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Transplantation Tool Integrated with MEMS Manipulator for Retinal Pigment Epithelium Cell Sheet

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Abstract— **This paper reports a transplantation tool for the retinal pigment epithelium in an eye. We have developed MEMS manipulator as an end-effector for transplantation of retinal pigment epithelium cell sheet. Typical size of MEMS manipulator is 3mm×3mm. MEMS manipulator was made of polydimethylsiloxane and driven by pneumatic balloon actuators. MEMS manipulator have been improved and integrated with several functions by sensors and actuators. MEMS manipulator is integrated into a transplantation tool. A whole tool also requires improvements based on our experimental results. We have improved our tool in terms of assembling, sealing, and operation.**

I. Introduction

Tissue engineering for regeneration medicine has been rapidly developing. Transplantation surgery of a cell sheet is strongly expected to cure inextirpable disease while DDS (Drug Delivery System) is expected to deliver drug to targeting areas in the body. Recently study on medical MEMS becomes popular by taking advantages of their integrated functions. We have studied MEMS devices for transplantation of retinal pigment epithelium (RPE) cell sheet. Various MEMS manipulators based on pneumatic balloon actuator (PBA) have been reported since 2006 [1-4]. This paper reports a whole transplantation tool including a MEMS manipulator and its peripheral mechanisms. Presented tool has been improved through continuous previous experimental evaluation of prototyped tools.

II. MEMS Manipulator for RPE Cell Sheet

MEMS manipulator has been designed by taking account of proposed transplantation operation of RPE cell sheet (see Fig. 1 and Fig. 2). Developed MEMS manipulator was basically composed of a head (3 mm×3 mm), an arm (40 mm long), and a base with interconnection. Details of fabrication and principle has already reported elsewhere [2].

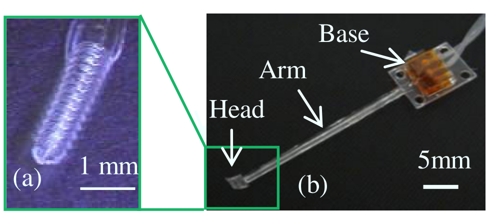

Figure 1 MEMS manipulator for RPE transplantation. (a) Driving head [2], (b) Whole view.

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The head made of polydimethylsiloxane (PDMS) can be retracted into a cylindrical shape to be accommodated in a needle. Initially, retinal dome is formed by filling subretinal space with physiological saline. The head of manipulator holds RPE sheet. The MEMS manipulator is driven by PBA actuation. The cylindrical head of manipulator holding RPE sheet is then accommodated into a hollow needle. The hollow needle with the manipulator holding RPE sheet is subsequently introduced into the retinal dome. The manipulator is pushed into the dome from the opening of the hollow needle. Then the head of manipulator is opened in the dome to release. RPE sheet is supported at corner of manipulator by gel so as to follow the deformation of manipulator. As a result of these sequential procedures, RPE sheet is carried and transplanted on the bottom of the eye.

III. Transplantation Tool

A. *Previous tool*

A transplantation tool is equipped with a MEMS manipulator. Surgeon can operate a MEMS manipulator by using driving mechanism of tool. Figure 3 shows previous tool. Previous tool could move MEMS manipulator back and forth in a hollow needle. Previous tool was composed of a hollow needle, a grip equipped with mechanism for linear motion of manipulator. A MEMS manipulator with a RPE sheet is pushed out from a hollow needle in an eye (see Fig. 3(a) and Fig. 3(b)).

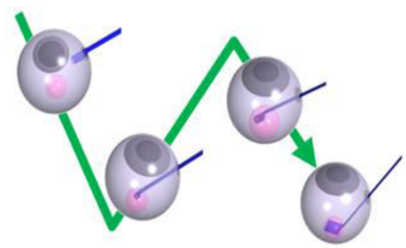


Figure 2 Outline of transplantation operations [2].
A needle tool holding MEMS manipulator is inserted into an eye. MEMS manipulator is actuated and opened in an eye.

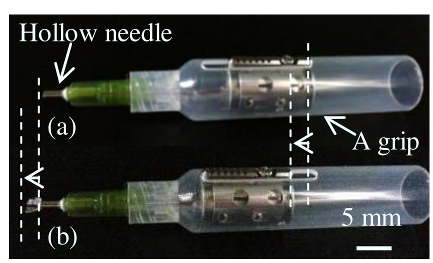


Figure 3 Appearance of previous tool. (a) Retracted status, (b) Releasing status.

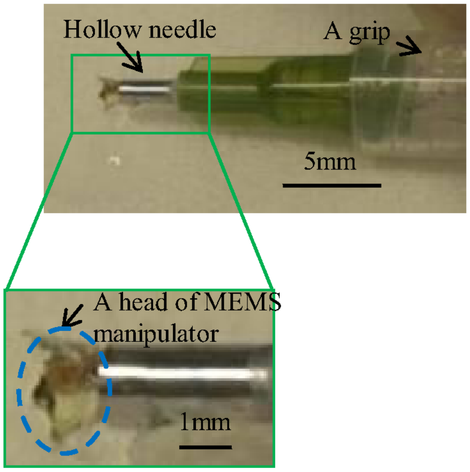


Figure 4 Sticking problem in previous tool.
A MEMS manipulator was stuck by friction force on the inner wall of needle both during assembly and operation.

Previous tool still had a room to be improved in consideration for experimental results. For example, we had following problems in experiments:
1) MEMS manipulator was stuck against an inner wall of hollow needle,
2) RPE sheet was flowed out by backward flow generated by pressurized saline filled in subretinal space of an eye.
Figure 4 shows sticking problem of MEMS manipulator on the inner wall of needle. A MEMS manipulator was stuck and deformed by friction force on the inner wall of a needle.
Figure 5 shows a pseudo experiments using syringe as high pressure source. Figure 5(a) explains set up of pseudo experiment. Water in a syringe was pressurized by a pressure regulator. Figure 5(b) shows the initial state. RPE sheet peeled from MEMS manipulator by backward flow at 1.2kPa (Fig. 5(c)). Pressure difference between subretinal space and outside caused the backward flow. We have improved the transplantation tool based on our experimental results.

B. Improvement of transplantation tool

First of all, sticking problem of MEMS manipulator is discussed. It was also hard to assemble MEMS manipulator made of PDMS (polydimethylsiloxane) into a hollow needle. We designed and employed separated needle structures composed of upper and lower parts (see Fig. 6). The needle was made of stainless steel (SUS304). It becomes possible to settle MEMS manipulator into a lower separated needle in advance and cover by an upper needle structure as shown in Fig. 7. Next, we improved linear back and forward motion of MEMS manipulator in a hollow needle. Friction between MEMS manipulator and needle wall was reduced by Teflon coating on needle inner wall by spray coating. We also had a problem of backward flow generated by pressurized saline filled in subretinal space. We designed a pressure partition to isolate high pressure space in an eye from outside space.

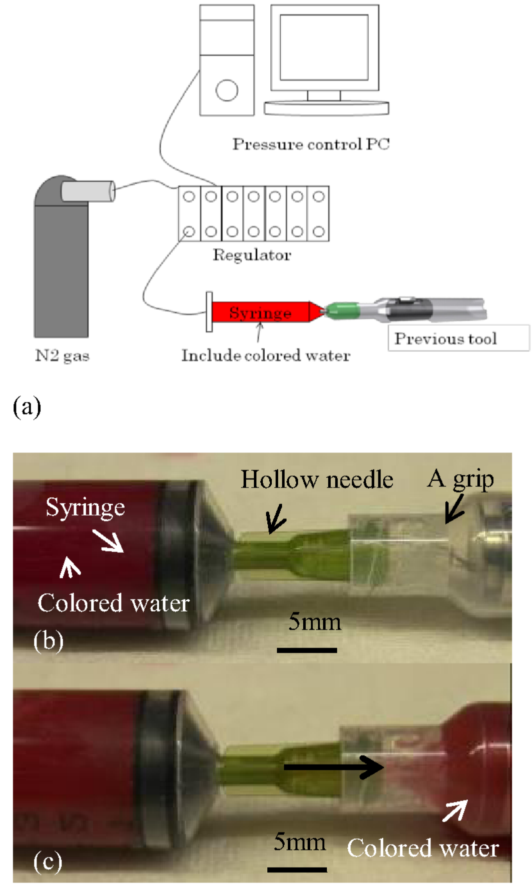


Figure 5 Backward flow in pseudo experiments using syringe as high pressure source.
(a) Set up of pseudo experiment, (b) Initial state,
(c) Pressurized at 1.2 kPa by. RPE sheet on a manipulator was peeled and moved by backward flow.

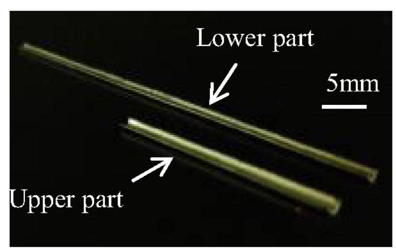


Figure 6 Separated needle structures (SUS304).

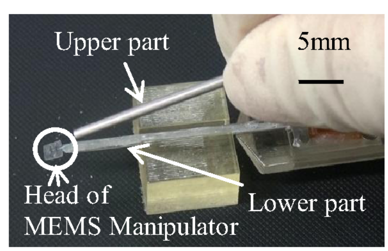


Figure 7 Assembled MEMS manipulator on a lower part.

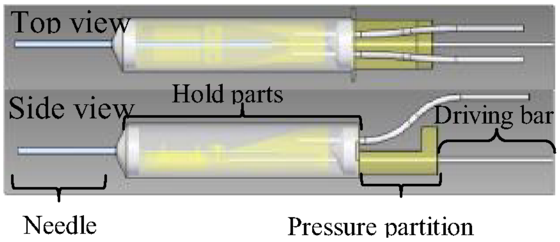
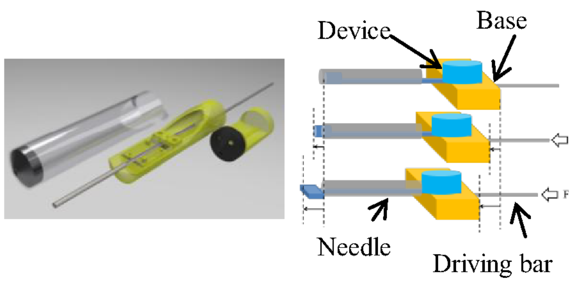
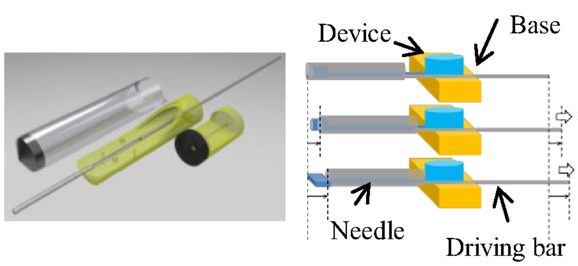


Figure 8 Schematic drawing of improved tool



(a) Movable MEMS manipulator type
Left is the whole view and right is the principle view.



(b) Movable needle type
Left is the whole view and right is the principle view.

Figure 9 Two types of driving mechanism. (a)Movable MEMS manipulator type. (b) Movable needle type. Driving bar is manually driven (Back and forth operation).

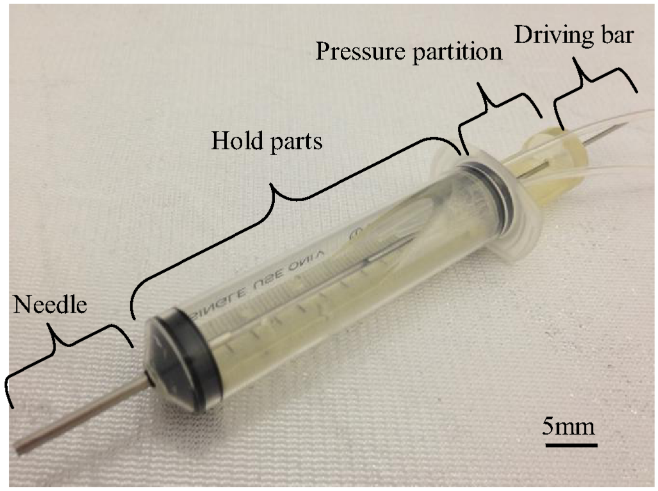
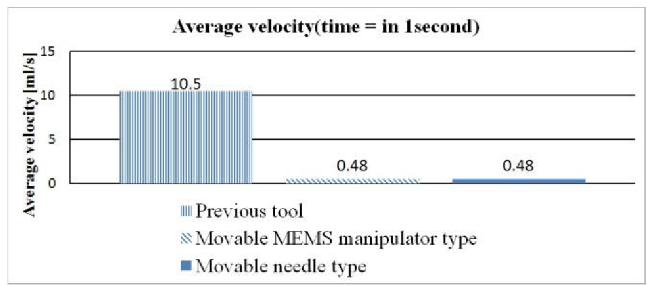


Figure 10 Photograph of implemented tool.



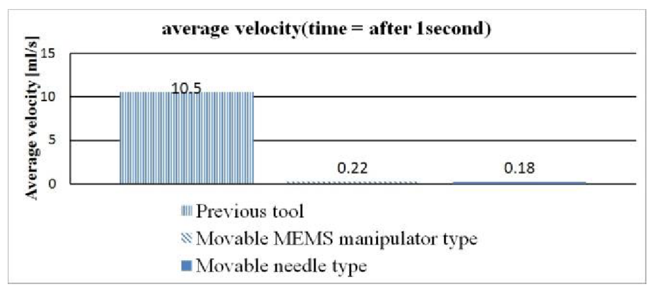


Figure 11 Average velocity of backward flow into tool at 3.0 kPa.
(a) Average velocity of backward flow within 1 second,
(b) Average velocity of backward flow after 1 second.

IV. IPLEMENTATION OF TRANSPLANTATION TOOL

We improved transplantation tool by taking into above consideration as shown in Fig. 8. Transplantation tool consist of MEMS manipulator, needle, syringe, pressure partition, and structure for driving mechanism. We designed two types of tools: movable MEMS manipulator type and movable needle type. Individual composition was illustrated in Fig. 9. Movable structures were driven by a driving bar. ø2.0 mm needle was designed 35 mm long in correspondence to 40 mm long MEMS manipulator. ø17 mm syringe was 78 mm long. Movable MEMS manipulator type employs the same way as previous tool to expose the head of MEMS manipulator in subretinal space while the other moves a needle (see Fig.9 (a)). Movable MEMS manipulator type moves MEMS manipulator itself. On the other hand, movable needle type moves a needle to expose the head of MEMS manipulator. These motions were driven by a driving bar (see Fig.9 (b)). Figure 10 shows completed movable needle type.

V. EVALUATION

We evaluated newly implemented transplantation tools in terms of pressure partition and back and forward motion. A pressure sensor was set to monitor sealing of tools by the partition. Different types of tools were compared: previous tool and two types of improved tools. Figure 11 shows the average velocity of backward flow generated at 3.0 kPa. Backward flow into our improved tool was very small amount and drastically decreased within a second (please compare Fig. 11 (a) with (b)). Strong backward flow was observed in previous tool. Improved tool could achieve high sealing performance while previous tool showed serious leakage. An experiment using a laver sheet as a pseudo RPE sheet was executed to confirm its feasibility. RPE sheet is very precious so laver which had the characters similar to RPE sheet is used.

In our experiment, the improved tool could keep pseudo RPE sheet without generating backward flow by 1.2 kPa pressure. Next, we evaluated back and forward motion. Both movable MEMS manipulator type and movable needle type were characterized. Figure 12 shows back and forth motion by improved tool. Figure 12 shows the motion of movable MEMS manipulator type. MEMS manipulator was pushed out from a nozzle successfully. Improved tool could move MEMS manipulator without serious friction problem. Contrary, the motion of movable needle type moves needle without moving the manipulator. Backward motion of needle exposes the head of manipulator.

VI. SUMMARY

This paper presented improvements of transplantation tool for the RPE cell sheet in an eye. We could improve a whole tool accommodating MEMS manipulator as an end-effector in order to satisfy requirements from experimental results. Assembly and driving mechanism of MEMS manipulator were improved successfully. Pressure partition could solve the backward flow from the subretinal space. Ex-vivo and in-vivo experiments will verify the practical usability of the improved tool.

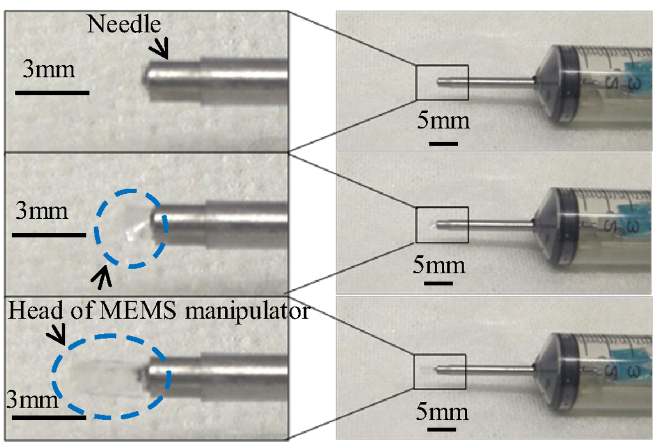


Figure 12 Back and forth motion by improved tool.
(a) Initial state, (b) Middle position, (c) Exposed head of manipulator.

VII. ACKNOWLEDGEMENT

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VIII. REFERENCE

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