Supplementary Material

Study of Long-Term Biocompatibility and Bio-Safety of Implantable Nanogenerators

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Figure S1. Preparation of i-NGs and cross-section image characterization. (a) Fabrication process of i-NGs with different encapsulation strategy. A group of i-NGs were packaged by PDMS, while another group of i-NGs were packaged by PDMS/Parylene-C encapsulation structures. (b) The SEM of cross-section of PDMS packaged i-NGs. The Au-coated PVDF film was encapsulated well by PDMS on both sides.
Figure S2. XRD patterns of PVDF films at different fabrication stages. Black curve: original PVDF film; blue curve: PVDF film after Au electrode deposition; red curve PVDF film after Parylene-C deposition.
Figure S3. Current output of a PVDF film when bended at a frequency of 2 Hz.
**Figure S4.** Voltage outputs of a PVDF film before (left figure) and after (right figure) PDMS package. Both were tested by applying a force of 6 N at a frequency of 2 Hz.
Figure S5. In-vitro stability test of i-NGs. (a) Digital image of releasing and bending of an i-NG. Inset is a photo of PDMS-Packaged PVDF NG. Scale bar in the inset is 5 mm. (b) 7200 cycles bending fatigues test of i-NGs. (c) Detailed information of voltage outputs at the beginning and end of the fatigue test. The i-NG was bended and released at a bending radius of 0.63 cm for each cycle driven by a magnetic shaker with a frequency of 2 Hz.
Figure S6. Photoacoustic (PA) and Ultrasound (US) imaging of implanted devices. (a) 3D PA images. (b) US images. (c) PA images. The upper side images include PDMS packaged i-NGs and surrounding tissues. The bottom side images involve PDMS/Parylene-C packaged i-NGs and surrounding tissues. Gold electrodes were shown as high density (white line) in the middle of i-NGs.
Figure S7. Gross pathology analyses at different time. Left part includes photographs of tissues of ICR mice at 2, 4, 12, 24 weeks, respectively. No observation of changes of shape, color and structure of tissues around i-NGs. The dashed box (right panel) covers photographs of implantation sites before and after skins were peeled off at 12 weeks. Insets are i-NGs taken out from sacrificed mice. The scale bar is 1 mm.
Figure S8. *In vivo* voltage output of a PDMS-packaged PVDF NG. (a) A photograph of the connection setup during the *in vivo* measurement of the electricity generation. The inset image is a photo of the implanted device, and the scale bar is 5 mm. (b) *In vivo* voltage output measured under different frequencies.
Figure S9. Stray Current Test. (a) Electrical circuit design for the stray current test of PDMS package materials in 0.9% NaCl saline solution. (b) Stray current recorded at day 1, 4, 7, and 16 when the device was immersed in 0.9% NaCl saline solution. The device was immersed in the saline solution for 21 days.

Video S1. ICR mouse with implanted NG for 3 months showing normal activity.

Video S2. The in vivo motion of PDMS-encapsulated NG in response to muscle movements.

Video S3. The in vivo motion of PDMS/Parylene C-encapsulated NG in response to muscle movements.
S2. PDMS toxicity and long-term biocompatibility

Figure S10. 3T3 fibroblast cells growth on PDMS film (PDMS group) and in 24-well cell plates (Normal group) for four days

Table S1. Other works related to PDMS/silicone rubber long-term biocompatibility

<table>
<thead>
<tr>
<th>No.</th>
<th>Device Structure and Application</th>
<th>Experimental Model</th>
<th>Experimental Period</th>
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<tbody>
<tr>
<td>1</td>
<td>PDMS (Dow Corning) Breast implants</td>
<td>Patient</td>
<td>3 months to 32 years</td>
<td>[1, 2]</td>
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<td>2</td>
<td>PDMS Thin film substrate for electrode array</td>
<td>Dog</td>
<td>6 months</td>
<td>[3]</td>
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<tr>
<td>3</td>
<td>PDMS Thin film window for in vivo imaging</td>
<td>Rat</td>
<td>Up to 15 weeks</td>
<td>[4]</td>
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<tr>
<td>4</td>
<td>PDMS Thin film substrate for electrode</td>
<td>Saline solution</td>
<td>Up to 330 days</td>
<td>[5, 6]</td>
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<tr>
<td>5</td>
<td>PDMS Encapsulation for cardiac pacemaker lead</td>
<td>Patient</td>
<td>$\geq$ 5 years</td>
<td>[7]</td>
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<tr>
<td>5</td>
<td>Silicone rubber Encapsulation for bladder stimulator</td>
<td>Patient</td>
<td>Up to 25 years</td>
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3T3 fibroblast cells were cultured on PDMS film (experimental) and in 24-well cell plates (control group) for four days (Figure 1). The cytoskeleton and nucleus were stained with Texas red-X phalloidin (591/608 nm) and blue fluorescent Hoechst (352/461 nm) (Thermo Fisher Scientific), respectively. From cell morphologies and viabilities, no significant difference between the cells on PDMS films and cells in culture plates was observed, which indicates PDMS is nontoxic to cells.

There are other publications reporting the long-term stability of PDMS inside body. More specifically, for in vitro stability investigation, Wang et al reported a long-term stable and implantable interdigital electrode systems by utilizing PDMS encapsulation (total thickness of 200-350 μm). The lifetime of the PDMS packaged implantable devices were estimated up to ~3.6 year by a saline bath test. [5,6] For in vivo stability test, long-term implantations of inactive epiretinal PDMS-electrode array in dogs was reported by Güven et al. The PDMS implant (4 mm×40 mm×55-60 μm) including 4-8 embedded electrodes were implanted epiretinally in four normal dogs. The authors demonstrated that the PDMS device shows good biocompatibility and electrical stability without significant damage to the retinal up to six months.[3]

References