Synthesis of a BioMEMS Device for Direct Delivery of Cancer Drugs

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Abstract:

This project focused on optimizing the fabrication process of a biological microelectromechanical systems (bioMEMS) device for direct delivery of cancer drugs. A photolithographic process was used to fabricate 50 × 50 μm "step" groove patterns on aluminum substrates, which were then used to make a metal mold for device synthesis with the inclusion of grooves. Heat was incorporated during PDMS curing to drastically reduce production time.

Introduction:

Direct delivery of cancer drugs is a topic of increasing importance, as current methods of cancer treatment are expensive and inefficient. High concentrations and large dosages are required for chemotherapy drugs and other substances to have a significant effect in treating cancer, driving up treatment costs as chemotherapy drugs are expensive to make. Direct delivery of cancer drugs increases the efficiency of treatment, lowers the costs as less drugs and lower concentrations are required, and reduces the severity of side-effects.

One method for implementing direct delivery is to implant a biocompatible device made of polydimethylsiloxane (PDMS) containing cancer drugs into sites of recently removed tumors. The drugs are dispensed from a hydrogel inside the device, using a hyperthermia coil to supply heat for activating the gel's contraction mechanism, with micro-channels acting as delivery pathways for drug flow.

This project focuses on the inclusion of microgrooves onto the device surface for cell attachment, fostering biocompatibility with the human body. The grooves can be tailored to the average size of the specific cancer cell type for optimum cell adhesion.

Procedure:

SU-8 50 microgrooves were made on 0.5 in × 0.5 in aluminum 5052 alloy substrates of thickness 0.3 mm, following the procedures outlined by MicroChem for 50 μm films [1]. It should be noted that: the final ramp-up spin speed was ~ 2180 RPM; all bakes were done in convection ovens, so heating times were 50% longer than outlined in procedures; and a hard-bake of 2 hrs minimum was carried out on the aluminum substrates. After making four substrates, a mold was assembled so that the bottom had a cylindrical piece of metal with diameter of 0.6-0.7 cm and height of 0.9 cm, and the interior length and width (on the inside of the mold) was 1 cm each, with the height at 1.1 cm. Under a fume hood, the mold was placed on a Petri dish with a few drops of silanizing agent. The dish was placed into a vacuum desiccator and was left in chamber for 1 hr under a pressure of 12.5 psi.

Two pieces of aluminum foil were molded onto the bottoms of 250 ml and 150 ml beakers. Using materials from a 184 Sylgard kit, PDMS was prepared by mixing at a weight ratio of 10:1 monomer to curing agent on a chemistry boat. Once the mixture became cloudy due to bubbles, the boat was degassed in vacuum at 12.5 psi for 45 min. Afterwards, any remaining bubbles were removed and the mold was placed on large foil boat. Next, the mixture was poured into a mold and small foil boat and re-degassed at 12.5 psi for a minimum of 1 hr, with pressure throttled every 20 min to assist with bubble removal. The boat was then placed on a hot plate, set to 125°C, for 20 min until the PDMS cured. After air cooling,

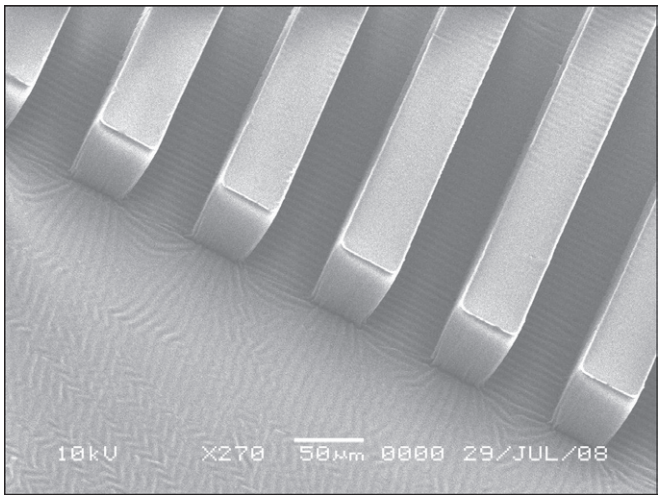

Figure 1: SEM of PDMS replica of microgroove pattern.

the mold was disassembled, using a razor to remove excess PDMS and foil from the small boat while carefully removing the substrates from casing. Using a micropipette to drop a small amount of curing agent on the side of the casing with a hole, the thin piece of PDMS from the small foil boat was cured onto a PDMS casing at 125°C for 20 min. After an air cool, the excess PDMS was removed using a razor.

Results and Discussion:

Using scanning electron microscopy (SEM) images of PDMS replicas such as in Figure 1, we confirmed the process conditions for good resolution replica molding of SU-8 microgrooves, and then fabricated the casing mold with the substrates. The original processing time, without the addition of heat, was dramatically reduced from 48 hours to 45 minutes with the inclusion of heat during PDMS curing. Figure 2 shows the completed device casing, and Figure 3 demonstrates the successful microgroove pattern replication onto the device surface. A preliminary experiment monitoring the cell attachment to microgrooves was conducted, and initial results showed that cells were in fact attached to the microgroove walls, as shown in Figure 4.

Conclusion:

In conclusion, the process and conditions used were successful in the fabrication of microgrooves on the bioMEMS device surface, potentially allowing the device to integrate with the human body without rejection. Along with the reduction in production time, our findings increase the viability of the device as an alternative to current cancer therapy methods.

Future Work:

For future work, long term studies of cell adhesion to device microgrooves will be conducted, flow-rate measurements of drug delivery via the hydrogel will be obtained, and efficacy of iron-oxide nanoparticles as a potential therapy in conjunction with the device will be determined.

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References:

[1] MicroChem, NANO™ SU-8 Negative Tone Photoresist Formulations 50-100.

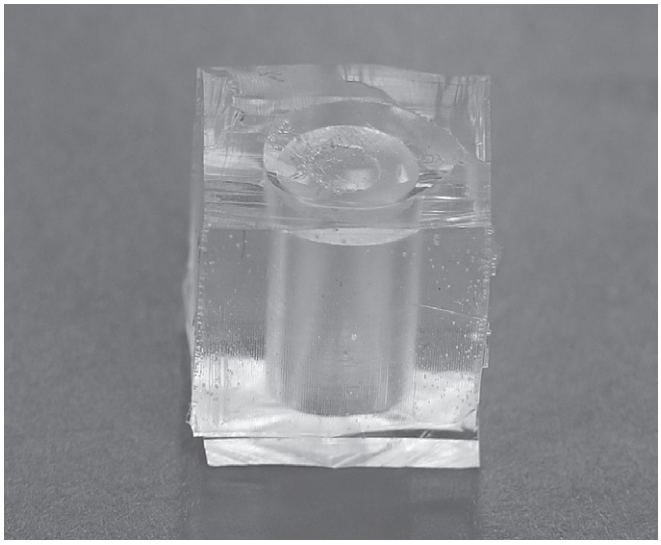

Figure 2: Photo of finished device casing.

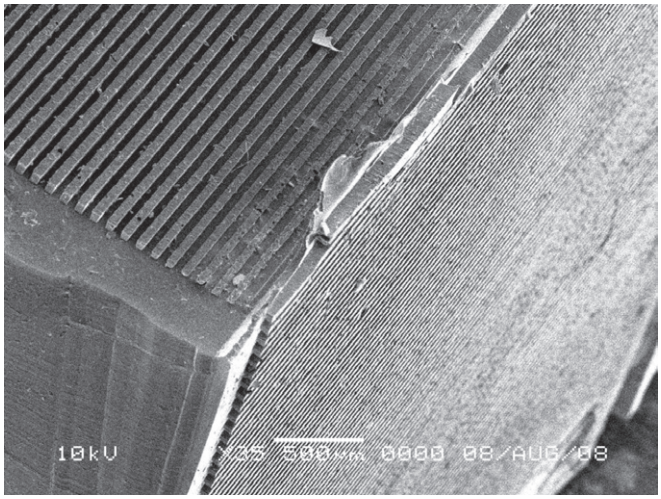

Figure 3: SEM micrograph of a corner of PDMS casing.

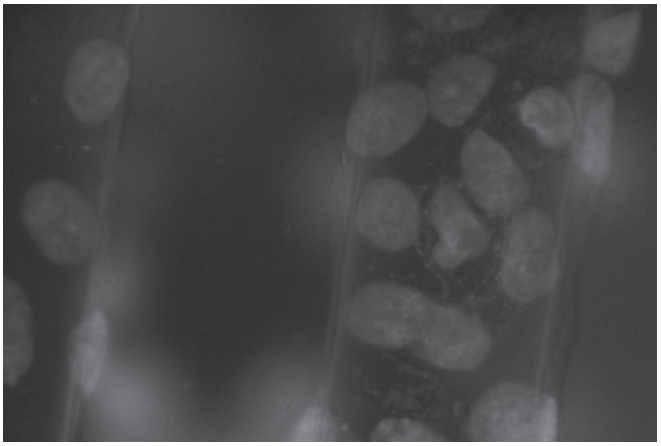

Figure 4: Photo of nuclear-stained cancer cells attached to microgrooves.