tumor injection (right). Fluorescent heat mapping of the injection sites demonstrates the efficiency of GFP delivery. (c) Skin cross-section highlighting MN penetration into the epithelial layer with GFP injection gradients. (Scale Bar: 200 µm).