WORLD'S FIRST BIO-DEGRADABLE ACTUATOR FOR REMOVAL-FREE IMPLANTABLE MEMS

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ABSTRACT

We propose a new concept of an implantable device totally made of bio-degradable polymers such as Poly(lactic acid) (PLA). Since the bio-degradable polymer is decomposed and absorbed in a human body, the removal surgery after use is not required. A micro fabrication process of bio-degradable polymer has already developed [1,2]. In addition to the fabrication of micro structure, we succeeded to develop a "bio-degradable actuator" with a two-way motion in this paper. This actuator needs no electric power because it utilizes a chronological change of mechanical property of bio-degradable polymers. The driving principle of the actuator was verified successfully. The total bio-degradable micro device concept should open new field of an implantable micro device.

NEW CONCEPT OF BIO-DEGRADABLE IMPLANTABLE DEVICE

Bio-degradable Micro Device with Actuator

The bio-degradable actuator proposed in this paper incarnates *in vivo* actuation without needs of surgery to take out after use and energy supply via electricity, magnetism, etc. With this novel actuator, removal-free implantable device loading movable parts can be constructed and various applications for medical field is conceivable. For example, a bio-degradable drug delivery system where the amount of drug release over time changes as it is designed, can be realized (Figure 1).

The device is totally made of bio-degradable polymer and consists of a capsule containing drug and a valve attached to the capsule. The valve is actuated by the bio-degradable actuator to controls the time variation of the amount of drug release. In Fig.1, the valve opens and the drug release begins after implanting to raise the drug concentration. After drug concentration reaches the enough level, the valve closes and the small amount of drug is released to retain the drug level. Finally, the whole device resolves and accordingly the surgical removal is unnecessary.

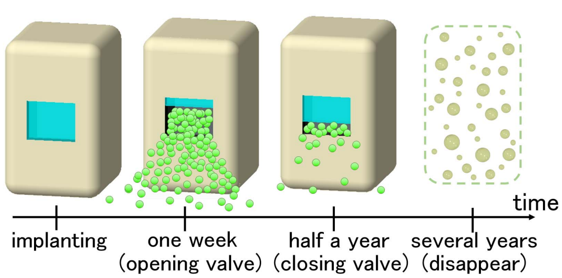

Figure 1: Proposed concept of bio-degradable drug delivery system with actuators. The amount of released drug is controllable by movement of the valve. This device decomposes and absorbs into the human body after use.

Driving Principle

The actuator consists of two or more springs made of different bio-degradable polymers. It is known that after put into liquid, the rigidity of a bio-degradable material steadily decreases, and consequently the spring constant of the bio-degradable spring decreases as it is proportional to the rigidity. Thus, if two or more bio-degradable springs that have different time courses of rigidity are balanced, the balanced point moves as time passes after immersion (Figure 2). This movement of balanced point was utilized as the actuation of implanted medical devices. The above mentioned driving principle can be applied to any kinds of bio-degradable polymers. In this paper, Poly(L-lactic acid) (PLLA) was used as the bio-degradable polymer. It is known that the rigidity of PLLA decreases through degradation process, which is known to be a long term reaction extending over several months or years after immersion [3]. In addition to this, it was shown in this paper that the rigidity of PLLA also decreased not so long after the immersion. Figure 3 shows the change in Young's modulus over time when a

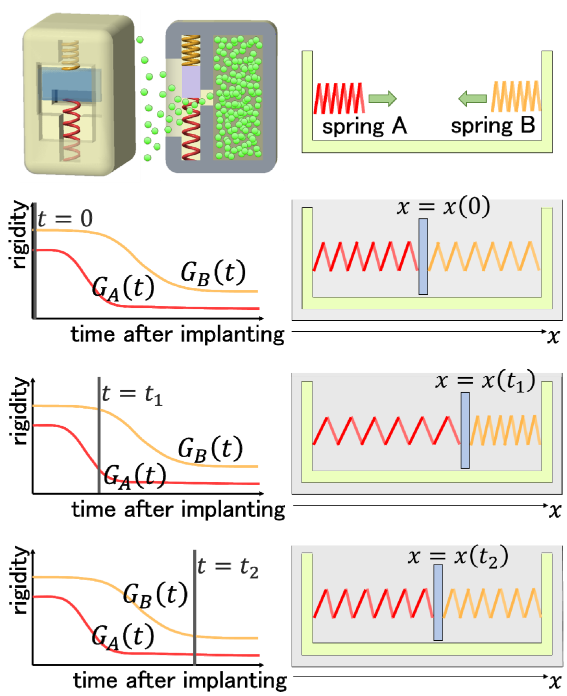

Figure 2: The driving principle of proposed bio-degradable actuator with two-way motion. The actuator utilizes the chronological change in rigidity of each spring. The balanced point of two springs moves according to the rigidity change of each spring.

PLLA specimen was put into liquid. Young's modulus continued to decrease until 2 hours after immersion. PLLA used in this measurement was Poly(L-lactic acid) Mw 50,000 produced by Polyscience, Inc., and the liquid was phosphate buffered saline (PBS) at 37°C. The detailed experimental methods are stated later in MATERIALS AND METHODS chapter. It seems that this short term change in Young's modulus was caused by swelling of PLLA.

Therefore, it can be said that PLLA has two different modes of decrement in Young's modulus: the first decrement probably caused by swelling and the second decrement caused by degrading. Since the amount of change in Young's modulus and the time when decrement occurs in each mode differ in the kind of PLLA, two-stage actuation is feasible by combining two springs made from different kinds of PLLA.

In this paper, the prototype bio-degradable actuator was fabricated and its actuation *in vitro* was measured and evaluated in order to verify the driving principle.

MATERIALS AND METHODS

Material

In this paper, Poly(L-lactic acid) (PLLA) was chosen to be used as bio-degradable polymer. Poly(lactic acid) (PLA) is the most widely produced bio-degradable polymer and used for a wide range of medical devices due to its bio-compatible nature [4]. PLLA is one of stereoisomers of PLA and is also a common choice for bio-resorbable applications. In addition to its long degradation time [3], PLLA shows a wide range of degradation characteristic according to its molecular weight and crystallinity [5]. Thus, time scale of the degradative actuation can be chosen from a wide range, which varies from months to years, by choosing appropriate material depending on its application.

Fabrication Methods

The bio-degradable spring fabricated in this paper was spiral shape, not coil shape. The spiral springs were fabricated by the casting. The procedure was as follows:

1. Male mold was fabricated by microstereolithography (Figure 4(a)) [6].
2. Silicon rubber was casted to the male mold to fabricate female mold (Figure 4(b), (c)).
3. PLLA pellets were casted to the female mold to fabricate the desired shape (Figure 4(d), (e), (f)).

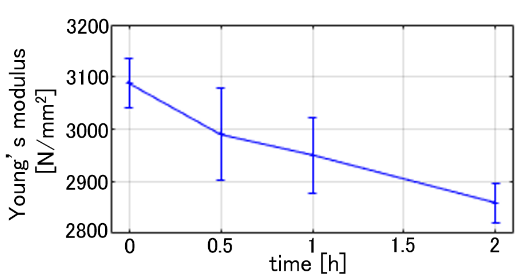

Figure 3: Young's modulus decrement observed immediately after immersion of PLLA into PBS at 37°C. This phenomenon seems to have been caused by swelling.

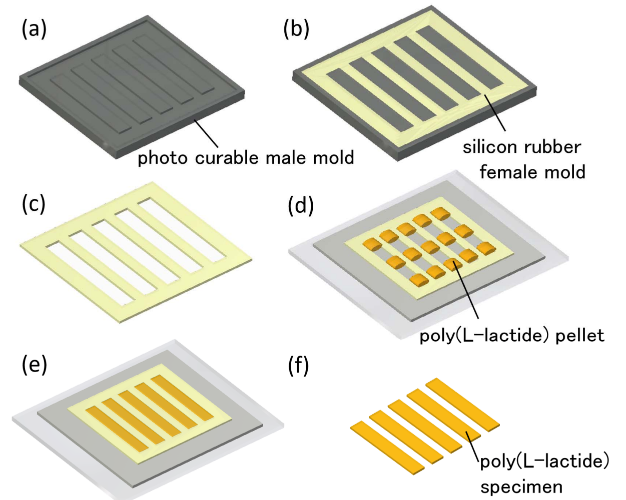

Figure 4: The fabrication method of PLLA specimens. (a): Male molds were made of photo curable resin and fabricated by microstereolithography. (b), (c): Female molds were made of silicon rubber. (d), (e), (f): PLLA pellets were casted to the female mold to fabricate PLLA specimens of desired shape.

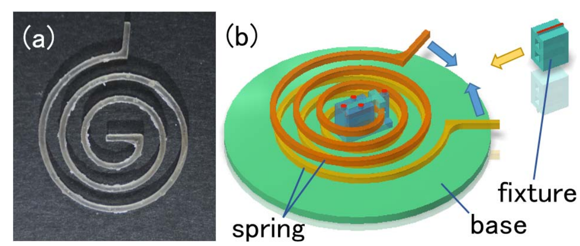

Figure 5: (a) Fabricated spring made of bio-degradable polymer used in setting II. (b) Design of the actuator. Two springs fixed to the base were stretched and joined by the fixture. This device was immersed into the solution and the displacement of the fixture was measured.

Figure 5(a) shows the actual spiral spring fabricated by following this procedure. Two spiral springs made from different kind of PLLA were combined to compose an experimental model of the actuator. Figure 5(b) shows the design of the actuator. Two springs fixed to the base were stretched and joined by the fixture. The position of fixture indicated balanced point of two springs and moved according to the change in rigidity of each spring.

Experimental Methods

In this paper, the change in the rigidity of each bio-degradable material over time was measured to calculate and predict the actuation of the device in experiment 1, and the actual movement of the actuator consisting of two spiral springs (Figure 5) was measured in experiment 2. The procedure of experiment 1 was as follows:

1. Specimens were fabricated from PLLA according to the method stated in Fabrication Method section. The shape of the specimen was rectangular parallelepiped

(3.0×20.0×0.5 [mm]), which was decided to meet the requirement of three-point bending test.

2. The specimens were soaked into solution. The temperature of the solution was kept constant using thermostat. The kind of solution and its temperature are shown in Table 1.
3. Young' s modulus of each specimen was measured by three-point bending test. The specimens were taken out from the solution and droplets were wiped off before measurement.

Five specimens were measured for each material and the mean value of each material were combined to simulate the movement of actuator.

The procedure of experiment 2 was as follows:

1. The actuator was fabricated according to the method stated in Fabrication Method section (Figure 5).
2. The actuator was soaked into solution. The temperature of the solution was kept constant using thermostat. The kind of solution and its temperature are shown in Table 1.
3. The actuator was photographed at a constant interval after soaked. Movement of the position of the fixture (Figure 5(b)), which represents the balanced point of two springs, was measured from the pictures.

The experimental setting is shown in Table 1 and the PLLA materials used in each setting is shown in Table 2. Both experiment 1 and 2 were conducted in setting I. In addition, experiment 2 was also conducted in setting II. The temperature and pH in setting I was decided to imitate the environment of internal body. However, it took several years to observe the actuation caused by degradation in setting I. Thus, the temperature and pH of setting II were decided to accelerate intrinsically slow degradation reaction. Winding number of the springs in setting I was 0.5, which is less than 3 of the spring shown in Figure 5.

RESULTS AND DISCUSSION

Figure 6 shows the simulated actuation calculated from material properties obtained in experiment 1 and the actual actuation measured in experiment 2 in setting I. Compared with the simulation, the balanced point of the actuator moved to the same direction almost at the same time, and the magnitude of the displacement was the same order. Rigidity of material A decreased but that of material B did not change significantly, and thus the balanced point actuated. This decrement in rigidity seems to have been caused by swelling, not by degradation since degradation of PLLA is a longer-term reaction than the length of this measurement. Although one-way motion observed in this experimental setting was almost consistent to the simulation, the magnitude of the displacement was about 4-5 times larger in actual measurement than simulated result. This error seems to have been caused by the difference in applied strain. In the actuator, a spring were pulled by the other spring and tensile stress was applied inevitably (experiment 2). On the other hand, the specimens were kept in the solution without strain in Young' s modulus measurement (experiment 1). In future research, the simulation should be improved to consider the effect of applied stress. Since no significant change in young's modulus of material B was observed in experiment 1, the young's modulus of material B was assumed to be constant in the time range of this experiment, in order to reduce the effect of measurement error on simulated result.

Figure 7 shows measured displacement of the actuator and Figure 8 shows pictures of the actuation, both in setting II. The two-way motion of clockwise and counterclockwise was realized. The clockwise movement was caused in one hour after immersion. It seems to have been caused by swelling of the material A, alike in the setting I. After 20 hours of immersion, the balanced point actuated to the opposite direction gradually. This second movement seems to have been caused by the different degradation characteristics between two materials.

Table 1: The experimental setting. Setting 1 was decided to imitate the environment of internal body and setting 2 was modified to accelerate intrinsically slow degradation reaction.

Experimental Setting	Material	Solution	Duration
setting I	material A and B	PBS at 37°C	72 [h]
setting II	material A and C	standard buffer solution pH 9.0 at 50°C	144 [h]

Table 2: The kind of PLLA used in this paper.

Name	Manufacturer and Trade name
material A	Polyscience, Inc. Mw 50,000, I.V. = 1.0
material B	Polyscience, Inc. Mw 100,000, I.V. = 1.8
material C	PURAC PURASORB PL I.V. = 4.5

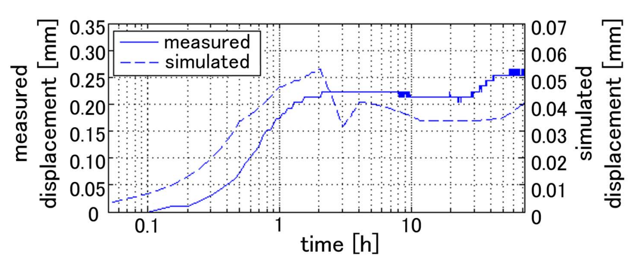

Figure 6: The result of setting 1. The balanced point of the device actuated to the same direction at the same time as the simulation. The magnitude of the actual movement was 4-5 times larger than that of the simulated movement.

CONCLUSIONS

In this paper, a novel actuator utilizing the change in rigidity of bio-degradable polymer was proposed for removable-free implantable device. It was shown in this research that PLLA has two mode of rigidity decrement: short term decrement probably caused by swelling and long term decrement caused by degradation. The prototype actuator was fabricated from PLLA and two-way motion was realized by different characteristics of rigidity change between two materials at each rigidity decrement mode. In addition to this, the actual movement of the actuator was compared with simulated movement calculated from measured material property as for first decrement mode. Compared with the simulation, the actual movement occurred to the same direction almost at the same time, and the magnitude of the displacement was the same order. Therefore, it can be said that the driving principle proposed in this paper was verified successfully.

In future experiments, the two-way motion of swelling and degradation (setting II) must also be validated by compared with simulated motion predicted from the rigidity measurement. In this paper, experiment 1 was conducted once for each experimental setting, thus more trial is needed to improve reliability.

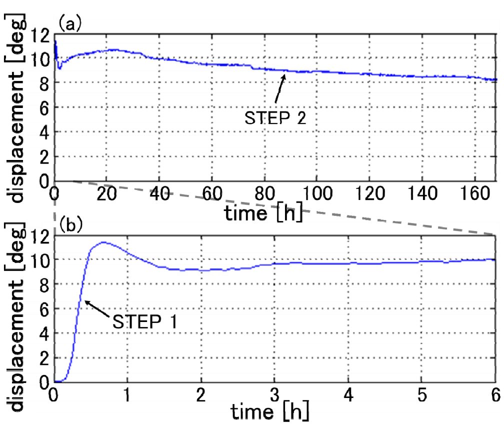

Figure 7: The result of setting 2. The actuation toward one direction was observed immediately after immersion (STEP 1). The movement toward the opposite direction was also observed after 20 hours (STEP 2).

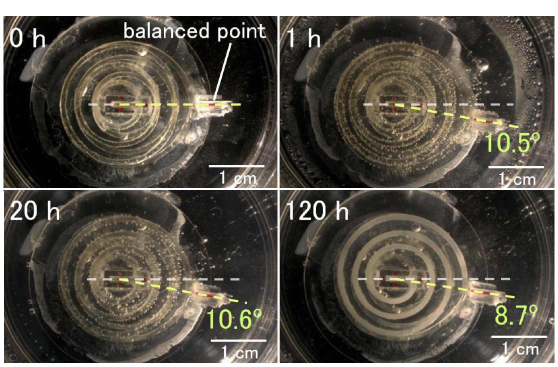

Figure 8: Two-way actuation of the prototype. Balanced point rotated clockwise one hour after immersion and it rotated counterclockwise after 20 hours.

PLA is relatively low-cost and widely used for 3D printing. Thus, the actuator is expected to be miniaturized adequately for implanting uses and be manufactured automatically and inexpensively in the future. In addition, the actuation timing and displacement can be pre-determined by selecting appropriate bio-degradable polymers. Since chronological change in rigidity of bio-degradable polymers vary according to their molecular weight, crystallinity, etc., the actuator for wide range of purposes is feasible. The driving mechanism proposed in this paper is applicable to various solution and bio-degradable material. Therefore, it has applicability to not only for the medical uses but for other MEMS fields as a micro-actuator for long-term quasi-static actuation.

REFERENCES

[1] K. Ikuta, A. Yamada, and F. Niikura, "Real Three-Dimensional Microfabrication for Biodegradable Polymers -Demonstration of High-Resolution and Biocompatibility for Implantable Microdevices-," *Proc. of The 26th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBS04)*, pp. 2679-2682, 2004.

[2] A. Yamada, F. Niikura, and K. Ikuta, "A three-dimensional microfabrication system for biodegradable polymers with high resolution and biocompatibility," *Journal of Micromechanics and Microengineering*, Vol. 18, No. 2, pp. 25-35, 2008.

[3] J. S. Bergström and D. Hayman, "An Overview of Mechanical Properties and Material Modeling of Polylactide (PLA) for Medical Applications," *Annals of Biomedical Engineering*, Vol. 44, No. 2, pp. 330-340, 2016.

[4] J. S. Soares, J. E. Moore Jr, and K. R. Rajagopal, "Constitutive framework for biodegradable polymers with applications to biodegradable stents," *Asaio Journal*, Vol. 54, No. 3, pp. 295-301, 2008.

[5] H. Tsuji and Y. Ikada, "Properties and morphology of poly (L-lactide) 4. Effects of structural parameters on long-term hydrolysis of poly (L-lactide) in phosphate-buffered solution," *Polymer Degradation and Stability*, Vol. 67, No. 1, pp. 179-189, 2000.

[6] K. Ikuta and K. Hirowatari, "Real three dimensional micro fabrication using stereo lithography and metal molding," *Micro Electro Mechanical Systems, 1993, MEMS'93, Proceedings An Investigation of Micro Structures, Sensors, Actuators, Machines and Systems. IEEE*, pp. 42-47, Feb. 1993.

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