INTEGRATION OF METALLIC MICRONEEDLES WITH DISPOSABLE BIOCHIPS FOR MINIMALLY INVASIVE BLOOD SAMPLING

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ABSTRACT

In this work we have developed and characterized the integration of metallic microneedles with biochips for minimally invasive blood sampling. A commercially available stainless steel needle is used in this approach and the integration is achieved during biochip assembly. The type of needle used in this work is approved for blood sampling and can be used to sample capillary and venous blood. The microneedle performance has been simulated and experimentally characterized to evaluate pressure required to initiate flow, and we show that very small pressure (2 KPa) is required for sampling blood.

KEYWORDS: Metallic microneedle, disposable biochip, blood sampling, venous

INTRODUCTION

The development of reliable and efficient Lab-On-A-Chip technology has made it possible for developing diagnostic tools for monitoring clinically relevant parameters from human blood. However, blood sampling remains a challenging issue for μTAS devices. Previously researchers have developed microfabricated needle structures for sampling and drug delivery applications on silicon and plastic substrates [1,2,3]. However, because of the limited size (length) of the microfabricated needle structures it is difficult to sample blood directly from veins [4]. Table 1 lists the typical concentrations of a few clinically significant parameters at different sampling locations.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Typical values</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Arterial</td>
<td>Venous</td>
</tr>
<tr>
<td>O2</td>
<td>90 ± 10</td>
<td>70 ± 10</td>
</tr>
<tr>
<td>CO2</td>
<td>40 ± 5</td>
<td>46 ± 5</td>
</tr>
<tr>
<td>pH</td>
<td>7.4 ± 0.05</td>
<td>7.36 ± 0.05</td>
</tr>
<tr>
<td>Glucose</td>
<td>4.9 ± 0.9</td>
<td>4.9 ± 0.9</td>
</tr>
<tr>
<td>Sodium</td>
<td>142 ± 4</td>
<td>142 ± 4</td>
</tr>
<tr>
<td>Potassium</td>
<td>4.2 ± 0.7</td>
<td>4.2 ± 0.7</td>
</tr>
</tbody>
</table>

Widely accepted clinical data is not available.
Of the above listed values, typically venous blood sample is most commonly used. It is preferable to avoid arterial sampling because of the risk of severe hemorrhages. Since microfabricated needles cannot penetrate to the required depth we have developed an integration scheme for commercially available 36 gauge stainless steel microneedles. Figure 1 shows a schematic sketch of the biochip with integrated microneedle.

MICROFLUIDIC SIMULATION

Fluidic simulations were conducted using the CFD-ACE™ module to investigate the effect of dissimilar material (steel and plastic) and changing hydraulic diameter on the microneedle sampling performance. Figure 2(a)-(d) show the fill sequence of the composite assembly. The model used for simulations has a different geometry than the actual structure for expediency in grid generation. As Figure 2(e) shows, initially the liquid is drawn in by a capillary suction force since the needle has a hydrophilic surface. Upon reaching the laser machined groove, a positive pressure is needed to push the liquid out of the needle. The simulations predict that ~ 3000 Pa pressure will be required to force liquid out of a 100 μm internal diameter needle.

Figure 2. Simulation results: (a)-(d) liquid filling behavior in simulated model and (b) dynamic pressure response at microneedle-channel interface.
FABRICATION

The biochip is fabricated using UV-LIGA lithography followed by electroplating and injection-molding as previously reported [5]. Laser micromachining using a 248 nm Excimer laser is used to etch a groove within the inlet microchannel. After laser machining the groove dimensions (depth and width = 250 μm) match the outer diameter of the microneedle.

Figure 3. Microneedle assembly: (a); (b) schematic sketch showing laser machining and assembly of microneedle; (c); and (d) SEM micrographs of biochip after laser machining.

The microneedle is positioned in the groove during thermoplastic fusion bonding. The fusion bonding process is a part of the biochip assembly sequence hence no extra step is required to assemble the microneedle. Figure 3 shows a schematic sketch of the assembly sequence and SEM micrographs of the laser machined channel. Figure 4 shows a micrograph of the assembled biochip with the microneedle compared to a 21 gage needle.

RESULTS

The disposable biochip with the integrated metallic microneedle was tested with a simulated blood source as shown in Figure 5. A pressure sensor was connected to near the microneedle insertion point (in the deformable reservoir) and the dynamic pressure response was monitored using a LabVIEW system. The biochip was withdrawn from the reservoir when the liquid filled up to the passive valve as shown in Figure 5(d). Figure 6 shows the measured dynamic pressure response where \( t_1 \) corresponds to the capillary suction duration, \( t_2 \) corresponds to the time when liquid enters the biochip and at \( t_3 \) the biochip is withdrawn from the reservoir. Comparison with Figure 2(e) shows that the value of pressure required to push liquid into the biochip matches the simulated values. The slight variation can be
attributed to variations in needle internal diameter. The negative pressure corresponding to capillary filling of the needle is not seen in Figure 6 because the pressure sensor is not capable of vacuum measurements and can only record positive pressures. The pressure required to push liquid into the biochip is of the order of 2 KPa (corresponding to 0.56 mm Hg). Hence, we believe that if the microneedle is used for venous sampling, blood samples can be easily drawn to fill up the desired volume on the biochip.

CONCLUSION

This work addresses an issue of concern to the Lab-On-A-Chip community; namely the development of an efficient sampling method that can be easily integrated with disposable biochips. The microneedle requires very low pressures to sample blood. Furthermore, the developed integration scheme uses commercially available, certified biocompatible metallic microneedles that be directly applied towards venous blood sampling. We believe this modular integration approach will greatly enhance the application of disposable biochips for point-of-care health monitoring applications.

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Reference: