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## Tissue Scaffold Engineering by Micro-Stamping

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### ABSTRACT

A hand operated benchtop stamping press was developed to conduct research on microscale hole fabrication in polymer membranes for applications as scaffolds in tissue engineering. A biocompatible and biodegradable polymer, poly( $\epsilon$ -caprolactone), was selected for micropunching. Membranes between 30  $\mu\text{m}$  and 50  $\mu\text{m}$  thick were fabricated by hot melt extrusion, but could not be stamped with a 200  $\mu\text{m}$  circular punch at room temperature, regardless of die clearance due to excessive strain to fracture. This problem was overcome by cooling the membrane and die sets with liquid nitrogen to take advantage of induced brittle behavior below the polymer's glass transition temperature. While cooled, 203  $\mu\text{m}$  hole patterns were successfully punched in 33  $\mu\text{m}$  thick poly( $\epsilon$ -caprolactone) membranes with 11% die clearance, achieving 71% porosity.

### INTRODUCTION

Tissue engineering provides an opportunity to develop patient specific implants comprised of scaffolds seeded with donor cells. Conventional methods such as solvent-casting with particulate leaching, gas foaming, phase separation, melt molding, freeze drying, and solution casting are not adequate to produce an engineered microarchitecture [1][2][3]. Scaffolds with engineered pores and internal channels can direct cell growth and provide transport to and from seeded cells [4]. Solid freeform fabrication (SFF) methods developed to engineer microarchitecture include 3D printing, stereolithography, fused deposition modeling, and phase-change jet printing, however most SFF methods require an internal support structure that must be dissolved with solvents, where residuals pose a risk of toxicity to seeded cells.

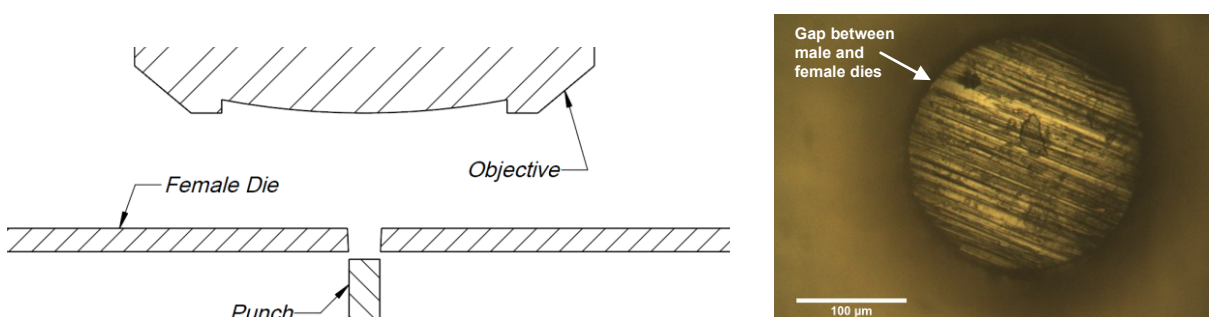
Scaffold engineering through multi-layer construction is a relatively new field where microarchitecture is created by stacking porous 2D membranes into 3D structures [5][6]. In general, these methods and the aforementioned SFF methods are time consuming, which is to say it takes hours rather than seconds to produce a single scaffold layer. One underlying reason for manufacturing inefficiency is the pursuit of scaffold material production at the same time as hole creation by rapid prototyping or molding methodologies. The novel approach presented in this paper is to separate these manufacturing processes by first pursuing high efficiency methods of material film production and then fabricating hole patterns via micromechanical punching.

Micro-punching first emerged in 2001 with the development of a micro-punching machine by Joo et al., who punched 100  $\mu\text{m}$  holes in 100  $\mu\text{m}$  brass sheets using dies fabricated with micro electrical discharge machining [7]. Subsequent research has almost exclusively been focused on micro-punching various metals 1.5-200  $\mu\text{m}$  thick [7-12]. Polymers, however, present a different set of challenges for microscale punching, the topic of the present study.

## MATERIALS AND METHODS

The design of the custom punching machine has several key elements. A microscope camera is set up on a 3-axis micrometer stage for x, y, and z movement and looks down through the female die to align the male die. The male die sits on x, y, z, and  $\theta$  stages with precision micrometers, whereas the female die is fixed in place. A frame is used to mount the stages and secure the dies relative to one another. Because of the small size of the dies, vacuum is used to hold the male and female dies in place.

The design of the stamping press ultimately revolves around the male and female dies and how they are aligned. The female dies were laser cut from stainless steel sheets, while gauge pins were used as the male dies. The two were aligned using a microscope to look at the male die through the female die (Figure 1). By focusing on the male die and bringing it close to the female die, the gap between the bottom of the female die and the top of the male die can be observed.

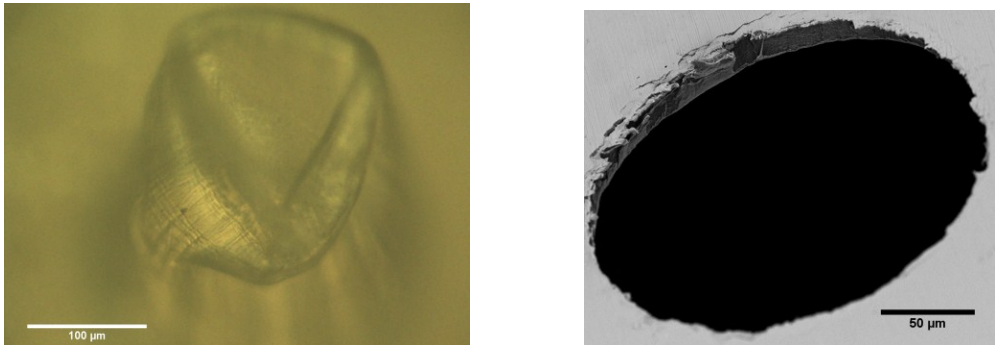


**Figure 1.** The microscope is used to align the male and female dies. (Left) Concept, not to scale. (Right) Microscope image of a gauge pin punch being aligned with a female die. Magnification: 200x.

The poly( $\epsilon$ -caprolactone) (PCL) was extruded through a thin die using a DSM Xplore Micro 15 cc twin-screw microcompounder. A precise thickness was achieved by controlling the tension in the solidifying film. Films with thicknesses from 30 to 50 microns and a width of roughly 15 mm were produced. From the opacity of the film, it was determined to be semi-crystalline.

## RESULTS & DISCUSSION

When attempting to punch PCL at room temperature, it was found to have a very high strain to fracture and would stretch into virtually any clearance between the male and female die. The result was forming the PCL into a bag-like structure (Figure 2, Left). The solution to punching PCL was to cool it down below its glass transition temperature of  $-60^{\circ}\text{C}$ . At this point, the PCL would fracture instead of stretching during punching (Figure 2, Right).

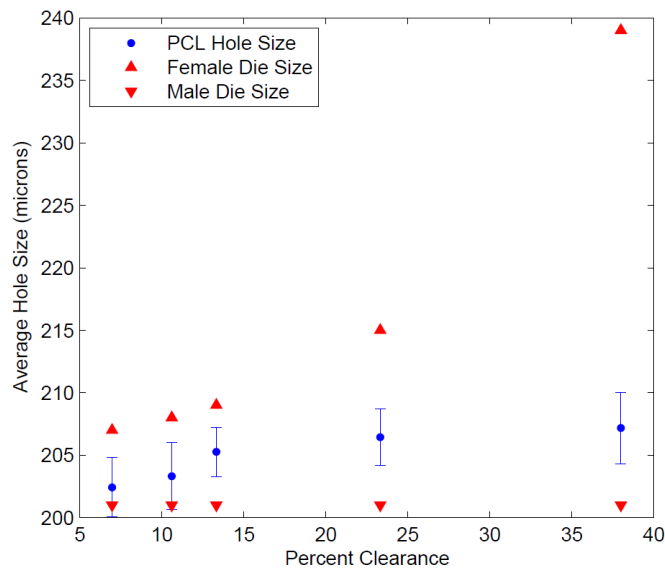


**Figure 2.** (Left) PCL stretched into a bag-like structure after attempted punching at room temperature. 37 μm thick PCL was punched with a 204 μm pin in a 213 μm female die, for a clearance of 12%. Magnification: 200x. (Right) PCL was successfully punched if cryogenically cooled below its glass transition temperature. 43 μm thick PCL film punched with a 201 μm male die and 207 μm female die for 7% clearance. View of exit side at 45°. SEM voltage: 5 kV.

The effect of die clearance on hole diameter, hole quality, minimum web thickness, and punching mechanics was investigated. PCL films were punched with die clearances of 38%, 23%, 13%, 11%, and 7%. The PCL thickness depended on the strip of material, which for these tests ranged from 30-50 μm. In each strip of PCL, rows of holes were punched with variable spacing. In four of the films, a final row of interrupted punches was performed with varying stroke.

**Hole Diameter**

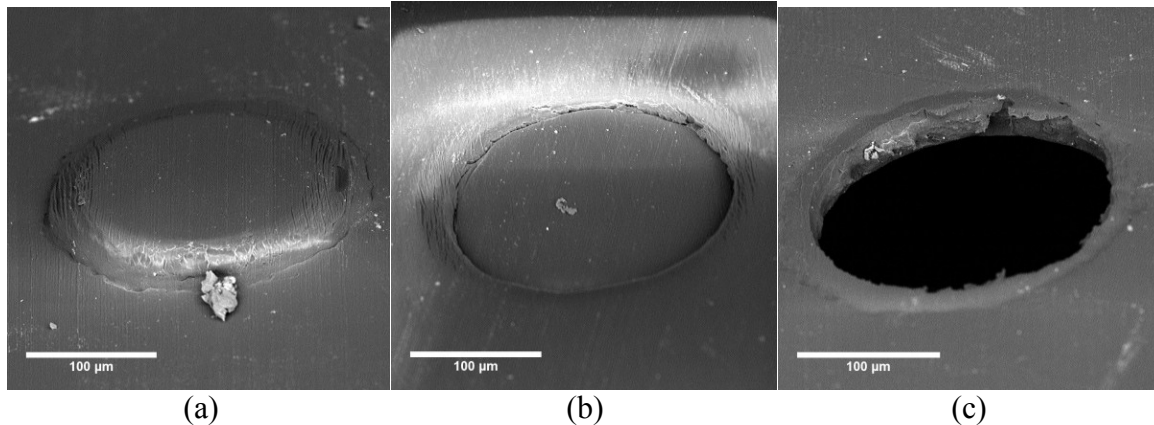
When punching PCL films with a 201 μm gauge pin and a range of stainless steel female dies, there was only a slight correlation between hole size and female die size (Figure 3). The resulting holes were much closer in size to the male die. The shear diameter has a propensity towards the male die because the shear stress is higher on the male side.



**Figure 3.** Effect of die clearance on hole size in 30-50 μm PCL.

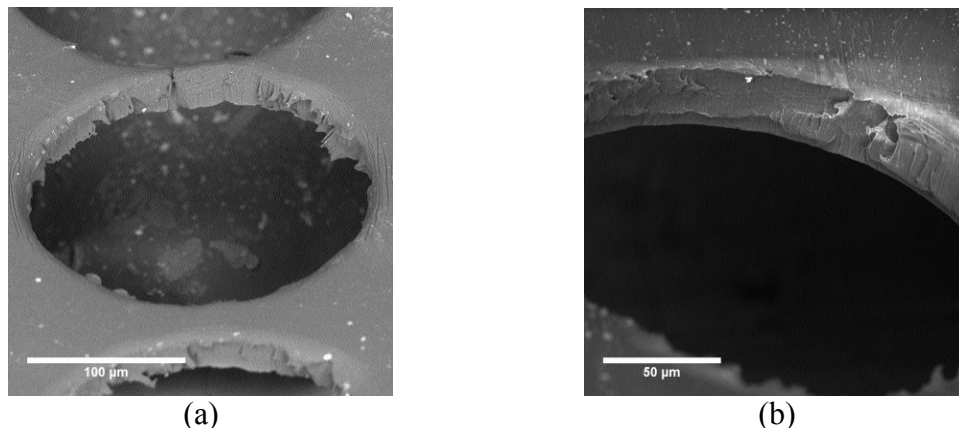
### Hole Quality

Figure 4 (a) and (b) show the exit and entrance sides of an interrupted punch with a clearance of 38%. Figure 4 (c) shows a hole produced with the same clearance. A 38% clearance makes it very easy to align the male and female dies, but is much larger than the standard 5-10% used in metal stamping [7].



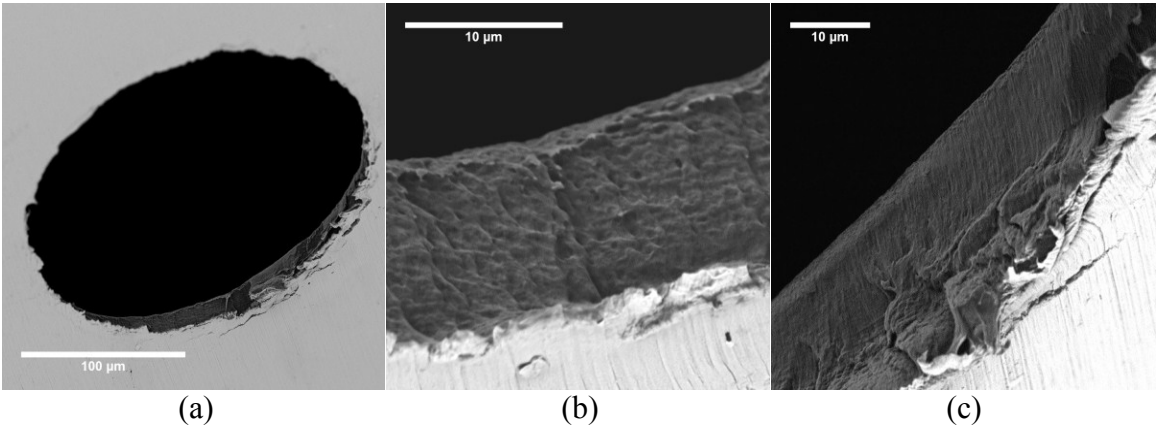
**Figure 4.** 50  $\mu\text{m}$  thick PCL film stamped with a 201  $\mu\text{m}$  male die and 239  $\mu\text{m}$  female die for 38% clearance. SEM voltage: 5 kV. (a) View of exit side at 45°. (b) View of entrance side at 45°. (c) View of exit side at 45°.

In Figure 4, cracks can be seen around the edges of the hole on the entrance side (b) and the resulting hole quality is quite poor (c), with very rough fracture zones spanning the entire thickness. From the interrupted punches, it is apparent that the material is bending up into the female die rather than cleanly shearing. The large, rough fracture zones indicate that most of the material is failing in tension as it is bent and stretched into the female die. When punching progressively, this tension could cause the web to tear between two consecutive punches. For a 23% clearance, cracks can also be seen in the film at the edges of the hole, and are oriented in the direction of extrusion (Figure 5). Hole quality seems quite variable, with large roughness in some parts (a), and relatively smooth and burr-less sections elsewhere (b).



**Figure 5.** 30  $\mu\text{m}$  thick PCL film punched with a 201  $\mu\text{m}$  male die and 215  $\mu\text{m}$  female die for 23% clearance. SEM voltage: 5 kV. (a) View of entrance side at 45°. (b) View of exit side at 45°.

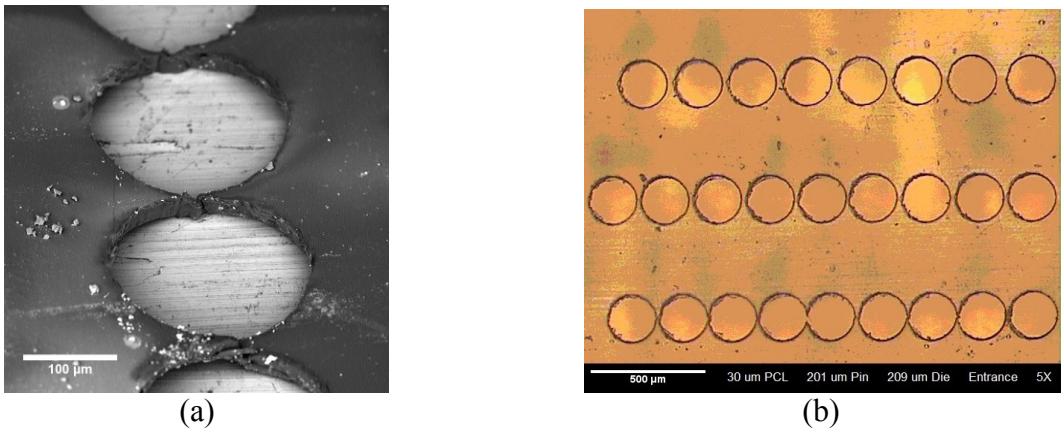
Figure 6 shows scanning electron microscope (SEM) images of PCL punched with a 7% die clearance. Certain sections, as seen in (b), resemble pure brittle fracture across the entire thickness of the workpiece. Other sections, as seen in (c), appear to exhibit a 50% burnish land and 50% (ductile) fracture zone. Overall, the results of punching with 7% clearance seem relatively clean with a small burr.



**Figure 6.** 43  $\mu\text{m}$  thick PCL film punched with a 201  $\mu\text{m}$  male die and 207  $\mu\text{m}$  female die for 7% clearance. View of exit side at 45°. SEM voltage: 5 kV.

**Punch Spacing**

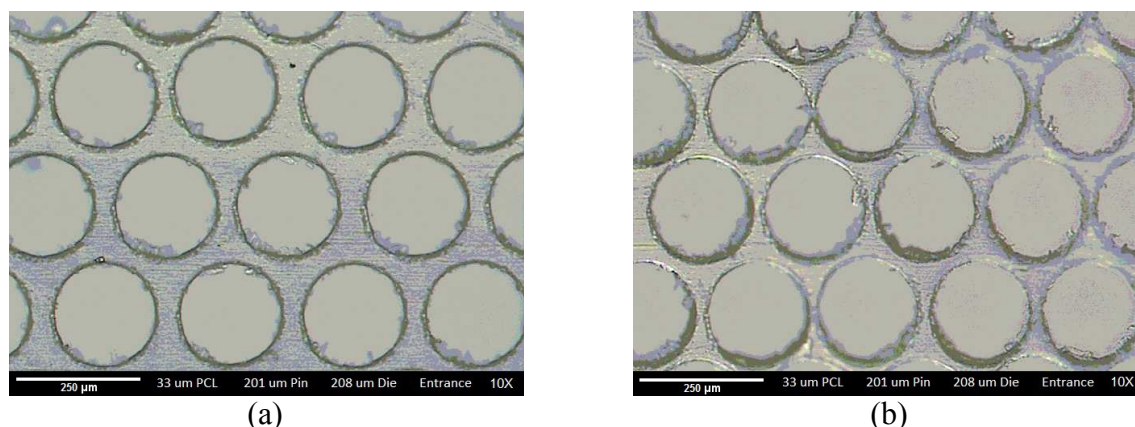
Punching of PCL was able to achieve extremely thin webs without tearing. However, the strength and practicality of such a web is questionable, as they can become so thin as to pinch in on themselves due to film stresses (Figure 7).



**Figure 7.** 30  $\mu\text{m}$  thick PCL film punched with a 201  $\mu\text{m}$  male die and 209  $\mu\text{m}$  female die for 13% clearance. (a) SEM view of exit side at 45. (b) Optical microscope view of entrance side.

Such thin sections may maintain their shape during and shortly after punching, but once the PCL is reheated to room temperature, it loses its rigidity and becomes extremely flexible again. Porosity tests were conducted in order to gain a practical understanding of the potential of these micro-punched holes. Figure 8 (a) shows a 5x5 pattern of nested holes, 203  $\mu\text{m}$  in diameter, with 47  $\mu\text{m}$  thick webs, and an overall porosity of 60%. Figure 8 (b) shows a similar pattern, but with 27  $\mu\text{m}$  webs, and 71% porosity. Higher porosities might be attainable with better alignment and temperature control.





**Figure 8.** Porosity study on a 33  $\mu\text{m}$  thick PCL film punched with a 201  $\mu\text{m}$  male die and 208  $\mu\text{m}$  female die for 11% clearance. (a) Porosity: 60%. Magnification: 100x. (b) Porosity: 71%.

## CONCLUSIONS

A micro-stamping press was developed with the capability of producing micro-hole arrays in extruded films of the biodegradable polymer poly( $\epsilon$ -caprolactone) (PCL). Successful die alignment was achieved by looking through the female die to align the male die. PCL was successfully punched only after cooling below its glass transition temperature. Hole quality improved significantly below a 10% die clearance and PCL hole arrays exhibiting up to 71% porosity were progressively punched.

## ACKNOWLEDGMENTS

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