SOLUTE DIFFUSION THROUGH THE FIBROTIC TISSUE FORMED AROUND A PROTECTIVE CAGE SYSTEM FOR IMPLANTABLE SENSORS

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ABSTRACT

Biocompatible packaging is crucial in developing implantable sensors. It should allow solutes of interest to diffuse through while minimizing inflammatory response to the packaging and the sensors. In this study, a cage system made of a metal mesh cylinder surrounded by a polyvinyl alcohol (PVA) sponge material was implanted into rats, and fibrotic tissue was formed around the cage system. We then experimentally investigated the permeation rate of solutes (Na, K and Cl) through the fibrotic tissue using a microfluidic device, and found that diffusion coefficients with respect to all the solutions were on the order of 10^{-10} m^2/s, which increased with the flow rates.

KEYWORDS:

Biocompatible packaging, Fibrotic tissue, Diffusion

INTRODUCTION

Implantable sensors have been studied to achieve in situ and long-term monitoring of our health without restricting patients' activities. Biocompatible packaging is crucial in such applications that allow the sensors to access target physical and state quantities while minimizing the effect of the body's inflammatory response onto the sensors. A cage implant system was previously proposed, onto which fibrotic tissue formed as a part of the body's natural reaction to foreign materials [1]. It is important to calculate the diffusivity of the solutes of interest because some sensors, such as glucose sensors, need contact with the solutes to measure their quantities. In the present study, a cage system made of a metal mesh cylinder surrounded by a polyvinyl alcohol (PVA) sponge material was implanted into rats, and fibrotic tissue was formed around the cage system. In this paper, we investigated the diffusivity of solutes to be measured through the fibrotic tissue.

THEORY

Figure 1 illustrates the concept of the micro fluidic system to calculate solute diffusion coefficients through fibrotic tissues. This device has a micro channel whose cross section is a rectangle with a depth of h, width of w and length of L. Two types of liquids, as solutions A and B, flow in the two separate channels. The diffusion coefficient Dc [m^2/s] of a solute can be calculated using the following equation;

$$Dc = \frac{Q \cdot H}{Ar} ln \frac{C_{B,in} - C_{A,in}}{C_{B,out} - C_{A,out}},$$

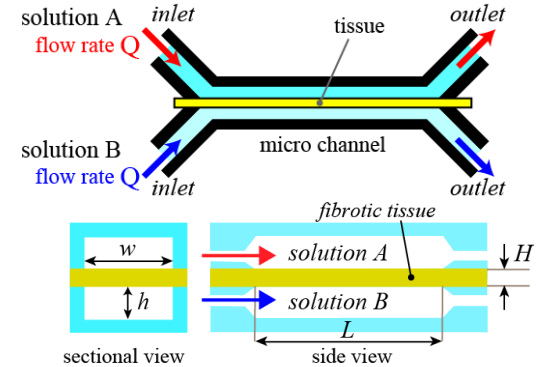

Figure 1. Microfluidic diffusion experiment setup using the fibrotic tissue. The diffusion coefficient can be derived from the measurement of the solute concentrations at the outlets.

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where Q is the flow rate [m^3/s], H the tissue thickness [m], Ar the channel area [m^2], C the concentration [M], $_{A,B}$ the solution type, and $_{in}$, $_{out}$ indicating inlet/outlet.

EXPERIMENTAL

As shown in figure 2, we manufactured metal mesh cages made of a stainless steel mesh sheet rolled into a cylindrical shape, which were then covered with a PVA sponge sheet. They were implanted into the back flanks of rats (n=two cages/rat) for five weeks, during which fibrotic tissues were uniformly formed around the cages. We carefully peeled off the tissue from the cages and sandwiched it in between two microfluidic channels. The tissue thickness was found to be approximately 300 μm.

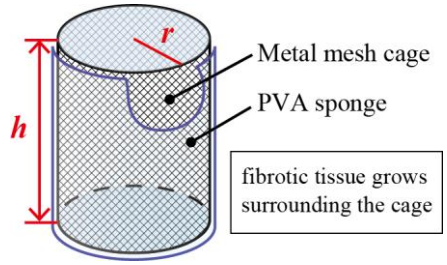

Figure 2. Schematic of a cage system for implantation into rats. A metal mesh cage is wrapped with a PVA (polyvinyl alcohol) sponge sheet.

Figure 3 shows the schematic of the microfluidic device made of polymethyl methacrylate (PMMA). The two opposing plates with channel structures were screwed together with the fibrotic tissue in between to make sure no leakage took place. We used sodium, potassium, and chloride as the solutes. We had phosphate buffered saline (PBS) with a solute dissolved on one side and pure PBS on the other side of the channel, flowing at the same flow rate and in the same flow direction. We then calculated the diffusion coefficients of six cage samples with respect to the flow rates of 5 to 100 μL/min.

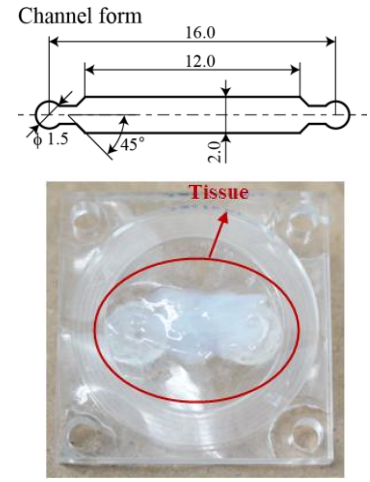

Figure 3. Microfluidic device to measure diffusivity of solutes through a fibrotic tissue

RESULT AND DISCUSSION

Figure 4 shows the photos of a fibrotic tissue formed around a mesh cage covered with PVA sponge. Only a small amount of tissues were formed inside the cage.

As shown in Figure 5, the diffusion coefficients with respect to all the solutes were on the order of 10^{-10} m^2/s. The diffusion coefficients increased with the flow rates, the cause of which still needs to be investigated, since the diffusion coefficient is a property of a tissue and should not be dependent on the flow rates. We hypothesize that this phenomenon may be due to the affinity of the solutes with the membrane. Large flow rates might have induced large shear stresses on the membrane, which could have facilitated the solutes to be diffused into the media.

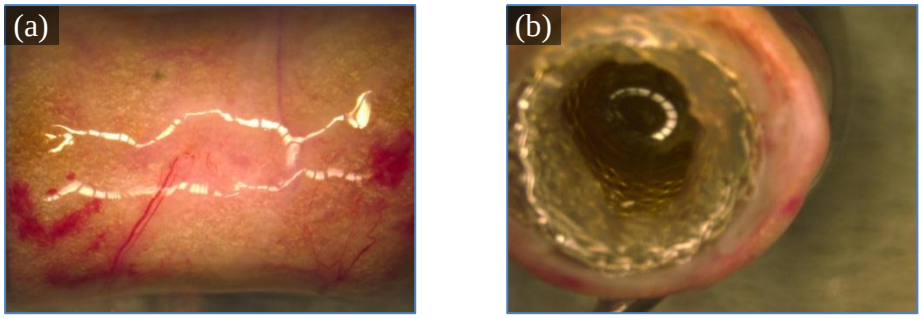

Figure 4. Photos of a fibrotic tissue formed around a mesh cage covered with PVA sponge. (a) Side and (b) cross-sectional views of the tissue and the cage.

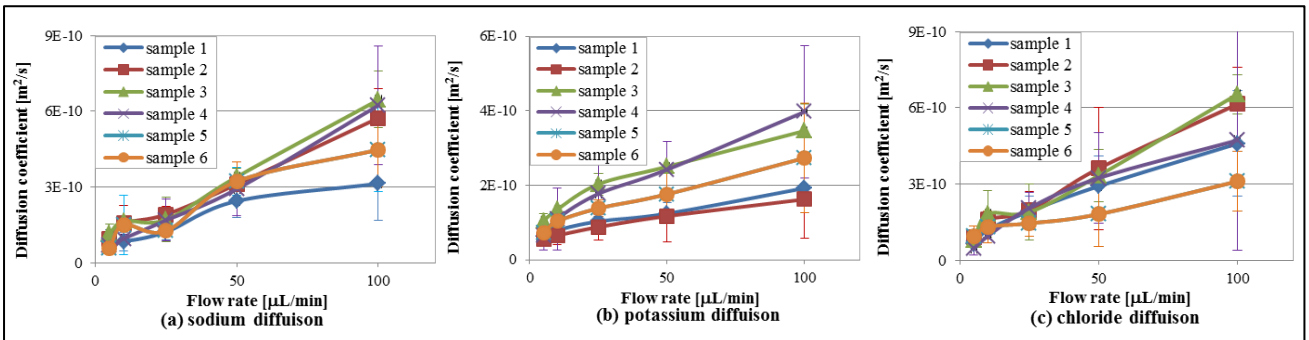

Figure 5. Relationship between the flow rate and the diffusion coefficient using tissues explanted at 5-week time point (n=6; 3 measurements/sample). The diffusion coefficients increased with the flow rate.

CONCLUSIONS

We experimentally investigated the diffusion coefficients of some salts found in the body fluid through the fibrotic tissues formed around a protective cage system, which can potentially be used as a biocompatible packaging system. The results show that it is possible to build a protective cage system that allows passage of salts through the fibrotic tissue and potentially house an implantable sensor *in vivo*.

ACKNOWLEDGMENTS

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[1] "*In vivo* biocompatibility studies. I. The cage implant system and a biodegradable hydrogel," Roger Marchant et al., Journal of Biomedical materials Research, 17, 301-325 (1983)