

INTRODUCTION

BACKGROUND

Many patients with extremity lymphedema anticipating lymphaticovenous anastomosis cannot tolerate the pain caused by numerous intradermal contrast injections during lymphatic mapping in the outpatient setting. Performing lymphatic mapping intraoperatively incurs increased costs and morbidity associated with longer anesthesia. The use of microneedles is an attractive alternative that may reduce pain for the patient while also providing sufficient intradermal contrast.

OBJECTIVE

The purpose of this proof-of-concept project was to design, fabricate, and test microneedles tailored for intradermal contrast delivery in the context of lymphatic mapping using both microbubbles for contrast-enhanced ultrasound and indocyanine green (ICG) for near-infrared imaging.

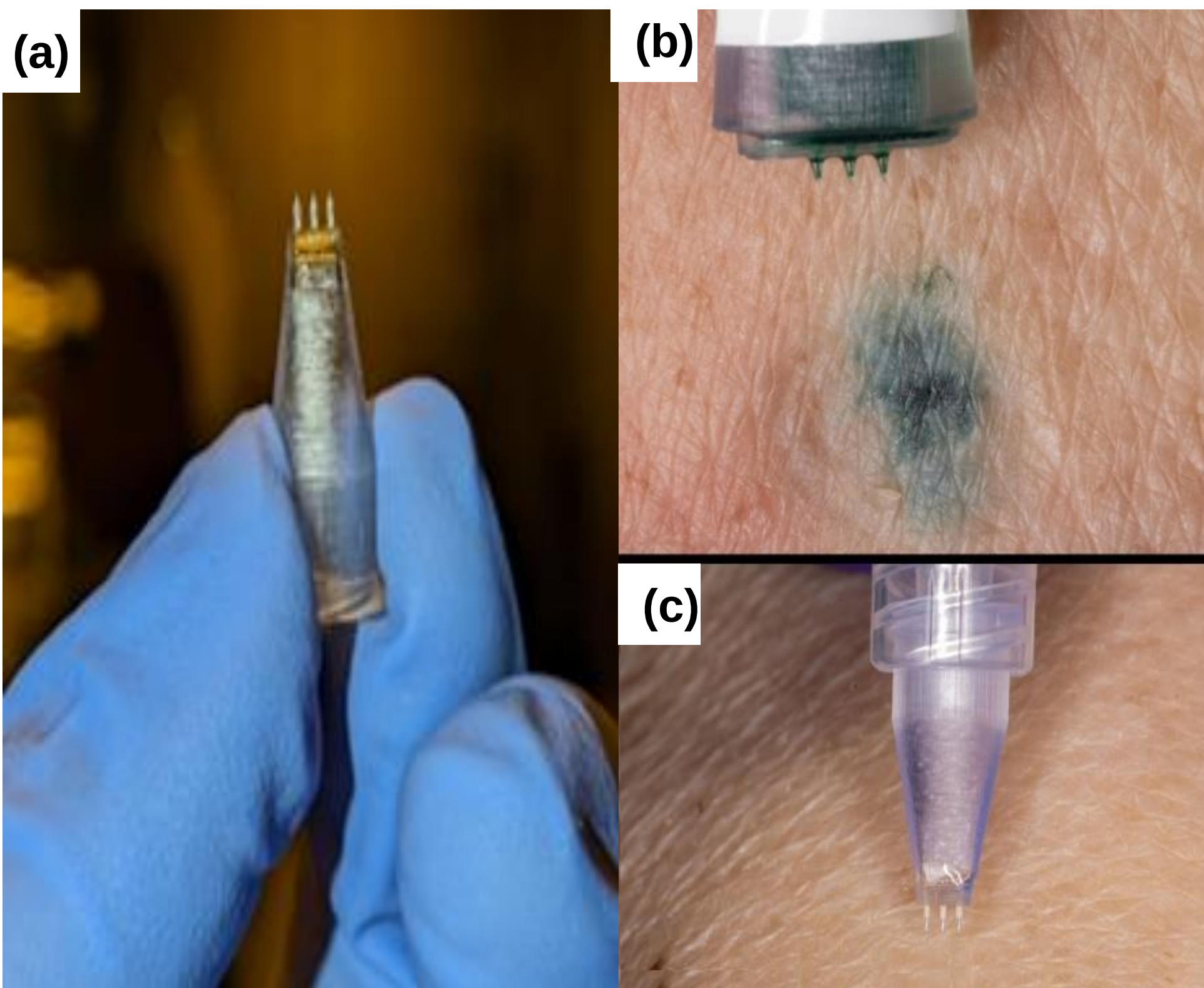


Figure 1: (a) 3-Microneedle device (micro-hypodermic needles on sharp tapered Luer lock) and injection of indocyanine green (ICG) during skin testing using the (b) half-eccentric needles on a tapered Luer lock and (c) micro-hypodermic needles on a sharp tapered Luer lock

METHODS

Two array configurations (27-microneedle and 3-microneedle), two lumen diameters (100 μm and 200 μm), and two needle lengths (1.1 mm and 1.6 mm) were tested in *ex vivo* porcine skin, in an animal model, and in cadaveric skin.

A microscale 3D printer (Dilase 3D, Kloé) was used to fabricate each design. The current device comprises an elliptical base measuring 3 mm to 6 mm in width, over which three needles are linearly placed 1mm apart from each other. The base has a height of 1.2 mm. The needle designs include half eccentric, conical tip shapes, and one design mimicking a hypodermic needle (Figure 1a). This device is then assembled onto a 3D printed Luer lock to connect with a syringe. Various Luer Lock designs were evaluated to optimize visual and haptic feedback for the clinician.

Microneedle performance was tested with isosulfane blue and ultrasound microbubbles contrast in the animal study and in the cadaveric study with ICG. These prototype microneedle variations were tested by a plastic surgeon, two plastic surgery residents, and two radiologists in an IACUC-approved porcine model and in cadaveric breasts.

FABRICATION PROCEDURE

The Luer lock and microneedle arrays were designed in CAD (Solidworks, Dassault Systems) as separate components. The components were 3D printed separately and then assembled to create complete devices. To optimize print time and resolution, the microneedles were printed using a micro-vat photopolymerization 3D printer (Dilase 3D, Kloé) while the Luer lock components, which had looser resolution requirements, were printed using a conventional vat photopolymerization 3D printer (Form 3B, Formlabs). Before assembling the device, the microneedle arrays were characterized under a digital microscope (VHX-7000 Keyence). The components were assembled and bonded with UV-cured resin to create a hermetic seal.

DESIGN

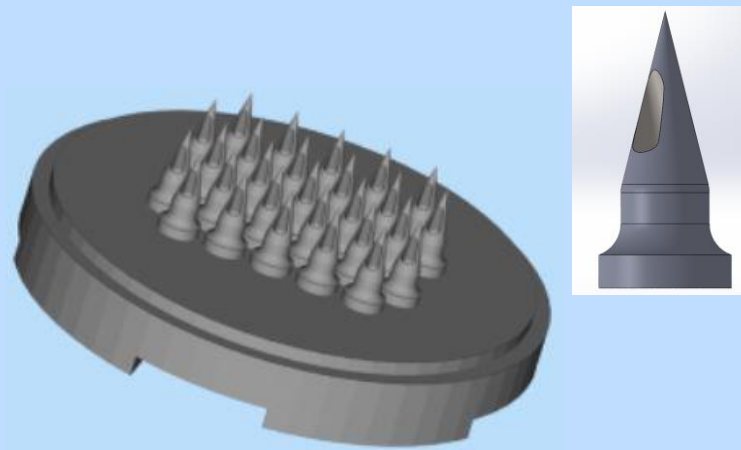
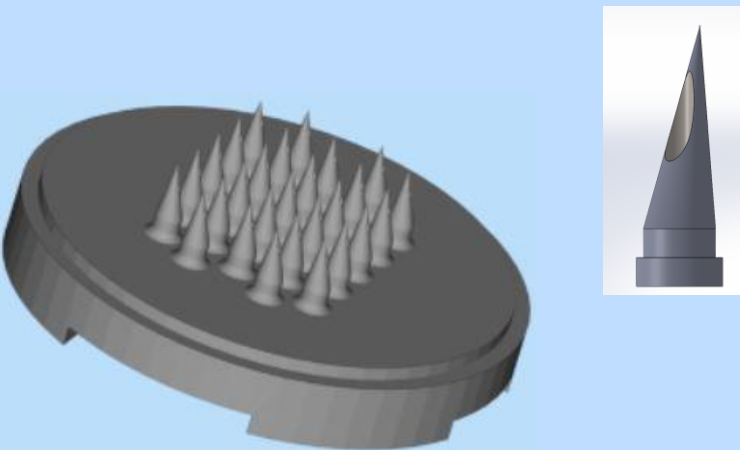
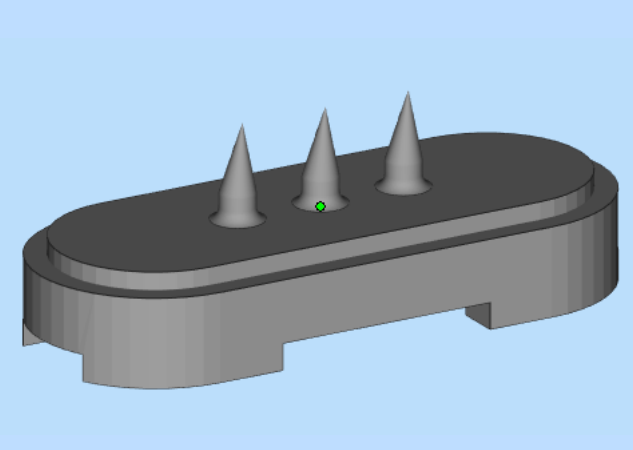
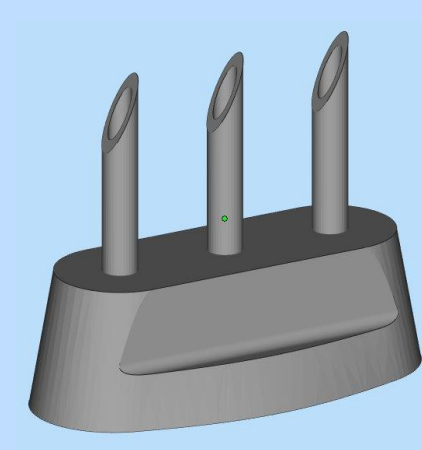
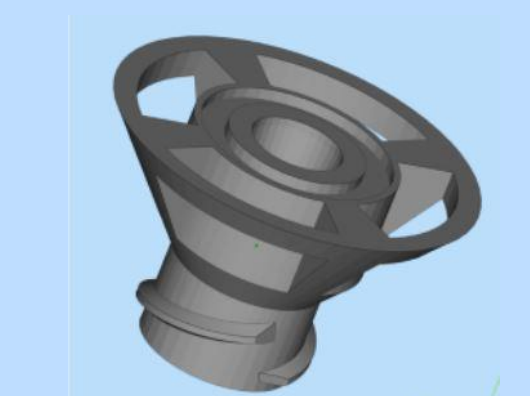
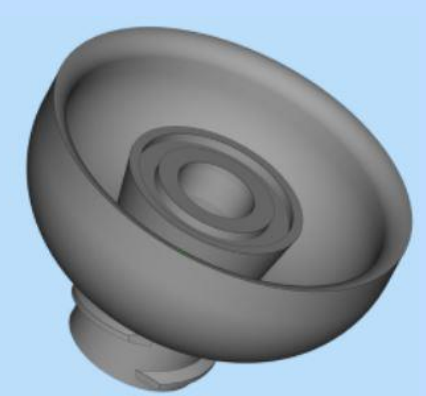
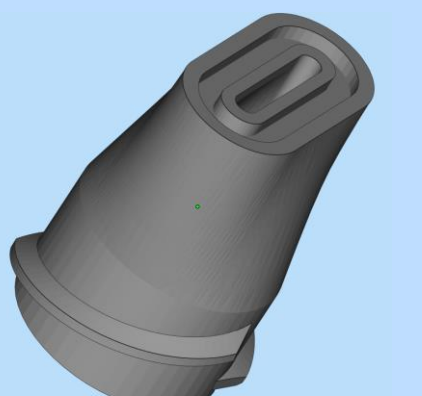
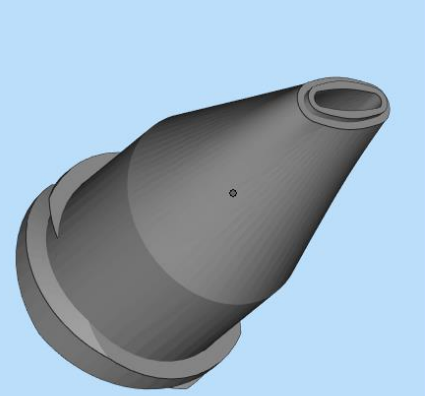
	27-Microneedle arrays		3-Microneedle arrays	
Microneedle array	 Conical needles	 Half-eccentric needles	 Half-eccentric needles	 Micro-hypodermic needles
Luer lock	 Rigid open window	 Flexible	 Tapered	 Sharp tapered

Table 1: CAD designs of different versions of microneedles and Luer locks

PRINTED DEVICES

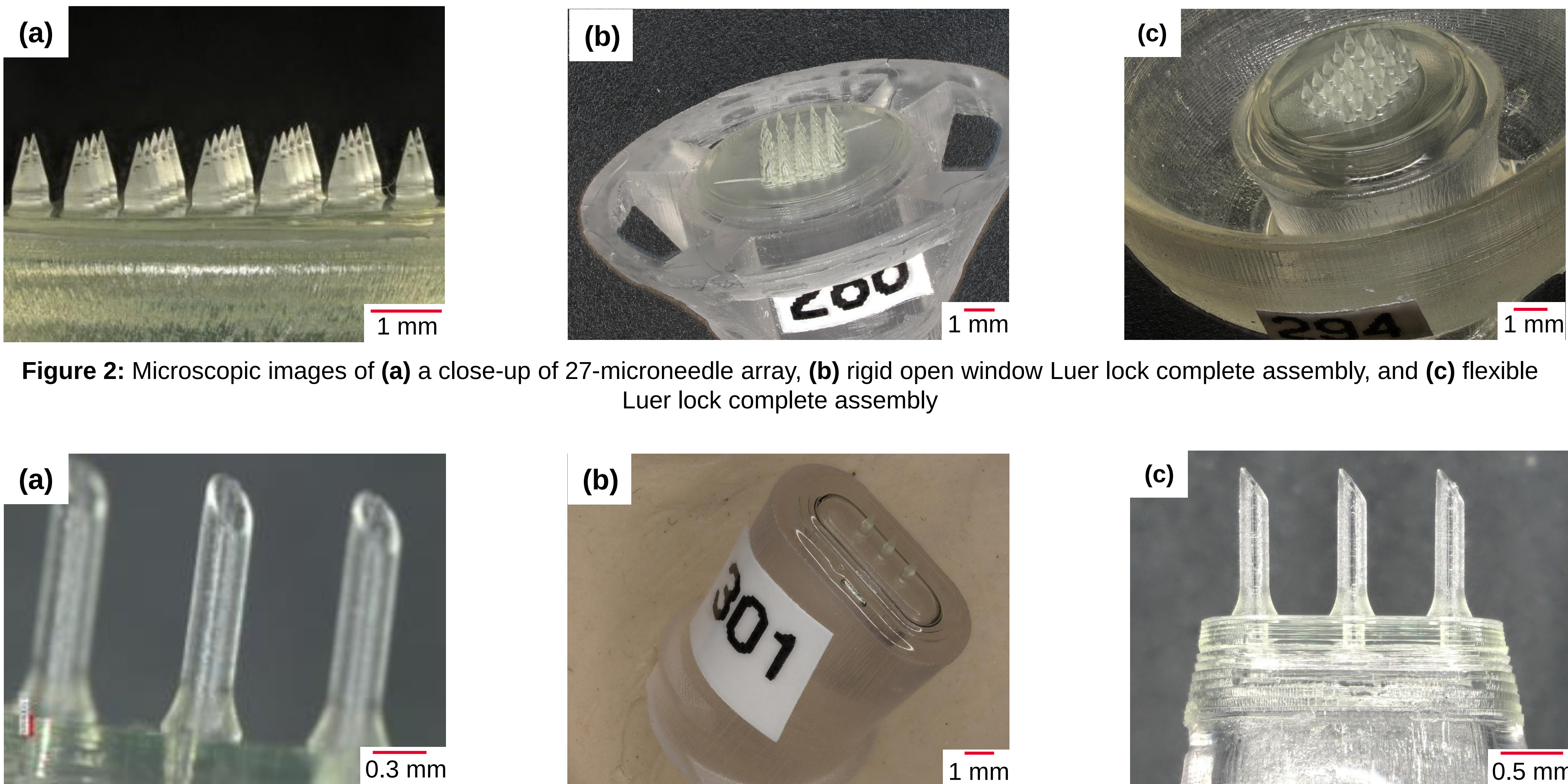


Figure 2: Microscopic images of (a) a close-up of 27-microneedle array, (b) rigid open window Luer lock complete assembly, and (c) flexible Luer lock complete assembly

Figure 3: Microscopic images of (a) a close-up of micro-hypodermic 3-microneedle array, (b) tapered complete assembly, and (c) sharp tapered complete assembly

CONCLUSIONS

In this work, we developed 3D printed microneedles specifically designed for intradermal injections of contrast for lymphatic mapping. Various microneedle designs, array configurations, and Luer lock designs were evaluated for optimal intradermal contrast delivery.

ARRAY CONFIGURATION

The 27-microneedle devices did not uniformly penetrate the dermis. Some needles failed to penetrate and completely insert the needle lumen into the dermis, causing fluid leakage on the skin during injection. Consequently, the number of needles in the latest device was reduced to three to ensure consistent penetration of the dermis. Subsequent trials confirmed that all three needles in the latest device successfully penetrated the dermis (Figure 4).

MICRONEEDLE LENGTH

Cadaver testing demonstrated that shorter microneedles (1.1mm) are preferable over longer microneedles (1.6mm). Although the longer microneedles facilitated visual confirmation of intradermal penetration, they were more prone to breakage, both during insertion and during injection.

LUMEN DIAMETER

A major concern with the use of microneedles for the delivery of microbubble contrast agent is the potential for microbubble breakage in the small lumen diameters of microneedles. Initial testing of microbubble breakage after injection through devices with 100 and 200 μm lumen diameters has thus far been inconclusive. Additional testing is planned to optimize this parameter.

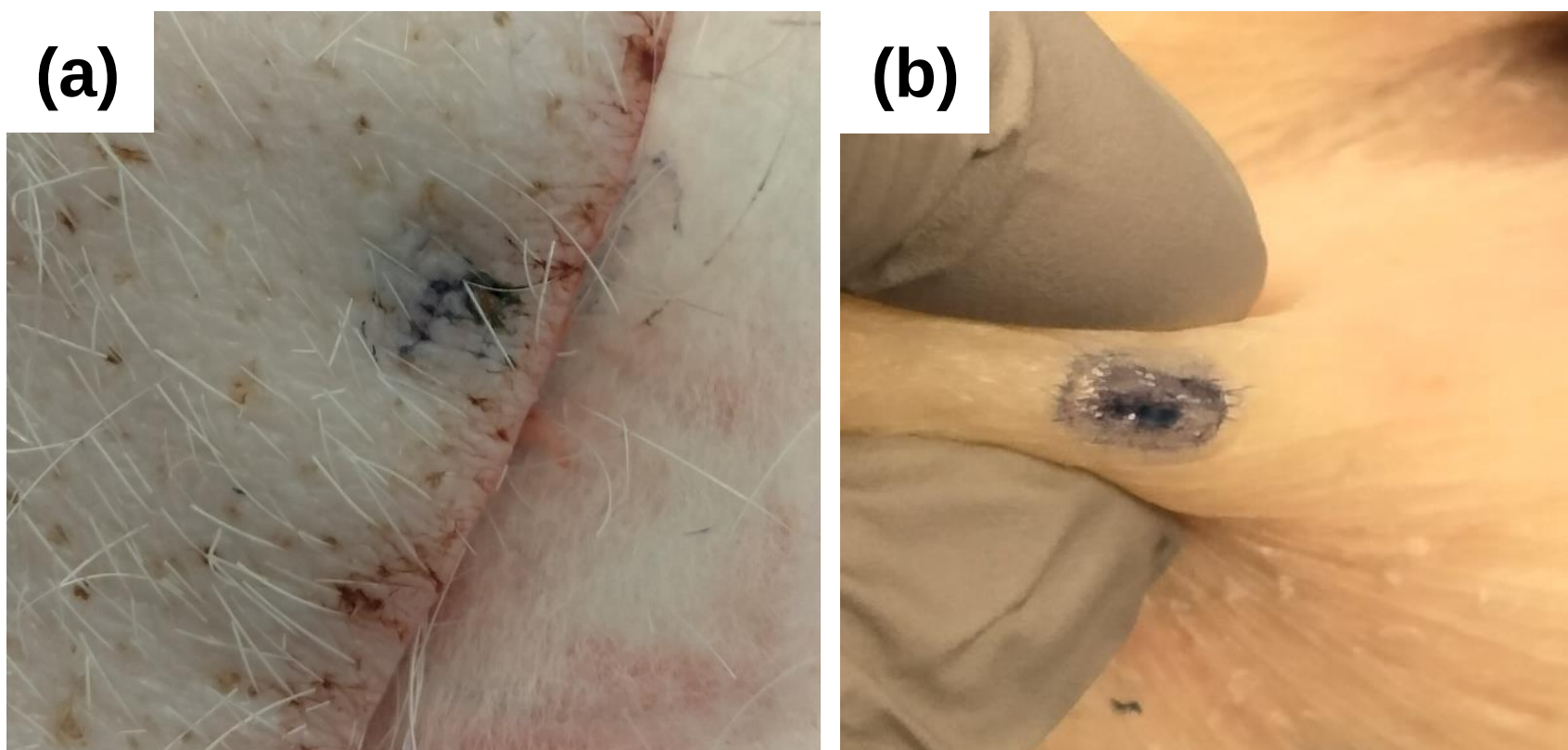


Figure 4: Confirmation of consistent penetration of 3-microneedle device on (a) porcine skin (b) cadaver skin