

## Research on Pneumatic Cell Sheet Delivery System for Laparoscopic Surgery

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Endoscopic submucosa dissection (ESD) procedures, used to remove cancerous tissue from thin-walled organs such as the duodenum, often result in compromising the organ's functionality, resulting in problematic leakage. While a device has been developed to enable the adherence of a cell sheet to provide additional protection (thickness) to the lining, the device is not suited to laparoscopic application. We have developed and tested a new device and procedure that can be used laparoscopically to adhere cell sheets to organs.

### 1. Introduction

The duodenum is the organ that follows the stomach and is the first part of the small intestine. Surgical operations, such as partial duodenectomy and pancreaticoduodenectomy, remove cancer at the duodenum by using laparoscopic or open surgery in the case of early-stage duodenal cancer and benign border tumors; currently endoscopic submucosa dissection (ESD)<sup>(1)</sup> may be used for this surgery. Figure 1 illustrates a typical ESD procedure.

The ESD procedure involves first marking around the cancer using a high-frequency knife. Next, a solution is injected into the submucosal layer to float the cancerous tissue to the surface. This is followed by cutting the mucosa around the affected area with a knife. However, in up to 50% of the cases, complications occur such as postoperative perforation, causing the leakage of pancreatic and bile acids and resulting in injury to surrounding organs. As a countermeasure against perforation, we are endeavoring to transplant a cell sheet to the thinned part of the wall laparoscopically.

Figure 2 shows actual images taken during an ESD procedure. Although it is not visually apparent, in image 5, after the cancerous tissue has been removed, the remaining organ wall is very thin.

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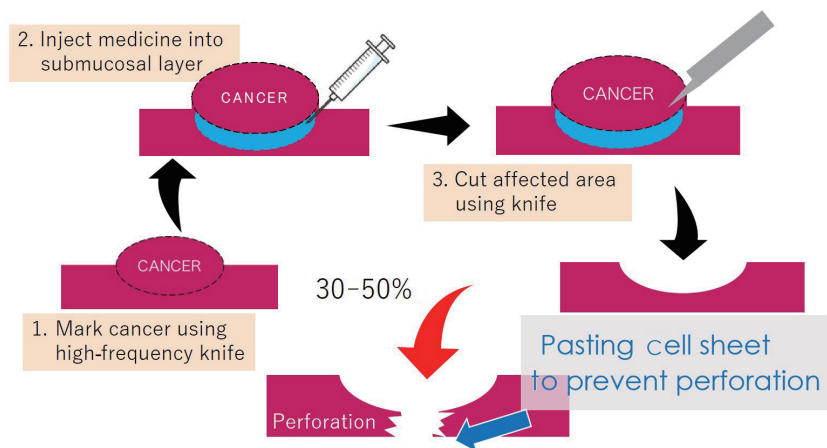


Fig. 1. (Color online) ESD.

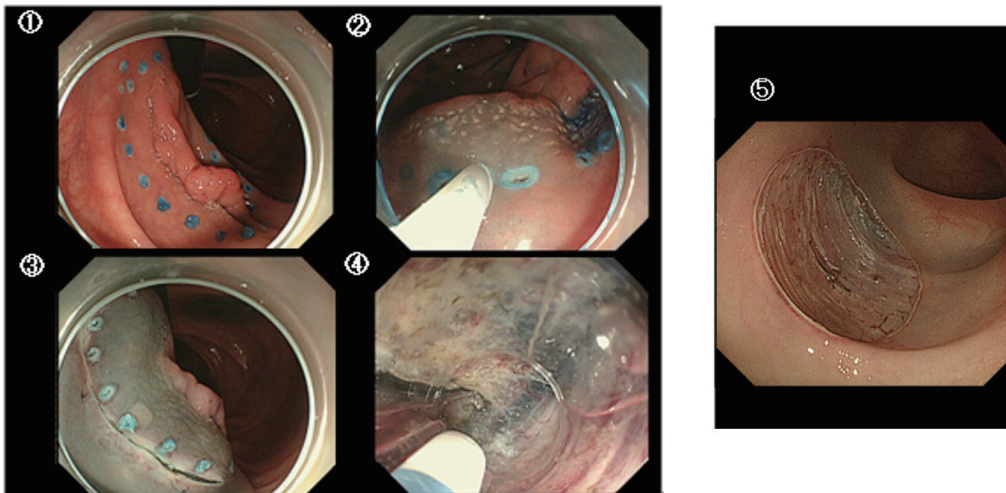


Fig. 2. (Color online) Actual images of ESD.<sup>(1)</sup>

Note that the cell sheet is adhered to the outer wall of the duodenum, and clearly the cell sheet must be adhered precisely behind the ESD site to be effective. Figure 3 shows the cell sheet.

The size of the cell sheet varies from 15 to 25 mm according to the surgical site. The cell sheet assists the recovery of the surgical site as well as helps prevent perforation. However, the cell sheet is very thin and is easily damaged, reducing its effectiveness.

The conventional method of transplanting a cell sheet is to use a SWITL device,<sup>(2)</sup> which is made by Furukawa Machine Co. and was developed by a collaboration between Tokyo Women's Medical University and Osaka University. This device was made to transplant a cell sheet called a "heart sheet" to the heart. An advantage of this device is that it is easy to detach the cell sheet from the tip; however, this device is too large to use for laparoscopic surgery.

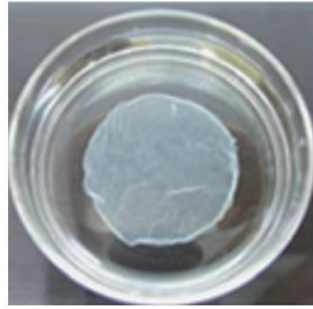


Fig. 3. (Color online) Cell sheet.

The aim of our research is to develop a device that assists the delivery and adherence of a cell sheet to the duodenum laparoscopically after ESD. We assume the use of a 12 mm trocar (actual internal diameter is 12.5 mm). Key aspects of this device are the reliable transportation of the cell sheet so as to avoid damage or wrinkling through the trocar and its accurate adherence to the ESD site.

## 2. Proposed Device

The proposed device is shown in Fig. 4, which shows the mechanism's structure. The outer housing of 12 mm diameter contains a 10-mm-diameter air tube that transports the cell sheet and releases the cell sheet at the target location from the tip. Note that during laparoscopic surgery, the abdominal region is pressurized to create a working area, and the air release mechanism must counter this pressure.

The left image in Fig. 5 shows the air release holes for the first prototype. The right image shows the storage mechanism, whereby the cell sheet is carefully rolled then passed through the outer tube.

Figure 6 shows the second prototype, which features a finer array of holes. The hole diameters are 0.5 mm and the holes are set at 1 mm spacings. This prototype supports cell sheets up to 20 mm in diameter. The release mechanism is shown in the center, where the air pressure enables the uniform release of the cell sheet on the target organ surface.

We used a wet tissue to simulate the cell sheet because it reflects the susceptibility of the cell sheet to tearing and wrinkling, and a silicone tube was used to simulate the intestine. Dots were added to the tissue to make it more visible. Using air, the tissue can be released on the surface of the silicone tube, but the tissue could not be released without using air. This simple simulation confirmed the effectiveness of the air release system. Refer to Ref. 3 for our prior work on the development of more elaborate silicone-based models, to Refs. 4 and 5 for an evaluation of the laparoscopic forceps grasping pressure, to Refs. 6 and 7 for more detail on the first prototype laparoscopic cell sheet transportation system, and to Ref. 8 for work on the development of articulated laparoscopic instruments.

The storage mechanism is shown in Fig. 7. Firstly, the cell sheet is placed on the tip (top left), then the tip is retracted into the 12 mm tube (top center) to transport the cell sheet through

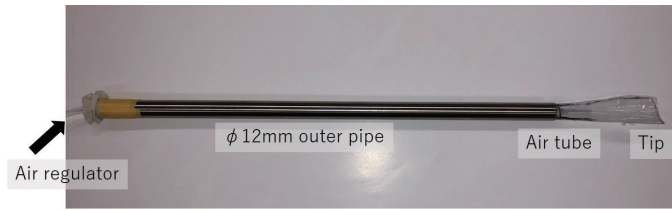


Fig. 4. (Color online) Proposed pneumatic cell sheet delivery device for laparoscopic surgery.

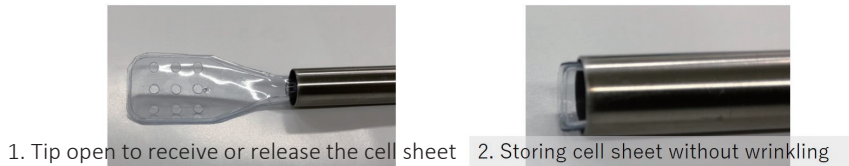


Fig. 5. (Color online) Proposed device (first prototype).

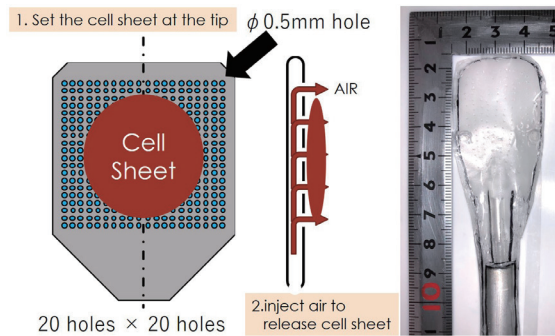


Fig. 6. (Color online) Releasing the cell sheet.



Fig. 7. (Color online) Storage system (first prototype tip).

a trocar to the target area, where the cell sheet is unraveled and placed carefully on the target intestine location. This location is the reverse side of the ESD procedure location explained earlier. This system makes it possible to transfer the cell sheet onto the outer surface of the duodenum laparoscopically without tearing or wrinkling the cell sheet. The cylinder is then

inserted through a trocar (not shown here). Then the tip is carefully aligned with the reverse side of the EDS site, the tip is opened, exposing the cell sheet, and the cell sheet is lightly pressed onto the target surface. Finally, compressed air releases the cell sheet onto the target surface. We found that even if we bend the cell sheet, we can transport it to the target without tearing or wrinkling.

### 3. Experiment

Figure 8 shows the device with the second prototype tip used in a porcine experiment. This experiment was carried out laparoscopically via a monitor. In this case, although the target was not the duodenum, it can be clearly seen that this device is fully functional. A red circle was added to the cell sheet to increase its visibility.

Figure 9 shows improvements made to the second prototype. The previous coarse array of perforations was replaced with a precision array of fine perforations, reducing air leakage and

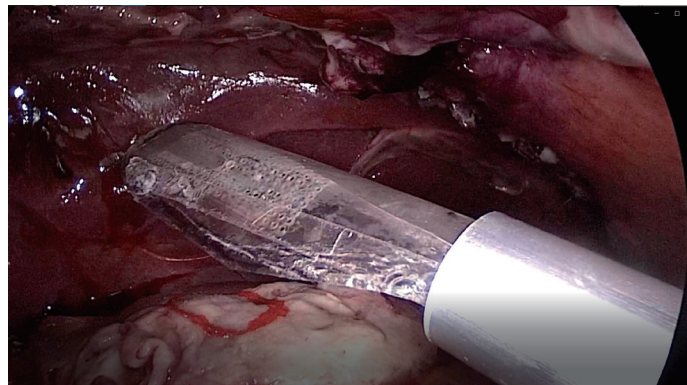


Fig. 8. (Color online) Porcine experiment.

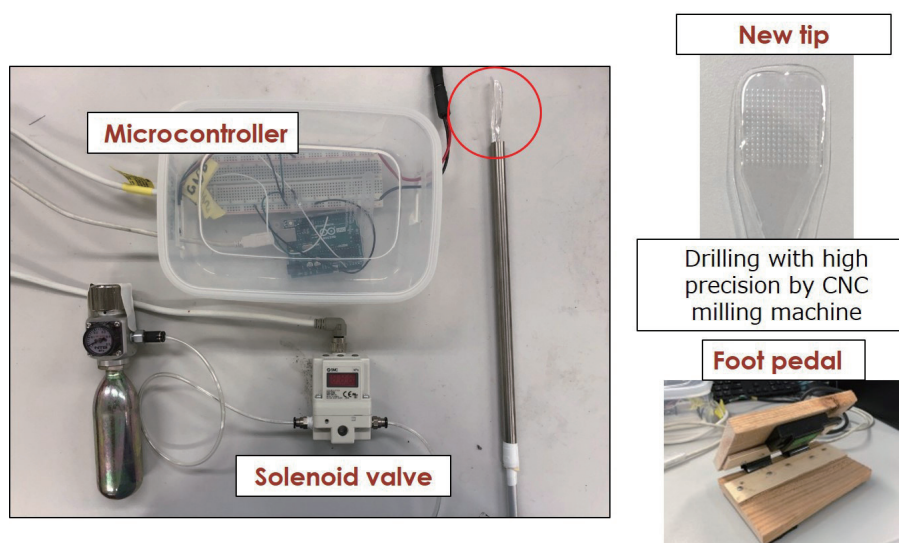


Fig. 9. (Color online) Improvements made to second prototype.

improving the uniformity of the release mechanism. Regarding the release control mechanism, the previously used on/off air pressure control operated by a hand switch was replaced with a foot control that provides proportional control of the air using pulse width modulation (PWM) control. As a result, the flow rate of air can be adjusted, and it is possible to perform operations with different sizes of the sheet and attachment locations.

#### **4. Discussion**

Regarding the placement of the cell sheet, in the experiment illustrated in Fig. 8, the placement plane was aligned with the cell sheet placement instrument; however, in many situations, this will not always be possible. To facilitate the application of the cell sheet in the widest possible range of scenarios, some kind of articulation will be required at the tip. Currently, the tip is made of polyethylene terephthalate and is quite rigid. This limits the application of the cell sheet in the direction of application. However, the use of a softer grade of plastic is currently being considered to allow the operator to flex the tip to apply the cell sheet to organs from a wider range of angles/orientations. If the application of the cell sheet from a wider range of angles and orientations is possible, it will make the instrument more convenient/practical. If passive manipulation is not possible, some kind of articulation will be required at the tip. However, additional articulation tends to increase complexity and cost.

#### **5. Results**

All three cell sheet tests, where cell sheets with sizes varying from 30 to 40 mm were placed on the tip, transferred to a target test site, and adhered to a target organ, were successful. The 40-mm-wide cell sheet overlapped a little when placed in the tube; however, a special coating on the cell sheet prevents the cell sheet edges from adhering to each other.

#### **6. Conclusions**

We have developed a cell sheet delivery device that can paste a cell sheet on an organ laparoscopically. This device transfers the cell sheet to the target site without tearing or wrinkling and releases the cell sheet onto the target organ surface using proportionally controlled compressed air. In future work, we plan to experiment with alternative air hole patterns and increase the flexibility of the system at the tip to allow a wider variety of release orientations.

#### **Acknowledgments**

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