ABSTRACT
In this study, we report two new fabrication processes for making thin, transparent, flexible and biocompatible polyurethane (PU)-based microfluidic devices. We detail not only the fabrication of microchannels but also their bonding, integration of fluidic interconnections as well as surface modification with hydrophilic polyethylene oxide (PEO) to improve their biocompatibility in blood contacting applications. These processes produced microchannels with high transparency (96% of glass in visible spectrum), high bond-strength (326.4kPa) and low fibrinogen (Fg) adsorption (80% reduction), which is critical for its anti-thrombotic property. Based on these results, PU could serve as an effective alternative to PDMS in many blood contacting biomedical applications.

KEYWORDS: Polyurethane, Solvent Casting, Soft Lithography, Blood, Surface Modification

INTRODUCTION
Polyurethanes are used widely in medical devices industry, especially in implantable devices due to their flexibility, abrasion resistance, adhesive strength and unique antithrombotic properties. However, they are usually not transparent and hence have not been widely investigated in the fabrication of microfluidic devices. Microfabrication of PU has typically involved injection molding [1] or reaction polymerization [2] that are not suited for rapid prototyping due to high-cost intermediate molds and high-intensity UV sources. They also produce rigid non-elastomeric and non-transparent substrates. Solvent casting [3] is more suitable but suffer from weak bonding, forms opaque channels and is difficult to attach interconnects. Here we present a modified the solvent casting method and develop new bonding, interconnection and surface modification methods to produce PU elastomeric devices that could be rapidly prototyped for blood contacting applications.

FABRICATION
The process flow of PU soft-lithography is depicted in Figure 1. The molds were made by SU-8 photoresists through a conventional photolithography process. The thickness of SU-8 molds ranged from 0.5µm to 80µm by choosing different SU-8 and varying the rate for spin coating. The PU resin was prepared by dissolving 10 wt% Tecothane® PU pellets in tetrahydrofuran (THF) and then casting on SU-8 molds. After the PU was cured, the interconnects (either Tygon® or silicone tubing) were attached using a solvent sealing method. In this method, THF was used to partially dissolve the surface to be bonded on the PU replica and the tubing. They were then placed together and allowed to dry. A strong bond was formed by fusing the two materials together and no fitting was required. The PU replica with integrated interconnects was then peeled from the mold. Punch tools were used to clean residual PU inside the tubing. To obtain sealed microchannels, two bonding methods were developed including oxygen plasma treatment and micro-contact printing. The surfaces of both PU replicas can either be activated in an oxygen plasma chamber with 60W RF power for 1min or be solvated by THF which can be spin-coated or dip-coated before placing together. The former was found to be more suited for nanochannels (<1µm) as the latter can cause channel blockage. A common method to reduce non-specific protein adsorption in biofluid contact is to graft polyethylene oxide (PEO) to the surface [4]. In this work, NCO groups were introduced on PU by reaction with methylene-bis-(4-phenylisocyanate). PEO was then grafted by reaction with the NCO groups. The PEO modified PU surfaces were characterized by fibrinogen adsorption from PBS (114I-labeling).

Figure 1. Process flow of PU soft-lithography
RESULTS AND DISCUSSION

Physical characterization of PU channels fabricated by this replica molding technique was performed by optical profilometry and SEM. The quality of the replica can be seen in Figure 2a. The casting technique is capable of replicating microstructures as small as a few hundred nanometers. Microchannels with feature sizes from 0.5-80 µm were easily replicated using this technique. The SU-8 mold can be repeatedly used a number of times (≥10) without any damage or degradation. Various bonding methods were investigated to attach the replicated microchannel layer with a base substrate to seal the microchannels. A cross section of the bonded microchannel is shown in Figure 2b. The interface between the top and the bottom PU layers is invisible, demonstrating the high quality of the bond formed. The bonding strength was characterized by the burst test and the data are summarized in Table 1. The first method used to bond was the exposure of the top and bottom PU substrates to an oxygen plasma. This resulted in a bond strength of about 42 kPa which was very weak. A similar technique employed for bonding PU to glass resulted in a slightly higher bonding strength of 150 kPa. A different method, where the PU base substrate was dipped in THF and then bonded to the microchannel PU layer, yielded a bond strength of 230 kPa which was substantially higher than the oxygen plasma method. Here, the dip coating transfers some of the THF on to the PU surface, dissolves it and when bonded to the other PU forms a tighter interconnection between the polymers on either substrate. Similarly, using a more precise microcontact printing method where the amount of THF loaded onto the PU substrate is controlled and uniform yielded an even higher bond strength of 326 kPa. The failure occurred at the fittings connected to the pressure sensor. These results show that a leak-proof interconnection and high bond-strength of >320 kPa (highest for PU) can be achieved in the formation of PU microchannels which is comparable to PDMS devices. Water contact angle measurement showed PU was significantly more hydrophilic (θ = 63°) than PDMS (sessile drop method). In addition, optical transmission showed that the cast PU was highly transparent and had very similar optical transmission characteristics to glass as shown in Figure 3. PEO was grafted inside the microchannel and characterized by fibrinogen adsorption from PBS (125I-labeling). PU modification with PEO was confirmed by a reduction in fibrinogen adsorption from PBS of over 80% compared to PDMS and PU as shown in Figure 4.

Figure 2. SEM photography of (a)&(b) Unsealed PU replica (45µm high); (c) cross-section of PU channels before bonding; (d)&(e) cross-section of PU sealed channels after bonding by µcontact printing (45µm high). No bonding interface as evidence of strong bonding; (f) cross-section of high-aspect ratio PU sealed channels after bonding by µcontact printing (10µm high and 150 µm)
**Table 1. Burst pressure test for sealed PU microchannels**

<table>
<thead>
<tr>
<th></th>
<th>PU/PU O₂ plasma</th>
<th>PU/Glass O₂ plasma</th>
<th>PU/PU dip-coating</th>
<th>PU/PU μcontact printing</th>
<th>PDMS/PDMS O₂ plasma</th>
</tr>
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<tbody>
<tr>
<td>pressure (kPa)</td>
<td>42.2 ±3.3</td>
<td>150.4 ±10.1</td>
<td>229.9 ±24.3</td>
<td>326.4 ±19.6</td>
<td>300</td>
</tr>
</tbody>
</table>

**Figure 3. Optical transmission spectrum of PU film and the image of C. elegans nematode through PU microchannel**

**Figure 4. Fibrinogen adsorption to devices and films made by PDMS, native PU and PEO-modified PU**

**CONCLUSION**

We have developed a new fabrication process for PU microchannels with properties that are better suited for blood contacting microfluidics. These devices have high bond-strength and optical transparency comparable with PDMS. They have the surface properties such as hydrophilicity and low protein adsorption that are superior to PDMS.

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**REFERENCES**


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