저작자표시-비영리-변경금지 2.0 대한민국

이용자는 아래의 조건을 따르는 경우에 한하여 자유롭게

- 이 저작물을 복제, 배포, 전송, 전시, 공연 및 방송할 수 있습니다.

다음과 같은 조건을 따라야 합니다:

저작자표시. 귀하는 원저작자를 표시하여야 합니다.

비영리. 귀하는 이 저작물을 영리 목적으로 이용할 수 없습니다.

변경금지. 귀하는 이 저작물을 개작, 변형 또는 가공할 수 없습니다.

- 귀하는, 이 저작물의 재이용이나 배포의 경우, 이 저작물에 적용된 이용허락조건을 명확하게 나타내어야 합니다.
- 저작권자로부터 별도의 허가를 받으면 이러한 조건들은 적용되지 않습니다.

저작권법에 따른 이용자의 권리는 위의 내용에 의하여 영향을 받지 않습니다.

이것은 [이용허락규약\(Legal Code\)](#)을 이해하기 쉽게 요약한 것입니다.

[Disclaimer](#)

Ph.D. DISSERTATION

**A Polymer Cochlear Electrode Array:
Atraumatic Deep Insertion, Tripolar
Stimulation, and Long-Term
Reliability**

폴리머 인공와우 전극: 비외상성 심부 삽입, 3극 자극,
장기 신뢰성

BY

Tae Mok Gwon

FEBRUARY 2018

**DEPARTMENT OF ELECTRICAL ENGINEERING AND
COMPUTER SCIENCE
COLLEGE OF ENGINEERING
SEOUL NATIONAL UNIVERSITY**

**A Polymer Cochlear Electrode Array:
Atraumatic Deep Insertion, Tripolar
Stimulation, and Long-Term Reliability**

지도 교수 김 성 준

이 논문을 공학박사 학위논문으로 제출함
2018년 2월

서울대학교 대학원
전기·컴퓨터공학부
권 태 목

권태목의 공학박사 학위논문을 인준함
2018년 2월

위 원 장 전 국 진 (인)

부위원장 김 성 준 (인)

위 원 오 승 하 (인)

위 원 이 종 호 (인)

위 원 민 규 식 (인)

Abstract

Biocompatible polymers have gained widespread interest in implantable biomedical applications due to their flexibility and compatibility with micro-fabrication processes. Liquid crystal polymer (LCP) is an inert, highly water-resistant, and thermoplastic polymer suitable for the encapsulation of electronic components and as a base material for fabricating neural interfaces. Feasibility of monolithic integration of neural interface and electronics packaging and its extremely low water absorption rate ($< 0.04\%$) enable LCP-based implantable devices that have salient benefits in terms of performance and reliability. In this dissertation, new design of LCP-based neural interfaces, especially cochlear electrode arrays, are proposed and evaluated within their purposes on fabrication process, functionality, and reliability. The following issues of LCP-based cochlear electrode arrays are studied: atraumatic deep insertion, tripolar stimulation, and long-term reliability.

Flexible LCP-based cochlear electrode array has been studied, but, there is no electrode design for an atraumatic insertion in terms of structural approach. An atraumatic cochlear electrode array has become indispensable to high-performance cochlear implants such as electric acoustic stimulation

(EAS), wherein the preservation of residual hearing is significant. A new design of cochlear electrode array based on LCP for an atraumatic implantation using precise batch fabrication and thermal lamination process unlike conventional wire-based cochlear electrode array is proposed. Multi-layered structure with variable layers of LCP films depending on the parts of the array to achieve a sufficient degree of basal rigidity and a flexible tip is devised and a peripheral blind via contributes to reduction of the width of the array. The diameters of the finalized electrode arrays are 0.3 mm (tip) and 0.75 mm (base). *In vitro* force measurements in a customized experimental setup reveal that the insertion force with a displacement of 8 mm from a round window and the maximum extraction force are 2.4 mN and 34.0 mN, respectively. Five human temporal bone insertion trials show that the electrode arrays can be inserted from 360° to 630° without trauma at the basal turn. Electrically evoked auditory brainstem responses are successfully recorded acutely in a guinea pig model, which confirms the efficacy of the array. Hearing preservation and tissue reaction are investigated during and after 4 weeks implantation of LCP electrode array.

For high-density and pitch-recognizable cochlear implant, channel interaction should be concerned. There have been efforts to increase distinct stimulation channel using advanced focused current stimulation methods

including tripolar stimulation. In this dissertation, structural considerations on electrode sites are approached for locally focused stimulation. A 3-dimensional arrangement of electrode site in multi-layered structure is practicable to be fabricated because differently patterned LCP layers can be merged into one substrate by thermal compression bonding. 3-dimensional electrode site structures for locally tripolar stimulation are simulated about electrical field distribution using finite element method. LCP electrode array of center stimulation channel with side wall auxiliary channel for tripolar stimulation is fabricated from the result of simulation. Compared with conventional monopolar and tripolar stimulation, locally tripolar stimulation on the proposed electrode site structure is more focused through *in vitro* measurements, which shows that spreading of electrical stimulation in electrolyte.

Device reliability is one of the most significant issues in polymer-based neural prostheses. Two technical strategies are suggested in this dissertation. One strategy adopts mechanical interlocking structure at metal-polymer interface, which is started by J. H. Kim. This study deepens his works and analyzes the impact of the strategy in terms of device reliability. The polymer-metal interface is vulnerable to water penetration that causes detrimental device failure. A goal is to suggest a feasible fabrication method

using mechanical interlocking to improve polymer-metal adhesion in polymer-based neural electrodes and evaluate its impact on device reliability quantitatively through *in vitro* measurements. After the metal patterns with undercut profile cross-sections are fabricated using a dual photolithography process and electroplating, the LCP interlocks with the metal during the lamination process. In a 180° peel test, the average maximum adhesion force of the samples with and without mechanical interlocking was 19.24 N and 14.27 N, respectively. *In vitro* accelerated soak tests that consist of interdigitated electrode patterns and a customized system for measuring the leakage current show that samples with and without interlock fail to function after 224 days and 185 days, respectively, in a 75°C saline. Scanning electron microscopy images reveal that the interlocked LCP-metal interfaces remained intact after water leakage.

The other strategy is to use dielectric materials in LCP-based neural implants. Dielectric materials such as silicon dioxide and silicon nitride have been used in neural implants to prevent water and ion penetration. In addition to these features, dielectric materials can maintain the metal patterning during lamination bonding process which causes migration of metal patterning on LCP substrate. With consideration on the role of dielectric materials in the LCP-based device and their effects on device

reliability, preliminary tests, including peel test to evaluate adhesion strength between LCP and dielectric materials compared with that of LCP-LCP interface and thermo-compression bonding process of LCP and dielectric materials with metal patterning to observe metal migration, are performed. LCP-dielectric materials interface is more adhesive than weakly bonded LCP-LCP interface and there is no metal migration after lamination process (295 °C, 1 MPa). The results confirm the possibility of the strategy.

Finally, a review of long-term reliability in LCP-based neural prosthetic devices including recently developed enabling technologies, demonstrated prototype devices and their performance capabilities as well as theoretical fundamentals is presented in the dissertation. Verification foretells the development of cochlear electrode array for an atraumatic deep insertion, advanced stimulation, and long-term clinical implant.

Keywords: polymer-based neural prosthesis, cochlear electrode array, liquid crystal polymer, atraumatic insertion, focused stimulation, long-term reliability

Student Number: 2012-20740

Contents

Abstract	3
Contents	8
List of Figures	15
List of Tables	24
List of Abbreviations	25
Chapter 1 Introduction	28
1.1 Overview of Neural Prostheses and Cochlear Implant	29
1.2 Review of Cochlear Electrode Array	32
1.2.1 Conventional Cochlear Electrode Array	33
1.2.2 Polymer-Based Cochlear Electrode Array	34
1.3 Proposed Polymer Cochlear Electrode Array	35
1.3.1 Electrode Array for Atraumatic Deep Insertion	36
1.3.2 Electrode Array for Tripolar Stimulation	37
1.4 Long-Term Reliability of Polymer-Based Neural Prostheses	38

1.5 Objectives of the Dissertation	40
Chapter 2 Materials and Methods	43
2.1 Liquid Crystal Polymer (LCP)	44
2.1.1 Material Properties and Types of LCP	46
2.1.2 MEMS Technologies compatible with LCP	49
2.2 Cochlear Electrode Array for Atraumatic Deep Insertion	51
2.2.1 Electrode Design	51
2.2.2 Fabrication Process	55
2.2.3 Experimental Setup and Protocol of <i>In Vitro</i> and <i>In Vivo</i> Evaluation Tests	57
2.2.3.1 Insertion and Extraction Force Measurements in Scala Tympani Model	57
2.2.3.2 Human Temporal Bone Insertion Studies	58
2.2.3.3 <i>In Vivo</i> Animal Study	60
2.2.3.3.1 Acute Implantation and Electrically Evoked Auditory Brainstem Response (EABR) Recording	60
2.2.3.3.2 Hearing Preservation and Histologic	

Evaluation	61
2.3 Polymer Electrode Array for Tripolar Stimulation	63
2.3.1 Modeling and Simulation of Polymer-Based Cochlear Electrode Array for Tripolar Stimulation	63
2.3.1.1 Simulation Tool and Modeling	65
2.3.1.2 Electrode Designs	66
2.3.2 Fabrication Process	68
2.3.3 <i>In Vitro</i> Measurements	69
2.3.3.1 Test Board for Tripolar Stimulation	69
2.3.3.2 Experimental Setup and Protocol	70
2.4 Long-Term Reliability Analysis of LCP-Based Neural Implants	71
2.4.1 Overview of the Long-Term Reliability	73
2.4.1.1 Failure Mechanism	73
2.4.1.2 Measurement Methods for Reliability Analysis	74
2.4.2 Technical Strategies to Improve Reliability of LCP- Based Implantable Device	76
2.4.2.1 Mechanical Interlocking to Strengthen Metal-LCP	

Adhesion	76
2.4.2.1.1 Fabrication Process using Dual Lithography and Electroplating	77
2.4.2.1.2 <i>In Vitro</i> Peel Test and Electrochemical Measurements	80
2.4.2.1.3 <i>In Vitro</i> Accelerated Soak Test	81
2.4.2.1.4 Visual Inspection and Statistical Analysis -	83
2.4.2.2 Fabrication using LCP and Dielectric Materials --	84
2.4.2.2.1 Role of Dielectric Materials	84
2.4.2.2.2 Proposed Fabrication Process	85
2.4.2.2.3 Preliminary Study	86
2.4.3 Experimental Comparison LCP-Based to Wire-Based Electrode Array	87
Chapter 3 Results	90
3.1 LCP-Based Cochlear Electrode Array for Atraumatic Deep Insertion	91
3.1.1 Fabricated Electrode Array	91
3.1.2 Insertion and Extraction Force Measurements	91

3.1.3	Insertion Trauma in Human Temporal Bone Insertion Study	93
3.1.4	Electrically Evoked Auditory Brainstem Response Recording	98
3.1.5	Histological Change and Hearing Preservation	100
3.2	Polymer Electrode Array for Tripolar Stimulation ---	103
3.2.1	Simulation Results according to Electrode Site Design --	103
3.2.2	Fabricated Electrode Array	107
3.2.3	<i>In Vitro</i> Measurements	109
3.3	Long-Term Device Reliability	111
3.3.1	LCP-Based Neural Electrode Array using Mechanical Interlocking at Metal-LCP Interface	111
3.3.1.1	Fabricated Electrode Array and Metal-LCP Interface	111
3.3.1.2	Adhesion Force and Electrochemical Measurements	113
3.3.1.3	Accelerated Soak Test and Lifetime Estimation -	115
3.3.2	Fabrication Method using LCP and Dielectric Materials -	117
3.3.2.1	Adhesion Strength of Bonding between LCP and	

Dielectric Materials	117
3.3.2.2 Lamination Result of the Proposed Fabrication Method	117
3.3.3 Impedance Measurements of LCP-Based and Wire-Based Electrode Array	118
Chapter 4 Discussion	121
4.1 LCP-Based Cochlear Electrode Array for Atraumatic Deep Insertion	122
4.1.1 Comparison of the Current Proposed Electrode Array to the Previous Electrode Array	122
4.1.2 Suggestion of Improvement in Electrode Design Related with Insertion Depth and Trauma	127
4.1.3 Point to Improve in Fabrication Process	129
4.1.4 <i>In Vivo</i> Implantation	132
4.2 Power Consumption and Stimulation Threshold of Tripolar Stimulation	134
4.3 Technical Strategies to Improve Device Reliability ...	136
4.3.1 Mechanical Interlocking at Metal-Polymer Interface -	136
4.3.2 Hybrid Device Based on Polymer and Dielectric	

Materials	143
4.4 Review of Long-Term Reliability of LCP-Based Device	145
Chapter 5 Conclusion	154
References	158
Abstract in Korean	170
감사의 글	174

List of Figures

Figure 2.1 Conceptual view of LCP-based implantable neural prosthesis -----	46
Figure 2.2 (a) LCP film (Kuraray, Tokyo, Japan) (b) Optical image of LCP surface -	47
Figure 2.3 (a) Basic fabrication process of LCP-based neural implants using MEMS technologies (b) Results of photolithography (i), electroplating and seed layer etching (ii) -----	51
Figure 2.4 Cross-section view of the design of tapered LCP-based cochlear electrode array for atraumatic deep insertion -----	54
Figure 2.5 Image of proposed cochlear electrode array using blind via -----	54
Figure 2.6 Fabrication process flow of tapered LCP-based cochlear electrode array using MEMS technologies, thin-film process, and thermal lamination process (a) Seed layer (Titanium and gold) deposition (b) Photolithography using AZ 4620 photoresist (c) Electroplating for thick metal lines (d) Developing photoresist and wet etching seed layer using nitrohydrochloric acid and hydrofluoric acid (e) Laser cutting of align holes and aligning LCP layers with pre-cut cover layer (f) Thermal lamination process for monolithic encapsulation -----	56
Figure 2.7 Experimental setup of insertion and extraction force measurements in plastic scala tympani model [51] -----	58

Figure 2.8 Human temporal bone insertion study and insertion depth [39] -----	59
Figure 2.9 3D Slicer version 4 -----	60
Figure 2.10 Acute implantation of the LCP-based cochlear electrode array into guinea pig (a) ABR recording in the soundproof room (b) Implantation surgery -----	61
Figure 2.11 Dummy LCP electrode array implantation surgery for hearing preservation and histological evaluation -----	63
Figure 2.12 Explanation of current focusing stimulation method -----	64
Figure 2.13 Modeling of human cochlea and implantation of an electrode array -----	66
Figure 2.14 Designs of electrode sites in the simulation -----	68
Figure 2.15 PWM data structure and Serial data format [91] -----	70
Figure 2.16 Outline of the test board used <i>in vitro</i> measurements of current focusing -----	70
Figure 2.17 (a) Block diagram and (b) Image of the experimental setup for <i>in vitro</i> current focusing measurements -----	71
Figure 2.18 Water penetration in (a) Metal-based neural prosthesis and (b) LCP- based neural prosthesis -----	73
Figure 2.19 Three pathways through which water ingress occurs -----	74
Figure 2.20 Conceptual view of mechanical interlocking at metal-polymer interface	

in the polymer-based neural electrode array -----	77
Figure 2.21 Fabrication processes of a LCP-based neural electrode with mechanical interlocking using MEMS technologies, including oxygen plasma, e-gun evaporation, dual steps of photolithography and electroplating, and wet etching -----	
	77
Figure 2.22 Design of test samples categorized according to the formation of the mechanical interlocking structures -----	
	79
Figure 2.23 Experimental setup for <i>in vitro</i> accelerated soak test (a) Test samples are immersed in PBS at 75°C to imitate a body environment. The test setup consists of a multichannel current stimulator to apply continuous biphasic pulses, a picoammeter for leakage current measurements, an interfacing circuit to switch between the stimulation mode and the leakage current measurement mode, and a deionized water tank to maintain the ion concentration of the PBS. (b) The interfacing circuit board, with the switch for mode conversion, and the test electrode sample are connected with an extension cable and a board.-----	
	82
Figure 2.24 Migration of metal pattern after lamination process -----	
	85
Figure 2.25 Experimental setup of customized peel test -----	
	86
Figure 2.26 (a) Experiment setup for comparison metal wire to polymer electrode array (b) Mold design for silicone elastomer curing (c) Mask design for photolithography (d) Metal-patterned LCP film -----	
	89

Figure 3.1 LCP-based cochlear electrode array with tapered structure	91
Figure 3.2 Insertion force measured in the plastic scala tympani model	92
Figure 3.3 Extraction force measured in the plastic scala tympani model	93
Figure 3.4 Human temporal bone insertion study of electrode 1 (Round window approach) (a) Micro-CT image for insertion depth (450°) (b) Reconstructed 3-D image (c) Cross-sectional views of cochlea where LCP electrode array is inserted (Trauma 0)	94
Figure 3.5 Human temporal bone insertion study of electrode 2 (Round window approach) (a) Micro-CT image for insertion depth (450°) (b) Reconstructed 3-D image (c) Cross-sectional views (Trauma 0)	95
Figure 3.6 Human temporal bone insertion study of electrode 3 (Round window approach) (a) Micro-CT image for insertion depth (360°) (b) Reconstructed 3-D image (c) Cross-sectional views (Trauma 0)	96
Figure 3.7 Human temporal bone insertion study of electrode 4 (Round window approach) (a) Micro-CT image for insertion depth (630°) (b) Cross-sectional views (Trauma 3)	97
Figure 3.8 Human temporal bone insertion study of electrode 5 (Cochleostomy approach) (a) Micro-CT image for insertion depth (495°) (b) Cross-sectional views (Trauma 0)	98
Figure 3.9 ABR recording which indicates the threshold level at 35 dB SPL	99

Figure 3.10 Recorded EABR with Stimulation (a) On and (b) Off -----	100
Figure 3.11 ABR threshold shift after (a) 4 days, (b) 1 week, (c) 2 weeks, (d) 3 weeks, and (e) 4 weeks implantation -----	101
Figure 3.12 (a) Enucleated cochlea after 4 weeks implantation (b) Cross-section of the cochlea with LCP electrode implantation -----	102
Figure 3.13 Cross-section view of stained cochlea in (a) Middle and (b) Basal turn ---	102
Figure 3.14 Simulation results of tripolar stimulation according to electrode designs (a) Design 1-1 (b) Design 1-2 (c) Design 2 (d) Design 3-1 (e) Design 3-2 (f) Design 3-3 ((i) electrode structure, (ii) absolute value of e-field at the plane of analyzing, (iii) picture of vector distribution of e-field) -----	104
Figure 3.15 Fabrication process of LCP cochlear electrode array for locally tripolar stimulation using MEMS technologies, laser micromachining, and thin-film processes -----	108
Figure 3.16 Results of fabrication process (a) Metal patterning after wet etching of seed layer (b) Via opening using laser ablation (c) Laser micromachining of site opening (d) Opened electrode site showing center and side electrodes -----	109
Figure 3.17 PWM data and biphasic pulses generated by ASIC chip and test board --	110
Figure 3.18 Optical images of Electrode site and IDE pattern in fabricated	

electrode array with and without mechanical interlocking pattern ---- 111

Figure 3.19 SEM images of fabricated electrode array with mechanical interlocking

(a) Electrode site opening (b) Seamless lamination result of upper and substrate layer of LCP (c) Mechanically interlocked LCP film with undercut metal pattern ----- 113

Figure 3.20 Impedance measurements of fabricated test samples with and without

mechanical interlocking used in accelerated soak test ----- 114

Figure 3.21 Cyclic voltammogram to calculate charge storage capacitance

(cathodic) of group 1 and group 2 ----- 115

Figure 3.22 Leakage current measurements during the *in vitro* 75°C accelerated

soak tests ----- 116

Figure 3.23 Metal patterning (a) Before and (b) After lamination process using

dielectric material and LCP ----- 118

Figure 3.24 Impedance measurements of wire- and LCP-based electrode array ---- 119

Figure 4.1 Comparison of LCP-based cochlear electrode arrays between the

previous and the current designs (a) The thickness of the previous LCP structure is 50 μm along its entire length. Its diameters at the tip and at the base are 0.5 mm and 0.8 mm, respectively, and its length was 28 mm. (b) The thickness of the current LCP structure in the cochlear electrode array varies from 25 μm (tip) to 75 μm (base). (c) Previously reported array employed a design scheme

which arranges stimulation sites at the center with the lead wires around the stimulation sites. (d) In this design, a peripheral via is employed so as to protect the lead wires at the center from the cutting laser beam. ----- 123

Figure 4.2 (a) Optical image of fabricated LCP-based cochlear electrode arrays with and without tapered structure (b) Side and cross-sectional views of the arrays with and without peripheral blind via ----- 125

Figure 4.3 Insertion force measured in a customized insertion setup (25 μm and 50 μm tip mean the current design and the previous design, respectively.) ----- 126

Figure 4.4 Extraction force measurements ----- 127

Figure 4.5 Insertion depth and trauma in human temporal bone insertion studies of LCP-based cochlear electrode arrays ----- 128

Figure 4.6 Fabrication processes and their results ----- 130

Figure 4.7 Deformation of metal line after lamination process ----- 131

Figure 4.8 Comparison of fibrosis between conventional and LCP-based cochlear electrode array ----- 134

Figure 4.9 Figure 4.9 Scheme of electrical pulse trains of sequential and paired stimulation ----- 136

Figure 4.10 Optical microscope images of test samples (a) Electrode site of test sample without mechanical interlocking in the course of accelerated

soaking (b) Electrode site of test sample with mechanical interlocking after water penetration (c), (d) Backlight microscope Images of test samples without and with mechanical interlocking after device failure (e) Side view of delamination of LCP film (f) Breakage of metal lines after water penetration ----- 138

Figure 4.11 SEM images of cross-section views of test samples after accelerated soak tests (a) Without mechanical interlocking (b) With mechanical interlocking ----- 139

Figure 4.12 Fabrication process of mechanically interlocked metal deposition onto LCP film (1st sacrificial layer and SiO₂ deposition on Si or Glass wafer → Interlocking patterning using photolithography and SiO₂ etching → 2nd Sacrificial layer and noble metal deposition → Lamination metal patterning onto LCP film → SiO₂ and 2nd sacrificial layer removal) -- 141

Figure 4.13 Mechanical interlocked metal-LCP in the substrate layer ----- 142

Figure 4.14 (a) TEM and (b) FIB-SEM images of micro-crack in electrode site ----- 143

Figure 4.15 Images of LCP-LCP interface (a) Using high temperature and high pressure lamination process and (b) Low temperature and low pressure lamination process after peeling off ----- 144

Figure 4.16 Fabrication flow feasible to make LCP-dielectric material hybrid implantable device ----- 145

Figure 4.17 Electrical modeling of crosstalk analyzation in stimulation electrode

when water penetration occurs ----- 148

List of Tables

Table 2.1 Properties of silicon, silica, and polymeric biocompatible materials [36] -----	48
Table 2.2 Conditions of current stimulation in the simulation -----	66
Table 2.3 Features of electrode site designs for locally tripolar stimulation -----	67
Table 3.1 Summarized results of absolute value of e-field distribution -----	106
Table 3.2 Summarized results of relative ratio of e-field distribution -----	107
Table 3.3 Comparison of reduction ratio of voltage amplitude at 1 mm distant from the center electrode -----	111
Table 3.4 Results of peel tests in test samples with and without mechanical interlocking -----	113
Table 3.5 Results of customized peel tests to compare bonding strength of LCP- LCP with LCP-dielectric materials -----	117
Table 4.1 Summarized results of reliability tests of LCP-based devices and the conditions of each specimen -----	150

List of Abbreviations

Abbreviation	Term
ABR	Auditory Brainstem Response
ASIC	Application Specific Integrated Circuit
CSCc	Cathodic Charge Storage Capacity
CVD	Chemical Vapor Deposition
DAC	Digital to Analog Converter
DBS	Deep Brain Stimulation
EABR	Electrically evoked Auditory Brainstem Response
EAS	Electric Acoustic Stimulation
EIS	Electrochemical Impedance Spectroscopy
FEM	Finite Element Method
FIB	Focused Ion Beam
FPC	Flexible Printed Circuit
ICP	Inductively Coupled Plasma
IDE	Inter-Digitated Electrode

Abbreviation	Term
ISO	International Organization for Standardization
LCP	Liquid Crystal Polymer
MEMS	Microelectromechanical System
MRI	Magnetic Resonance Imaging
MTTF	Mean Time To Failure
PBS	Phosphate Buffered Saline
PCB	Printed Circuit Board
PFOA	Perfluorooctanoic Acid
PTFE	Polytetrafluoroethylene
PWM	Pulse Width Modulation
RF	Radio Frequency
SEM	Scanning Electron Microscopy
SPL	Sound Pressure Level
TEM	Transmission Electron Microscopy

Note

Some parts of this dissertation are extracted and adapted from the journal publications which were published during the course of this study:

- ♦ Tae Mok Gwon, Kyou Sik Min, Jin Ho Kim, Seung Ha Oh, Ho Sun Lee, Min-Hyun Park, and Sung June Kim, “Fabrication and evaluation of an improved polymer-based cochlear electrode array for atraumatic insertion,” *Biomedical Microdevices*, 17(2), 2015.
- ♦ Tae Mok Gwon, Jin Ho Kim, Gwang Jin Choi, and Sung June Kim, “Mechanical interlocking to improve metal-polymer adhesion in polymer-based neural electrodes and its impact on device reliability,” *Journal of Materials Science*, 51(14), pp.6897-6912, 2016.
- ♦ Tae Mok Gwon, Chaebin Kim, Soowon Shin, Jeong Hoan park, Jin Ho Kim, and Sung June Kim, “Liquid crystal polymer (LCP)-based neural prosthetic devices,” *Biomedical Engineering Letters*, 6(3), 2016

Chapter I

Introduction

1.1 Overview of Neural Prostheses and Cochlear implant

Neural prostheses are electronic devices that can restore or substitute the partially damaged or profoundly impaired nervous system from neural diseases. Great developments from basic scientific discoveries to practical engineering technologies have been achieved in many applications [1-4]. These findings and researches combined to medical approaches have led to success in commercialization of neural prostheses such as cochlear implant, deep brain stimulation (DBS), and artificial retina. Cochlear implant devices have been implanted into over 300,000 worldwide recipients who have impaired auditory function from hair cell damage [5-8]. DBS is clinically qualified neuromodulation method for effective alleviation of symptoms in Parkinson's disease, essential tremor, and dystonia [9-11]. Visual prostheses including artificial retina, which replace the function of retina, for people who have retinitis pigmentosa or age-related macular degeneration have been manufactured and allowed as an implantable devices in recent years [12, 13].

Neural implants consist of microelectrode array, microelectronics, and implantable microsystem package. Neural microelectrode array is an interface where electrical pulses and signals delivered into neural tissue. Various materials have been used to fabricate microelectrode array such as metal wire, silicon, polymer, and carbon fiber [1, 14-17]. Metal wire-based electrode is one of the most powerful and reliable tool to both stimulate and record the nervous system [1]. Silicon-based neural probe is also widely used due to its elaborate structure and

precise size control from semiconductor fabrication process [18, 19]. Polymers and carbon fiber have consistently gained interests in implantable biomedical devices because of its flexibility, durability and compatibility with micro-fabrication process [20-22]. There are many types of neural electrode array, because the electrode size, design and stiffness depend on the target neural tissue and biological anatomy where electrode array is to be implanted. Therefore, the fundamental requirements for the neural electrode array are different in each application. For example, neural depth probe, which is used to record the neural signal in brain, must have enough stiffness to insert brain tissue, but non-breakable characteristics to be maintained in brain tissue. Cochlear electrode array must have both insertability and flexibility because the shape of cochlea is a spiral structure. Cuff-type electrode array has been used in peripheral neural tissue to cover axil nerve without insertion and damage in nerve tissue. On the other hand, microelectronics for stimulation, recording, and power-data transmission has been developed to satisfy minute control of neural response and derive diverse effect in local space. It is obvious that application-specific integrated circuit (ASIC) chip for neural stimulation, wireless transmission technology including inductive link, Bluetooth and Zigbee, data transmission algorithm strategies, and signal processing strategies have contributed the success of high performance neural implant. Implantable microsystem package is the technology which enable electronics to be implanted in human body. Without hermetic packages, neural implants would be imaginary device which can only apply to animal test. Conventional implantable devices have been fabricated using metal- and ceramic-encased packaging technologies [23-26].

Recently, polymer-based packages have been actively studied due to their compatibility with micro-fabrication process, size reduction, lightness, transparency to radio frequency (RF) wave, and cost reduction [27-33].

Cochlear implant is a class of neural prosthesis which replace the role of hair cell that convert mechanical energy to electrical signal in the cochlea. Movements of the stereocilia of the hair cells are detected and converted to electrical signals which pass through the upper auditory pathway. Cochlea implant copies the role of hair cell generating electrical pulse according to external sound signal and delivers the pulses directly into next auditory path past hair cells such as spiral ganglion cells. Cochlear implant is one of the most successful commercial neural implantable device. Internal device of cochlear implant is composed of intracochlear electrode array and electronics package including coil for data-power transmission, current pulse generator, data receiver. External device of cochlear implant consists of microphone for receiving sound signal, analog to digital converter, signal processor for data conversion, and transmission coil.

Conventional cochlear implant devices have been manufactured by major three global companies (Cochlear Ltd., MED-EL, Advanced Bionics). Most implantable devices implanted in human cochlea are based on metal-encased electronics packages and platinum-iridium wire-assembled electrode arrays. The fabrication process of the conventional devices demand laborious manual process, which leads to low throughput. Feedthrough for connection between electrode array and electronics package need heterogeneous hermetic sealing which requires complicated and high cost technologies [34, 35]. Additionally, metal-encased

package blocks electromagnetic waves penetration, which prevents coil integration into electronics package. Size reduction of implantable unit is difficult because of the external coil. The number of stimulation channel of intracochlear electrode array which determines maximum data and information quantity is limited to capability of metal-wire fabrication process. There have been efforts to solve the problem that conventional cochlear implant confronts by using new polymer materials and micro-fabrication process compatible with mass-production [34, 36].

1.2 Review of Cochlear Electrode Array

Cochlear electrode array plays important role in delivering electrical pulses to neural tissue in the auditory pathway. Because electrode array contacts directly neural tissue and is exposed to electrical stimuli and electrolyte, material for implantable electrode array must be selected with consideration of characteristics such as biocompatibility, durability, charge storage capacity, encapsulation ability, and reliability. Moreover, electrode design must fit into cochlea structure. Unlike other neural implant application, the spiral structure of cochlea is highly complicated. Human cochlea is occupied with 3 spaces which are scala tympani, scala vestibule, and scala media. Cochlear electrode array is inserted into the scala tympani which meets scala vestibule at basilar membrane. Electrode array must be in scala tympani during insertion to protect cochlea tissue. Insertion depth and the number of stimulation channel affect the perception ability of the recipients. Basal and apex turns of the cochlea response to high and low frequency, respectively.

Atraumatic and deeper insertion can be advantageous for perception of pitch perception and the recognition of noise [37-39]. On the other hand, localized current stimulation enables high performance cochlear implant. There have been various stimulation techniques designed to increase the number of distinguishable channel and reduce channel interaction which is supposed to cause difficulties in pitch perception and listening in noise [40-43].

1.2.1 Conventional Cochlear Electrode Array

Conventional cochlear electrode arrays are based on Teflon-insulated Pt-Ir wire and silicone elastomer. Manual processes of aligning wire electrode and making ball- or band-type electrode site are laborious and cost high with low throughput [44]. The number of stimulation channel is ranging from 12 to 26 [45]. The length of the electrode arrays is ranging from 19 to 31.5 mm. The short electrode array is used for electrical acoustic stimulation system which stimulates low frequency region by sound signal and high frequency region by electrical pulses. The diameter of basal end is ranging from 0.8 to 1.3 mm. Flexible array tip for minimal insertion trauma is essential property of cochlear electrode array.

The electrode shape has been studied and developed for high performance and minimal insertion trauma [46, 47]. Pre-curved (perimodiolar) electrode array with insertion tool has been developed to be closed to target neuron cell such as spiral ganglion cell. This modiolus hugging structural electrode array showed low threshold compared to straight electrode array due to the distance between the stimulation electrode site and target tissue [48, 49].

1.2.2 Polymer-Based Cochlear Electrode Array

Biocompatible polymers such as polyimide, parylene-C, silicone elastomer, and SU-8 have attracted attention as substrate materials of microelectrode array due to their flexibility and feasibility of micro-fabrication (thin-film fabrication). Among these biocompatible polymers, liquid crystal polymer (LCP) is a rising alternative biocompatible polymer for biomedical implantable devices. It has one of the most reliable polymers in water because water absorption rate of LCP is less than 0.04%. LCP-based devices offer the monolithic integration of the electrode array and electronic package for enhanced reliability. LCP-based electrode arrays are non-breakable because these arrays simply consist of flexible polymers and metal patterns. Cochlear electrode arrays using LCP have been studied in several groups. The first LCP-based cochlear electrode array was fabricated in 2006 using 50- μm -thick LCP films with a higher melting temperature, on which metal is deposited [50]. Films with a lower melting temperature were used as a bonding layer during the thermal lamination process. The length of the electrode array was less than 30 mm, and there were 12 contacts. The apical dimensions of the array were about 250 μm (Width) $\times$ 250 μm (Height). Medical-grade silicone was adopted as an overmold material for better positioning of the electrode array near the cochlea. It was found in an acute animal insertion trial that it was too stiff for clinical use with humans. Next, improved LCP-based highly flexible cochlear electrode array was fabricated and evaluated [51]. Only two 25- μm -thick LCP layers with a lower melting temperature for metal patterning and bonding were used, resulting in a 50- μm -thick electrode. Medical-grade silicone elastomer

encapsulated 50- μ m-thick along its entire length using a novel self-aligned molding method. Its diameters at the tip and at the base were 0.5 mm and 0.8 mm, respectively, and its length was 28 mm. The electrochemical properties showed that it could be used as a stimulation electrode, and the insertion force was half that of a comparative wire-based electrode array. The results of human temporal bone insertion studies revealed insertion trauma and feasibility of its clinical use.

There have been batch-fabricated cochlear electrode arrays using bulk micromachining and lithographically defined thin-film technology [52-54]. Silicon-based hybrid thin-film cochlear electrode array was encapsulated using Parylene-C and integrated with position sensors. Silicon-based and LCP-based cochlear electrode arrays offer a higher density of electrode sites compared to conventional cochlear electrode arrays owing to the use of the precise thin-film processes and less manual process. Position sensor was adopted to minimize insertion damage.

1.3 Proposed Polymer Cochlear Electrode Array

The issues of cochlear electrode array under consideration in this dissertation are as follows.

- (1) Compatibility with micro-fabrication process for mass-production
- (2) Atraumatic insertion for hearing preservation
- (3) Low frequency region stimulation
- (4) High-density electrode array and reduction of channel interaction

between electrode sites for locally distinct stimulation

Polymer cochlear electrode array has been studied to be a possible alternative to the conventional cochlear electrode array about the aforementioned issues. Cochlear electrode array based on thin-film polymers can be compatible with reliable micro-fabrication such as semiconductor fabrication process, microelectrodemechanical systems (MEMS) technologies, and monolithic encapsulation. A differentiated design of cochlear electrode arrays are suggested, fabricated and evaluated for the purpose of atraumatic deep insertion. Also, a novel electrode structure, which is enabled in the multi-layered thin-film electrode array, is proposed and evaluated to verify the feasibility of localized current stimulation for reduction of channel interaction.

1.3.1 Electrode Array for Atraumatic Deep Insertion

Atraumatic electrode insertion and stable interface between electrode array and neural tissue are essential for high performance cochlear implant, because electrode insertion without trauma is highly significant for hearing preservation in cochlear implantation especially for electric acoustic stimulation (EAS), which uses both high-frequency electrical stimulation and low-frequency sound stimulation. Deeper insertion is advantageous for the perception of music and the recognition of noise [38, 39].

In this study, LCP-based cochlear electrode array for atraumatic and deep insertion is proposed. The electrode array compatible with precise batch process,

thin-film process and a thermal lamination process is proposed. Differentiated design of the proposed LCP-based cochlear electrode array adopts a multi-layered structure with variable layers of LCP films depending on the parts of the electrode array to achieve a sufficient degree of basal stiffness and a tip flexibility. The electrode array design also uses shadow masking method with blind via to reduce the width of the electrode array, resulting in finer electrode array compared to previous cochlear electrode array.

1.3.2 Electrode Array for Tripolar Stimulation

Limitation of the number of stimulation channel in current cochlear implant comes from not only the manual fabrication process using wire-based electrode array, but also channel interaction which leads to insignificant effect when increasing the number of stimulation channel more than 8 [55]. Low spectral resolution could affect pitch perception and hearing in noise environment. Current steering and focusing stimulation method have been studied to increase the number of distinguishable perceptual channels [40, 42, 43, 56]. Especially, current focusing exploits multi-polar current stimulation techniques to prevent spread of electrical field. Tripolar stimulation method, which uses electrode channels adjacent both sides as a reference for current pulses, has shown its effect in reducing current spread and increasing spectral resolution [43]. Although there are controversy about the effect of tripolar stimulation in pitch perception, some reported spatial selectivity helps to analyze tuning position and improve cochlear implant performance [57, 58].

In this study, a novel electrode structure that can enhance the spatial resolution in tripolar stimulation is proposed. This structure is feasible in multi-layered thin-film electrode array. Previous tripolar stimulation is performed at 3 stimulation channels, but, in the proposed strategy, locally tripolar stimulation on one electrode channel using another layer of auxiliary electrode site for tripolar stimulation. In other words, Stimulation channel and auxiliary tripolar stimulation channel are separated in different LCP layer. Computer simulation program is used to verify possibility of the proposed electrode structure and field distribution according to the various designs. Choosing the best electrode design, laminated LCP-based electrode array with laser ablation is fabricated.

1.4 Long-Term Reliability of Polymer-Based Neural Prostheses

Long-term reliability is one of the most implant issue in the use of polymer-based neural prostheses. It is known that polymer-based neural implants are vulnerable to electrolyte ingress compared with conventional metal-encased and ceramic-based packages due to their fundamental non-hermeticity and high permeability to water and gas. Device reliability in polymer-based neural implants is difficult to measure using conventional helium leak tests, an industry standard methods to quantify the hermeticity of metal or ceramic cases because polymer has permeable surface where the helium absorbed during bombing. The absorbed helium gradually is released, resulting in misleading in leak rate [59-62]. Despite

there is no practically accepted standard testing methods to measure long-term reliability of polymer-based neural implants, LCP-based implantable devices have been evaluated using the helium fine leak test and accelerated soak test. The accelerated soak test is a testing method to measure relevant value on device reliability in a wet environment mimicking the body fluidic condition at elevated temperature for estimation of device lifetime in a shorten time. The estimation of lifetime of device at body temperature is based on Arrhenius equation using the calculated reaction rate and the mean time to failure at the accelerated temperature. Moreover, *in vivo* device stability experiments has also been conducted as well as *in vitro* reliability tests [63]

Delamination in polymer-based devices causes detrimental effect on device reliability. Most polymer-based devices suffers from delamination by water ingress into the surface of polymer and the weak bonded interfaces. Therefore adhesion of the interfaces should be enhanced using mechanical or chemical modification. There have been many studies for long-term reliability of implantable polymer-based devices and looking for methods to enhance the device reliability. For polyimide, effective annealing steps to prevent delamination was developed [64, 65]. For parylene-C, chemical modification, adhesion promoter, and structural approach to increase adhesion reliability were used in parylene–metal interface [66, 67].

In this dissertation, long-term reliability of LCP-based neural implants is analyzed and reviewed. Failure mechanism of LCP-based thin-film neural implants is arranged. Two technical strategies to improve reliability of LCP-based

implantable device are suggested and evaluated using *in vitro* measurements. Strategy 1 mentions about mechanical interlocking to strengthen metal-LCP adhesion where the most vulnerable part to water penetration, which has been started by Kim [68]. This study deepens his works and analyzes the impact of the strategy on device reliability. Metal patterning onto electrode site using dual photolithography and electroplating interlocks with LCP insulation layer during thermal lamination process. *In vitro* measurements of adhesion test and accelerated soak test are used to verify the impact of mechanical interlocking on device reliability. Strategy 2 deals with fabrication method for micro-implantable device using LCP and dielectric materials. To enhance device reliability, the role of dielectric materials to prevent water penetration and metal migration is introduced and hybrid structure is proposed. The feasibility of the proposed method is investigated by preliminary tests including peel test and thermos-compression bonding process with high temperature and high pressure using hybrid LCP-dielectric materials structure.

1.5 Objectives of the Dissertation

In this study, tapered and multi-layered LCP-based cochlear electrode array for atraumatic deep insertion is suggested. Metal lines and electrode sites are patterned on a flexible LCP film using MEMS technologies and thin-film process. Electrode array is designed with variable thermo-compression laminated layers and peripheral blind vias. Employing the proposed design scheme, the width of the

electrode array becomes smaller than that of previously reported LCP-based cochlear electrode arrays. Consequently, the possibility of insertion trauma is reducible. The measurements to prove atraumatic insertion are presented. Insertion force and extraction force in scala tympani model are measured and compared with conventional previous cochlear electrode array. Insertion trauma and depth are investigated through human temporal bone insertion studies.

Local tripolar stimulation method using multi-layered electrode structure is also proposed in this dissertation. Simulation results which designs enlarge the effect of current focusing to reduce current spread are presented. Fabrication process feasible to make multi-layered local tripolar stimulation electrode array is devised and fabricated electrode array is evaluated through *in vitro* measurements using test board based on ASIC chip for current pulse generation.

Long-term reliability of LCP-based neural implants is analyzed and discussed basically. Failure mechanism of LCP-based implantable device and suggestions to improve long-term reliability are presented. Adopting MEMS technologies, mechanical interlocking patterns on the electrode site for enhancement in metal-LCP adhesion and fabrication method using LCP and dielectric material are suggested and evaluated. Results of peel tests and *in vitro* accelerated soak tests show that the device reliability can be improved. Long-term reliability of LCP-based neural implantable device is reviewed and the quest for desirable ways to enhance reliability is described

The specific objectives of the dissertation are as follows.

- (1) Fabrication and evaluation of a LCP-based cochlear electrode array for atraumatic deep insertion.
- (2) The Suggestion and feasibility of an LCP-based cochlear electrode array for tripolar stimulation
- (3) The Suggestion and evaluation of technical strategies to enhance long-term reliability of LCP-based neural implants: mechanical interlocking to strengthen metal-LCP adhesion and LCP-dielectric material hybrid fabrication method
- (4) Review and analysis of reliability of LCP-based implantable device.

Chapter II

Materials & Methods

2.1 Liquid Crystal Polymer (LCP)

Biocompatible polymers such as polyimide, parylene-C, SU-8, and silicone elastomer have gained great interests in neural implants due to their flexibility and compatibility with micro-fabrication. In recent studies, polymer-based or hybrid with conventional neural implants have been developed and evaluated for clinical uses [69]. Polyimides have been widely used as insulation and substrate materials for medical devices. Polyimides can be used bulk film type or spun onto thin films as both photopatternable and non-photopatternable types. Polyimides are mainly served as substrates of flexible microelectrode arrays including cuff electrodes for peripheral nerve stimulation and micro-channel for nerve regeneration, and insulation materials for MEMS sensor. Moreover, high light transmittance property with wide range of wavelengths enable polyimide to be an optoelectronics material. Parylene-C has very low water absorption rate and chemical inertness. Chemical vapor deposition (CVD) process without any additives is needed to deposit parylene-C onto biomedical devices. It is mostly used as a coating material for implantable devices because a few micrometer of insulation layer is possible using parylene-C. SU-8 in MEMS have been famous due to its patternable property using photolithography and various types with usable thickness ranging from a few to hundreds of μm . Tunable electrical, mechanical, and optical properties make it more attractive biomaterials to be used in structural molds for soft lithography, optical waveguides, and neural probes.

Liquid crystal polymer (LCP) is another rising biocompatible material for

biomedical devices. It has one of the lowest water absorption rate ($<0.04\%$) and highest Young's Modulus among biocompatible polymers. Thermo-compression bonding and thermoforming technologies enable monolithic encapsulation of LCPs with variable designs, which makes it an attractive packaging material for implantable neural prosthetic devices [70]. MEMS technologies including metal deposition, photolithography, wet etching, dry (plasma) etching, and laser machining can be utilized on LCP film. As shown in Figure 2.1, LCP is used not only for packaging material, but also electrode substrate. Figure 2.1 shows conceptual view of LCP-based neural implants. LCP-based neural electrode array and LCP-based electronics packaging enable homogeneous adhesion at feedthroughs. Patterned metal lines and electrode sites on LCP substrate are insulated with another LCP layer and exposed by laser ablation [71]. LCP-based multichannel electrode arrays fabricated for stimulation or recording neuronal function can be monolithically encapsulated with the same LCP material for electronics packages [72]. This monolithic fabrication without feedthrough technologies enhances reliability of LCP-based neural implant. Thermal bonding and thermal forming process using mold with desired design allow tissue-conformable structure, which is a great advantage in relation to effectively functional implantation of devices. RF transparency of LCP and integrated coils onto LCP achieve miniaturized and wireless operated electronics packages [73]. In recent years, LCP-based microelectrode arrays for CI, artificial retina, DBS, electrocorticogram, and peripheral nerve stimulation have been developed and evaluated both *in vitro* and *in vivo* [51, 72, 74-82]. Electrochemical and mechanical

properties are enough to be used in clinical applications. Further, animal studies for efficacy of LCP-based microelectrode arrays and good magnetic resonance imaging (MRI) compatibilities and long-term evaluation tests show possibility of LCP-based implantable prostheses as substitutes of conventional neural implants [34, 63, 72, 83, 84].

Figure 2.1 Conceptual view of LCP-based implantable neural prosthesis

2.1.1 Material Properties and Types of LCP

LCP forms aligned molecule chains with a crystalline structure composed of rigid and flexible monomers. LCPs are distinguished by their mechanical,

electrical, and optical properties because they are fabricated using chemically different base materials and processes for specific intended applications. The material properties of LCPs are summarized and compared with those of silicon, silica, and other biocompatible polymers in Table 2.1. Their Young's moduli range from 2 to 40 GPa. LCP is one of the most stable biocompatible polymers in water, making it a strong candidate substrate material for long-term implants. The melting points of LCPs range from 275 to 335 °C. It has an extremely low water absorption rate, and superior barrier performance against water vapor and gas (oxygen, hydrogen, and other gases). Its water absorption rate (<0.04%) is similar to that of glass (<0.01%). It is also chemically inert, exhibiting excellent resistance to chemicals including high temperature organic solvents and cleaning agents.

Figure 2.2 (a) LCP film (Kuraray, Tokyo, Japan) (b) Optical image of LCP surface

The commercial products of LCPs are various such as pure fibers, film types, copper cladding films, and pellets. There are in several families, including

brands of Vectra LCP (Celanese, Texas, U.S.A), Zenite (Celanese, Texas, U.S.A), Vecstar LCP (Kuraray, Tokyo, Japan), Vectran LCP (Kuraray, Tokyo, Japan), and copper foil-cladded Ultralam Series (Rogers Corporation, Connecticut, U.S.A). Each LCP has specific properties, for example, in Kuraray Vecstar LCP films, CT-Z is suitable for high speed transmission flexible printed circuit (FPC) and high frequency antenna because its melting temperature is 335 °C. Another Vecstar CT-F film, which is used as bonding layer in multilayer fabrication process, has relative low melting temperature 280 °C. The thickness units of commercial LCP film product are 25 µm, 50 µm, and 100 µm. In this study, CT-F and CT-Z films are used to make cochlear electrode array.

Table 2.1 Properties of silicon, silica, and polymeric biocompatible materials [36]

	Silicon	Glass	Polyimide	Paylene-C	PDMS	SU-8	LCP
Moisture absorption (%)	-	<0.01	0.24-4	0.06-4	0.1-1.3	0.55-0.65	<0.04
Melting temperature (°C)	1414	1252	>400	290	200-250	>300	275-335
Glass transition temperature (°C)	-	821	290-430	35-80	125-150	200-210	82-280
Young's modulus (MPa)	130000-188000	62750	1800-15000	2800-3200	100-870	2000	2000-40000
Coefficient of thermal expansion (ppm/K)	2.6	3.25	3-60	35	180-907	52	4-50
Dielectric constant	11.68 (1 kHz)	4.1 (1 MHz)	3.3 (1 MHz)	3.1 (1 kHz)	2.6 (1 MHz)	3.2 (10 MHz)	2.9 (1 MHz)

Biocompatibility of LCP has been evaluated. The requirements and general testing procedures described in the International Organization for Standardization (ISO) 10993 that provides necessary guidelines for the materials to be used in medical devices have been met in some grades of Vectra LCP. Vecstar LCP-based gold microelectrode arrays met criteria of ISO 10993-5 like other polymer-based arrays [83, 85]. *In vivo* implantation animal test of LCP-based package revealed that the possibility of LCPs for long-term implant [63].

2.1.2 MEMS Technologies compatible with LCP

It is highly advantageous that LCP is compatible with micro-fabrication processes using MEMS technologies such as metallization, photolithography, plasma etching, wet etching, and laser machining. Fabrication methods using MEMS technologies allow high-density microelectrode arrays and high-integration neural prosthetic systems. To use the micro-fabrication technologies, which are optimized for silicon wafer, it is necessary to attach LCP film onto silicon wafer because LCP cannot be spin-coated while polyimide and SU-8 can be. Flatness of uniform LCP surface is significant to realize ultrafine pitch of metal lines through photolithography. Spin-coated photoresist or silicone elastomer can be used to attach LCP films onto silicon wafer. Flatness is improved when using silicone elastomer by more than 50% and no bubble is found. Then, metal deposition onto

LCP substrate needs surface modification technologies. Using oxygen plasma to activate LCP surface breaking C–C bond and titanium adhesion layer to form chemically strong Ti–C bond, reliable metallization onto LCP surface is possible [86]. After photolithography, wet etching, and dry etching, metal lines and electrode sites are patterned onto LCP substrate. The basic fabrication processes and scanning electron microscope (SEM) and optical images of the metal patterning on LCP substrates are shown in Figure 2.3. For insulation layer, another LCP layer can be laminated onto the patterned LCP substrate. The condition of lamination process requires enough pressure, melting temperature, and accurate lasting time. In recent years, electroplating process is added to fabricate thicker metal lines enduring lamination pressure because high-pressure results in more reliable LCP–LCP and LCP–metal bond [71]. Wavy metal lines are also used to bare high pressure in lamination process. Through lamination process, monolithically encapsulated LCP-based devices can be achieved. Pre-cut insulation layers have been used to secure electrode site exposed for neural stimulation or recording. With the development of laser machining technology, laser ablation after lamination process has been also utilized to expose desired area and location with high-accuracy.

Figure 2.3 (a) Basic fabrication process of LCP-based neural implants using MEMS technologies (b) Results of photolithography (i), electroplating and seed layer etching (ii)

2.2 Cochlear Electrode Array for Atraumatic Deep Insertion

2.2.1 Electrode Design

In the LCP structure of the LCP-based cochlear electrode array, the width of the electrode (W_s), the number of channels ($N_{channel}$), the minimal line pitch (P), the error in the laser machining (electrode site: E_s , outline: E_o) and the number of LCP layers (N_{layer}) determine the total width of the electrode array (W_T). Design schemes of the previously reported LCP-based microelectrode arrays arrange stimulation sites at the center and lead wires around the stimulation sites [51]. Because the cover layer is pre-cut by the laser for site openings, the marginal spacing for lamination alignment error should be secured such that it does not

expose the lead wires through the site windows. If all of the electrode contacts and lead wires are located in the same LCP film, the total width is expressed by the following equation [51]:

$$W_T = W_S + P \times N_{channel} + 2(E_S + E_O),$$

where $P = 0$ and $E_O = 0$ if $N_{channel} = 1$.

Total width of the LCP-based electrode array increases in proportion to the number of channels and the line pitch. 0.3-mm-wide electrode sites means that the total width of the 16-channel LCP-based electrode array ranges from 0.5 mm (tip) to 1.02 mm (base) if E_S and E_O are 0.1 mm and P is 20 μm .

To avoid the aforementioned drawback of the previous design scheme, the design of a side via and a cover electrode site is suggested as shown in Figure 2.4 and Figure 2.5. Instead of positioning an electrode at the center of the lead wires, a peripheral via so as to protect the lead wires at the center from the cutting laser beam is used. The final laser-cutting process is followed by metallization processes, sputtering and electroplating of the cover layer. Using this method, the laser-cutting of the electrode site opening windows on the cover layer only has to protect the inner lead wires because the electrode sites on the cover layer have minimal contact with the via holes. The fabrication error, $2(E_S + E_O)$, is reduced to $(E_V + E_O)$, which results in the following equation:

$$W_T = \max \left(W_S, (P \times N_{channel} + E_V + E_O) N_{layer} \right),$$

where $P = E_O = E_V = 0$ if $N_{channel} = 1$,

$$N_{channel} = N_{MWL} \text{ if } N_{layer} \geq 2,$$

N_{MWL} : Maximum number of lead wires per layer

In this case, in the current design, the width of the LCP-based electrode array with 0.3-mm-wide electrode sites ranges from 0.3 mm to 0.36 mm

On the basis of the minimal width described above, the LCP-based electrode array with silicone encapsulation is proposed. From channel 1 to channel 8, the contact vias and lead wires are patterned on the first substrate layer of the LCP film. The thickness of this region is 50 μm , including the inter-cover layer, except for the first channel, which is 25 μm thick because there is no cover layer. From channel 9 to channel 16, the contact vias and lead wires are patterned on the aforementioned inter-cover layer. The thickness of this basal region is 75 μm , including the cover layer.

The axial stiffness (k) is expressed by the following equation

$$k = \frac{AE}{L}$$

Here, A is the cross-section area, E is tensile modulus, and L is the length of the element. Because the tensile modulus of LCP is more than one hundred times that of the silicone elastomer used in biomedical applications [32, 87, 88], the stiffness of the electrode results from the thickness of the LCP film. Therefore, it is possible to offer a variety of stiffness depending on the parts of the electrode using the current design. After laminating the substrate layer, the inter-cover layer, and

the cover layer, gold and iridium oxide electrode sites are sputter-deposited and electroplated onto the exposed layers.

Figure 2.4 Cross-section view of the design of tapered LCP-based cochlear electrode array for atraumatic deep insertion

Figure 2.5 Image of proposed cochlear electrode array using blind via

2.2.2 Fabrication Process

Advances in LCP-based micro-fabrication process for cochlear electrode arrays include the minimization of the line pitch using a novel LCP-film mounting method. The conventional film-based micro-fabrication process uses a photoresist to attach a film to a silicon wafer [78]. In this study, a silicone elastomer is used as an adhesion layer to enhance the flatness, which is related to the photolithography resolution [89]. Micro-fabrication process flows are shown in Figure 2.6. A silicon wafer is spin-coated using a silicone elastomer (Nusil Silicone Technology, MED 6233, Carpinteria, CA, USA) at 2000 rpm for 70 seconds. The silicone elastomer is then cured on a 150 °C hotplate for 30 minutes. On the cured silicone elastomer, a 25- μm -thick LCP film (Kuraray, Vecstar CT-F 25 μm , Tokyo, Japan) is attached using a roller. To clean the surface of the LCP film, the wafer onto which the LCP film is attached is immersed in acetone, methanol and isopropyl alcohol for 1 minute, sequentially. Then, inductively coupled plasma (ICP) etcher for three minutes in an O₂ gaseous environment is used to clean and activate the surface of the LCP film. Subsequently, 50 nm of titanium and 150 nm of gold are deposited using an e-gun evaporator (Maestech Co., Ltd., ZZS550-2/D, Pyungtaek, South Korea) as electroplating seed layers. Next, photolithography using a mask aligner machine (SUSS MicroTec, MA6/BA6, Garching, Germany) is used to pattern a 10- μm -thick photoresist, followed by 5- μm -thick gold electroplating. An align hole for lamination and an align key for laser-cutting are also patterned. After removing photoresist using a remover and the etching of the seed layer using nitrohydrochloric acid and hydrofluoric acid, the LCP substrate is detached from

the elastomer surface.

Figure 2.6 Fabrication process flow of tapered LCP-based cochlear electrode array using MEMS technologies, thin-film process, and thermal lamination process (a) Seed layer (Titanium and gold) deposition (b) Photolithography using AZ 4620 photoresist (c) Electroplating for thick metal lines (d) Developing photoresist and wet etching seed layer using nitrohydrochloric acid and hydrofluoric acid (e) Laser cutting of align holes and aligning LCP layers with pre-cut cover layer (f) Thermal lamination process for monolithic encapsulation

The first 25- μm LCP substrate for channels 1 to 8 is fabricated. In the same way, the second 25- μm LCP substrate for channels 9 to 16 is fabricated. Alignment holes 1 mm in diameter for the second substrate and the cover film which is the

same film of the substrate are laser-cut using a UV laser machining system (Electro Scientific Industries, Flex5330, Portland, OR, USA). In addition to the align holes, the laser-cutting design should include the outlines of the via-openings, the align key for the final laser cutting process, and the contact pads. Using a thermal press machine (Carver, Model 4122, Wabash, IN, USA), the mold is heated up to 285 °C at 7 °C/minute. At 285 °C, the mold maintains a pressure of 250 kg for 40 minutes. The LCP layers are then laminated into a united body. Therefore, as shown in Fig. 2(g), there are different thicknesses depending on the parts of the electrode array. The thicknesses of the LCP films are 25 µm at channel 1 (tip), 50 µm at channels 2 to 8 (middle), and 75 µm at channels 9 to 16 (base). A disposable shadow mask which is laser-cut using 100-µm-thick LCP film is used to deposit the site seed layer. Then, platinum or iridium oxide layers are electroplated onto the contact pads. Finally, a medical-grade silicone elastomer using a previously reported custom molding process [51] encapsulates the current LCP-based electrode array.

2.2.3 Experimental Setup and Protocol of *In Vitro* and *In Vivo* Evaluation Tests

2.2.3.1 Insertion and Extraction Force Measurements in Scala Tympani Model

The insertion force and extraction force of the finalized cochlear electrode array were measured and compared to that of a previously reported wire-based cochlear electrode array fabricated using conventional process and LCP-based cochlear electrode array which had a uniform thickness of its LCP structure. Test electrode arrays were fixed to a load cell (ATI, Nano17, Pinnacle Park, Apex, NC,

USA) which was controlled by a motorized linear actuator (Newport, LTA-HS, Irvine, CA, USA). The displacement and the force applied to the load cell were recorded when the electrode arrays were inserted into a transparent plastic human scala tympani model using a customized program based on Labview® [51].

Figure 2.7 Experimental setup of insertion and extraction force measurements in plastic scala tympani model [51]

2.2.3.2 Human Temporal Bone Insertion Studies

The insertion depth and the insertion safety were evaluated in human temporal bone insertion studies. Five human temporal bone insertions were attempted using a cochleostomy and round window approach. The insertion depth was measured using a micro-CT (computerized tomography) scanned image. The insertion trauma is standardized using the following grades: 0, no trauma; 1, elevation of the basilar membrane; 2, rupture of the basilar membrane or spiral

ligament; 3, dislocation into the scala vestibuli; 4, fracture of the osseous spiral lamina or modiolar wall [90].

Human temporal bone with LCP-based cochlear electrode array can be reconstructed using 3-dimensional reconstruct program (3D Slicer version 4). CT images are integrated in the program and the threshold values with each materials are designated. Cochlear electrode array is distinguishable in the reconstructed image.

Figure 2.8 Human temporal bone insertion study and insertion depth [39]

Figure 2.9 3D Slicer version 4

2.2.3.3 *In Vivo* Animal Study

2.2.3.3.1 Acute Implantation and Electrically Evoked Auditory Brainstem Response (EABR) Recording

Acute implantation of the cochlear electrode array to record ABR and EABR levels was performed on an anaesthetized guinea pig (female, 327 g) using the smartEP USB Box system (Intelligent Hearing Systems, Miami, FL, USA). The procedures used to record the ABR and EABR using this system are similar to those described in the literature [91]. To verify the hearing ability of the ear and to measure the ABR threshold, the ABR was recorded initially with sound stimuli (24 kHz tone bursts; burst amplitude: 30-70 dB SPL; burst rate: 19 Hz; burst duration:

1.6ms). The ABR threshold was determined as the minimum sound intensity level required to evoke identifiable waves. Then, the LCP-based electrode array was inserted at a displacement of 5mm from a round window and was fixed using biocompatible glue. The Impedance of the stimulation electrode site of the electroplated gold was 3.7 k Ω at 1 kHz. As the sound stimuli (4 kHz tone burst; burst amplitude: 100dB SPL (Sound pressure level); burst frequency: 5 Hz; burst duration: 0.8 ms) was converted into cathodic first biphasic current stimuli (amplitude: 0.5 mA; duration: 30 μ s/phase; rate: 1000/s) using an application specific integrated circuit (ASIC), the EABR was recorded using the same process used for the ABR with the cochlear stimulator condition, i.e., on or off. All procedures conformed to protocols approved by the Institutional Animal Care and Use Committee of Seoul National University.

Figure 2.10 Acute implantation of the LCP-based cochlear electrode array into guinea pig (a) ABR recording in the soundproof room (b) Implantation surgery

2.2.3.3.2 Hearing Preservation and Histologic Evaluation

Seven-week-old male Dunkin-Hartley guinea pigs weighing from 410 to 450 g were used for hearing preservation and histologic evaluation study after LCP-based cochlear electrode array insertion. All surgical procedures and auditory brainstem response (ABR) recordings were performed after anaesthesia with intramuscular administration of ketamine (40 mg/kg) and xylazine (4 mg/kg). Six guinea pigs were randomly chosen. This study was approved by the Institutional Animal Care and Use Committee of Boramae Medical Center (2015-0010).

The hearing level of both ears of all animals was measured using ABRs before surgery. The Intelligent Hearing System (IHS Inc., Miami, FL, USA), employing HIS high-frequency transducers (HFT9911–20–0035) and IHS high-frequency software (ver. 2.33), was used to record ABRs. Tone pips of 2, 8, 16, and 32 kHz were used as the sound stimuli (5-ms duration, cos shaping, 21 Hz). Electrode-dummy was inserted and then, ABR thresholds were measured at 4 days and 1, 2, 3 and 4 weeks. The definition of the threshold shift was a value obtained by subtracting the preoperative threshold from each of the postoperative thresholds.

Histological analyses of the basal, middle and apical turns of the cochlea were performed using light microscopy (CX31; Olympus, Tokyo, Japan). The tissue responses, including intracochlear fibrosis, ossification, and spiral ganglion cell density were evaluated using the results of Masson's Trichrome staining. Microscopic images of five sequential sections around the area with the most apparent tissue responses were taken and converted to JPEG files. The area of the scala tympani, and of the tissue responses surrounding it, were measured using Image J software (National Institutes of Health, Bethesda, MD, USA). The

percentage of the area occupied by tissue responses in the scala tympani was calculated in each section and a mean percentage was obtained for each animal.

Figure 2.11 Dummy LCP electrode array implantation surgery for hearing preservation and histological evaluation

2.3 Polymer Electrode Array for Tripolar Stimulation

2.3.1 Modeling and Simulation of Polymer-Based Cochlear Electrode Array for Tripolar Stimulation

Current steering and focusing stimulation method have been studied to reduce current spread and increase distinct stimulation channel. It is important that channel interaction between stimulation channels hinders high-density electrode array and high-performance cochlear implant. Electronics can provide enormous

data and information around us to internal device, but electrode array implanted in cochlea cannot accommodate and exploit the information received owing to limits of the number of stimulation channel in electrode array. Current focusing is a one of alternatives to increase effective stimulation channel without physical growth of the number of stimulation channel. Figure 2. 12 explain stimulation method. Monopolar stimulation uses one stimulation channel and one reference channel, but multi-polymer stimulation such as bipolar and tripolar stimulation do not use the separated reference channel. Instead, multi-polar stimulation method uses fixed stimulation channel and surrounded auxiliary channel to flow current path. This flow of current prevents current spreading in the body fluid which is an electrolyte. Conventional tripolar stimulation uses 3 channels to stimulation local area. Two adjacent channels play a role of reference electrode.

Figure 2.12 Explanation of current focusing stimulation method

More locally stimulating method through design of electrode site structure

is proposed in this study. Unlike conventional electrode array, the proposed electrode array has multi-layered structure wherein the layer of auxiliary channels are separated from that of stimulation channels. This structure of electrode array is possible only in multi-layer integrated materials. Because LCP is thermoplastic material, same kind of LCP layers can be a united layer by thermo-compression lamination process.

2.3.1.1 Simulation Tool and Modeling

Commercial field element method (FEM) solver ANSYS High Frequency electromagnetic Field Stimulation (HFSS) is used to simulate the spreading electrical field when tripolar stimulation is implemented in the proposed electrode design. Modeling replicates human cochlea and cochlear electrode implantation. Simulation modeling of human cochlea refers to the literature [43]. The structure of scala tympani where the cochlear electrode array implanted is assumed as cylinder. Its radius is 1 mm. Perilymph, which is an extracellular fluid located in the scala tympani, and bony wall that surround cochlea are included in the modeling. The location of target cells, which are spiral ganglion cells, is 1.25 mm distant from the center of scala tympani. The radius of bony wall and analyzing space of cylindrical structure of cochlea are 1.15 and 2.5 mm, respectively.

Monopolar, tripolar, and locally tripolar (proposed stimulation structure) are simulated. The conditions of current stimulation are followed as shown in Table 2.2. In the plane where target cells are locate, relative absolute e-field amplitude at 1 mm from the position of the maximum e-field spot is calculated and analyzed.

More reduction ratio of the amplitude of e-field means more focused current stimulation.

Figure 2.13 Modeling of human cochlea and implantation of an electrode array

Table 2.2 Conditions of current stimulation in the simulation

Classification	Condition
Kinds of stimulation method	Monopolar, Tripolar, Locally Tripolar
Analyzing time	0 ~ 300 μ s (stimulation starts at 0 s)
Phase of current pulse	Biphasic
Amplitude of current pulse	400 μ A
Duration of current pulse	50 μ s

2.3.1.2 Electrode Designs

Electrode array is fabricated using only 25 μ m-LCP films. The width and length of electrode stimulation site are 300 μ m same. Only gold and LCP are used

in electrode array. The thickness of electroplating (metal) is 5 μm (Center) or 10 μm (Auxiliary). Reference electrode which is needed in monopolar stimulation is 18 mm distant from the stimulation sites. Total 6 electrode site designs are simulated. After analyzing relative amplitude of e-field, one electrode design showing the most effective focused stimulation is chosen to fabricate. This design of electrode site structure is evaluated through *in vitro* measurement. Table 2.3 and Figure 2.14 show the features of each electrode site designs.

The pitch of stimulation channel is 1 mm. Design 0 means general cochlear electrode array which is used in conventional monopolar and tripolar stimulation. Design 1- proposes center (stimulation) electrode site is at the lower LCP layer and auxiliary electrode site for locally tripolar stimulation is at the upper LCP layer, but Design 2 does in reverse. Design 3- suggests that center electrode site is at the lower LCP layer and auxiliary electrode site at the side wall in both sides of center electrode. There are slight differences that with and without insulation space between center site and auxiliary sites in the Design 1-1 and 1-2. Length of electrode site and distance between center site and auxiliary sites are different in the Design 3-1, 3-2, and 3-3.

Table 2.3 Features of electrode site designs for locally tripolar stimulation

Design	Subordinate Design	Feature
1	1-1	Center site (stimulation): lower layer Auxiliary site: upper layer Width of electrode site: 300 μm Length of electrode site: 100 μm

	1-2	10 μm -thick insulation area between center and auxiliary site
2		Center site: upper layer Auxiliary site: lower layer Width of electrode site: 300 μm Length of electrode site: 100 μm
3	3-1	Center site (stimulation): lower layer Auxiliary site: upper layer (Side wall) Height of auxiliary site: 10 μm Length of electrode site: 100 μm
	3-2	Length of electrode site: 300 μm
	3-3	Length of electrode site: 100 μm Distance Between center and side site: 100 μm

Figure 2.14 Designs of electrode sites in the simulation

2.3.2 Fabrication Process

Fabrication process of multi-layered electrode array is more complicated than that of mono-layered electrode array. Alignment in lamination process and

laser ablation process play key role in the multi-layered LCP-based electrode array for locally tripolar stimulation. To reduce width of the electrode array and enable the proposed design, via structure is necessary using laser ablation and electrical contact with conductive paste. Micromachining laser equipment (Samurai UV Marking System, DPSS Lasers Inc., Santa Clara, CA, USA) is used to make via structure and electrode site opening. Detailed fabrication process of the chosen electrode design is shown in *Result* section (3.2.2).

2.3.3 *In Vitro* Measurements

2.3.3.1 Test Board for Tripolar Stimulation

Neural stimulator using ASICs to increase the effective number of stimulation channels via pseudo channel stimulation is implemented. The designed chip was fabricated using 0.18 μm BCDMOS process [92]. Figure 2.15 explains PWM data structure and serial data format. ASICs have their own 4-bit address and the data receiver converts amplitude modulated data into clock. Logical data using pulse width modulation (PWM) control ASICs to change stimulation mode (Monopolar, tripolar). The setup mode determines duration and current pulse polarity, phasic type, and current pulse amplitude. The current digital to analog converter (DAC) with 3-bit binary weighted transistors generates current in two pairs between center electrode site and auxiliary electrode sites. Ratio of the left to right pulse generator is ranging from 0:7 to 7:0 in 8 steps. The ratio used in this *in vitro* experiment is 3:4. As shown in Figure 2.16, 4 ASIC chips can be loaded in the test board.

Figure 2.15 PWM data structure and Serial data format [92]

Figure 2.16 Outline of the test board used *in vitro* measurements of current focusing

2.3.3.2 Experimental Setup and Protocol

Figure 2.17 shows experimental setup for measuring current spreading in

phosphate buffered saline (PBS) solution to copy body fluid. Stimulation electrode designed from simulation results is fabricated using LCP films. It is attached on a recording electrode based on printed circuit board (PCB). Test board generates data and power for ASCII chip that generates current pulse according to PWM signals. Current pulse of monopolar or tripolar stimulation mode is transferred to stimulation electrode array designed for locally tripolar stimulation. Current spreading by stimulation current pulse is recorded in the recording electrode and the measurements is saved in an oscilloscope. The space between the recording and stimulation electrode is 0.5 mm. Like analyzing method in FEM simulation, the reduction ratio of voltage level at the site of 1 mm distant from the center electrode site to that at the center electrode site is calculated and compared. More reduction ratio means more focused current stimulation.

Figure 2.17 (a) Block diagram and (b) Image of the experimental setup for *in vitro* current focusing measurements

2.4 Long-Term Reliability Analysis of LCP-Based Neural

Implants

Polymer-based and hybrid metal- or silicon-based neural implant devices have been widely used to overcome the limitations of the conventional neural implant systems which are bulky, heavy, and stiff. However, these devices cannot be completely free from long-term reliability issue, because polymers are basically less hermetic than metallic and ceramic materials. Moreover, heterogeneous interfaces where water penetration occurs exist in the polymer-based neural implants. Although LCP is one of the most reliable polymers in body fluid due to its extremely low water absorption rate ($<0.04\%$) and compatibility with monolithic seamless encapsulation process, it is essential for LCP-based implantable devices to evaluate and verify long-term reliability for the purpose of clinical use. In this dissertation, long-term reliability of LCP-based implantable devices are studied and analyzed synthetically from failure mechanism and technical strategies to improve reliability of LCP-based implantable devices to review of device reliability.

As shown in Figure 2.18, LCP-based neural implant with monolithic integration of electronics package and electrode array has buried feedthrough that can be encapsulated by LCP homogeneous adhesive layers. Duration of water penetration through 0.1 mm-thick LCP surface when the relative humidity reaches 63 % is calculated 64.3 years using parameters of LCP about solubility, diffusion coefficient, and moisture permeability [63]. When considering reliability of LCP-based device, water penetration into electrode array wherein LCP-LCP and Metal-

LCP interface exist is more critical than that through electronics package. In this dissertation, technical strategies to improve reliability of LCP-based device is focused in electrode array.

Figure 2.18 Water penetration in (a) Metal-based neural prosthesis and (b) LCP-based neural prosthesis

2.4.1 Overview of the Long-Term Reliability

2.4.1.1 Failure Mechanism

In the LCP-based neural electrodes, there are three pathways through which water ingress occurs: through the LCP surface, through the interface between the LCP layers, and through the interface between the LCP and the metal (Figure 2.19). Among these pathways, the polymer-metal interface is the limiting factor of the long-term reliability of LCP-based neural implantable devices [63].

Fundamentally, the delamination of a polymer from a metal in an electrolyte has been investigated, and studies have proven the basic delamination mechanism of polymers coated with steel [93-95]. An examination of images taken after water leakage into the electrodes verifies that the LCP-metal interface is most vulnerable to water penetration. The water penetration distance through the LCP-LCP interface is shorter than that through the LCP-metal interface.

Figure 2.19 Three pathways through which water ingress occurs

2.4.1.2 Measurement Methods for Reliability Analysis

Helium leak measurements are the general standard method used in the industrial field to ensure the hermeticity of metal-based implantable devices. The detected helium leakage can be estimated with that of water using the square root of their ratio of the molecular mass [96] and measured leak rate can be used to

calculate device lifetime using following equation.

$$t = -\frac{V}{L_{H_2O}} \left[\ln \left(1 - \frac{Q_{H_2O}}{\Delta p_{i_{H_2O}}} \right) \right]$$

Q_{water} = the water that has leaked in the device in atm

V = the available internal volume of the package (volume of the parts inside the package should be subtracted) in cc

t = the time in seconds

L_{water} = the true water leak rate = $0.471 * L_{\text{He}}$ in atm-cc/sec

$\Delta p_{i_{\text{water}}}$ = the initial difference in the water partial pressure on the outside less the partial pressure on the inside the package (water vapor partial pressure in human body is 0.061 atm)

However, it is difficult to measure correct helium leakage in polymer-based devices accurately, as organic polymers such as LCPs naturally absorb helium [60, 61]. Besides, the range of precision of current helium leak test device is 1×10^{-13} atm-cc/sec, but, measurement level about 1×10^{-15} atm-cc/sec is needed to guarantee that LCP-based package with 0.005 cc free volume endure in relative humidity 100 % environment.

Also, in terms of the electrode, water ingress from the interface between the polymer and the metal at the electrode site cannot be separated from that at the surface of the electrode. Therefore, the accelerated soak test in this study is conducted to measure and compare the long-term reliability of the LCP-based neural devices. Lifetime estimation is calculated and analyzed using Arrhenius equation and activation coefficient.

2.4.2 Technical Strategies to Improve Reliability of LCP-Based Implantable Device

2.4.2.1 Mechanical Interlocking to Strengthen Metal-LCP Adhesion

Adhesion between polymers and metals can be strengthened both mechanically and structurally. To enhance adhesion strength at the metal-polymer interface, mechanical interlocking using micro-patterning at the polymer-metal interface can be effective way [97-100]. Depending on the surface topography, the adhesion strength can be modified due to energy expenditure when a fracture occurs [97]. The proposed concept of mechanical interlocking at metal-polymer interface in the polymer-based neural electrode array is shown in Figure 2.20. The polymer neural electrodes fabricated using consist of three parts: 1) the polymer substrate; 2) the patterned metal lead wires and electrode sites, and 3) insulating polymer with an exposed area for electrode-tissue interaction. The exposed area, which has a heterogeneous interface consisting of a metal electrode site and a polymer insulating layer, is where this study concerns. This part is where water penetration causes metal corrosion, interconnection failures, and delamination. The noble metal is used as surface for the electrode sites. However, noble metals cannot form long-term stable carbide bonds in contrast to adhesion metals such as Ti, Cr, and Ni. Alternatively, mechanical approach between a noble metal and a polymer using surface modification by means of micro-patterning. The surface metal is patterned to interlock with polymer. With undercut structure of metal patterning and nanoporous surface, the noble metal can be adhered to polymer strongly.

Figure 2.20 Conceptual view of mechanical interlocking at metal-polymer interface in the polymer-based neural electrode array

2.4.2.1.1 Fabrication Process using Dual Lithography and Electroplating

Figure 2.21 Fabrication processes of a LCP-based neural electrode with mechanical interlocking using MEMS technologies, including oxygen plasma, e-gun

evaporation, dual steps of photolithography and electroplating, and wet etching

Figure 2.21 explains the processes to fabricate the proposed LCP-based neural electrode with mechanical interlocking structure on the electrode sites. The fabrication processes using MEMS technologies include double steps of photolithography and electroplating to form the metal pattern. First, the surface of a LCP substrate (Vecstar CTF-100, Kuraray, Tokyo, Japan) attached onto a silicon wafer using a silicone elastomer (MED 6233, Nusil Silicone Technology, Carpinteria, CA, USA) is cleaned in acetone, methanol, and isopropyl alcohol, sequentially. Seed layers consisting of titanium and gold (Ti/Au) are deposited onto the surface of the LCP substrate using an e-gun evaporator (ZZS550-2/D, Maestech Co., Ltd., Pyungtaek, Korea) at 50 nm and 150 nm, respectively, after which the surface is activated by oxygen plasma using an ICP etcher for three minutes. Subsequently, a 10- μ m-thick positive photoresist (Hoechst Celanese, AZ 46020, Somerville, NJ, USA) is spin-coated onto the surface of the LCP substrate (Figure 2.21 (a)). Then, the first photolithography step using a mask aligner machine (MA6/BA6, SUSS MicroTec, Garching, Germany) is carried out for the first electroplating of gold (Figure 2.21 (b)). After the removal of the remaining photoresist and the spin-coating of a new photoresist, the second photolithography step with the intentional overexposure of light to generate a trapezoidal cross-sectional photoresist and an electroplating step to create the anti-trapezoidal cross-sectional metallic structures (undercut structure) are performed using the same equipment (Figure 2.21 (c), (d)). The remaining photoresist and the thin seed layers

of Ti/Au are then removed by a wet etching process (Figure 2.21 (e)). Lastly, a layer of LCP film for insulation (Vecstar CTF-25, Kuraray, Tokyo, Japan) with a site window pre-cut by laser micromachining (Samurai UV Laser, DPSS Laser Inc., CA, USA) is laminated onto the patterned LCP substrate using a thermal press (Model 4122, Carver, Wabash, IN, USA) at 285°C for 30 minutes while maintaining 200 kg of lamination pressure (Figure 2.21 (f)). During the lamination process, the LCP layers are melted into the space between the metal pattern, becoming a united body and resulting in the mechanically interlocking shapes.

Figure 2.22 Design of test samples categorized according to the formation of the mechanical interlocking structures

Two types of LCP-based neural electrode samples are fabricated with the aforementioned methods. Group 1, with a mechanical interlocking structure, and group 2 (control group), without a microscale interlocking structure, are shown in Figure 2.22. Both samples have electroplated nanoporous gold surface. In group 1,

microscale metallic lines with a 50 μm width at 50 μm intervals are patterned by photolithography. The fabrication processes of the control group are identical to those of group 1 except for the second photolithography step to form the metal pattern for interlocking.

2.4.2.1.2 *In Vitro* Peel Test and Electrochemical Measurements

Adhesion strength is evaluated by peel test. The principle of the 180° peel test is demonstrated in earlier work [101]. The test specimens (25 × 190 × 0.2 mm) are prepared using the fabrication processes described above. The bonded area of each specimen is 25 × 70 mm². A universal testing machine (WL2100, Withlab, Daegu, Korea) is used to peel the upper LCP film at an angle of 180° with a speed of 300 mm/min following the standard test method for the peel adhesion of pressure-sensitive tape (ASTM D3330). The peel strength (N/mm) is determined as the recorded maximum force divided by the width of the specimen. Peeling force causes the mode of failure that is classified three categories: adhesive, indicating peeling from the substrate; tearing, indicating a rupture of the upper LCP within the bonded area; or snapping, indicating that the upper LCP was ruptured away from the bonded area.

Electrochemical impedance spectroscopy (EIS) and cyclic voltammetry (CV) in PBS solutions (Invitrogen Life Technologies, Gibco 10010, Carlsbad, CA, USA) at pH 7.2 are measured using a potentiostat (Solartron Analytical, 1286 and 1287A, Farnborough, UK) and a three-cell electrochemical system with a platinum counter electrode and a silver/silver chloride (Ag/AgCl) reference electrode. EIS is

measured at frequencies ranging from 10 Hz to 10 kHz using 10 mVrms of excitation. Cyclic voltammetry is also measured using an identical electrochemical cell and the electrochemical potential from -0.6 to 0.8 V versus an Ag/AgCl electrode at a rate of 100 mV/s is swept. The cathodal charge storage capacity (CSCc) is determined from the obtained cyclic voltammogram.

2.4.2.1.3 *In Vitro* Accelerated Soak Test

Accelerated soak tests are used to evaluate the long-term reliability of the implantable device. The soak tests are carried out in a 75°C PBS condition. Although the elevated temperature for the accelerated aging of polymers is generally recommended to be at or below 60 °C [102], a temperature of 75°C is chosen here in an effort to expedite encapsulation failure within the limited period of the experiment and to compare the “relative” reliability depending on the surface condition of the mechanical interlocking structure. The test setup for the accelerated soak test of the LCP-based neural electrodes is shown in Figure 2.23. The samples under testing are immersed with PBS-filled bottles then placed in a 75°C convection oven. A flow regulator (DOSI-FLOW 10, Leventon, Spain) is connected to a water tank to supply deionized water to maintain the water level and the ion concentration. In order to simulate electrical stress, a customized multi-channel current stimulator generates biphasic current pulses with stimulation parameters of a 1 mA amplitude, a 32 μ s duration/phase, and 1 kHz pulses per second continuously.

Figure 2.23 Experimental setup for *in vitro* accelerated soak test (a) Test samples are immersed in PBS at 75°C to imitate a body environment. The test setup consists of a multichannel current stimulator to apply continuous biphasic pulses, a picoammeter for leakage current measurements, an interfacing circuit to switch between the stimulation mode and the leakage current measurement mode, and a deionized water tank to maintain the ion concentration of the PBS. (b) The interfacing circuit board, with the switch for mode conversion, and the test electrode sample are connected with an extension cable and a board.

Device failure is determined through the presence of leakage current using inter-digitated electrodes (IDEs), with a width of 80 μm and a pitch of 100 μm , integrated into the test electrodes. Leakage currents are periodically measured in the four samples of group 1 and the five samples of group 2 using a picoammeter (Model 6485, Keithley Instruments, Inc., Cleveland, OH, USA) with 5 volts of DC bias. A customized interfacing board provides switching between the stimulation mode and the leakage current measurement mode. LabView software was used to

control the picoammeter with a GPIB controller (GPIB-USB-HS, National Instruments, Austin, TX, USA). Averages and standard deviations are calculated from one hundred measurements of the leakage current value. The failure criterion for the electrode samples is set to 1 μA , which is a rough level sourced from previous work [72].

Given that the mean time to failure (MTTF) of the test samples is measured at an accelerated temperature, the lifetime at the regular body temperature (37°C) can be calculated using the following common 'ten-degree rule', which is based on the assumption that the rate of a chemical reaction is doubled for every 10°C elevation in the temperature.

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

f: increased rate of aging

T: elevated temperature (75°C), T_{ref} : reference temperature (37°C)

2.4.2.1.4 Visual Inspection and Statistical Analysis

For visual images, optical microscopy and SEM are used to compare the junction between the LCP and the noble metal layers before and after water ingress in each test group during the accelerated soak tests. Transmission electron microscope (TEM) and focused ion beam (FIB) are also used to inspect micro-crack at the surface and interface of electrode site. All data including the peel test results, the electrochemical characterization results and the lifetime data values from the accelerated soak tests are also investigated using the Wilcoxon rank-sum

test.

2.4.2.2 Fabrication using LCP and Dielectric Materials

2.4.2.2.1 Role of Dielectric Materials

In fabrication process of LCP-based neural implants, lamination using thermo-compression bonding press as well as photolithography is limiting factor in determining metal patterning because high temperature and high compression pressure can affect migration of metal lines. Metal patterning can be broken if the pressure used in lamination exceeds the pressure level that metal layer can withstand. To solve this problem, electroplating to increase the thickness of metal layer is used after photolithography. However, simply increment of metal thickness has limitations in enduring pressure and pattern resolution. The line pitch resolution of metal pattern is limited to 160 μm when high temperature and high pressure (295 °C, 1 Mpa) is used in lamination process, which prevent high-density electrode array and interconnections. Low temperature and low pressure (285 °C, < 500 kPa) in lamination process can realize 20 μm -line pitch resolution, but reliability problem can arise from weak LCP-LCP interface.

Figure 2.24 Migration of metal pattern after lamination process

Silicon dioxide (SiO_2) on the surfaces of silicon wafer offers excellent barrier properties in flexible electronic implants [103]. Silicon nitride films deposited by plasma-enhanced CVD play a role of barrier to water and oxygen for flexible display applications [104]. Silicon neural probe have utilized triple dielectric layers to prevent water and ion penetration [105]. In this regard, fabrication process using dielectric materials with LCP is proposed to enhance reliability. Bonding strength between LCP and dielectric material is important to apply dielectric material between LCP layers. The roles of dielectric material in LCP-based implantable devices are to grip metal pattern during lamination process and delay the penetration of body fluid.

2.4.2.2.2 Proposed Fabrication Process

Silicon dioxide and silicon nitride are deposited on a silicon wafer using

CVD process (PlasmaPro System 100, Oxford Instruments). After CVD, ICP (O_2 , 100 sccm, 0.1 torr, 150 W, 3 mins) is utilized to activate the surface of LCP film (Vecstar CTF-25, Kuraray) and dielectric materials for bonding enhancement. Plasma treatment increases surface hydrophilicity which affect bonding strength [106]. Identical plasma enhancement is applied in all test samples. For test samples of adhesion strength measurements, lamination process using thermo-compression press (Model 4122, Carver, Wabash, IN, USA) is carried out in low temperature and low pressure conditions ($282\text{ }^{\circ}\text{C}$, $< 500\text{ kPa}$). High temperature and high pressure condition is used in lamination process to evaluate that the dielectric materials prevent migration and breakage of metal lines patterned on the LCP.

2.4.2.2.3 Preliminary Study

Figure 2.25 Experimental setup of customized peel test

Customized peel test method is utilized to compare adhesion strength between LCP and dielectric materials. Test specimens of which width is 5 mm are

fixed to a load cell (ATI, Nano17, Pinnacle Park, Apex, NC, USA) which is controlled by a motorized linear actuator (Newport, LTA-HS, Irvine, CA, USA). Peeling force is measured until the upper LCP film is peeled off 4 mm from the bottom layer and the average force is calculated during peeling off. Silicon dioxide and silicon nitride are deposited on a silicon wafer. LCP films are thermally laminated onto the dielectric materials-deposited surface. Adhesion strengths of LCP-LCP (result from low temperature and low pressure lamination), LCP-SiO₂, and LCP-SiN_x are compared by the means of peel test method.

Lamination process using high temperature and high pressure with dielectric materials is also evaluated to verify whether metal patterning is stable in dielectric material during highly reliable lamination process.

2.4.3 Experimental Comparison LCP-Based to Wire-Based Electrode Array

Conventional wire-based electrode array uses generally Teflon-coated Pt or Pt-Ir wires for metal lines and silicone elastomer as a carrier. It is well-known that Teflon (Polytetrafluoroethylene, PTFE)-coated wire electrode array is stable in body fluid and Teflon is not peeled off from metal wire. PTFE is composed of carbon and fluorine and carbon-fluorine bonds is non-reactive and resistant to humidity. Its coefficient of friction and hydrophilicity is extremely low [107]. However, it has not been evaluated in highly accelerated condition in saline. In other words, long-term reliability of metal wire-based electrode array has not been compared to that of polymer-based electrode array in identical condition.

Fundamental characteristics of materials cannot determine practically the long-term reliability of device in ionic electrolyte. Moreover, in recent years, Perfluorooctanoic acid (PFOA), which is a material used in adhesion of PTFE and metal, was reported as a carcinogen. PFOA-free PTFE-coated metal wire has been reported that flaking occurs in humid condition [108]. Therefore, wire-based neural electrode array needs to be compared with polymer-based neural electrode array in a body fluid condition for device reliability.

Experimental setup is depicted in Figure 2.26 (a) . Accelerated soak test and impedance measurement are carried out to evaluate wire- and LCP-based electrode array. To fabricate wire-based electrode array, mold is designed to cure silicone elastomer for carrier of wires. Metal patterning of LCP electrode array is shown in Figure 2.26 (d). Four-channel wire- and LCP-based electrode array is soaked in 60 °C PBS. Impedance is measured using the same aforementioned equipment. Decreasing value of impedance data means PBS penetrates into the interface between metal and PTFE or metal and LCP, which indicates delamination. Metal line is open or electrode site loses its role to stimulation when impedance increase 100 times more than the initial value

Figure 2.26 (a) Experiment setup for comparison metal wire to polymer electrode array (b) Mold design for silicone elastomer curing (c) Mask design for photolithography (d) Metal-patterned LCP film

Chapter III

Results

3.1 LCP-Based Cochlear Electrode Array for Atraumatic Deep Insertion

3.1.1 Fabricated Electrode Array

LCP-based cochlear electrode array for atraumatic deep insertion is fabricated using MEMS technologies and thin-film process. The number of stimulation channel is sixteen and two reference electrodes are at 72 mm apart from the end of stimulation channel. The lengths of electrode array is 28 mm and the thickness of the current LCP structure varies depending on the part of the cochlear electrode array, which is 25 μm at the tip, 50 μm at the middle, and 75 μm at the base. The diameters of the electrode array are 0.3 mm (tip) and 0.75 mm (base). The dimensions of the current LCP-based cochlear electrode array are similar or finer than that of a conventional cochlear electrode array due to peripheral vias and via-openings.

Figure 3.1 LCP-based cochlear electrode array with tapered structure

3.1.2 Insertion and Extraction Force Measurements

The average of measured insertion force of the electrode array, shown in Figure 3.2, is 2.4 mN at a displacement of 8 mm from the round widow. The average measured maximum extraction force is 33.0 mN as shown in Figure 3.3.

Figure 3.2 Insertion force measured in the plastic scala tympani model

Figure 3.3 Extraction force measured in the plastic scala tympani model

3.1.3 Insertion Trauma in Human Temporal Bone Insertion Study

In the present human temporal bone insertion studies, the insertion depths of the electrode arrays in the human temporal bone, which are measured in micro-CT images, are 450° , 450° , 360° and 630° in the round window approach and 495° in the cochleostomy approach. Insertion trauma is investigated in the cross-section view of enucleated cochlea. Five electrode arrays are inserted without trauma (grade 0) at the first turn. However, for the 630° insertion, dislocation into the scala vestibuli (grade 3) is observed at the tip of the electrode array. There is no observable trauma in the other cases.

Figure 3.4 Human temporal bone insertion study of electrode 1 (Round window approach) (a) Micro-CT image for insertion depth (450°) (b) Reconstructed 3-D image (c) Cross-sectional views of cochlea where LCP electrode array is inserted (Trauma 0)

Figure 3.5 Human temporal bone insertion study of electrode 2 (Round window approach) (a) Micro-CT image for insertion depth (450°) (b) Reconstructed 3-D image (c) Cross-sectional views (Trauma 0)

Figure 3.6 Human temporal bone insertion study of electrode 3 (Round window approach) (a) Micro-CT image for insertion depth (360°) (b) Reconstructed 3-D image (c) Cross-sectional views (Trauma 0)

Figure 3.7 Human temporal bone insertion study of electrode 4 (Round window approach) (a) Micro-CT image for insertion depth (630°) (b) Cross-sectional views (Trauma 3)

Figure 3.8 Human temporal bone insertion study of electrode 5 (Cochleostomy approach) (a) Micro-CT image for insertion depth (495°) (b) Cross-sectional views (Trauma 0)

3.1.4 Electrically Evoked Auditory Brainstem Response Recording

Impedance amplitude and phase angle of the stimulation electrode site of the nanoporous electroplated gold at frequencies ranging from 0.1 Hz to 100 kHz indicates 3.66 k Ω and -43.2 degrees at 1 kHz. A 24 kHz-tone burst-evoked ABR is shown in Figure 3.9 wherein the ABR threshold is measured at 35 dB SPL. The EABR recordings, which are recorded when the current stimulator was on and off, respectively, are depicted in Figure 3.10. The measured peak-to-peak amplitudes are 9.2 μ V and 1.93 μ V without filtering, respectively. When operating the current stimulator, the EABR waveform shows positive peak value that is a meaningful neural signal. When the stimulator is off, there is a significant change in the EABR

waveform. The signal magnitude becomes much weaker and there is no obvious neural signal. It is assumed and evaluated that the guinea pig is not able to recognize the sound stimuli.

Figure 3.9 ABR recording which indicates the threshold level at 35 dB SPL

Figure 3.10 Recorded EABR with Stimulation (a) On and (b) Off

3.1.5 Histological Change and Hearing Preservation

There are shifts in ABR threshold at all frequency measured. Threshold shift levels at all frequency range from 25.6 to 38 dB. The mean and standard deviation of the shift results are arranged in Figure 3.11. The threshold shift levels have been maintained during 4 weeks.

Figure 3.11 ABR threshold shift after (a) 4 days, (b) 1 week, (c) 2 weeks, (d) 3 weeks, and (e) 4 weeks implantation

Cochlea is enucleated after 4 weeks implantation, as shown in Figure 3.12.

In the cross-sectional view of cochlea, dummy LCP cochlear electrode array is inserted in the scala tympani without any trauma. Stable implantation has been maintained during 4 weeks.

Figure 3.12 (a) Enucleated cochlea after 4 weeks implantation (b) Cross-section of the cochlea with LCP electrode implantation

Figure 3.13 Cross-section view of stained cochlea in (a) Middle and (b) Basal turn

In Figure 3.13, there is fibrosis at the site where cochlear electrode array was inserted. Using Masson's Trichrome, stained color is different in each tissue: collagen fiber and bone to blue, Muscle fibers, cytoplasm, erythrocytes, keratin, and fibrin to red, and nuclei to black or blue. White circle areas indicate fibrosis.

3.2 Polymer Electrode Array for Tripolar Stimulation

3.2.1 Simulation Results According to Electrode Site Design

Figure 3.14 shows the simulation results depending on electrode site designs. Center electrode site for stimulation is at the lower layer in Design 1 and the upper layer in Design 2. Design 3 utilizes the side wall electrode site for tripolar stimulation. The value of e-field at the plane where spiral ganglion cells exist are calculated using finite element method. The obtained values are arranged in the Table 3.1 and 3.2. According to the simulation results, Design 3-3 shows the most effective focused stimulation to be chosen to fabricate. The fabricated electrode structure is evaluated in *in vitro* test setup.

(a)

(b)

(c)

(d)

Figure 3.14 Simulation results of tripolar stimulation according to electrode designs (a) Design 1-1 (b) Design 1-2 (c) Design 2 (d) Design 3-1 (e) Design 3-2 (f) Design 3-3 ((i) electrode structure, (ii) absolute value of e-field at the plane of analyzing, (iii) picture of vector distribution of e-field)

Table 3.1 Summarized results of absolute value of e-field distribution

	Design 0 (MP)	Design 0 (TP)	Design 1-1	Design 1-2	Design 2	Design 3-1	Design 3-2	Design 3-3
Max. E-field	4.51×10^{-7}	2.00×10^{-1}	6.87×10^{-1}	1.80×10^{-1}	8.50×10^{-1}	9.36×10^{-2}	8.46×10^{-1}	6.97×10^{-1}
1-mm-Left	2.77×10^{-7}	4.86×10^{-2}	2.26×10^{-1}	8.33×10^{-2}	3.60×10^{-1}	4.76×10^{-2}	3.20×10^{-1}	2.02×10^{-1}
1-mm-right		9.98×10^{-2}	4.13×10^{-1}	1.27×10^{-1}	3.97×10^{-1}	4.45×10^{-2}	4.78×10^{-1}	2.40×10^{-1}
500- μ m-left	3.16×10^{-7}	1.02×10^{-1}	2.95×10^{-1}	1.54×10^{-1}	6.76×10^{-1}	6.70×10^{-2}	5.59×10^{-1}	2.49×10^{-1}
500- μ m-right	3.31×10^{-7}	1.53×10^{-1}	5.55×10^{-1}	1.47×10^{-1}	6.65×10^{-1}	6.85×10^{-2}	6.59×10^{-1}	5.13×10^{-1}

Table 3.2 Summarized results of relative ratio of e-field distribution

	Design 0 (MP)	Design 0 (TP)	Design 1-1	Design 1-2	Design 2	Design 3-1	Design 3-2	Design 3-3
Max. E-field	1	1	1	1	1	1	1	1
1-mm-Left	0.615	0.243	0.329	0.463	0.424	0.508	0.378	0.290
1-mm-right		0.499	0.601	0.703	0.467	0.475	0.0566	0.344
500- μ m-left	0.701	0.509	0.429	0.856	0.795	0.716	0.661	0.357
500- μ m-right	0.734	0.765	0.808	0.815	0.783	0.731	0.780	0.736

3.2.2 Fabricated Electrode Array

Electrode array following Design 3-3 can be fabricated using laser ablation technology and multi-layered through via structure. The fabrication process and result at each process are presented in Figure 3.15 and 3.16. Via at back side of micro-patterned LCP film is made using laser ablation. Silver paste (EPO-TEK H20E, Epoxy Technology Inc., MA, USA) is selected in this fabrication process as a material for via-fill due to its easy curing process. Four-channel LCP-based electrode array for locally tripolar stimulation is fabricated. Pitch of the stimulation channel is 1 mm and the distance between center and auxiliary site is 100 μ m. The width of electrode sites is 300 μ m.

Figure 3.15 Fabrication process of LCP cochlear electrode array for locally tripolar stimulation using MEMS technologies, laser micromachining, and thin-film processes

Figure 3.16 Results of fabrication process (a) Metal patterning after wet etching of seed layer (b) Via opening using laser ablation (c) Laser micromachining of site opening (d) Opened electrode site showing center and side electrodes

3.2.3 *In Vitro* Measurements

Figure 3.17 PWM data and biphasic pulses generated by ASIC chip and test board

Biphasic current pulses are generated by ASIC chip. PWM data to generate current pulses from test board is delivered to ASIC chip. Duration of cathodic pulse of biphasic current pulse is 120 μ s and amplitude of pulses is 1.24 mA in monopolar stimulation mode. In tripolar stimulation mode, the current is divided into ratio of 5.8:4.8 at left and right auxiliary electrode, respectively.

Reduction ratio is compared according to stimulation methods. The proposed locally tripolar stimulation using multi-layered electrode array indicates the most effective focused stimulation. Tripolar stimulation is more balanced reduction of current pulse from the center electrode than monopolar stimulation, which shows imbalanced spread of stimulation due to the position of reference electrode.

Table 3.3 Comparison of reduction ratio of voltage amplitude at 1 mm distant from the center electrode

Stimulation Method	Reduction Ratio (%)	Voltage (V)	Reduction Ratio (%)
	Left	Center (Stimulation)	Right
Monopolar	-	-0.32	37.5
Tripolar (Conventional)	28.57	-0.28	28.57
Locally Tripolar (Proposed)	39.29	-1.12	42.86

3.3 Long-Term Device Reliability

3.3.1 LCP-Based Neural Electrode Array using Mechanical Interlocking at Metal-LCP Interface

3.3.1.1 Fabricated Electrode Array and Metal-LCP Interface

Figure 3.18 Optical images of Electrode site and IDE pattern in fabricated electrode array with and without mechanical interlocking pattern

Metal patterning for mechanical interlocking between noble metal and LCP is fabricated using double steps of photolithography and electroplating. Surface of electrode site is nanoporous electroplated gold. All test samples have IDE pattern for current detection in accelerated soak tests. The microscale metallic lines composed of both a width of 50 μm and pitch of 50 μm are successfully patterned on the electrode site using double steps of photolithography and electroplating. IDEs with a width of 80 μm and a pitch of 100 μm is patterned onto the LCP substrate to measure leakage current indicating device failures

As shown in Figure 3.19, the pre-cut LCP insulation layer with exposed area is aligned to the center of electrode site and laminated onto the LCP substrate using thermal compression bonding. It is shown in cross-section of electrode site that undercut metal patterns surrounded by LCP film are mechanically interlocked with the upper LCP insulation layer. Moreover, LCP layers form monolithic seamless adhesion and bond to the interlocking structures without voids.

Figure 3.19 SEM images of fabricated electrode array with mechanical interlocking
 (a) Electrode site opening (b) Seamless lamination result of upper and substrate layer of LCP (c) Mechanically interlocked LCP film with undercut metal pattern

3.3.1.2 Adhesion Force and Electrochemical Measurements

Table 3.4 shows results of peel test to evaluate adhesion force. There were specific differences in peel strength between the test group 1 with interlocking structures and the control group 2 ($p < 0.1$). In comparison with the control group, the maximum force per width of the test specimens with interlocking interface between LCP and noble metal has increased by 34.8 percent.

Table 3.4 Results of peel tests in test samples with and without mechanical interlocking

Classification	Maximum force/width (N/mm)	Mode of failure
	Mean (SD)	
w/ interlocking	0.7696 (0.0230)	peel + snap or tear
w/o interlocking	0.5707 (0.0131)	snap, peel + snap

Figure 3.20 Impedance measurements of fabricated test samples with and without mechanical interlocking used in accelerated soak test

Figure 3.21 Cyclic voltammogram to calculate charge storage capacitance (cathodic) of group 1 and group 2

Figure 3.20 and 3.21 show electrochemical measurements of test samples. Group 1 (with mechanical interlocking) shows lower amplitude of impedance and larger CSCc than Group 2 ($p < 0.01$). Impedances at 1 kHz are measured as 356.99Ω and 474.31Ω in group 1 and 2, respectively. The measured and calculated cathodal charge storage capacities are 1.388 mC cm^{-2} in group 1 and 1.031 mC cm^{-2} in group 2.

3.3.1.3 Accelerated Soak Test and Lifetime Estimation

Figure 3.22 Leakage current measurements during the *in vitro* 75°C accelerated soak tests.

Leakage current measurements and MTTF of LCP-based electrode test samples using mechanical interlocking at the interface between the LCP and the gold during the lamination process and LCP-based electrode test samples without interlocking patterns are shown in Figure 3.22. Threshold level of 1 μA indicating that device failure is determined from the earlier accelerated soak test results. The average days of soaking when the device failure occurred due to water penetration into the exposed electrode site are observed as 224 days in group 1 and 185 days in group 2, respectively. If we apply '10-degree rule', the estimated lifetimes of two groups are about 8.55 years and 7.06 years, respectively. However, there is less

significant difference in data ($p > 0.05$).

3.3.2 Fabrication Method using LCP and Dielectric Materials

3.3.2.1 Adhesion Strength of Bonding between LCP and Dielectric Materials

There are significant differences in bonding strength among LCP-LCP, LCP-SiO₂, and LCP-SiN_x ($p < 0.05$). As shown in table 3.5, LCP-LCP interface shows weaker bonding than LCP-dielectric materials under the low temperature and low pressure condition. This result reveals feasibility of dielectric material bonded to LCP.

Table 3.5 Results of customized peel tests to compare bonding strength of LCP-LCP with LCP-dielectric materials

Interface	Maximum force/width (N/mm) Mean (SD)	Mode of failure
LCP-LCP	0.2365 (0.0212)	Peel
LCP-SiO ₂	0.5412 (0.0446)	Peel
LCP-SiN _x	0.4027 (0.0369)	Peel

3.3.2.2 Lamination Result of the Proposed Fabrication Method

Figure 3.23 Metal patterning (a) Before and (b) After lamination process using dielectric material and LCP

In Figure 3.23, results of lamination process using LCP and dielectric materials on which metal is patterned are shown. There is no metal migration on the dielectric material. Dielectric materials protect metal patterning from high pressure and temperature as well as water penetration.

3.3.3 Impedance Measurements of LCP-Based and Wire-Based Electrode Array

(a)

(b)

Figure 3.24 Impedance measurements of wire- and LCP-based electrode array

Impedance measurement data is arranged in Figure 3.24. The experiments are ongoing at the day of writing of this dissertation. Gradual increase of impedance is observed in LCP-based electrode arrays, whereas impedance in wire-

based electrode arrays is maintained during days of soaking except for failure sample.

Chapter IV

Discussion

4.1 LCP-Based Cochlear Electrode Array for Atraumatic Deep Insertion

4.1.1 Comparison of the Current Proposed Electrode Array to the Previous Electrode Array

Adopting peripheral blind via and tapered structure, the current proposed cochlear electrode array reduces width of electrode array with variable stiffness depending on the part of the electrode array. Figure 4.1 shows comparison of the current electrode array design with the previous LCP cochlear electrode array which used uniform thickness throughout the total electrode array. If 20- μ m line pitch, 0.3-mm-wide electrode sites, 16-channel electrode array, and 0.1-mm laser machining error are assumed, the total width of the previous design ranges from 0.5 mm (tip) to 1.02 mm (base) and that of the proposed design ranges from 0.3 mm (tip) to 0.36 mm (base). The tip and base of the current electrode array can be reduced to 60 % and less than 40 % of those of the previous design, respectively. This reduced width and more flexible tip result in decrease of insertion and extraction forces. As shown in Figure 4.3, the measured insertion forces of the electrode arrays are 2.4 mN (current version), 8.2 mN (previous version), and 17.2 mN (wire-based cochlear electrode array) at a displacement of 8 mm from the round widow. The current cochlear electrode array is inserted 3 mm deeper than the previous cochlear electrode array. This means lower frequency area can be stimulated using the current design. According to Greenwood function, 3 mm difference in insertion depth is approximately converted into the displacement of

array tip at the region of frequency from 4009 to 6592 Hz, if the less inserted array is inserted at 20 mm [109]. The measured maximum extraction forces are 33.0 mN (current version), 110.4 mN (previous version), and 158.5 mN (wire-based cochlear electrode array), respectively. In addition to the reduced insertion force, the extraction force in the current version is lower than that of the previous LCP-based electrode array and the conventional wire-based cochlear electrode array. These results are desirable for residual hearing and reimplantation surgery without insertion trauma, which is critical for children who have experienced device failure due to the short lifespan of the device compared to the lengths of time these patients require the device [37, 38, 110, 111]. Moreover, It is possible that chemical or dry etching and laser micromachining process make thinner LCP films, which lead to a more flexible tip.

(c)

(d)

Figure 4.1 Comparison of LCP-based cochlear electrode arrays between the previous and the current designs (a) The thickness of the previous LCP structure is $50\text{ }\mu\text{m}$ along its entire length. Its diameters at the tip and at the base are 0.5 mm and 0.8 mm , respectively, and its length was 28 mm . (b) The thickness of the current LCP structure in the cochlear electrode array varies from $25\text{ }\mu\text{m}$ (tip) to $75\text{ }\mu\text{m}$ (base). (c) Previously reported array employed a design scheme which arranges stimulation sites at the center with the lead wires around the stimulation sites. (d) In this design, a

peripheral via is employed so as to protect the lead wires at the center from the cutting laser beam.

(a)

(b)

Figure 4.2 (a) Optical images of fabricated LCP-based cochlear electrode arrays with and without tapered structure (b) Side and cross-sectional views of the arrays with and without peripheral blind via

Figure 4.3 Insertion force measured in a customized insertion setup (25 μm and 50 μm tip mean the current design and the previous design, respectively.)

Figure 4.4 Extraction force measurements

4.1.2 Suggestion of Improvement in Electrode Design Related with Insertion Depth and Trauma

The insertion force needed for deeper insertion into the scala tympani increases as the insertion depth increases because the increased friction necessitates greater insertion force [112]. If exceeding the mechanical tolerant level of the basilar membrane, resulting in trauma in the cochlea. Uniform thickness along the entire length leads to insufficient supportability in the basal region for full insertion. In the present study, the number of LCP layers varies from the tip to the base. For a more flexible tip, channel 1 is not covered by another LCP layer, and the exposed plane is used as the stimulation electrode contact. From channels 2 to 8, the

substrate layer and inter-cover layer are used for the patterns and the cover, respectively. From channel 9, inter-cover layer is used for the patterning of the electrodes and wires, and the outermost insulation layer is laminated onto this layer. The more flexible tip and stiffer base result in less insertion trauma and more insertion depth as well as deeper insertion with less insertion force.

Figure 4.5 Insertion depth and trauma in human temporal bone insertion studies of LCP-based cochlear electrode arrays

The insertion trauma and depth in human temporal bone insertions are investigated to evaluate the proposed LCP-based cochlear electrode array with a layered and tapered design. In the present study, the measured insertion depths of

the electrode arrays in the human temporal bone are 630°, 470°, 450°, and 360° in the round window approach and 500° in the cochleostomy approach (Figure 4.5). Four cases show enhanced results of the insertion depth, but for one case the insertion length was shorter compared to the previous result (405°). Insertion trials generally encounter considerable resistance from 13th of 16th electrode site insertion. There is no significant difference between round window approach and the cochleostomy approach about the resistance. The insertion trauma continues to exist only in the 630° temporal bone insertion trials, with evidence that the electrode array causes no trauma in the basal turn. In 630° insertion trial, the LCP-based cochlear electrode array is found to be wavy structure from the result of treatment and handling by accident. Therefore, wavy structure in electrode substrate may help reduce insertion force because film-type LCP-based cochlear electrode arrays undergo resistance at perpendicular direction from the grain or plane of LCP surface. Although atraumatic deep insertability are observed in the proposed finer and multi-layered electrode array, additional approaches such as more flexible tip and wavy substrate are needed to insert LCP-based cochlear electrode array deeper without trauma in basal and second turn.

4.1.3 Point to Improve in Fabrication Process

Multi-layered structure can be also used to provide a manufacturing method for a high-density implantable polymer-based electrode array. Using multi-layered structure and micro-fabrication processes allows more electrode stimulation channels given a restricted electrode dimension. This is not easily

achieved in a manual wire-based cochlear electrode array. The more LCP layers, the more stimulation channels we can use. This can be another advantage as a cochlear electrode array which has limited number of stimulation channels compared to the number of hair cells until the LCP layers are too stiff to be inserted stably.

Figure 4.6 Fabrication processes and their results

Figure 4.6 shows fabrication processes and their results. In lamination process to transform multi-layered films to one united substrate, the alignment and even pressure is significant factor determining the success in the fabrication of the

LCP electrode array. As in Figure 4.7, metal lines in bottom layer is moved to upper layer because of stepped pulley structure show. This often causes short or open of metal lines, resulting in detrimental effect in production throughput. Partially stepped structure is inevitable as long as via structure and thermally compressive lamination process are used.

Figure 4.7 Deformation of metal line after lamination process

For atraumatic insertion, it is also important to produce a finer electrode array. The finer electrode array cause less damage to the cochlear tissue. To reduce the width of the electrode array, fine metal patterns are useful. Because the metal is evaporated and patterned onto LCP film on a silicon wafer, uniform flatness of the attached LCP on the silicon wafer is a significant condition. Therefore, it is necessary to use proper adhesive material to attach the LCP film onto the silicon

wafer. Conventionally, photoresist has been used to attach LCP film to silicon wafers. In micro-fabrication processes, the evaporation of the solvent on the photoresist occurs. The flatness of the LCP film attached using the photoresist layer here worsens over time, and this method cannot support fine metal patterns through the entire manufacture process. Specifically, equipment using a vacuum chamber creates more serious situations, resulting in a limitation of the dimensions of the metal pattern. In contrast to a photoresist, a silicone elastomer does not create any bubbles or voids. Moreover, it is resistant to chemical solution. Also, the detachment of the LCP films should be considered for micro-patterning. The LCP film should adhere onto the wafer during the process with a chemical etchant and solvent. If an adhesion layer is damaged or dissolved in these chemicals, the microstructure likely cannot be patterned onto the LCP film. The degree of non-flatness of the LCP films attached to a silicon wafer using a photoresist and a silicone elastomer is found to be greater than 43.7 μm and 16 μm , respectively [89]. Because the size of the electrode array is related to the degree of trauma, it is important to use uniform and flat adhesion layer in manufacture process of LCP-based electrode array. The silicone elastomer shows better uniformity and durability compared to a photoresist. Unless peeling stress is applied, film adhered with the silicone elastomer is not detached. Because the Van der Waals force [113, 114] is applied between the silicone elastomer and the LCP film, the elastomer-coated silicon wafer can be reused for repetitive micro-fabrication processes.

4.1.4 *In Vivo* Implantation

As shown in EABR recordings, electrical stimulation is successfully delivered into the cochlea of a guinea pig through the current electrode array. Acute insertion and stimulation steps confirm its functional operation as an electrode. As a future work, it is necessary to implant the entire LCP-based cochlear implant system into an animal model. Chronic electrical stimulation in order to analyze the long-term reliability and histological changes of the device.

From the results of 4 weeks implantation of dummy LCP electrode arrays in guinea pigs, electrode implantation is maintained stably. Tissue reaction is comparable level with that of conventional cochlear electrode array implantation. It is calculated that scala tympani area occupied by tissue responses are 52 % (Control group, CochlearTM electrode array) and 43 % (Experimental group, LCP electrode array), respectively. Figure 4.8 shows fibrosis in both electrode array implantation. The electrode array is implanted in scala tympani and fixed at its position where there is no significant difference between two images. Feasibility of clinical use of LCP-based cochlear electrode array is corroborated by these *in vivo* implantation results.

Figure 4.8 Comparison of fibrosis between conventional and LCP-based cochlear electrode array

4.2 Power Consumption and Stimulation Threshold of Tripolar Stimulation

Tripolar stimulation for current focusing is effective in reducing crosstalk between electrode stimulation channels at the cost of a high power consumption [115-117]. Multipolar strategies utilize concurrent stimulation of multiple electrode sites, resulting in the increased power consumption. Besides, high threshold and comfort levels can decrease the time that batteries can be used [115, 118]. The growth of loudness (amplitude of stimulation current pulse) can be limited by compliance voltage due to highly increased threshold level. Larger channel-to-channel variability in stimulation level is another consideration from focused

current and reduced reactive area. There are alternatives to the trade-off of reduction in channel interaction and power consumption such as reducing stimulation pulse rate, reduced distance from electrode to target tissue, and limiting the number of channel in use. Paired stimulation (depicted in Figure 4.9), which is stimulation method using two electrode sites simultaneously, can reduce overall stimulation rate in half [117]. This method is interrupted by channel interaction to be used practically. Convergence tripolar stimulation and paired stimulation can compensate each other in terms of the increased power consumption and channel interaction. If the proposed electrode site design for locally tripolar stimulation adopts paired stimulation, adjacent electrode sites can be used in stimulation simultaneously, which increase physically the number of stimulation channel in tripolar stimulation at the same time the power consumption is halved by reduction of stimulation rate.

Figure 4.9 Scheme of electrical pulse trains of sequential and paired stimulation

4.3 Technical Strategies to Improve Device Reliability

4.3.1 Mechanical Interlocking at Metal-Polymer Interface

Metallic lines in the electrode site are patterned using double steps of photolithography and electroplating to make mechanical interlocking pattern. Overexposure of UV light forms trapezoidal photoresist patterns, which results in anti-trapezoidal metallic patterns during electroplating process. Thermal lamination bonding process interlocks LCP insulation layer with anti-trapezoidal (undercut) metal structures without voids as forming monolithic seamless bonding between

LCP film for electrode substrate and insulation LCP films.

Optimal adhesion of joint strength between two materials is defined as following equation [119].

$$\begin{aligned} \text{Optimum joint strength} = & (\text{constant}) \\ & \times (\text{mechanical interlocking component}) \\ & \times (\text{interfacial chemical component}) \end{aligned}$$

Interfacial chemical bonding is determined by the reactive willingness of involved materials [120]. Polymers are attached onto the noble metals by intermolecular electrostatic and weak chemical bonding of van der Waals force because noble metals have no reactive willingness with organic polymers like LCPs [121]. In this strategy, the mechanical interlocking using microscale metallic lines for interfacial mechanical bonding is adopted to improve interfacial adhesion strength between LCP and noble metal for long-term device reliability. In peel tests, the adhesion strength are significant different between test samples with and without mechanical interlocking. Metal surface topography modification causes failure mode transition from adhesive to cohesive [97]. Both groups with and without interlocking structures have nanoporous surfaces formed by electroplating in electrode site, which leads to the fact that failure modes in both groups are not adhesive only. The mechanical interlocking provides the energy expending process for crack propagation, makes the interface more cohesive. In addition to the enhancement of adhesion strength, the structures remained on the exposed area in the electrode site window have an additional effect on the increase of geometry

area. In comparison with the control group, the impedance decreases 24.8 % and CSCc increases 34.6 % due to larger surface area.

Figure 4.10 Optical microscope images of test samples (a) Electrode site of test sample without mechanical interlocking in the course of accelerated soaking (b) Electrode site of test sample with mechanical interlocking after water penetration (c), (d) Backlight microscope Images of test samples without and with mechanical interlocking after device failure (e) Side view of delamination of LCP film (f) Breakage of metal lines after water penetration

Size of interlocking patterns is critical point in the adhesion strength [97]. In the previous study, the failure load of adhesive joints increase according to the increment of the ratio of the patterned width to the preserved width. In this strategy, size and morphology of metallic pattern for interlocking on the polymer film need

to be split and studied. However, in this study, the effect of mechanical interlocking pattern on the adhesion strength and device reliability is proved by comparing the test samples with and without mechanical interlocking, though the condition of the interlocking pattern of noble metal is not optimized.

(a)

(b)

Figure 4.11 SEM images of cross-section views of test samples after accelerated soak tests (a) Without mechanical interlocking (b) With mechanical interlocking

Accelerated soak testing method is used in this study to investigate device reliability. In addition to the results of peel tests, result of accelerated soak tests reveals practical reliability of LCP-based devices. In Figure 4.10, water penetration at metal-LCP interface cause detrimental effect in LCP adhesion, resulting in metal

line breakage and device failure. However, mechanical interlocking between noble metal and LCP is intact even after water penetration as shown in Figure 4.11. Both top and bottom surfaces of metal are peeled off from the LCP insulation film and electrode substrate in non-mechanical interlocking samples, but, adhesion between interlocked metal and LCP is maintained after water ingress. In mechanical interlocking samples, there is further delamination at interface without interlocked structure. The interlocked interface between LCP and undercut metallic structure remains intact after device failure, while the other interface without interlocking is delaminated even in the same test specimen. Therefore, this result derive that double-sided mechanical interlocking is needed to enhance device reliability. Mechanical interlocking at the fabrication steps of metal deposition on LCP film can be realized using following fabrication process (Figure 4.12). In Figure 4.13, mechanical interlocked metal-LCP in the substrate (bottom) layer on which metal patterning can be fabricated.

Figure 4.12 Fabrication process of mechanically interlocked metal deposition onto LCP film (1st sacrificial layer and SiO_2 deposition on Si or Glass wafer → Interlocking patterning using photolithography and SiO_2 etching → 2nd Sacrificial layer and noble metal deposition → Lamination metal patterning onto LCP film → SiO_2 and 2nd sacrificial layer removal)

Figure 4.13 Mechanical interlocked metal-LCP in the substrate layer

Titanium can be used to strengthen the interfacial chemical bonding as an adhesion promotion layer, but, more complicated and delicate fabrication processes are needed due to the risk of galvanic corrosion from multiple metal layers exposed to ionic water [122]. When using different metals, micro-crack in the electrode site can be critical factor in device reliability. Micro-crack exposed to electrolyte accelerates water penetration. Figure 4.14 shows TEM and FIB images of micro-crack in the LCP-based neural electrode due to mishandling. Water ingress into the micro-crack can cause damage of electrode site (Figure 4.10) and galvanic corrosion at the interface of two different metals.

Figure 4.14 (a) TEM and (b) FIB-SEM images of micro-crack in electrode site

4.3.2 Hybrid Device Based on Polymer and Dielectric Materials

The results of customized peel test reveal that LCP-dielectric material bonding is more reliable than LCP-LCP bonding when using low temperature and low pressure lamination method, even though bonding conditions such as plasma treatment are not optimized. This results show feasibility of fabrication process using dielectric materials with LCP. However, as in the results of peel tests, LCP-dielectric materials interface is adhesive from the failure mode. Conversion adhesive interface to cohesive interface should be needed for better reliability using anodic bonding method and optimization in plasma condition for surface activation.

Figure 4.15 shows the peeled interface of LCP-LCP bonding according to lamination temperature and pressure. In samples with high temperature and high pressure lamination process, the film does not peel neatly and it is difficult to

distinguish the interface. In contrast, the LCP film bonded in low temperature and low pressure lamination is peeled off from bottom LCP film and the interface is clearly distinguished. In this regard, it is essential to use high temperature and high pressure in lamination process for long-term device reliability. To prevent migration of metal lines, which is a disadvantage in high temperature and high pressure lamination, dielectric material can be utilized to grab the metal patterning during lamination process. There is no significant change in metal patterns between before and after lamination process.

Figure 4.16 shows feasible fabrication process and metal pattern with dielectric material onto LCP film. With this fabrication process, long-term reliable and high-density LCP-based neural implant is expected to realize. It is difficult to handle layer of dielectric materials due to their ultra-thin thickness ($< 5 \mu\text{m}$). LCP plays a role of handling substrate as well as final encapsulation cover layer.

Figure 4.15 Images of LCP-LCP interface (a) Using high temperature and high pressure lamination process and (b) Low temperature and low pressure lamination process after peeling off

Figure 4.16 Fabrication flow feasible to make LCP-dielectric material hybrid implantable device

4.4 Review of Long-Term Reliability of LCP-Based Device

Helium leak test is the general and standard method used in the industrial field to measure the hermeticity of metal-based implantable devices. The detected helium leakage in this test is estimated with that of water using the square root of

their ratio of the molecular mass [96]. However, in polymer-based devices, it is difficult to measure correct helium leakage, as organic polymers such as LCPs naturally absorb helium [60, 61]. Also, in terms of the electrode, water ingress at the interface between the polymer and the metal at the electrode site cannot be separated from that at the surface of the electrode. An absolute value of long-term reliability of polymer-based implantable devices is hard to measure using conventional testing method for metal-based devices. Therefore, testing method such as accelerated soak tests is needed to compare the “relative long-term reliability” of the test samples. As mentioned in the section 2, Materials and Methods, there are three pathways through which water ingress occurs in the LCP-based neural electrodes: through the LCP surface, through the interface between the LCP and the LCP layers, and through the interface between the LCP and the metal. Among these pathways, the polymer-metal interface is the limiting factor of the long-term reliability of LCP-based neural implantable devices [63]. An examination taken after water leakage into the electrodes corroborates that the LCP-metal interface is the most vulnerable region to water penetration.

The accuracy of lifetime estimations at body temperature using the ‘ten-degree rule’ is not completely acceptable. The ten-degree rule is based on gross approximations from the Arrhenius reaction rate function. In order to obtain an accurate lifetime estimation, the activation-energy-related mechanism should be identical at the body and accelerated temperature. In this regard, an accelerated temperature above 60°C is not recommended in a polymer-related aging test due to the non-Arrhenius behavior during polymer degradation [123]. Other activation-

energy-related mechanisms which do not occur at a typical body temperature can occur at an elevated temperature. Preliminary accelerated soak tests using LCP-based neural electrodes at a temperature of 110°C and 95°C also reveal that theoretical predictions of device lifetime based on only the ten-degree rule are not in good agreement with empirical data. The ten-degree rule provided conservative predictions of lifetime expectancy levels [124]. The temperature of 75°C used in the accelerated soak tests in this paper was chosen as an elevated temperature to expedite encapsulation failure within the limited time period. In addition, Temperatures above 60°C have been used in accelerated aging tests for polymer-based device such as parylene-C and LCP, which were used to prove the reliability of the fabrication methods [63, 102]. These results can be considered to compare the “relative” reliability of LCP-based neural electrodes depending on the mechanical interlocking at the LCP-metal interface. To obtain more accurate lifetime estimations in the body, an accurate temperature coefficient (Q_{10}), which is roughly assumed 2 generally, as a consequence of increasing the temperature by 10°C should be calculated through accelerated soak tests at multiple temperatures with a narrow temperature interval (such as 5°C and 10°C).

Figure 4.17 Electrical modeling of crosstalk analyzation in stimulation electrode when water penetration occurs

Electrical modeling analyzed in this dissertation refers to the literature [125] about modeling of recording electrode and it is transformed according to stimulation electrode array. It is assumed that LCP-LCP bonding is strong and delamination between LCP films does not occur when using lamination process with high temperature and high pressure. However, if insufficient temperature and pressure are given due to stability to secure metal patterning, LCP-LCP as well as metal-LCP bonding is delaminated when water penetrates into LCP-based device. LCP-LCP delamination affect metal lines stability and electrolyte penetrates into the space between metal lines, resulting in short of metal lines. This causes crosstalk between adjacent electrode stimulation sites. In the modeling (Figure 4.17), Crosstalk (dB) is calculated as following.

$$\text{Crosstalk (dB)} = -20 \log \left(\frac{V_{in1}}{V_{out2}} \right) \approx$$

$$-20 \log \left(\frac{1 - \frac{(Z_{site} \parallel Z_{c,site})(Z_{sh} \parallel Z_{c,line} \parallel Z_{site})}{Z_{site}^2} - \frac{(Z_{site} \parallel Z_{c,site})^2}{Z_{c,site}^2}}{\frac{(Z_{site} \parallel Z_{c,site})(Z_{sh} \parallel Z_{c,line} \parallel Z_{site})}{Z_{site} Z_{c,line}} + \frac{(Z_{site} \parallel Z_{c,site})^2}{Z_{site} Z_{c,site}}} \right)$$

It is assumed that Z_L and Z_{line} is small enough to be neglect in the calculation and Z_{sh} is much larger than other impedances. Pitch of metal lines is 20 μm and the conductivity of PBS is 15,000 $\mu\Omega^{-1}/\text{cm}$. Volume resistivity of LCP is larger than $10^{13} \Omega \text{ cm}$. Area of electrode site and distance between electrode sites are 0.1 mm^2 and 1 mm, respectively. In high temperature and high pressure lamination, $Z_{c,line}$ is approximate to R_{LCP} , which is calculated as $1.33 \times 10^{15} \Omega$. In low temperature and low pressure lamination, $Z_{c,line}$ is approximate to R_{PBS} after water ingress, which is calculated as a $8.89 \times 10^3 \Omega$. This low value of $Z_{c,line}$ increases the above crosstalk value, which leads to device failure. Therefore, high temperature and high pressure in lamination process is significant for device reliability.

The results of reliability tests for various LCP-based devices are summarized in Table 4.1. To predict the relative humidity inside the LCP-encased cavity, the moisture diffusion through the polymer was analytically calculated using Fick's diffusion law and Henry's law with solubility [63]. The theoretical lifetimes were proportional to the thickness of the LCP layers from the fact that time constants when the relative humidity reaches 63 % inside the LCP-based package, with LCP layers 25 μm , 50 μm , and 100 μm thick, were 15.3, 31.2, and

64.3 years, respectively..

Table 4.1 Summarized results of reliability tests of LCP-based devices and the conditions of each specimen

Classification	Interface	T* (°C)	MTTF** (days) or leak rate	Lamination Pressure (kPa)	Surface modification and bonding	Method
LCP encapsulation [63]	LCP surface	Body	>5000	-	25-μm thick LCP	Analytic calculation
Flat package [72]	LCP-LCP	75	390	< 100	O ₂ plasma fusion bonding	Soak (IDE)
Curved package [63]	LCP-LCP	87	87	500	O ₂ plasma fusion bonding	Soak (IDE)
Electrode [63]	LCP-metal	87	21	75	O ₂ plasma, electroplated gold fusion bonding	Soak (pulsing)
Electrode [63]	LCP-metal	87	114	500	O ₂ plasma, electroplated gold fusion bonding	Soak (pulsing)
Electrode [84]	LCP-metal	75	185	100	O ₂ plasma, electroplated gold fusion bonding	Soak (IDE)
Electrode [84]	LCP-metal	75	224	100	O ₂ plasma, electroplated gold, interlocking structure fusion bonding	Soak (IDE)
Flexible package [76]	LCP-LCP	Body	42	-	Fusion bonding	<i>In vivo</i>
Flexible package [76]	LCP-LCP	75	95	-	Fusion bonding	Soak (gate- drain leakage current)
Interconnection [126]	LCP-metal	-	<5×10 ⁻⁸ (mbar • l/sec)	-	Fusion bonding	Helium leak
Surface-mount package [60]	LCP-LCP	-	3.7×10 ⁻⁸ (atm•cc/s)	-	Fusion bonding	Helium leak

* Temperature used in the soak tests

** Mean time to failure

- Reprinted from the reference [36]

In a study to compare an LCP-based implant package with polyimide- and parylene-based packages using IDEs, the leakage current was not detected during more than one year of soaking in 75°C PBS [72]. In contrast, other polymer-based devices failed within 117 days. The leakage current in a retinal prosthesis with a curved package design was also measured [63]. After 87 days of soaking at 87°C PBS, water penetration occurred.

Ion diffusion and oxidation are the main causes of the delamination of polymer-metal interfaces in ion-contained saline [93-95]. Lee *et al.* evaluated the adhesion of LCP-LCP and LCP-Ti interfaces in 37 °C PBS soak tests which incorporated blister tests [78]. The test results showed that LCP-LCP and LCP-Ti interfaces were more reliable than polyimide-polyimide and polyimide-Ti interfaces. Methods to enhance the adhesion strength between LCPs and metals have been explored, and their effects on reliability were evaluated [63, 84]. A device created at a thermo-compression pressure of 500 kPa withstood operation 93 days longer (from 21 to 114 days) than another created at 75 kPa of pressure in

87°C PBS. Another method for enhancing the adhesion strength involved the use of mechanical interlocking between an LCP and metal [84]. Micro-metal patterns for mechanical interlocking of LCP with metal were fabricated onto LCP substrates. The LCP insulation layer and the metal patterns were interlocked during the thermo-compression bonding process. The test specimen with interlocking showed higher adhesion strength and improved device reliability from 185 to 224 days in a 75°C soak test.

In vivo device stability tests for LCP-based packaging technologies have been performed. An implantation of LCP-encapsulated wireless system was conducted in a rat during six weeks to verify the RF response stability of the device of which the external PCB linked to a network analyzer. Insertion loss and isolation remained constant for six weeks [76]. Non-functional dummy LCP devices for retinal prosthesis were implanted stably in two New Zealand white rabbits for 2.5 years without adverse effects or structural deformations [63, 78].

Although it has been argued whether helium leak tests can be used for polymer-based packages, as stated earlier, there have been a number of helium fine-leak-rate measurements of LCP encapsulations. High-density electrical interconnection feedthroughs, 1024-stimulator channels in a 5 mm × 5 mm area,

are realized utilizing a novel fusion bonding process [126]. Helium leak rates of $< 5 \times 10^{-8} \text{ mbar} \cdot \text{l s}^{-1}$ were measured, which is a reliable level compared to the leak rates of glass substrates with metallized vias. LCP cavity of LCP surface-mount packages for K α -band applications had a fine leak rate of $3.6 \times 10^{-8} \text{ atm} \cdot \text{cc s}^{-1}$ [127]. Another LCP-based package using the same thermo-compression sealing process showed a measured fine leak rate of $3.7 \times 10^{-8} \text{ atm} \cdot \text{cc s}^{-1}$. These results show that LCP is classified as a near-hermetic material for electronics packaging comparable to ceramic and metal [60].

Chapter V

Conclusion

In the present study, we develop LCP-based cochlear electrode array for atraumatic deep insertion using a novel design scheme and an advanced LCP-based micro-fabrication process. A tapered structure of multi-layer LCP substrates with 16-channel interconnection realized on LCP film is successfully fabricated. Variable layers depending on the parts of the electrode array are utilized for a more flexibility at tip and a sufficient rigidity at stiffer base. This design enables safer insertion with less insertion force. Dislocation into the scala vestibuli is observed in one of five trials at the tip of the electrode array in human temporal bone insertion studies, whereas there is no observable trauma at the basal turn. These are more atraumatic results compared to the conventional wire-based and the previous uniformly thick LCP-based electrode. The initial functional data by means of EABR recordings is obtained via acute electrical stimulation in the guinea pig model. It is revealed that the amounts of hearing preservation and tissue reaction are comparable with conventional electrode array after 4 weeks *in vivo* implantation.

We also propose a particular electrode site design for locally tripolar stimulation to increase spectral resolution in multi-channel polymer-based neural electrode array. Simulation results show the possibility of the proposed electrode site design and focused current stimulation. Multi-layered electrode sites of which center sites for stimulation is located on the bottom layer and auxiliary electrode sites are on side wall of upper layer of LCP films is realized using laser micromachining and via structure. The effect of structure of electrode sites is evaluated by *in vivo* measurements of spreading of current stimulation.

Long-term device reliability is a significant issue in polymer-based neural prosthesis to be used in clinical use. The long-term reliability of LCP-based implantable devices has been evaluated using analytic calculations, helium leak rate measurements, blister tests, and accelerated soak tests. Surface modifications such as those by oxygen plasma, and high-pressure lamination have been used to improve the interlayer bond strength and were shown to enhance device reliability levels. In this dissertation, technical strategies to enhance reliability of polymer-based device are suggested. An applicable fabrication method for polymer-based implantable neural interfaces which relies on mechanical interlocking at the interface between the polymer and a noble metal. Microscale undercut metal patterning by the dual steps of photolithography and electroplating are interlocked with LCP in a thermo-compression bonding process without voids. Results of peel test and cross-sectional images after device failures corroborate the effect of mechanical interlocking from the fact that the interlocked LCP-metal interface is intact while another interface without interlocking is delaminated, though it is difficult to estimate accurate lifetime. Mechanical interlocking has the effect of preventing water ingress into the exposed electrode site window where the LCP-metal interface exists. The proposed method using mechanical interlocking at the electrode site not only helps LCP-based neural prosthetic devices to gain widespread acceptance as long-term reliable implantable devices is also applicable to other polymer-based devices. Additional strategy to use dielectric material with LCP is also proposed and its feasibility in LCP fabrication process is investigated in preliminary tests. Surface-treated LCP and dielectric materials by oxygen plasma

are bonded using thermo-compression lamination process, resulting in reliable adhesion strength. Metal migration from heat and pressure in lamination process can be prevented using hybrid structure of LCP and dielectric materials.

Technical results, performance tests, and long-term reliability data foretell the promising future of safe, effective, and long-term reliable LCP-based neural electrode array, in spite of remaining several challenges and verifications for its clinical use.

References

- [1] S. F. Cogan, "Neural Stimulation and Recording Electrodes," *Annual Review of Biomedical Engineering*, vol. 10, pp. 275-309, 2008.
- [2] V. K. Khanna, "Biomaterials for Implants," in *Implantable Medical Electronics: Prosthetics, Drug Delivery, and Health Monitoring*, ed Cham: Springer International Publishing, 2016, pp. 153-166.
- [3] T. Stieglitz, M. Schuetter, and K. P. Koch, "Implantable biomedical microsystems for neural prostheses," *IEEE Engineering in Medicine and Biology Magazine*, vol. 24, pp. 58-65, 2005.
- [4] A. Prochazka, V. K. Mushahwar, and D. B. McCreery, "Neural prostheses," *The Journal of Physiology*, vol. 533, pp. 99-109, 2001.
- [5] B. J. Gantz, B. F. McCabe, and R. S. Tyler, "Use of multichannel cochlear implants in obstructed and obliterated cochleas," *Otolaryngology--Head and Neck Surgery*, vol. 98, pp. 72-81, 1988.
- [6] K. D. Brown and T. J. Balkany, "Benefits of bilateral cochlear implantation: a review," *Current opinion in otolaryngology & head and neck surgery*, vol. 15, pp. 315-318, 2007.
- [7] B. S. Wilson, C. C. Finley, D. T. Lawson, R. D. Wolford, D. K. Eddington, and W. M. Rabinowitz, "Better speech recognition with cochlear implants," *Nature*, vol. 352, pp. 236-238, 1991.
- [8] F.-G. Zeng, S. J. Rebscher, Q.-J. Fu, H. Chen, X. Sun, L. Yin, *et al.*, "Development and evaluation of the Nurotron 26-electrode cochlear implant system," *Hearing Research*, vol. 322, pp. 188-199, 2015.
- [9] D. S. Kern and R. Kumar, "Deep brain stimulation," *The Neurologist*, vol. 13, pp. 237-252, 2007.
- [10] H. S. Mayberg, A. M. Lozano, V. Voon, H. E. McNeely, D. Seminowicz, C. Hamani, *et al.*, "Deep brain stimulation for treatment-resistant depression," *Neuron*, vol. 45, pp. 651-660, 2005.
- [11] J. S. Perlmuter and J. W. Mink, "Deep brain stimulation," *Annual review of neuroscience*, vol. 29, p. 229, 2006.
- [12] M. S. Humayun, J. D. Dorn, L. da Cruz, G. Dagnelie, J. A. Sahel, P. E. Stanga, *et al.*, "Interim results from the international trial of Second Sight's visual

- prosthesis," *Ophthalmology*, vol. 119, 2012.
- [13] R. K. Shepherd, M. N. Shivdasani, D. A. X. Nayagam, C. E. Williams, and P. J. Blamey, "Visual prostheses for the blind," *Trends in Biotechnology*, vol. 31, pp. 562-571, 2013.
 - [14] M. HajjHassan, V. Chodavarapu, and S. Musallam, "NeuroMEMS: Neural Probe Microtechnologies," *Sensors*, vol. 8, p. 6704, 2008.
 - [15] L. Grand, A. Pongrácz, É. Vázsonyi, G. Márton, D. Gubán, R. Fiáth, *et al.*, "A novel multisite silicon probe for high quality laminar neural recordings," *Sensors and Actuators A: Physical*, vol. 166, pp. 14-21, 2011.
 - [16] G. Grigori, E. M. Jeffrey, A. L. William, and J. G. Timothy, "A carbon-fiber electrode array for long-term neural recording," *Journal of Neural Engineering*, vol. 10, p. 046016, 2013.
 - [17] J. W. Thomas, C. W. Michael, L. M. Janice, L. P. Rachel, and U. E. Jeremiah, "Nano-biotechnology: carbon nanofibres as improved neural and orthopaedic implants," *Nanotechnology*, vol. 15, p. 48, 2004.
 - [18] K. C. Cheung, "Implantable microscale neural interfaces," *Biomedical Microdevices*, vol. 9, pp. 923-938, December 01 2007.
 - [19] S. Herwik, S. Kisban, A. A. A. Aarts, K. Seidl, G. Girardeau, K. Benchenane, *et al.*, "Fabrication technology for silicon-based microprobe arrays used in acute and sub-chronic neural recording," *Journal of Micromechanics and Microengineering*, vol. 19, p. 074008, 2009.
 - [20] D.-H. Kim, J. A. Wiler, D. J. Anderson, D. R. Kipke, and D. C. Martin, "Conducting polymers on hydrogel-coated neural electrode provide sensitive neural recordings in auditory cortex," *Acta Biomaterialia*, vol. 6, pp. 57-62, 2010.
 - [21] V. S. Polikov, P. A. Tresco, and W. M. Reichert, "Response of brain tissue to chronically implanted neural electrodes," *Journal of Neuroscience Methods*, vol. 148, pp. 1-18, 2005.
 - [22] M. D. Johnson, R. K. Franklin, M. D. Gibson, R. B. Brown, and D. R. Kipke, "Implantable microelectrode arrays for simultaneous electrophysiological and neurochemical recordings," *Journal of Neuroscience Methods*, vol. 174, pp. 62-70, 2008.
 - [23] S. K. An, S. I. Park, S. B. Jun, C. J. Lee, K. M. Byun, J. H. Sung, *et al.*, "Design for a simplified cochlear implant system," *IEEE transactions on Biomedical engineering*, vol. 54, pp. 973-82, Jun 2007.

- [24] P. Maló, M. de Araújo Nobre, J. Borges, and R. Almeida, "Retrievable Metal Ceramic Implant-Supported Fixed Prostheses with Milled Titanium Frameworks and All-Ceramic Crowns: Retrospective Clinical Study with up to 10 Years of Follow-Up," *Journal of Prosthodontics*, vol. 21, pp. 256-264, 2012.
- [25] J. F. Patrick, P. A. Busby, and P. J. Gibson, "The Development of the Nucleus® Freedom™ Cochlear Implant System," *Trends in Amplification*, vol. 10, pp. 175-200, 2006.
- [26] C. M. Zierhofer, I. J. Hochmair, and E. S. Hochmair, "The advanced Combi 40+ cochlear implant," *The American journal of otology*, vol. 18, pp. S37-8, 1997.
- [27] A. J. T. Teo, A. Mishra, I. Park, Y.-J. Kim, W.-T. Park, and Y.-J. Yoon, "Polymeric Biomaterials for Medical Implants and Devices," *ACS Biomaterials Science & Engineering*, vol. 2, pp. 454-472, 2016.
- [28] V. Castagnola, E. Descamps, A. Lecestre, L. Dahan, J. Remaud, L. G. Nowak, *et al.*, "Parylene-based flexible neural probes with PEDOT coated surface for brain stimulation and recording," *Biosensors and Bioelectronics*, vol. 67, pp. 450-457, 2015.
- [29] R. A. Normann, E. M. Maynard, P. J. Rousche, and D. J. Warren, "A neural interface for a cortical vision prosthesis," *Vision research*, vol. 39, pp. 2577-2587, 1999.
- [30] F. J. Rodri, D. Ceballos, M. Schu, A. Valero, E. Valderrama, T. Stieglitz, *et al.*, "Polyimide cuff electrodes for peripheral nerve stimulation," *Journal of neuroscience methods*, vol. 98, pp. 105-118, 2000.
- [31] L. Kee-Keun, H. Jiping, S. Amarjit, M. Stephen, E. Gholamreza, K. Bruce, *et al.*, "Polyimide-based intracortical neural implant with improved structural stiffness," *Journal of Micromechanics and Microengineering*, vol. 14, p. 32, 2004.
- [32] C. Hassler, T. Boretius, and T. Stieglitz, "Polymers for neural implants," *Journal of Polymer Science Part B: Polymer Physics*, vol. 49, pp. 18-33, 2011.
- [33] B. J. Kim and E. Meng, "Review of polymer MEMS micromachining," *Journal of Micromechanics and Microengineering*, vol. 26, p. 013001, 2015.
- [34] J. H. Kim, K. S. Min, S. K. An, J. S. Jeong, S. B. Jun, M. H. Cho, *et al.*, "Magnetic Resonance Imaging Compatibility of the Polymer-based Cochlear Implant," *Clinical and Experimental Otorhinolaryngology*, vol. 5, pp. S19-S23, 2012.
- [35] G. Jiang and D. D. Zhou, "Technology Advances and Challenges in Hermetic Packaging for Implantable Medical Devices," in *Implantable Neural Prostheses 2:*

- Techniques and Engineering Approaches*, D. Zhou and E. Greenbaum, Eds., ed New York, NY: Springer New York, 2010, pp. 27-61.
- [36] T. M. Gwon, C. Kim, S. Shin, J. H. Park, J. H. Kim, and S. J. Kim, "Liquid crystal polymer (LCP)-based neural prosthetic devices," *Biomedical Engineering Letters*, vol. 6, pp. 148-163, August 01 2016.
 - [37] S. J. Rebscher, A. Hetherington, B. Bonham, P. Wardrop, D. Whinney, and P. A. Leake, "Considerations for design of future cochlear implant electrode arrays: electrode array stiffness, size, and depth of insertion," *Journal of rehabilitation research and development*, vol. 45, pp. 731-47, 2008.
 - [38] R. Shepherd, K. Verhoeven, J. Xu, F. Risi, J. Fallon, and A. Wise, "An improved cochlear implant electrode array for use in experimental studies," *Hearing Research*, vol. 277, pp. 20-27, 2011.
 - [39] P. Wardrop, D. Whinney, S. J. Rebscher, J. T. Roland Jr, W. Luxford, and P. A. Leake, "A temporal bone study of insertion trauma and intracochlear position of cochlear implant electrodes. I: Comparison of Nucleus banded and Nucleus Contour™ electrodes," *Hearing Research*, vol. 203, pp. 54-67, 2005.
 - [40] C. K. Berenstein, L. H. M. Mens, J. J. S. Mulder, and F. J. Vanpoucke, "Current Steering and Current Focusing in Cochlear Implants: Comparison of Monopolar, Tripolar, and Virtual Channel Electrode Configurations," *Ear and Hearing*, vol. 29, pp. 250-260, 2008.
 - [41] J. B. Firszt, D. B. Koch, M. Downing, and L. Litvak, "Current Steering Creates Additional Pitch Percepts in Adult Cochlear Implant Recipients," *Otology & Neurotology*, vol. 28, pp. 629-636, 2007.
 - [42] D. M. Landsberger and A. G. Srinivasan, "Virtual channel discrimination is improved by current focusing in cochlear implant recipients," *Hearing Research*, vol. 254, pp. 34-41, 2009.
 - [43] B. H. Bonham and L. M. Litvak, "Current focusing and steering: Modeling, physiology, and psychophysics," *Hearing Research*, vol. 242, pp. 141-153, 2008.
 - [44] K. S. Min, S. B. Jun, Y. S. Lim, S.-I. Park, and S. J. Kim, "Modiolus-Hugging Intracochlear Electrode Array with Shape Memory Alloy," *Computational and Mathematical Methods in Medicine*, vol. 2013, p. 9, 2013.
 - [45] Product brochure. *Electrode Arrays: Designed for atraumatic implantation providing superior hearing performance.* Available: <http://s3.medel.com/pdf/21617.pdf>

- [46] B. K. Chen, G. M. Clark, and R. Jones, "Evaluation of trajectories and contact pressures for the straight nucleus cochlear implant electrode array — a two-dimensional application of finite element analysis," *Medical Engineering & Physics*, vol. 25, pp. 141-147, 2003.
- [47] M. Tykocinski, L. T. Cohen, B. C. Pyman, T. J. Roland, C. Treaba, J. Palamara, *et al.*, "Comparison of Electrode Position in the Human Cochlea Using Various Perimodiolar Electrode Arrays," *Otology & Neurotology*, vol. 21, pp. 205-211, 2000.
- [48] E. Saunders, L. Cohen, A. Aschendorff, W. Shapiro, M. Knight, M. Stecker, *et al.*, "Threshold, Comfortable Level and Impedance Changes as a Function of Electrode-Modiolar Distance," *Ear and Hearing*, vol. 23, pp. 28S-40S, 2002.
- [49] M. L. Hughes and P. J. Abbas, "Electrophysiologic channel interaction, electrode pitch ranking, and behavioral threshold in straight versus perimodiolar cochlear implant electrode arrays," *The Journal of the Acoustical Society of America*, vol. 119, pp. 1538-1547, 2006.
- [50] S. Corbett, J. Ketterl, and T. Johnson, "Polymer-Based Microelectrode Arrays," *MRS Online Proceedings Library Archive*, vol. 926, pp. 0926-CC06-02 (6 pages), 2006.
- [51] K. S. Min, S. H. Oh, M. H. Park, J. Jeong, and S. J. Kim, "A Polymer-Based Multichannel Cochlear Electrode Array," *Otol Neurotol*, vol. 35, pp. 1179-1186, 2014.
- [52] P. T. Bhatti, "A High-Density Thin-Film Electrode Array for a Cochlear Prosthesis", *Thesis University of Michigan*, 2006.
- [53] J. Wang and K. D. Wise, "A Hybrid Electrode Array With Built-In Position Sensors for an Implantable MEMS-Based Cochlear Prosthesis," *Microelectromechanical Systems, Journal of*, vol. 17, pp. 1187-1194, 2008.
- [54] J. Wang and K. D. Wise, "A Thin-Film Cochlear Electrode Array With Integrated Position Sensing," *Microelectromechanical Systems, Journal of*, vol. 18, pp. 385-395, 2009.
- [55] L. M. Friesen, R. V. Shannon, D. Baskent, and X. Wang, "Speech recognition in noise as a function of the number of spectral channels: Comparison of acoustic hearing and cochlear implants," *The Journal of the Acoustical Society of America*, vol. 110, pp. 1150-1163, 2001.
- [56] J. D. Falcone and P. T. Bhatti, "Current steering and current focusing with a high-

- density intracochlear electrode array," *Conference proceedings: Annual International Conference of the IEEE Engineering in Medicine and Biology Society. IEEE Engineering in Medicine and Biology Society. Conference*, pp. 1049-52, 2011.
- [57] C. A. Fielden, K. Kluk, and C. M. McKay, "Place specificity of monopolar and tripolar stimuli in cochlear implants: The influence of residual masking," *The Journal of the Acoustical Society of America*, vol. 133, pp. 4109-4123, 2013.
 - [58] Z. Zhu, Q. Tang, F.-G. Zeng, T. Guan, and D. Ye, "Cochlear-implant spatial selectivity with monopolar, bipolar and tripolar stimulation," *Hearing Research*, vol. 283, pp. 45-58, 2012.
 - [59] S. Costello, M. P. Y. Desmulliez, and S. McCracken, "Review of test methods used for the measurement of hermeticity in packages containing small cavities," *IEEE Transactions on Components, Packaging and Manufacturing Technology*, vol. 2, pp. 430-438, 2012.
 - [60] K. Aihara, M. J. Chen, C. Cheng, and A. V. H. Pham, "Reliability of liquid crystal polymer air cavity packaging," *IEEE Transactions on Components, Packaging and Manufacturing Technology*, vol. 2, pp. 224-230, 2012.
 - [61] A.-V. Pham, "Packaging with liquid crystal polymer," *IEEE Microwave Magazine*, vol. 5, pp. 83-91, 2011.
 - [62] B. Han, "Measurements of true leak rates of MEMS packages," *Sensors*, vol. 12, pp. 3082-3104, 2012.
 - [63] J. Jeong, S. H. Bae, J.-M. Seo, H. Chung, and S. J. Kim, "Long-term evaluation of a liquid crystal polymer (LCP)-based retinal prosthesis," *Journal of Neural Engineering*, vol. 13, p. 025004, 2016.
 - [64] J. S. Ordonez, C. Boehler, M. Schuettler, and T. Stieglitz, "Silicone rubber and thin-film polyimide for hybrid neural interfaces; A MEMS-based adhesion promotion technique," in *Neural Engineering (NER), 2013 6th International IEEE/EMBS Conference on*, 2013, pp. 872-875.
 - [65] J. S. Ordonez, C. Boehler, M. Schuettler, and T. Stieglitz, "Improved polyimide thin-film electrodes for neural implants," in *Engineering in Medicine and Biology Society (EMBC), 2012 Annual International Conference of the IEEE*, 2012, pp. 5134-5137.
 - [66] J. H. C. Chang, L. Yang, K. Dongyang, and T. Yu-Chong, "Reliable packaging for parylene-based flexible retinal implant," in *Solid-State Sensors, Actuators and*

- Microsystems (TRANSDUCERS & EUROSENSORS XXVII), 2013 Transducers & Eurosensors XXVII: The 17th International Conference on*, 2013, pp. 2612-2615.
- [67] R. von Metzen and T. Stieglitz, "The effects of annealing on mechanical, chemical, and physical properties and structural stability of Parylene C," *Biomedical Microdevices*, vol. 15, pp. 727-735, 2013/10/01 2013.
 - [68] J. H. Kim, "A study on low-cost, effective, and reliable liquid crystal polymer-based cochlear implant system," *Ph.D. Thesis*, Department of electrical engineering and computer science, Seoul National University, 2015.
 - [69] E. T. Kim, C. Kim, S. W. Lee, J.-M. Seo, H. Chung, and S. J. Kim, "Feasibility of Microelectrode Array (MEA) Based on Silicone-Polyimide Hybrid for Retina Prosthesis," *Investigative Ophthalmology & Visual Science*, vol. 50, pp. 4337-4341, 2009.
 - [70] S. W. Lee, J. Jeong, K. S. Min, S. Shin, S. B. Jun, and S. J. Kim, "Liquid Crystal Polymer (LCP), an Attractive substrate for Retinal Implant," *Sensors and Materials*, vol. 24, 2012.
 - [71] J. Jeong, S. Shin, G. J. Lee, T. M. Gwon, J. H. Park, and S. J. Kim, "Advancements in fabrication process of microelectrode array for a retinal prosthesis using Liquid Crystal Polymer (LCP)," in *2013 35th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)*, 2013, pp. 5295-5298.
 - [72] S. W. Lee, K. S. Min, J. Jeong, J. Kim, and S. J. Kim, "Monolithic Encapsulation of Implantable Neuroprosthetic Devices Using Liquid Crystal Polymers," *IEEE Transactions on Biomedical Engineering*, vol. 58, 2011.
 - [73] J. Jeong, S. H. Bae, K. S. Min, J. M. Seo, H. Chung, and S. J. Kim, "A Miniaturized, Eye-Conformable, and Long-Term Reliable Retinal Prosthesis Using Monolithic Fabrication of Liquid Crystal Polymer (LCP)," *IEEE Transactions on Biomedical Engineering*, vol. 62, pp. 982-989, 2015.
 - [74] E. Y. Chow, A. L. Chlebowski, and P. P. Irazoqui, "A Miniature-Implantable RF-Wireless Active Glaucoma Intraocular Pressure Monitor," *IEEE Transactions on Biomedical Circuits and Systems*, , vol. 4, pp. 340-349, 2010.
 - [75] T. Gwon, K. Min, J. Kim, S. Oh, H. Lee, M.-H. Park, *et al.*, "Fabrication and evaluation of an improved polymer-based cochlear electrode array for atraumatic insertion," *Biomedical Microdevices*, vol. 17, pp. 1-12, 2015.
 - [76] G.-T. Hwang, D. Im, S. E. Lee, J. Lee, M. Koo, S. Y. Park, *et al.*, "In Vivo Silicon-

- Based Flexible Radio Frequency Integrated Circuits Monolithically Encapsulated with Biocompatible Liquid Crystal Polymers," *ACS Nano*, vol. 7, pp. 4545-4553, 2013.
- [77] N. Laotaveerungrueng, C. H. Lin, G. McCallum, S. Rajgopal, C. P. Steiner, A. R. Rezai, *et al.*, "3-D microfabricated electrodes for targeted deep brain stimulation," in *2009 Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, 2009, pp. 6493-6496.
 - [78] S. W. Lee, J. M. Seo, S. Ha, E. T. Kim, H. Chung, and S. J. Kim, "Development of microelectrode arrays for artificial retinal implants using liquid crystal polymers," *Invest Ophthalmol Vis Sci*, vol. 50, pp. 5859-66, Dec 2009.
 - [79] C. Liu, "Recent Developments in Polymer MEMS," *Advanced Materials*, vol. 19, pp. 3783-3790, 2007.
 - [80] P. Sattayasoonthorn, J. Suthakorn, S. Chamnanvej, J. Miao, and A. G. P. Kottapalli, "LCP MEMS implantable pressure sensor for Intracranial Pressure measurement," in *Nano/Molecular Medicine and Engineering (NANOMED), 2013 IEEE 7th International Conference on*, 2013, pp. 63-67.
 - [81] S. E. Lee, S. B. Jun, H.-J. Lee, J. Kim, S. W. Lee, H-C. Shin, J. W. Chang, and S. J. Kim, "A Flexible Depth Probe Using Liquid Crystal Polymer," *IEEE Transactions on Biomedical Engineering*, vol. 59, pp. 2085-2094, 2012.
 - [82] W. Xuefeng, E. Jonathan, and L. Chang, "Liquid crystal polymer (LCP) for MEMS: processes and applications," *Journal of Micromechanics and Microengineering*, vol. 13, p. 628, 2003.
 - [83] S. H. Bae, J.-H. Che, J.-M. Seo, J. Jeong, E. T. Kim, S. W. Lee, K.-I. Koo, G. J. Suaning, N. H. Lovell, D.-I. Cho, S. J. Kim, and H. Chung, "In Vitro Biocompatibility of Various Polymer-Based Microelectrode Arrays for Retinal Prosthesis," *Investigative Ophthalmology & Visual Science*, vol. 53, pp. 2653-2657, 2012.
 - [84] T. M. Gwon, J. H. Kim, G. J. Choi, and S. J. Kim, "Mechanical interlocking to improve metal-polymer adhesion in polymer-based neural electrodes and its impact on device reliability," *Journal of Materials Science*, vol. 51, pp. 6897-6912, 2016.
 - [85] A. L. Chlebowski, "Advanced radio frequency materials for packaging of implantable biomedical devices," 2009.
 - [86] J. R. N. Dean, J. Weller, M. J. Bozack, C. L. Rodekohr, B. Farrell, L. Jauniskis, *et*

- al.*, "Realization of Ultra Fine Pitch Traces on LCP Substrates," *IEEE Transactions on Components and Packaging Technologies*, vol. 31, pp. 315-321, 2008.
- [87] R. Pelrine, R. Kornbluh, J. Joseph, R. Heydt, Q. Pei, and S. Chiba, "High-field deformation of elastomeric dielectrics for actuators," *Materials Science and Engineering: C*, vol. 11, pp. 89-100, 2000.
- [88] A. D. Woolfson, R. K. Malcolm, S. P. Gorman, D. S. Jones, A. F. Brown, and S. D. McCullagh, "Self-lubricating silicone elastomer biomaterials," *Journal of Materials Chemistry*, vol. 13, pp. 2465-2470, 2003.
- [89] K. S. Min, "A study on the liquid crystal polymer-based intracochlear electrode array," *Thesis Seoul National University*, 2014.
- [90] A. A. Eshraghi, N. W. Yang, and T. J. Balkany, "Comparative Study of Cochlear Damage With Three Perimodiolar Electrode Designs," *The Laryngoscope*, vol. 113, pp. 415-419, 2003.
- [91] M. Polak, A. A. Eshraghi, O. Nehme, S. Ahsan, J. Guzman, R. E. Delgado, *et al.*, "Evaluation of hearing and auditory nerve function by combining ABR, DPOAE and eABR tests into a single recording session," *Journal of Neuroscience Methods*, vol. 134, pp. 141-149, 2004.
- [92] J. H. Park, C. Kim, S. H. Ahn, T. M. Gwon, J. Jeong, S. Beom Jun, and S. J. Kim, "A distributed current stimulator ASIC for high density neural stimulation," in *2016 38th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)*, 2016.
- [93] A. Leng, H. Streckel, K. Hofmann, and M. Stratmann, "The delamination of polymeric coatings from steel Part 3: Effect of the oxygen partial pressure on the delamination reaction and current distribution at the metal/polymer interface," *Corrosion Science*, vol. 41, pp. 599-620, 1998.
- [94] A. Leng, H. Streckel, and M. Stratmann, "The delamination of polymeric coatings from steel. Part 2: First stage of delamination, effect of type and concentration of cations on delamination, chemical analysis of the interface," *Corrosion Science*, vol. 41, pp. 579-597, 1998.
- [95] A. Leng, H. Streckel, and M. Stratmann, "The delamination of polymeric coatings from steel. Part 1: Calibration of the Kelvinprobe and basic delamination mechanism," *Corrosion Science*, vol. 41, pp. 547-578, 1998.
- [96] A. Vanhoestenbergh and N. Donaldson, "The Limits of Hermeticity Test Methods for Micropackages," *Artificial Organs*, vol. 35, pp. 242-244, 2011.

- [97] W.-S. Kim, I.-H. Yun, J.-J. Lee, and H.-T. Jung, "Evaluation of mechanical interlock effect on adhesion strength of polymer–metal interfaces using micro-patterned surface topography," *International Journal of Adhesion and Adhesives*, vol. 30, pp. 408-417, 2010.
- [98] F. K. LeGoues, B. D. Silverman, and P. S. Ho, "The microstructure of metal–polyimide interfaces," *Journal of Vacuum Science & Technology A*, vol. 6, pp. 2200-2204, 1988.
- [99] D. E. Packham, "Surface energy, surface topography and adhesion," *International Journal of Adhesion and Adhesives*, vol. 23, pp. 437-448, 2003.
- [100] J. D. Venables, "Adhesion and durability of metal-polymer bonds," *Journal of Materials Science*, vol. 19, pp. 2431-2453, 1984.
- [101] J. F. McCabe, T. E. Carrick, and H. Kamohara, "Adhesive bond strength and compliance for denture soft lining materials," *Biomaterials*, vol. 23, pp. 1347-1352, 2002.
- [102] W. Chun, N. Chou, S. Cho, S. Yang, and S. Kim, "Evaluation of sub-micrometer parylene C films as an insulation layer using electrochemical impedance spectroscopy," *Progress in Organic Coatings*, vol. 77, pp. 537-547, 2014.
- [103] E. Song, H. Fang, X. Jin, J. Zhao, C. Jiang, K. J. Yu, *et al.*, "Thin, Transferred Layers of Silicon Dioxide and Silicon Nitride as Water and Ion Barriers for Implantable Flexible Electronic Systems," *Advanced Electronic Materials*, vol. 3, pp. 1700077, 2017.
- [104] D. S. Wu, W. C. Lo, C. C. Chiang, H. B. Lin, L. S. Chang, R. H. Horng, *et al.*, "Water and oxygen permeation of silicon nitride films prepared by plasma-enhanced chemical vapor deposition," *Surface and Coatings Technology*, vol. 198, pp. 114-117, 2005.
- [105] S. J. Oh, J. K. Song, and S. J. Kim, "Neural interface with a silicon neural probe in the advancement of microtechnology," *Biotechnology and Bioprocess Engineering*, vol. 8, pp. 252-256, 2003.
- [106] A. U. Alam, Y. Qin, M. R. Howlader, and M. J. Deen, "Direct bonding of liquid crystal polymer to glass," *RSC Advances*, vol. 6, pp. 107200-107207, 2016.
- [107] W. G. Sawyer, K. D. Freudenberg, P. Bhimaraj, and L. S. Schadler, "A study on the friction and wear behavior of PTFE filled with alumina nanoparticles," *Wear*, vol. 254, pp. 573-580, 2003.
- [108] A. K. Gupta, H. Basappa, K. S. Sadananda, and C. N. Manjunath, "*In vivo*

- delamination of coronary guidewire polytetrafluoroethylene layer – A dreaded complication," *Indian Heart Journal*, vol. 68, pp. 182-183, 2016.
- [109] D. D. Greenwood, "A cochlear frequency-position function for several species— 29 years later," *The Journal of the Acoustical Society of America*, vol. 87, pp. 2592-2605, 1990.
 - [110] S. C. Parisier, P. M. Chute, A. L. Popp, and G. D. Suh, "Outcome Analysis of Cochlear Implant Reimplantation in Children," *The Laryngoscope*, vol. 111, pp. 26-32, 2001.
 - [111] J. N. Fayad, T. Baido, and S. C. Parisier, "Revision cochlear implant surgery: causes and outcome," *Otolaryngol Head Neck Surg*, vol. 131, pp. 429-32, 2004.
 - [112] S. J. Rebscher, M. Heilmann, W. Bruszewski, N. H. Talbot, R. L. Snyder, and M. M. Merzenich, "Strategies to improve electrode positioning and safety in cochlear implants," *IEEE Transactions on Biomedical engineering*, vol. 46, pp. 340-52, 1999.
 - [113] B. Bhushan, "Adhesion and stiction: Mechanisms, measurement techniques, and methods for reduction," *Journal of Vacuum Science & Technology B*, vol. 21, pp. 2262-2296, 2003.
 - [114] C. J. Van Oss, R. J. Good, and M. K. Chaudhury, "The role of van der Waals forces and hydrogen bonds in "hydrophobic interactions" between biopolymers and low energy surfaces," *Journal of Colloid and Interface Science*, vol. 111, pp. 378-390, 1986.
 - [115] J. A. Bierer, S. M. Bierer, and J. C. Middlebrooks, "Partial tripolar cochlear implant stimulation: Spread of excitation and forward masking in the inferior colliculus," *Hearing Research*, vol. 270, pp. 134-142, 2010.
 - [116] D. Vellinga, J. J. Briare, D. M. P. van Meenen, and J. H. M. Frijns, "Comparison of Multipole Stimulus Configurations With Respect to Loudness and Spread of Excitation," *Ear and Hearing*, vol. 38, pp. 487-496, 2017.
 - [117] D. Vellinga, S. Bruijn, J. J. Briare, R. K. Kalkman, and J. H. M. Frijns, "Reducing interaction in simultaneous paired stimulation with CI," *PLOS ONE*, vol. 12, p. e0171071, 2017.
 - [118] J. A. Bierer, "Threshold and channel interaction in cochlear implant users: Evaluation of the tripolar electrode configuration," *The Journal of the Acoustical Society of America*, vol. 121, pp. 1642-1653, 2007.
 - [119] A. Kinloch, *Adhesion and adhesives: science and technology*: Springer Science &

Business Media, 2012.

- [120] J. Ordonez, M. Schuettler, C. Boehler, T. Boretius, and T. Stieglitz, "Thin films and microelectrode arrays for neuroprosthetics," *MRS Bulletin*, vol. 37, pp. 590-598, 2012.
- [121] A. S. Widge, "Self-assembled monolayers of polythiophene "Molecular wires": a new electrode technology for neuro-robotic interfaces," *Thesis Carnegie Mellon University*, 2007.
- [122] L. Reclaru and J. M. Meyer, "Study of corrosion between a titanium implant and dental alloys," *Journal of Dentistry*, vol. 22, pp. 159-168, 1994.
- [123] M. Celina, K. T. Gillen, and R. A. Assink, "Accelerated aging and lifetime prediction: Review of non-Arrhenius behaviour due to two competing processes," *Polymer Degradation and Stability*, vol. 90, pp. 395-404, 2005.
- [124] D. W. L. Hukins, A. Mahomed, and S. N. Kukureka, "Accelerated aging for testing polymeric biomaterials and medical devices," *Medical Engineering & Physics*, vol. 30, pp. 1270-1274, 2008.
- [125] A. A. C. M. Lopez, S. Mitra, M. Welkenhuysen, W. Eberle, C. Bartic, R. Puers, R. F. Yazicioglu, G. G. E. Gielen, "An Implantable 455-Active-Electrode 52-Channel CMOS Neural Probe," *IEEE Journal of Solid-State Circuits*, vol. 49, pp. 248-261, 2014.
- [126] V. Sundaram, V. Sukumaran, M. E. Cato, F. Liu, R. Tummala, J. D. Weiland, *et al.*, "High density electrical interconnections in liquid crystal polymer (LCP) substrates for retinal and neural prosthesis applications," in *2011 IEEE 61st Electronic Components and Technology Conference (ECTC)*, 2011, pp. 1308-1313.
- [127] K. Aihara, M. J. Chen, and A. V. Pham, "Development of Thin-Film Liquid-Crystal-Polymer Surface-Mount Packages for Ka-Band Applications," *IEEE Transactions on Microwave Theory and Techniques*, vol. 56, pp. 2111-2117, 2008.

국문 초록

액정 폴리머 (liquid crystal polymer, LCP)는 가장 낮은 수분 흡수율을 가지는($< 0.0.4\%$) 생체 이식에 적합한 (biocompatible) 폴리머 중에 하나이며, 열압착 공정을 이용한 성형 및 접합이 가능한 물질이다. 그리고, 반도체 공정 및 멤스(MEMS) 공정, 레이저 미세 가공(laser micromachining)과 호환성이 뛰어나, 초소형 생체 삽입 기기를 만드는데 장점이 많은 물질이다. 본 학위논문은 액정 폴리머 기반의 신경 자극 전극에 대한 내용을 다루고 있다.

인공와우(cochlear implant)는 달팽이관(와우) 내의 유모세포의 손상으로 소리 자극을 전기적인 자극으로 변환하지 못하여 생기는 청력 손상을 보완해주는 신경보철 기기로, 상용 체내 삽입 장치는 금속 기반 전자 패키지 및 금속 와이어 기반 인공와우 전극으로 이루어져 있다. 본 논문에서는 액정 폴리머 기반의 미세 인공와우 전극을 제작함에 있어, 달팽이관 내 삽입 시 비외상성 심부 삽입(atraumatic deep insertion)이 가능하도록 디자인하였다. 여러 층의 액정 폴리머 필름을 적층하는 구조를 활용하여, 상호 연결 라인(interconnection line)의 배치를 유동적으로 하는 한편, 전극의 각 위치에 따른 적층 두께를 달리 하여 전극의 유연성을 각 부분에 따라 달리 가져가는 구조를 이용했다. 유연성이 필요한 전극 팁 부분은 한 층의 $25\ \mu\text{m}$ 액정 폴리머 필름을 사용하고, 전극 삽입 시 전극을 지탱하는 힘을 받는 전극의 기초 부분은 세 층의 $25\ \mu\text{m}$ 액정 폴리머 필름을 사용하는 구조를 착안하였다.

그리고, 전기적 비아 구조를 활용하여 전극의 폭을 줄이는데 기여하였다. 멤스 공정 및 레이저 미세가공을 이용해 제작된 전극은 시험관 내(*in vitro*) 평가 실험 방법인 전기화학 테스트를 이용하여 자극 가능한 임피던스를 가지는지 측정을 하였고, 플라스틱 달팽이관 모형과 힘 측정 센서를 이용한 맞춤형 실험 설정을 통한 전극 삽입 및 추출 힘 측정을 통해 기존의 와이어 기반 전극과 단순 구조의 폴리머 전극에 비해 저항이 줄어든 삽입 및 추출이 가능함을 보였다. 그리고, 5 번의 인간 측두골 삽입 실험을 통해 전극의 삽입 깊이 및 삽입 외상을 평가하였다. 기니피그를 활용한 자극 실험에서 본 전극을 통한 자극이 청력 감지를 나타냄을 검증하였고, 4 주간 삽입 실험을 통해 전극 삽입 후 청력 보존과 조직학적인 분석을 시행한 결과, 기존 전극과 대비하여 비슷한 수준의 결과 및 안정적인 삽입 유지를 보였다.

또한, 본 논문에서는 폴리머 인공와우 전극의 활용에 있어, 집중적인 자극(current focusing)을 활용한 실제 자극 채널 개수의 증가 및 채널 간 간섭(channel crosstalk) 감소를 위해 전극의 자극 사이트(electrode site for stimulation) 구조적인 측면에서 새로운 구조를 제안하고 시뮬레이션을 통해 효과가 가장 높은 구조를 선정하여, 시험관 내 측정 실험을 통해 검증하였다. 다층 구조의 전극 제작이 용이한 액정 폴리머의 장점을 활용하여, 기존에는 세 개의 자극 사이트를 활용한 것에 반해, 본 논문에서 제안되는 구조는 하나의 전극 사이트에서 3 개의 채널을 다층 구조로 제작하여 더욱 국부적인 자극이 이루어지도록 하였다. 집중 자극을 위한 3 극 자극에서 전류 흐름을 위한 보조 전극 채널의 위치는 다층 구조의 측면에 위치하도록 하였다.

레이저 미세 가공을 이용한 전극 사이트를 노출시키는 기술을 사용하였다. 체액을 모사한 환경에서 개발된 전극을 활용하여 3 극 자극을 전달하고 전기적 자극의 집중도를 측정하여 기존의 3 극 자극 활용과 비교하는 실험을 수행하였다.

본 논문에서는 실제적인 임상적 적용에 필수적인 장기간 기기 신뢰성(long-term device reliability) 측면에서, 액정 폴리머 기반 생체 삽입 기기를 분석하고 기술적 접근을 통한 신뢰성 향상 방법에 대한 연구를 수행하였다. 이론적, 실험적 분석을 통해 액정 폴리머 기반 기기의 금속-폴리머 접합에서의 수분 침투를 막고자 하는 방법의 필요성을 도출하였고, 이를 방지하기 위한 방법으로 기계적 맞물림 구조를 활용한 금속-폴리머 접합 향상을 제안하였다. 기계적 맞물림 구조를 활용하여 제작한 액정 폴리머 기반 신경 전극은 박리 시험(peel test) 및 가속 수명 테스트(accelerated soak test)를 통해 맞물림 구조를 이용한 접합 향상이 실제로 기기의 신뢰성 향상과 미치는 영향에 대해서 검증하였다. 또 다른 신뢰성 향상 방안으로 열압착 공정 시 금속 패턴의 이동을 막고, 수분 및 이온의 침투를 방지하고자 유전체 물질을 액정 폴리머와 혼용하여 전극을 제작하는 방안을 제안하였다. 예비 실험으로 액정 폴리머와 유전체 물질의 접합을 박리 시험을 통해 비교와, 시험적인 열 접합 공정을 통해 액정 폴리머와 유전체 물질의 하이브리드(hybrid) 구조의 신경 전극 가능성을 확인하였다.

마지막으로, 본 논문에서는 현재까지의 실험적 데이터를 기반으로 한 액정 폴리머 기반 신경 보철 기기의 장기간 신뢰성에 대한

심층적으로 분석하고 결과를 정리하였다. 추가적인 연구 및 발전 방안이 필요함에도 불구하고, 이론적, 실험적 검증 결과를 토대로, 액정 폴리머 기반 신경 보철 기기의 임상적 적용 및 발전 가능의 결론을 도출 할 수 있었다.

주요어: 폴리머 기반 신경보철장치, 인공와우전극, 액정폴리머, 비외상성 전극 삽입, 집중 전기 자극, 장기간 신뢰성

학 번: 2012-20740