Development of a miniaturized, reconnectable, and implantable multichannel connector

Gwang Jin Choi 1,8, Hyun Ji Yoo 1,8, YoonKyung Cho 8, Shinyong Shim 1, Seunghyeon Yun 8, Jaehoon Sung 8, Yoonseob Lim 4,5,∗, Sang Beom Jun 2,6,7,∗ and Sung June Kim 1

1 Department of Electrical and Computer Engineering, Seoul National University, Seoul, Republic of Korea
2 Department of Electronic and Electrical Engineering, Ewha Womans University, Seoul, Republic of Korea
3 Department of Biomedical Engineering, Pratt School of Engineering, Duke University, Durham, United States of America (On a leave of absence)
4 Center for Intelligent and Interactive Robotics, Korea Institute of Science and Technology, Seoul, Republic of Korea
5 Department of HY-KIST Bio-convergence, Hanyang University, Seoul, Republic of Korea
6 Graduate Program in Smart Factory, Ewha Womans University, Seoul, Republic of Korea
7 Division of Brain and Cognitive Sciences, Ewha Womans University, Seoul, Republic of Korea
8 The first two authors contributed equally to this work.

* Authors to whom any correspondence should be addressed.

E-mail: yslim@kist.re.kr and juns@ewha.ac.kr

Keywords: implantable connector, liquid crystal polymer, neural implant

Supplementary material for this article is available online

Abstract

Objective. Connectors for implantable neural prosthetic systems provide several advantages such as simplification of surgery, safe replacement of implanted devices, and modular design of the implant systems. With the rapid advancement of technologies for neural implants, miniaturized multichannel implantable connectors are also required. In this study, we propose a reconnectable and area-efficient multichannel implantable connector. Approach. A female-to-female adapter was fabricated using the thermal-press bonding of micropatterned liquid crystal polymer films. A bump inside the adapter enabled a reliable electrical connection by increasing the contact pressure between the contact pads of the adapter and the inserted cable. After connection, the adapter is enclosed in a metal case sealed with silicone elastomer packing. With different sizes of the packings, leakage current tests were performed under accelerated conditions to determine the optimal design for long-term reliability. Repeated connection tests were performed to verify the durability and reconnectability of the fabricated connector. The connector was implanted in rats, and the leakage currents were monitored to evaluate the stability of the connector in vivo. Main results. The fabricated four- and eight-channel implantable connectors, assembled with the metal cases, had a diameter and length of 6 and 17 mm, respectively. Further, the contact resistances of the four- and eight-channel connectors were 53.2 and 75.2 mΩ, respectively. The electrical contact remained stable during repeated connection tests (50 times). The fabricated connectors with packings having 125%, 137%, and 150% volume ratios to the internal space of the metal case failed after 14, 88, and 14 d, respectively, in a 75 °C saline environment. In animal tests with rats, the connector maintained low leakage current levels for up to 92 d. Significance. An implantable and reconnectable multichannel connector was developed and evaluated. The feasibility of the proposed connector was evaluated in terms of electrical and mechanical characteristics as well as sealing performance. The proposed connector is expected to have potential applications in implantable neural prosthetic systems.
1. Introduction

Neural implants are electrical devices placed inside the body for restoration of neural functions by modulating neural signaling in the nervous system [1–8]. A neural implant generally comprises two components: a stimulator generating electrical stimulation pulses and neural electrodes interfacing neurons or nerves. These two parts can be integrated into a single implantable system or connected through connectors and cables [9–14]. Combining the stimulator and neural electrodes into a monolithic system has the advantage of superior long-term reliability because of the seamless system design. However, implant surgery has drawbacks because it can be complicated, particularly when the electrodes are located far from the stimulator in the body [9–11]. In addition, if the implanted system includes a battery, the entire system needs to be replaced with a new one after the battery life runs out. Accordingly, separating an electrical stimulator from neural electrodes using hermetically sealed connectors can make the implant surgery more flexible and reduce the risk of infection during replacement surgery [12–14].

As various regions in the nervous system are targeted and the number of neural electrodes increases, various implantable connectors with different connecting mechanisms and materials have been proposed [12–20]. The ‘Craggs connector’, which is a plug-and-socket-type connector sealed with silicone rubber, was introduced for a lumbar anterior root stimulator system and experimentally tested for its long-term stability in conjunction with the stimulator [13, 15]. Further, a two-male-plug-type connector, called ‘in-line connector’, was used with an implantable stimulator system for neuromuscular excitation [12]. Another implantable connector with circular contact pads sealed with silicone elastomer O-rings has been successfully used for pacemakers or deep brain stimulation (DBS) systems [14, 16]. In addition, research groups have developed implantable connectors with a high number of channels. A 32-channel connector was fabricated on a silicon or polyimide substrate, and electrical contact with the stimulator was achieved through external housing parts. However, the long-term reliability of these connectors has not been evaluated in vitro or in vivo [17–20].

In this study, we propose an implantable and reconnectable connector that comprises a metal case and a microfabricated multichannel adapter. The multichannel adapter and cables are microfabricated using a liquid crystal polymer (LCP), and three-dimensional structures are formed via a thermal-press bonding process. To block the possible leakage paths, silicone elastomer packings are used to seal the gap between LCP cables and the metal housing [12, 14, 16]. Repeated connection tests and acceleration leakage tests are performed to demonstrate the durability and long-term reliability of the proposed connectors. Moreover, the sealed connector is implanted into rats to evaluate the stability in vivo.

2. Materials and methods

2.1. Connector design

The configuration of the proposed connector with the LCP-based adapter, cable, and metal case (SUS 304 stainless steel) is shown in figure 1. The adapter and cables are fabricated with a micropatterned LCP film, and thin layers of LCP films are stacked via the thermal-press bonding process to create three-dimensional structures such as small bumps and walls (figure 1(c)). Inside the adapter, the contact pads are located at the bottom, and small bumps create uniform contact pressure on the cables to form a stable electrical connection with contact pads on the adapter. Two different types of silicone elastomer packings are placed to seal the gap between the cable and the metal case or the joint area of the metal cases. Wedge-shaped packings are attached on the cable to block the leakage path between the cables and metal case, and ring-shaped packings are placed on the joint area of the metal cases. On the outer surface of a metal case, screw threads are formed to create a hermetic seal around the leakage paths by physically deforming the silicone elastomer packings upon fastening.

2.2. Fabrication of LCP-based adapter and cable

The fabrication process of the proposed adapter following the lamination processes that have been previously reported is depicted in figure 2 [21–25]. First, a 4 inch silicon wafer (thickness of 525 µm) was spin-coated with a silicone elastomer (MED-6233, Nusil Technology, CA, USA) at 2000 rpm for 70 s. After the silicone elastomer was cured at 100 °C for 8 h, an LCP film (Vecstar CT-Z 25 µm, Kuraray, Tokyo, Japan) was attached to the silicone wafer (figure 2(a)). The LCP film fixed on the silicon wafer was immersed sequentially in acetone, methanol, and isopropyl alcohol for 1 min each for surface cleaning of the LCP film. Further, oxygen plasma (150 W, 100 sccm, 3 min: Plasmalab 80 plus, Oxford Instruments, UK) was used to clean and activate the surface of the LCP film. Subsequently, 50 nm Ti and 150 nm Au layers were deposited as metal seed layers using an electron gun evaporator (ZSS550-2/D, Maestech Co., Ltd, Pyungtaek, Republic of Korea) for the following electroplating process (figure 2(b)). A photoresist (AZ 4620, Clariant, USA) was spin-coated at 2000 rpm for 40 s onto the metal seed layers, and photolithography was performed using an aligner machine (vacuum contact, 70 s; MA6/B6, SUSS MicroTec, Garching, Germany). After electroplating of a 10 µm Au layer (figures 2(c) and (d)), the photomask was removed with AZ 700 and the
metal seed layers were wet-etched using aqua regia for the Au layer and hydrofluoric acid for the Ti layer. Then, the LCP film with metal patterns was prepared (figure 2(e)). The metal-patterned LCP film was detached from the silicon wafer and cut to the size of a metal-pressing jig using a UV laser machining system (Samurai UV Marking System, DPSS Lasers Inc., CA, USA). Meanwhile, additional LCP films with a low melting temperature (Vecstar CT-F series, Kuraray, Tokyo, Japan) were prepared for the adapter structure. Additional LCP films were aligned in the metal jig with the metal-patterned LCP film and laminated together using a thermal press (10 min, 290 °C, 1 kgf cm⁻²; Model 4122, Carver, IN, USA) (figure 2(f)). In this step, the empty space of the metal jig was filled with melted LCP to form the bumps. After the laser-cutting process, the LCP-based adapter was fabricated (figure 2(g)). The LCP-based cables were fabricated using the same LCP-fabrication processes with a planar metal-pressing jig (figures 2(f’) and (g’)). After the thermal lamination, the outline of the cable was cut with a laser machining system. Further, the lead part was ablated by the laser system to make it thinner than the insertion part inserted into the adapter.

2.3. Assembly procedure

Two different types of silicone elastomer packings were used to assemble the LCP-based adapter, LCP-based cables, and metal case (figure 3). First, the cables were inserted into the adapter and the wedge-shaped packings (MED 6233, Nusil Silicone Technology, CA, USA) were positioned on both sides of the adapter to block the gap between the adapter and cables (figure 3(a)). Then, the ring-shaped packing (MED 6233, Nusil Silicone Technology, CA, USA) was placed between the metal cases to block their joints (figure 3(b)). Finally, the metal cases were fastened to provide mechanical pressures to the wedge- and ring-shaped packings, achieving hermetic sealing (figures 3(c) and (d)).

2.4. Repeated connection test

To examine the reconnectability of the proposed connector, a repeated connection test was performed. The resistance of each conductor line was measured during the repeated connection of the adapter and cable. Figure 4 shows the measurement setup for the line resistance (R_{\text{line}}) and contact resistance (R_{\text{contact}}) of the adapter. The line resistance was determined from the current (I) through the load resistor (R_{\text{load}}) and the voltage (V_{\text{Line}}) across the assembled adapter and cable. Further, the contact resistance of the adapter was calculated using the transmission line...
Figure 4. Electrical characteristic measurement of LCP-based adapter. (a) Measurement of assembled connector resistance ($R_{\text{Line}}$: line resistance, $R_{\text{Load}}$: load resistance, $I$: current through load resistor, and $V_{\text{Line}}$: voltage across the assembled connector). (b) Measurement of contact resistance between the connector and cable ($R_{\text{Cable}}$: cable resistance, $R_{\text{Adapter}}$: adapter resistance, and $R_{\text{Contact}}$: contact resistance).

The line resistance can be expressed as follows:

$$2R_{\text{Cable}} + R_{\text{Adapter}} = \rho L/A \quad (1)$$

$$R_{\text{Line}} = 2R_{\text{Cable}} + R_{\text{Adapter}} + 2R_{\text{Contact}} = \rho L/A + 2R_{\text{Contact}} \quad (2)$$

$$L = L_1 + L_2 + L_3 \quad (3)$$

where

- $\rho$ = Resistivity of the conductor;
- $L$ = Length of a conductor line;
- $A$ = Cross-sectional area of a conductor line;
- $L_1, L_2$ = Length of the cable;
- $L_3$ = Length of the conductor line in the adapter.

Because the line resistance depends on the length of conductor line, several measurements were performed with different cable lengths. Then, a graph of the line resistance versus the length of the conductor line was obtained. In the limit of a zero-length adapter, the residual resistance, which is twice the contact resistance, is obtained by extrapolating the plot back to $L = 0$ mm.

As the LCP-based cables were inserted into the LCP-based adapters for each connection, the line and contact resistances were measured as described above. Three adapters with four and eight channels were tested for 50 cycles while monitoring the line and contact resistances.

2.5. Leakage current test

Accelerated soak tests were conducted to evaluate the long-term reliability of the proposed connector (figure 5). The four-channel connector samples were immersed in a 75 °C phosphate-buffered saline (PBS) solution (10 010–023, pH 7.4, Gibco, Thermo Fisher Scientific, MA, USA), and deionized water was frequently supplied to maintain the water level and ion concentration. To decide the optimal shape of the silicone packings, various wedge-shaped packings were prepared with volume ratios of 125%, 137%, and 150% with respect to the internal space of the metal case ($n = 3$ for 125% and 150% volume ratio; $n = 4$ for 137% volume ratio; figure 6). As control groups, connector samples without a metal case but sealed only with either dental resin (500 µm; Charmfil Flow A3, ELI-DENT Group SpA, Fiorentino, Italy) or silicone elastomer (500 µm) were also prepared ($n = 3$ for each) [27].

The water leakage was determined through the presence of leakage currents between each conductor line and a platinum-wire reference electrode. Similarly, the crosstalk was determined from the presence of currents between the contact pads resulting from water penetration into the connector. The leakage and crosstalk currents were measured daily using...
Figure 7. Equivalent circuits of (a) two parallel metal lines for the crosstalk current model and (b) a metal line for the leakage current model. Metal lines of the same length and width are assumed.

Figure 8. Animal experiment for in vivo preliminary study. (a) Illustration of in vivo current measurement setup. (b) Photograph of anesthetized rat with an implanted connector sample and a custom-made wireless ammeter. The connector sample is connected to the wireless ammeter, which delivers measured leakage and crosstalk current data through wireless ZigBee transmission.

Figure 9. (a) Photograph and (b) detailed illustration of the in vivo surgical setup using Vascular Access Buttons™.

2.6. Modeling failure criteria

The failure criteria (current threshold level) were decided theoretically by modeling the different impedances involved in the stimulation path. Figure 7 depicts the equivalent circuits of connector channels with leakage and crosstalk currents. In these models, $Z_{\text{Elec}}$ represents the interface impedance, $Z_{\text{Sh}}$ the wire shunt impedance to ground, $Z_{\text{C}}$ the coupling impedance between two channels due to leakage, and $Z_{\text{Seal}}$ the sealing impedance of the outer solution. Assuming that $Z_{\text{Sh}} \gg Z_{\text{Elec}}$ and 1% crosstalk is considerable, the crosstalk current ($I_2$) has the following relationship:

$$I_2 < I_1 / 100 = V_{\text{in}} / (100 \times Z_{\text{Elec}}).$$

(4)

Based on the same 1% crosstalk criterion, the leakage current ($I_3$) is also limited as follows:

$$I_3 < I_1 / 100 = V_{\text{in}} / (100 \times Z_{\text{Elec}}).$$

(5)

Thus, the threshold level is determined by $Z_{\text{Elec}}$. In this study, all the gold sites were assumed to have the same area as the metal contact pad. Moreover, the stimulation current ($I_1$) was measured using the same electrode with the gold sites, which yielded 0.731 $\mu$A as a threshold level of currents.

2.7. Estimation of connector lifetime

We first calculated the mean time to failure (MTTF), which is defined as the average time after which either leakage or crosstalk current is higher than the threshold current level. Then, MTTF is applied to the common ten-degree rule to estimate the approximate lifetime of the connector:

$$f = 2^{(\Delta T/10)}, \text{ where } \Delta T = T - T_{\text{ref}}$$

(6)

where

- $f =$ increased rate of aging;
- $T =$ elevated temperature (75 °C);
- $T_{\text{ref}} =$ reference temperature (37 °C).

2.8. Animal implantation test

To demonstrate the implantation stability of the connector, in vivo animal experiments were performed with Spraque-Dawley rats (age: 9 weeks, weight: 300–350 g, sex: male, $n = 3$) (figure 8). For easy maintenance and prevention of infection, an access interface was prepared by modifying the structure of a commercial product (Vascular Access Buttons™, Instech Laboratories, Inc., USA). As shown in figure 9, an LCP-based cable and a platinum wire pass through the hole, penetrating the access interface. To minimize the tissue damage due to the bare LCP-based
shows the metal cases, where the adapter and cable were 53.2 and 75.2 m respectively. The contact resistances of the antibiotic (Gentamicin) and analgesic (carprofen (rimadyl®)) were 1.85 and 13 respectively. The line resistances at both ends of the cables were measured under the 75°C soak test of the samples with three different designs of the wedge-shaped adapter and cable. The LCP-based cable was coated with a thin layer of silicone elastomer (thickness: 500 µm). The empty space of the hole was filled with hemostatic gelatin sponge (Cutanplast standard, Mascia Brunell, Italy) and non-absorbable felt pledget (Polytetrafluoroethylene Suture Buttress, Ethicon, NJ, USA). The outer side was covered with additional super glue for achieving water tightness. The platinum-wire reference electrode was sewn with an overcast stitch on the felt for stable placement after implantation. During surgery, anesthesia was induced using isoflurane, and the sterilized access interface combined with the connector was placed on the backside and implanted under the skin. After surgery, the wound was sutured and 20 mg kg⁻¹ antibiotic (Gentamicin) and 5 mg kg⁻¹ analgesic (carprofen (rimadyl®)) were administered to the animal subcutaneously. Upon suturing the skin with felt, the access interface maintained its position without additional anchoring. This access interface was located on the backside to prevent the rats from touching the wound site, allowing them to recover quickly. The protective metal cap was placed on the opposite side of the contact pads, having a radius of 100 µm (or height). The cables have two parts with different thicknesses; the thick part, which is inserted into the adapter, has a thickness of 450 µm, and the thin lead part has a thickness of 250 µm (figures 11(c) and (d)) shows the cross-sectional view of the adapter, where the cable is inserted to make contact with contact pads on the adapter. Figure 12 shows the metal cases, where the adapter and cables are inserted and sealed with the wedge and ring-shaped silicone packings. The outer diameter and length of the metal case are 6 and 17 mm, respectively. The ring-shaped packing is designed to be 100 µm thicker than the groove in the metal cases, and the wedge-shaped packing has a larger volume than the internal space of the metal case (see the details on the accelerated soak test result.). As the metal cases are fastened, mechanical pressure is applied to the wedge- and ring-shaped packings, creating a hermetic sealing for the connector.

3.2. Electrical and mechanical characteristics
Figure 13 shows the measured line resistance of the proposed connector of the four- and eight-channel adapters (n = 3 for each). The contact resistances of the adapters calculated in the limit of zero length (L = 0 mm) were 53.2 and 75.2 mΩ, respectively. To test the reliability of the electrical connections, the line resistances at both ends of the cables were measured by repeatedly inserting cables into the adapter. At the first connection, the average line resistance was 1.01 Ω for the four-channel adapters and 1.85 Ω for the eight-channel adapters. However, we did not find any significant changes in the measured resistance values over 50 cycles of insertion. In addition, there was no apparent damage to the contact pads of the LCP-based adapters and cables after the repeated tests.

3.3. Accelerated soak test
Figure 14 shows the leakage and crosstalk currents measured under the 75°C soak test of the samples with three different designs of the wedge-shaped
either the average leakage current or crosstalk current exceeded the threshold current level (threshold level = 0.731 µA).

The MTTF due to water penetration into the connector was 2 d for the dental resin sealing and 25 d for the silicone elastomer sealing (figures 14(a) and (b)), implying that the connector could be maintained without water leakage for 27 and 347 d at body temperature. For the connector samples with three different designs of the wedge-shaped packing, water penetration was observed after 14, 88, and 14 d, corresponding to 194, 1214, and 194 d, respectively (equation (6), ten-degree rule is applied) [28].

3.4. In vivo preliminary study
After the implantation of the sealed connector in the rat, the leakage and crosstalk currents were measured for 3 months. The connector samples with the wedge-shaped packing having 137% volume ratio, which showed the longest life expectancy in the leakage current test, were selected as a final design and implanted into the rat. In figure 15, the measured leakage currents upon application of a DC bias voltage during the in vivo stability test are plotted. For animal #1, the maximum leakage current was 1.771 ± 0.160 µA at day 25, and the maximum crosstalk current was 0.568 ± 0.211 µA at day 39. For animal #2, the maximum leakage current was 0.178 ± 0.081 µA (day 18), and the maximum crosstalk current was 0.102 ± 0.009 µA (day 78). For animal #3, the maximum leakage current was 0.206 ± 0.131 µA (day 36), and the maximum crosstalk current was 0.148 ± 0.021 µA (day 13). The measured leakage and crosstalk current levels remained below the threshold level (0.731 µA) for three months, excluding the leakage currents from animal #1 (25–41 d). This is considered to be because the reference electrode became unstable owing to an inflammatory reaction around it.
Figure 14. (a)–(e) Leakage and crosstalk current measurements during the accelerated soak test. Designs 1, 2, and 3 depict the connector samples with the wedge-shaped packing having 125%, 137%, and 150% volume ratio, respectively. Vertical lines represent the failure day of each connector sample. Among the measured currents in each four-channel connector sample, leakage and crosstalk currents that reached the threshold level first are shown. Among the four channels, connector sample W2-4 failed on day 105 owing to operation error. (f) MTTFs of the connector samples (threshold level: 0.731 µA; EL: estimated lifetime).

Figure 15. Leakage and crosstalk current measurements during the in vivo animal test. (a) In vivo leakage current measurement graph, (b) in vivo crosstalk current measurement graph over a period of approximately three months (threshold level: 0.731 µA).

4. Discussion

The proposed implantable and reconnectable connector comprises an adapter for linking multichannel cables (four or eight channels) and a metal case for hermetic sealing around the adapter and cables. The basic material of the adapter and cables is a thin LCP film, on which metal contact pads and
Conductor lines are microfabricated and each layer of the LCP film is stacked via simple thermal press bonding (figure 11). To block the leakage path between heterogeneous materials (e.g. between an LCP-based cable and a metal case), silicone elastomer packings are inserted on either the cable or metal case (figure 12). The proposed connector has a maximum diameter of 6 mm and a length of 17 mm (figure 12). Repeated connection tests revealed that the proposed connector was mechanically stable enough to maintain electrical connections for over 50 cycles. We also demonstrated the feasibility of the proposed connectors for neural implants through leakage current tests and in vivo experiments. Leakage current tests in an accelerated saline environment showed that the proposed connector could have a life expectancy of approximately three years (figure 14). Furthermore, the implantation stability was evaluated through three months of in vivo animal tests (figure 15).

To realize minimally invasive surgery for implantation, the implantable connector needs to be miniaturized and have a high channel density. However, previous implantable connectors were composed of metal wires sealed with relatively large housings that would guarantee a long-term electrical connection but with a small number of channels (up to four channels) [12–16] (table 1). Therefore, to overcome physical constraints such as size and number of channels, the proposed implantable connector is equipped with electrical sockets or adapters made of LCP, which is compatible for microfabrication and biocompatible for long-term implantation. We experimentally demonstrated that the proposed connector could provide stable electrical connections for up to eight channels sealed with a small metal housing (diameter: 6 mm, length: 17 mm). The developed four- and eight-channel connectors have channel densities of 14.2 and 28.3 channels cm⁻², respectively, which are similar to or higher than those of previously reported implantable connectors (table 1). However, for application to neural implant devices having a higher number of channels, such as cochlear implants, increasing the number of channels is necessary; this is achievable by patterning more contact pads with a higher density on the LCP film.

The primary material of the adapter and cables is LCP, which is well known for its biocompatibility and mechanical stability. However, we believe that the suggested connector could be fabricated using other biocompatible polymer materials such as polyimide, parylene C, and cyclo-olefin polymers [29–34], which enable small and lightweight packaging to be fabricated for neural implant systems [11, 27, 35]. Moreover, flexible multichannel neural electrodes have been proposed using similar biocompatible polymers compatible with microfabrication processes [29, 31, 33, 34]. This means that electrical cables with different materials (e.g. a polyimide-based neural electrode) could be connected with the proposed connector.

To deliver electrical pulses from a stimulator to a neural electrode, the contact resistance of the implantable connector should be small enough not to alter the electrical characteristics of the cable. Further, the lower the contact resistance, the larger is the compliance voltage for the stimulation electrode that can be obtained [36]. The electrical contacts of the proposed LCP-based adapter were successfully

| Type                                      | Number of channels | Diameter (mm) | Channel density (# of ch. cm⁻²) | Length (mm) | Sealing method       | Long-term reliability | Usage                      |
|-------------------------------------------|--------------------|---------------|---------------------------------|-------------|----------------------|-----------------------|--------------------------|
| Craggs connector                          | 1, 3               | 7.5           | 2.26, 6.79                      | 60          | Adhesive sealant      | 2 years (implant)      | Lumbar anterior root stimulator, Custom neural stimulator |
| In-line lead connector                    | 1                  | 3.5           | 10.4                            | 30          | Silicone elastomer suture packing | 49 months (implant)    |                         |
| Circular contact pad connector            | 1–4                | 4.06          | 7.72–30.9                       | 30          | Silicone elastomer packing Polyimide O-ring, vacuum | Application in the patient (pacemaker, DBS) | DBS, bladder stimulator |
| Modular micromachined high-channel connector | 32                | 12.5          | 26.1                            | 2.5         | Silicone elastomer packing | No leakage test, acute animal experiment (brain cortex recording) | <4 years (accelerated soak test, estimated) |
| Proposed connector                        | 4, 8               | 6             | 14.2, 28.3                      | 17          | Silicone elastomer packing |                       | —                        |
established using the bump structure inside the adapter and the inserted cable (figure 11(d)). In addition, the contact resistances of the four- and eight-channel adapters were measured to be 53.2 and 75.2 mΩ, respectively. The contact resistances were maintained over 50 cycles of repeated connection tests. Consequently, the fabricated LCP-based adapter could form an effective and secure electrical connection with the cable.

Hermetically sealing the implantable connector is essential for long-term usage and reliability. In addition, for repeated disassembly and reassembly procedures of the connector, sealing materials need to have good mechanical strength and stability. To provide a hermetic and durable barrier between implanted devices and body fluid, biocompatible metals have been used for achieving higher sealing performance and longer lifetime than other materials such as polymers or ceramics [28, 35, 37–40].

In this study, we used SUS 304 stainless steel to block the possible leakage paths along the fabricated adapter or cable. SUS 304 stainless steel is known to be biocompatible and is widely employed in biomedical applications [41, 42]. Moreover, owing to the good wear resistance characteristics of SUS 304 stainless steel, the metal cases are expected to withstand repeated mechanical abrasion from several reassembly procedures, which was confirmed from repetitive assembly and reassembly tests conducted in this study [43]. In this study, the hermeticity of the proposed connector was tested under two experimental conditions: accelerated soak test and in vivo animal test. In the accelerated soak tests, the connector samples with the metal cases exhibited an MTTF of 88 d (approximately three years in body fluid), whereas connectors sealed with only dental resin or silicone elastomer showed an MTTF of 2 or 25 d, respectively.

A preliminary study was conducted to optimize the in vivo animal study protocol. For monitoring animal behavior in the pilot test, above the skull or behind the neck was not a proper area for implanting the sealed connector. Considering the rodents’ grooming habit, without the access interface, the wound would get easily infected repeatedly. Consequently, at the end of the test, the implanted device was revealed through the wounds. Therefore, a protective structure for a stable experimental period longer than a month was required. The main animal study was conducted under a 3 month schedule; however, the animal subjects were healthy at the end of the study period, suggesting the possibility of long-term in vivo studies.

Although the feasibility of the proposed connector has been demonstrated by the accelerated soak test and in vivo preliminary study, further studies are needed to evaluate reliability in more detail. For example, in this study, the accelerated soak test was performed in a state of rest with no force applied to the connector. However, sustained or repeated stress may be applied to the implanted devices in long-term animal tests or clinical applications depending on the target region of the neural implant. Thus, additional accelerated tests with mechanical stress, such as flexural test, fatigue test, or tensile test, are necessary [44, 45]. Furthermore, additional accelerated tests can be considered to estimate lifetimes more accurately. The estimated lifetime of the proposed connector was obtained as the MTTF under one temperature condition (75 °C) by applying the ten-degree rule. The ten-degree rule assumes that increasing the temperature by about 10 °C roughly doubles the rate of aging [46]. However, if various MTTFs are compared under multiple temperatures, the lifetime can be estimated more accurately at the body temperature [28, 46].

In addition, other possible damages induced by biological sources such as fibrosis and enzymes can be verified. Tissue damage and blood leakage, which are inevitably generated during the implantation process, initiate an acute foreign body reaction (FBR) reaction of inflammatory-mediating cells. M1 macrophages (pro-inflammatory activation phenotype) form a layer around the implant and release degrading enzymes and reactive oxygen species for phagocytosis. This process can reveal surface degradation and cracking as factors affecting implant stability [47, 48]. In the chronic stage of FBR, M1 macrophages are converted to M2 macrophages (anti-inflammatory and tissue-generating phenotype), attracting and organizing fibroblasts to the implant surface, resulting in fibrous encapsulation.

Nonetheless, the estimated lifetime is still short for use in a clinical application. In this study, the silicone elastomer packings were placed between the cable and metal case or the joint area of the metal cases, which is known to have relatively high water-vapor permeability [49]. This means that water molecules could penetrate through the packings themselves. Several studies have proposed methods to control the permeability of silicone elastomers by synthesizing composites using different materials such as collagen, carbon black, and carbon nanotubes [49–51]. These studies have also demonstrated that silicone elastomer packings with lower water-vapor permeability could be fabricated, which may enhance long-term reliability and increase the lifetime of the proposed connector.

5. Conclusion

In this study, we have proposed an implantable and re-usable connector with high channel density. A female-to-female LCP-based adapter is fabricated using micropatterning and thermal bonding processes. The developed four- and eight-channel adapters tightened by metal cases have a diameter of 6 mm and a length of 17 mm, resulting in a channel density of 14.2 and 28.3 channels cm$^{-2}$, respectively.
We demonstrated its reconnectability and long-term reliability through a repeated connection test, leakage current test, and an in vivo test. The LCP-based adapter maintained a consistent contact resistance during 50 trials of repeated connections, and the connector sealed with silicone packings and metal cases lasted for 88 d in PBS at 75 °C (approximately three years in body fluid). The results of the current study demonstrate the feasibility of long-term implantation of LCP-based connectors sealed with stainless steel cases. However, increasing the channel number and lifetime of the connector for application to multichannel neural implants is necessary. In addition, long-term reliability needs to be further investigated using functioning neural implants for extended periods.

Data availability statement

All data that support the findings of this study are included within the article (and any supplementary files).

Acknowledgments

The authors disclose no conflicts of interest.

This research was supported by the CABMC grant funded by the Defense Acquisition Program Administration (UD170030ID) of Korea, the National Research Foundation of Korea (NRF) grant funded by project BK21 FOUR, the NRF funded by the Korea government (NRF-2022R1H1A4063209), the Korea Medical Device Development Fund grant funded by the Korea government (1711139110, KMDF_PR_20210527_0006), and the National Research Council of Science and Technology (NST) grant by the Korea government (MSIT) (No. CAP21051-200).

ORCID iDs

Gwang Jin Choi https://orcid.org/0000-0003-0212-2960
Hyun Ji Yoo https://orcid.org/0000-0001-5011-2084
YoonKyung Cho https://orcid.org/0000-0002-8166-4233
Seunghyeon Yun https://orcid.org/0000-0003-2885-043X
Jaehoon Sung https://orcid.org/0000-0002-2435-8344
Yoonseob Lim https://orcid.org/0000-0003-4754-6038
Sang Beom Jun https://orcid.org/0000-0003-3912-250X
Sung June Kim https://orcid.org/0000-0001-7902-1223

References

[1] Kessler D K, Loeb G E and Barker M J 1995 Distribution of speech recognition results with the Clarion cochlear prosthesis Ann Otol. Rhinol. Laryngol. 104 283–5 (available at: https://viterbi.usc.edu/pdfs/globel/49630.pdf)
[2] An S K, Park S I, Jun S B, Lee C J, Byan K M, Sung J H, Wilson B S, Rebischer S J, Oh S H and Kim S J 2007 Design for a simplified cochlear implant system IEEE Trans. Biomed. Eng. 54 973–82
[3] Wilson B S and Dormann M F 2007 The surprising performance of present-day cochlear implants IEEE Trans. Biomed. Eng. 54 969–72
[4] Johnson M D, Miocinovic S, McIntyre C C and Vitek J L 2008 Mechanisms and targets of deep brain stimulation in movement disorders Neurotherapeutics 5 294–308
[5] Arle J E and Shils J L 2008 Motor cortex stimulation for pain and movement disorders Neurotherapeutics 5 37–49
[6] Kelly S K et al 2011 A hermetic wireless subretinal neurostimulator for vision prostheses IEEE Trans. Biomed. Eng. 58 3197–205
[7] Weiland J D, Cho A K and Humayun M S 2011 Retinal prostheses: current clinical results and future needs Ophthalmology 118 2227–37
[8] Stangle K et al 2013 Artificial vision with wireless powered subretinal electronic implant alpha-IMS Proc. R. Soc. 280 20130077
[9] Jackler R K, Leake P A and McKernow W S 1989 Cochlear implant revision: effects of reimplantation on the cochlea Ann. Otol. Rhinol. Laryngol. 98 813–20
[10] Ray J, Proops D, Donaldson I, Fielden C and Cooper H 2004 Expantation and reimplantation of cochlear implants Cochlear Implants Int. 5 160–7
[11] Jeong J, Bae S H, Min K S, Seo J M, Chung H and Kim S J 2015 A miniaturized, eye-conformable, and long-term reliable retinal prosthetic device using monolithic fabrication of liquid crystal polymer (LCP) IEEE Trans. Biomed. Eng. 62 982–9
[12] Letechipia J E, Peckham P H, Gazdik M and Smith B 1991 In-line lead connector for use with implanted neuroprosthesis IEEE Trans. Biomed. Eng. 38 707–9
[13] Rushion D N, Tromans A M and de N Donaldson N 2002 A reconnectable multiway implantable connector Med. Eng. Phys. 24 691–4
[14] Mond H G, Helland J R and Fischer A 2013 The evolution of the cardiac implantable electronic device connector Pacing Clin. Electrophysiol. 36 1434–46
[15] Donaldson P K 1985 The Cragg connector: a termination for cooper cable Med. Biol. Eng. Comput. 23 195–6
[16] Lee S W, Lee M K, Seo I, Kim H S, Kim J H and Kim Y S 2014 A groove technique for securing an electrode connector on the cranial bone: case analysis J. Korean Nucl. Soc. 56 130
[17] Akin T, Zaia B and Najafi K 1996 A modular micromachined high-density connector for implantable biomedical systems Proc. Ninth Int. Workshop Micro Electron. Syst. pp 497–502
[18] Akin T, Zaia B, Nikles S A and Najafi K 1999 A modular micromachined high-density connector system for biomedical applications IEEE Trans. Biomed. Eng. 46 471–80
[19] Koch J, Ordonez J S, Steiglitz T and Schuettler M 2015 Development of a multichannel implantable connector 2015 37th Annu. Int. Conf. IEEE Eng. Med. Biol. Soc. (EMBC) pp 805–8
[20] Koch J, Schuettler M and Steiglitz T 2017 Design of contact zone topology for implantable high-channel electrical connectors 2017 39th Annu. Int. Conf. IEEE Eng. Med. Biol. Soc. (EMBC) pp 238–41
[21] Lee S W, Seo J M, Ha S, Kim E T, Chung H and Kim S J 2009 Development of microelectrode arrays for artificial retinal implants using liquid crystal polymers Investigative Ophthalmol. Vis. Sci. 50 5859–66
