FABRICATION OF FLEXIBLE DRUG DELIVERY CHANNEL EMBEDDED LCP BASED HYBRID NEURAL PROSTHESIS

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ABSTRACT
We developed a porous core architecture embedded flexible microchannel which can be applied widely in the field of film type implantable prostheses. Based on capillary action through porous fiber, we developed microfluidic channels that can be established between thin thermoplastic polymer film layers using a critical thermal press bonding condition that does not obstruct the fiber embedded microfluidic channel. Due to its robustness to biological environments and high mechanical durability, this fabrication method can be employed as a technology for drug delivery within implantable prosthesis devices.

KEYWORDS: Drug Delivery, Flexible Channel, Liquid Crystal Polymer, Neural Prosthesis

INTRODUCTION
The developed porous core architecture embedded microfluidic channel is composed of axially porous fiber bundles and the parallel voids. Two different types of channels, core fiber and void, deliver liquid simultaneously, however the physics of flow through each channel differ. Flow through fiber depends on the capillary action, resulting in the flow rate being determined by the physical constants such as the surface energy of the fiber or axial permeability, viscosity and density of the liquid. In the case of the void, however, the flow rate can be controlled by external pumping pressure which is induced at inlet ports.

Drug delivery channels in chronic implantable prosthesis is one of the important issues for the prevention of adverse reactions to inserted devices. Currently, biocompatible Liquid Crystal Polymer (LCP) thin film based electrode neural prosthesis are used as Deep Brain Stimulus (DBS) systems [1]. Our main goal is to embed our novel microfluidic channel on it for drug delivery.

THEORY
Microfluidic using fiber thread has many advantages for medical care products due to its wettability, flexibility and biocompatibility. However, thread fluidics also have several limitations of application in commercial products itself, such as the difficulty in fabricating isolated thread networks and concentration of transferred solution can be increased transiently due to the low flow speed and exposure to ambient conditions. In addition it is impossible to control flow rate actively using capillary driven flow or wicking through fibers. So threads which transport liquids need to be encapsulated and designed to be controllable as independent and active flow channels.

Capillary action depends mainly on four physical parameters: surface tension, gravitational, viscous drag and inertial forces [2]. In these four parameters, gravitational and inertial force can be ignored because the mass scale of thread fluidics itself is extremely low in order of pico-liters.

Figure 1: (Left) The illustration of flexible drug delivery channel embedded hybrid neural electrode prosthesis. (Right) Cross-section of end-tip. Triangular voids by the side of the fiber bundle works as active controllable drug delivery channel.
EXPERIMENTAL

Surface Treatment for hydrophilicity

To maximize the benefits of LCP based neural electrode[1], we tried to fabricate the flexible microfluidic channels between LCP film layers. As mentioned above, LCP has thermoplastic properties and is hydrophobic under normal conditions. During thermal press bonding of LCP films, the embedded fibers should endure the extremely high temperature of 280 °C and should not absorb any melted LCP. To increase wicking properties, we initially tested various type of fibers, 100% cotton, silk and nylon. However, thermal resistance was not only unacceptable, but these fibers also showed evidence of carbonization. Finally, Kevlar™ fiber was selected for its thermal resistance and bio-compatible property for the core architecture of the flexible microfluidic channel.

Table 1: Kevlar™ fiber vertical rising test according to surface condition

<table>
<thead>
<tr>
<th>Assessment item</th>
<th>Vertical rising height [mm]</th>
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<tbody>
<tr>
<td>Equilibrium height</td>
<td>Plasma + wetted (74)</td>
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Pure 100% Kevlar™ fiber can absorb aqueous solutions without any surface treatment. However, the inherent hydrophilicity of Kevlar™ fiber can be lowered during high temperature thermal bonding process of LCP. Table 1 shows the effect of air plasma treatment and the equilibrium of vertical rising height due to the surface condition of Kevlar™ fiber. Prior to packaging LCP and Kevlar™ fiber was treated with air plasma (100 W, 5 min, FemtoScience, Cube) to minimize the effect of high temperature [4].

Modified thermal press bonding process and linear fiber alignment

The thermal bonding process was modified for the development of the flexible drug delivery channel in the LCP film based electrode array, figure 2A. This modified process compare with monolithic thermal bonding processes is that melted LCP does not obstruct the Kevlar™ fiber nor the voids. Voids along the fiber play an critical rule for active flow rate control based on the pressure difference of inlet and outlet ports. Figures 2B shows the cross-section of Kevlar™ fiber embedded within the flexible microfluidic channel. Two different type of LCP were used, OCL (high T_g) and FA (low T_g). To fabricate fiber embedded LCP layers without structural damage, phase changes at the LCP interface should be minimized to achieve sufficient bonding force. Heat transfer from the bottom to the upper plate is the key point during the suggested method and different T_g of LCP helps focus localized melting.

Figure 2: (A) Modified LCP thermal press bonding process. Treat for 30 min at 270-280 °C at 1.20 – 1.60 x 10³ Pa (B) Cross-section of Kevlar™ fiber embedded flexible microfluidic channel.

To make linear alignment of Kevlar™ fiber on LCP [1], we also suggest a removable hook wiring alignment. Initially, non-adhesive ultra-thin Teflon wire is fixed at the end of the LCP electrode. Then weave single Kevlar™ fibers across Teflon hook and twist. Kevlar™ fiber can be linearly aligned by pre-tension and any multiple bending angles can be aligned.
RESULTS AND DISCUSSION

We inserted dH2O pre-filled hybrid neural prosthesis into an adult rat brain to assess drug delivery performance. After insertion, 10 μl of green aqueous solution was added to the inlet port. After 30 min, the hybrid neural prosthesis was removed and cerebral tissue cross sectioned Figure 3B.

Figure 3 : (A) Prototype of flexible drug delivery channel embedded hybrid neural electrode prosthesis. Kevlar ™ fiber is embedded along the yellow gold electrode wire and the diameter of laser holes is approximately 50 μm. (B) The result of adult rat brain insertion test. Green trace in yellow dash ellipse indicates colored solution.

CONCLUSION

In this paper, we present a simple technology to fabricate a drug delivery channel in LCP based neural prostheses and verified its ability to deliver drugs by capillary action. Nevertheless, this research approached fabrication method and simple verification of fiber embedded drug delivery channel, analytic modeling, quantitative analysis and clinical assessment will be reported in further study [3,5].

The proposed fiber embedded fluidic channel has several advantages of robustness, mechanical durability and biocompatibility. Most of all, we hope this fabrication method can be applied to chronic implantable prosthesis since biocompatible fiber can be embedded between film layer and also into various shapes and materials used in prostheses.

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REFERENCES


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