

Geometrical Improvements of Hollow Microneedle Fabrications by Alignment X-ray Lithography

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Abstract

An improvement in design and fabrication method of partial LIGA(Lithographie Electroformung, Abformung) microneedles with through holes is presented in this work. The development of microneedle fabricated by a technique, combining the conventional deep X-ray lithography process and PCT (Plane-pattern to Cross-section Transfer) process and the alignment X-ray lithography have been carried on since the last report in 2004. The method provides a precise hole-alignment with $\pm 3 \mu\text{m}$ tolerance. Formerly, we fabricated microneedle with $100 \mu\text{m}$ -base with $300 \mu\text{m}$ -height by right-triangular mask, the microneedle has a very sharp tip but excessively steep, thus it resulted in a very low strength. The improvement of strength and tip-sharpness was consequently done by changing mask-pattern and dimensions of the microneedle from triangular pattern to be polygonal mask and changing the dimension of microneedle to be $300 \mu\text{m}$ -base with various heights between $350\text{-}800 \mu\text{m}$. Totally 400 microneedles are standing on a 1 cm^2 chip. The molding process or electroplating of Nickel is correspondingly included in this paper.

1. Introduction

The synchrotron radiation deep x-ray lithography with PCT technique enhances the fabrication of three dimensional structure. Using the technique, we have succeeded in the fabrication of various microneedles including; single-tip[1, 2], quadruplets[3], and hollow[4] types. The selected microneedle to be discussed in this paper is the hollow microneedle. The fabrication method is based on LIGA that the product materials are selectable for the replication after manufacturing a metal mold. Therefore, the geometrical study on original microneedle structure has attracted our attention so that an operative mold can be developed afterward. It has been clearly known that the cost of processing X-ray lithography is extremely high. To optimize the mask design before fabrication has to be taken into account.



Fig. 1 Array of microneedles after optimizing hole-location and strength improvement

2. DESIGN AND FABRICATION TECHNIQUE

The accomplishment of strengthening and sharpening microneedle array is represented by SEM(Scanning Electron Microscope) photo in Fig. 1 as the array of microneedle the optimized microneedle. The exposure process has been divided into triple exposure-steps; twice PCT and once alignment exposure. The key process of revealing the slope side-wall structure is PCT technique [5]. It has been employed as an additional method for the fabrication of 3-dimensional structures whose cross-sections are similar to the two-dimensional patterns on the X-ray mask. A movable stage was equipped inward the exposed chamber at the tail of an SR beam. PMMA (Poly-methylmethacrylate) resist moves repeatedly with the scanning stage while X-ray is exposed through the X-ray mask. Prior to the exposure, PMMA sheet was glued by the liquid PMMA onto a silicon wafer coated by sputtered Au layer. Figure 2 shows the schematic of resulting structure after single scan and double scans with the triangular mask. The vertical movement(z-direction) of the work stage forms the three dimensional structures and gradually enlarges the exposed area on the PMMA. The brief exposure condition is as following. The PMMA substrates were exposed in the chambers of beamline-13 (BL-13) and beamline-6 (BL-6) for PCT and alignment X-ray lithography respectively. The beamlines were installed at synchrotron radiation source AURORA at SR center, Ritsumeikan University, Japan. Figure 3 shows a step-by-step schematic of fabrication process.

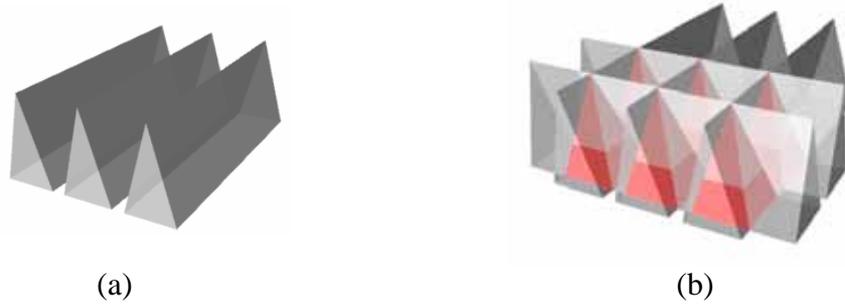


Fig. 2 The schematic of resulting structure after a PCT exposure with (a) single scan and (b) double scans.

For the alignment exposure, we developed low-cost equipment consisting of lateral, vertical and angular adjustable stages as reported in [4]. In addition, a digital microscope (KEYENCE VH-8000) which provides the mesh-frame for aligning hole mask to a proper location on the single microneedle structure. The conditions of AURORA storage ring is, the wavelength of the SR light between 0.15 to 0.73 nm, the applied electron energy and the maximum storage current in the experiment were 575MeV and 300mA respectively. The exposure environment was covered with Helium gas at 1atm. The exposed PMMA structures completely revealed after developing by the GG developer at 37°C for 3 hours.

3. EXPERIMENTAL

The improved microneedle has 300 μm -base and 350 μm -height exposed by pentagonal and heptagonal mask in replace of triangular mask. As a result, the new shape of microneedle was enhanced the strength for a safe penetration through skin whilst the sharp-tip is still exhibited. The study on an optimization of microneedle hole-location by a simulation of stress-analysis confirmed that the alignment #4 where the aligned hole at horizontally away from the center about 30 μm and vertically away from the microneedle tip about 50 μm as listed in Table 1 was the strongest pattern. The alignment #1 has been considered as useless microneedle for safety and high-efficient since the hole has been located onto the center of microneedle-tip. The tip was, thus removed and the microneedle has become blunt and decreased in length. Moreover, since the hole-plane is parallel to the skin surface, it has been considered to be easily blocked by skin clogging into the hole [6].

Table 1. Four different patterns for alignment exposures

Alignment #1	Alignment #2	Alignment #3	Alignment #4
hole mask I : center	hole mask II : center	hole mask I : 50 μm horizontally from center	hole mask II : 50 μm vertically from center
			
top-view of single-tip microneedle :			
hole masks I :	 centered	II :	 30 μm horizontally from center

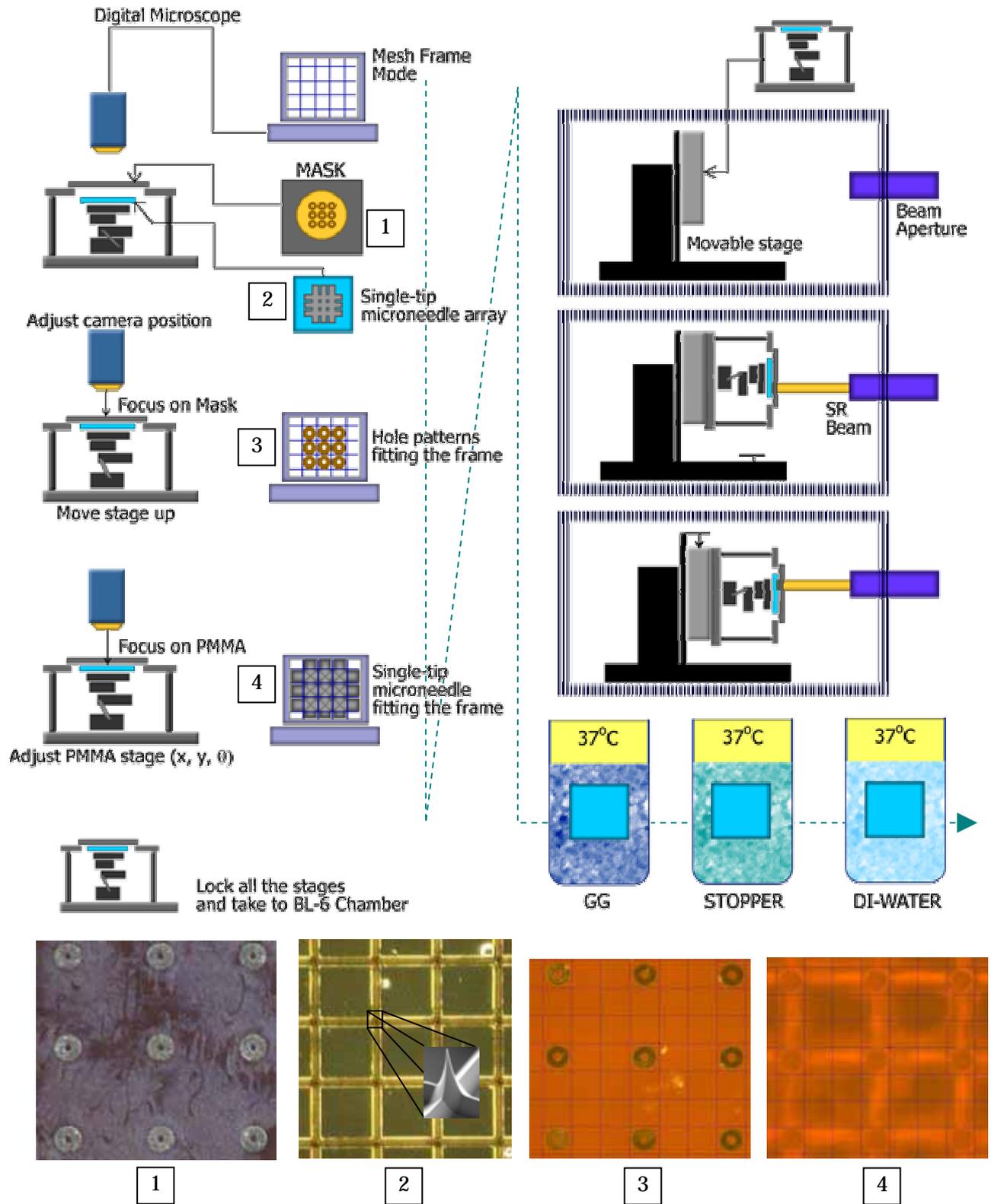


Fig. 3 Fabrication step of microneedle by alignment process in the chamber of BL-6

4. MOLDING PROCESS

As for reducing the cost of batch-fabrication, the molding process has been taken into account. Nickel electroplating was performed with the following conditions; electrolyte 350 g/l, nickel

sulfamate 30 g/l boric acid bath temperature 37 ° C, current 0.2 A/dm² , pH 4.8 and approximately 1 week time-consuming for the thickness of 400 μm. Figure 4(a) illustrates the sequence fabricating layers on a substrate and the nickel mold. The SEM photo shown in Fig. 4(c) confirmed that the microneedle with through hole can be molded since the counterpart of the hole has been apparently observed for the entire array.

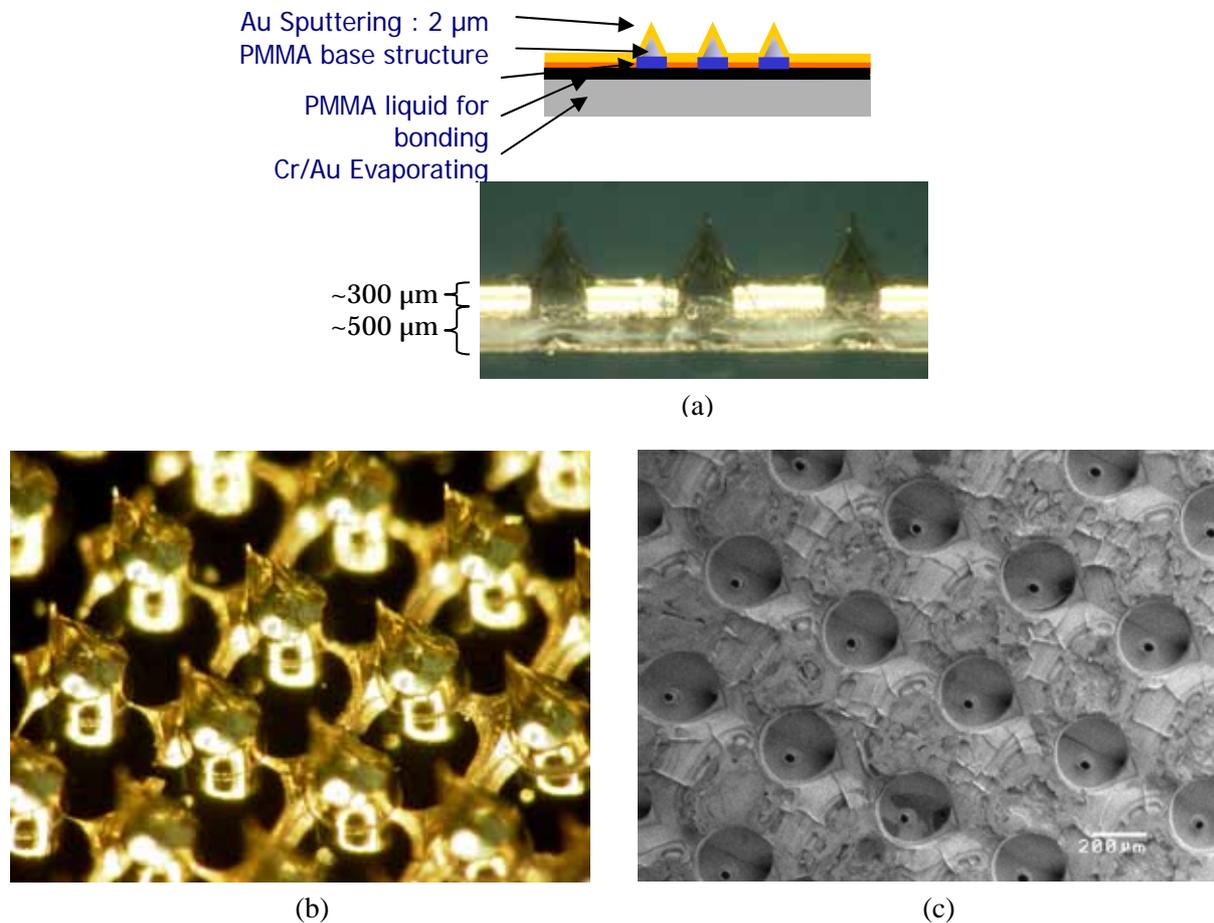


Fig. 4 Metal molding process; (a) sample preparation, (b) electro-conductive layer (Au) sputtering, (c) Nickel mold from electroplating

5. CONCLUSION

The microneedle while piercing a polyimide film is illustrated in Figure 5. We have tried to pierce the film by our previous microneedle type. It resulted as a broken tip. Contrary, piercing new type microneedle, it was still being complete (see Fig. 5(c)). In summarize, the recent microneedle reported in this work is more operative and more suitable for bio-medical uses. The optimization of hole-location is beneficial since the hole centrally located to the needle-tip has raised a trouble of clogging skin into the hole. The liquid or blood, thus, can not go through the hole and made microneedle useless. In this paper, although the benchmarking of different materials are not included, the techniques of strengthening and tip-sharpening of microneedle fabricated from any plastic material by shape-modification have been described

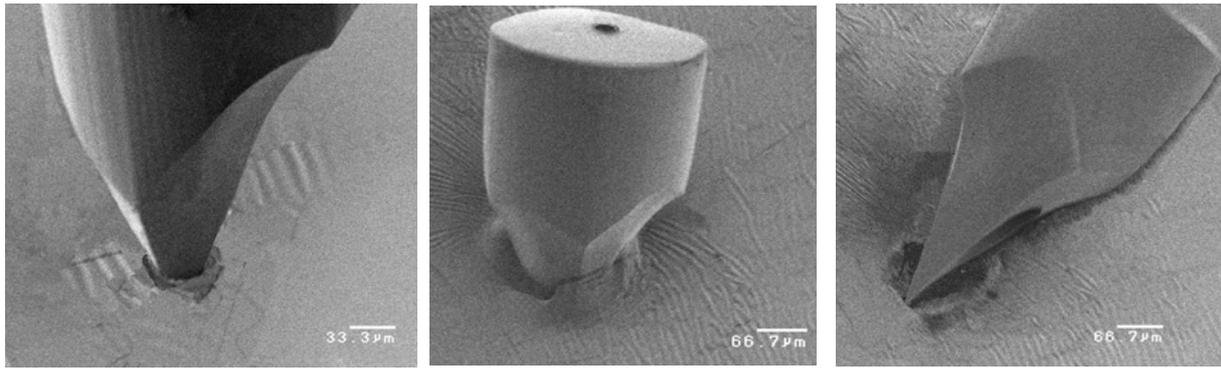


Fig. 5 Strength test of the microneedle with polyimide film at (a) 50µm-deep, (b) 120µm-deep and (c) after removal.

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