ULTRA RAPID MICROFABRICATION OF HOLLOW-WELL MICRONEEDLES BY DIFFRACTION ULTRAVIOLET (UV) LITHOGRAPHY

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Introduction

This paper presents one-of-a-kind hollow-well microneedles fabricated by unique diffraction UV lithography. The microneedles equip a small pocket (well) near the tip for the drug reservoir, which allows unprecedentedly effective drug delivery than a conventional drug-coated solid microneedle. The fabrication of the hollow-well microneedles involves diffraction UV lithography that enables a high aspect ratio microstructure. Due to simple, rapid, and scalable fabrication capability, a hollow-well microneedle fabrication takes less than 30 min from start to finish. Using a ring-shaped micropattern, the back-side UV exposure crosslinks a liquid-state photosensitive resin. The ring-shaped micropattern photomask is defined by translucent outer and opaque inner patterns. The outer shell first defines the overall microneedle shape. The resin residue that remains uncured inside the microneedle's hollow is then cured by second UV exposure from the topside, which forms a small pocket at the tip. The drug reservoir can be located while evading the tip by offsetting the inner pattern. It is also possible to realize multiple wells by increasing the number of inner patterns, which can be utilized for drug delivery with temporal control, a broader selection of drugs, or a higher dose. A 20×20 hollow-well microneedle array was fabricated, demonstrating the batch fabrication. A hollow-well microneedle was assessed with a mechanical test, affirming the skin penetration viability. The drug delivery of the hollow-well microneedle was evaluated using pigskin and blue dye. The diffused blue marks showed significant improvement as compared to the conventional drug-coated solid microneedle. The proposed hollow-well microneedles indeed show the feasibility to replace solid microneedles due to enhanced drug delivery capability for transdermal application.

Background and Fabrication Process

Microneedle has expanded the practicality of transdermal patches by improving the drug delivery capability through the skin. Solid microneedle has emerged as the most common option for drug delivery, granted by its ease of use and simple fabrication. However, drug delivery using solid microneedle is still limited due to low drug loading dosage, poor control of drug delivery and drug availability [1]. Inspired by these challenges and progressing on the basis of previous works [2][3], we develop a novel hollow-well microneedle, which contains an innate well-type reservoir at the needle tip or body for larger drug loading dosage and wider drug availabilities, as shown in Fig. 1. Fig. 2 illustrates the fabrication process of hollow-well microneedles. A ring-shaped micropattern was used as the substrate and coated with photosensitive resin. The first UV exposure was performed with a bottom-top direction through the micropattern to crosslink the resin and form the outer shell of the hollow-well microneedle while leaving the center uncrosslinked. The sample proceeded with a 2-min partial development process in isopropanol with moderate swirling. The sample was baked at 70°C for 1 min to produce the concave contour through the capillary effect. Second top-bottom UV exposure was followed to crosslink the uncured resin for the well formation, completing the hollow-well microneedle.

Experimental Results

Fig. 3 shows the hollow-well microneedle prototype using three different photomask designs, including the center-well microneedle, side-well microneedle, and dual-well microneedle. Fig. 4 shows the 20×20 microneedle array with a 300-µm diameter and 700-µm height, indicating high uniformity and reliability of the batch fabrication. Fig. 5 shows the mechanical strength of the hollow-well microneedle. A sudden decline of force was recorded during the compression, indicating a tip strength of 2 N. To analyze the drug delivery performance, the hollow-well microneedle was pre-filled with blue dye and inserted into a pig cadaver skin. The same procedure was repeated using solid microneedles for comparison. Wider dispersion of dye was observed at the inserted site, confirming a larger drug loading dosage for each administration.

Word count: 595

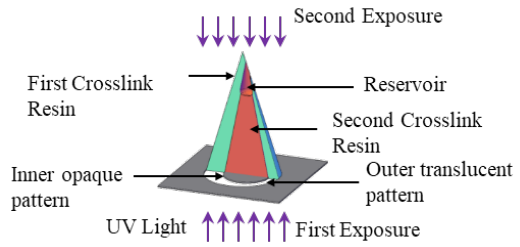

Figure 1. Conceptual drawing of hollow-well microneedle.

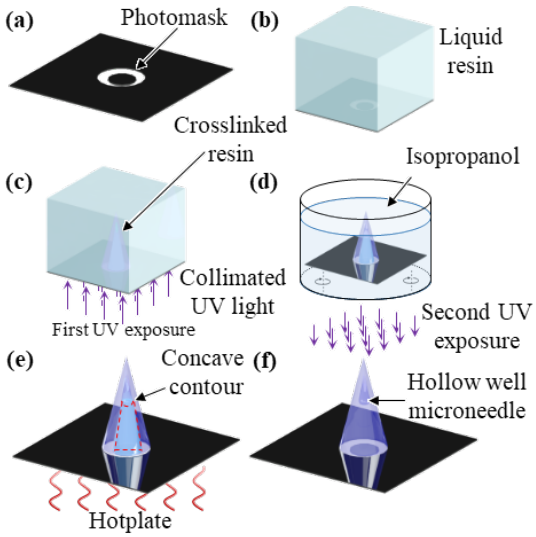

Figure 2. Fabrication process of hollow-well microneedle. (a) Photomask. (b) Resin coating. (c) First UV exposure. (d) Partial development. (e)Thermal treatment forms concave contour. (f) Second UV exposure and complete.

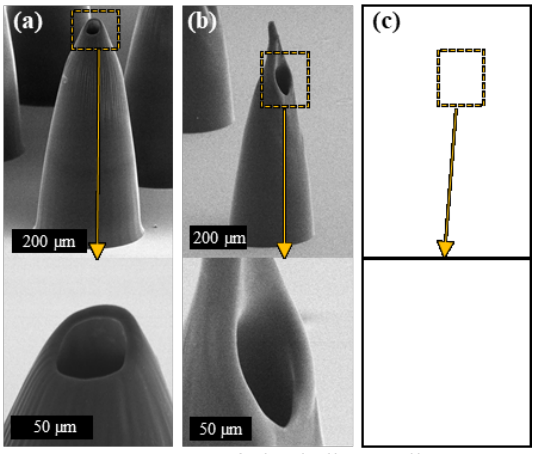

Figure 3. SEM images of the hollow-well microneedle fabricated with three photomask designs. (a) Center-well, (b) side-well, (c) dual-well (upper) and close-up (lower).

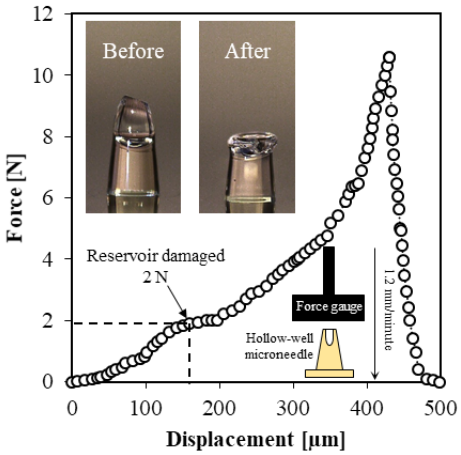

Figure 4. Mechanical test result of hollow-well microneedle.

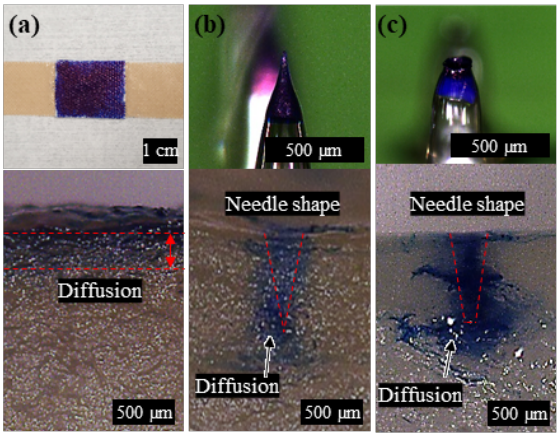

Figure 5. Drug delivery analysis on pig cadaver skin. Blue tissue dye coated (a) adhesive bandage, (b) solid microneedle, (c) hollow-well microneedle (upper) and drug dispersion result (lower).

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