Results

Infrared absorption spectra

The absorption spectra of the mucosa, submucosa, and muscularis propria were almost identical (Fig. 2). The absorption spectra of saline and 0.4 % sodium hyaluronate displayed similar curves in the mid-infrared range and exhibited absorption values of ~850 cm^{-1} at a wavelength of 10.6 μm (Fig. 3). The absorption coefficients of these solutions were markedly higher than that of the lamina propria at a wavelength of 10.6 μm, suggesting that laser absorbents, such as saline and sodium hyaluronate, absorb enough of the energy produced by CO_2 lasers to protect the muscularis propria from damage caused by laser irradiation.

Preliminary study

To investigate whether the submucosal injection of saline prevents the muscularis propria from being injured and to determine the optimal CO_2 laser output power for ESD, a preliminary study was performed. In the absence of saline injection, at cutting speeds of 0.5 and 1.0 mm/s performing the CO_2 laser irradiation at 6 W damaged the muscularis propria, and performing it at 10 W damaged the muscularis propria at all speeds (Fig. 4A, C). On the other hand, in the presence of saline, irradiation did not damage the muscularis propria at any speed or output power (Fig. 4B, D). Thus, the injection of saline prevented the laser's energy from passing through the submucosa, and hence, protected the muscularis propria from injury.

When sodium hyaluronate was injected into the submucosa, performing the CO_2 laser irradiation at 12 W and 0.5 mm/s, which were the conditions that were found to be most likely to induce injury in the saline experiment, laser irradiation did not damage the muscularis propria (data not shown).

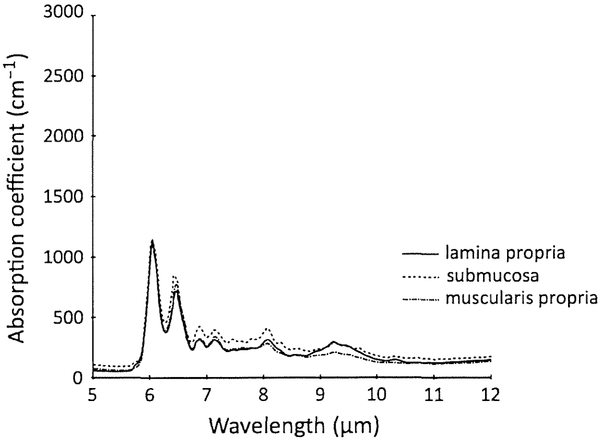

Fig. 2 Absorption spectra of the porcine stomach. The infrared absorption spectra of the lamina propria, submucosa, and muscularis propria are shown. These spectra were similar in the infrared region

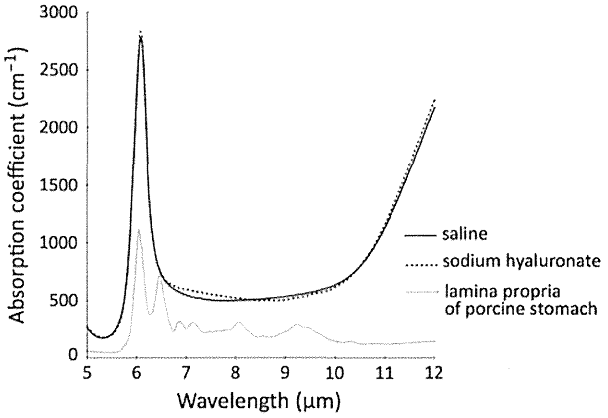

Fig. 3 Absorption spectra of saline and sodium hyaluronate. The infrared absorption spectra of saline, sodium hyaluronate, and the mucosa of the porcine stomach are shown. The spectra of saline and sodium hyaluronate were similar. The absorption coefficients of these solutions were higher than that of the lamina propria at a wavelength of 10.6 μm

These results showed that both saline and sodium hyaluronate stopped the energy of the CO_2 laser from passing through the submucosa and prevented the muscularis propria from being injured.

Ex vivo porcine study

To investigate whether performing ESD using a CO_2 laser with laser absorber is a safe and feasible method, an *ex vivo* study, in which a porcine gastric model was subjected to the procedure, was performed.

The procedure time was measured from the first submucosal injection to the end of the complete resection of the lesion. Grossly, all specimens included all of the markings caused by electrocautery, which formed the equivalent of a tumor-free resection margin. Hypothetical lesions were produced in the antrum, lower body, central body, and upper body. En bloc resections were achieved in all cases. The mean diameter of the resected specimen was 31.6 mm, and the mean procedure time was 26.2 min (Table 1).

The gastric wall resection sites were examined. However, no gastric wall perforation was encountered, and no muscular injuries were detected during histological examinations.

The resected specimens also were collected and histologically evaluated. The mucosae of the resected specimens were not damaged by the submucosal dissection, and histological evaluations could be performed in all of the resected specimens (Fig. 5A). The resection margins were very clear, and almost no burn effects were seen. In

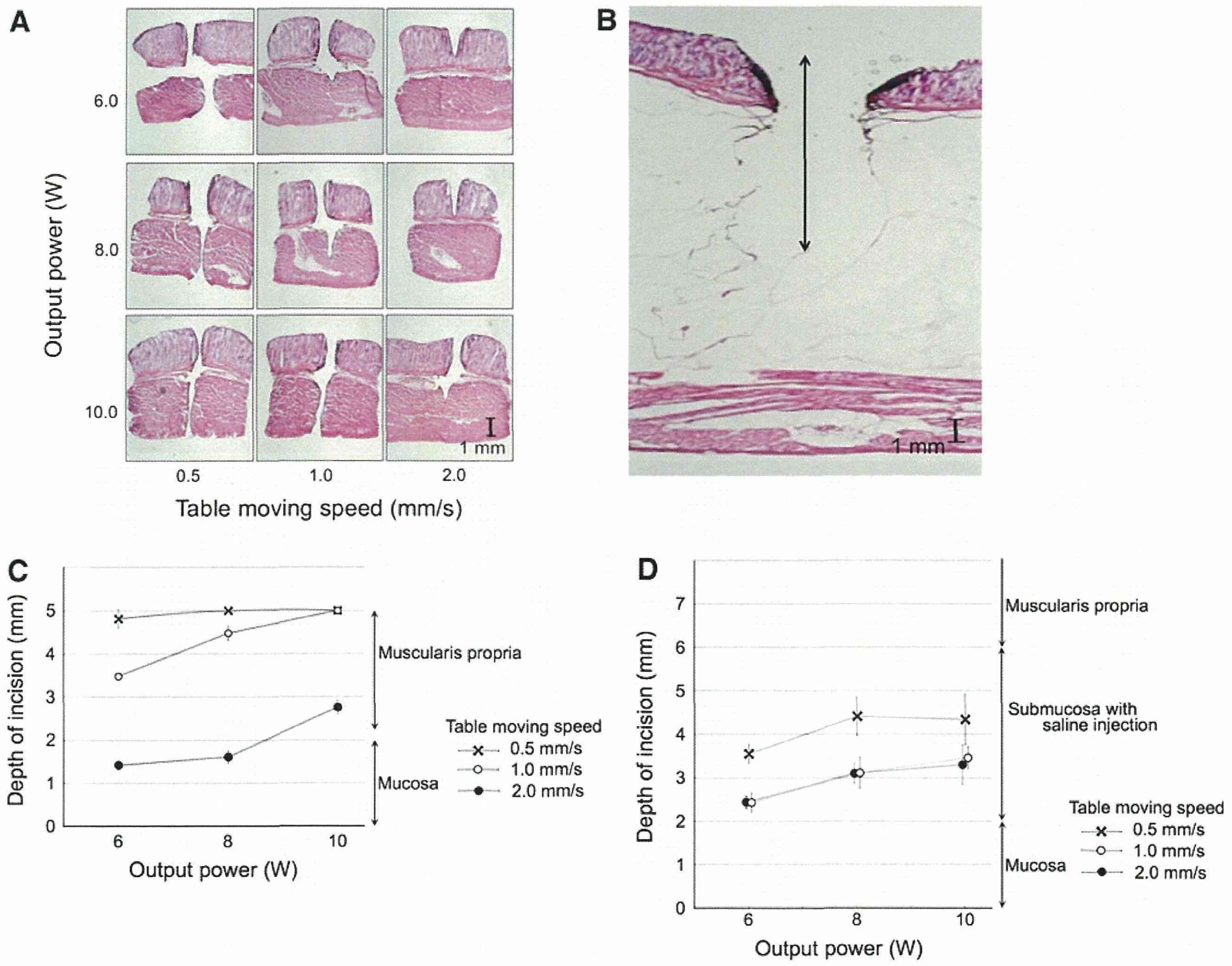

Fig. 4 Incision depth in various conditions. In the absence of saline injection, performing the CO_2 laser irradiation using an output power of 6 W damaged the muscular layer at incision speeds of 0.5 and 1.0 mm/s. Performing the CO_2 laser irradiation at an output power of 10 W damaged the muscular layer at all speeds (**A**). When the CO_2 laser incision was performed at an output power of 12 W and a speed of 0.5 mm/s, it did not reach the muscular layer (**B**). These conditions were considered to produce the deepest incisions according to the findings obtained without saline injection. **C** Depth of the incisions produced in the absence of saline injections. **D** Depth of the incisions produced in the presence of saline injections

Table 1 Results of CO_2 laser ESD in a resected porcine stomach

Case	Procedure time (min)	Major axis (mm)	Minor axis (mm)	Perforation
1	22.3	32.6	26.7	None
2	26.6	31.1	26.3	None
3	24.1	30.2	25.8	None
4	22.7	33.6	21.8	None
5	35.5	30.3	29.7	None
Mean	26.2	31.6	26.1	0
SD	5.5	1.5	2.8	0

ESD was performed using a CO_2 laser for five hypothetical lesions

The mean size of the resected specimens was 31.5 mm, and the mean procedure time was 26.2 min. No perforation occurred during the procedures

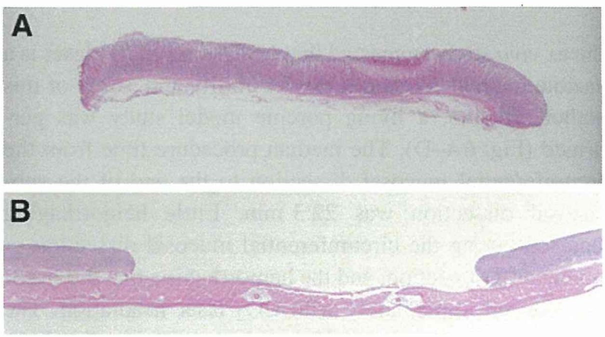

Fig. 5 Histological findings of the resected lesion and resected site. **A** Histological findings of the resected lesion after laser ESD. Enough of the submucosa remained to allow submucosal invasion and lymphovascular invasion to be evaluated. **B** Histological findings of the laser ESD site. No muscular damage was seen

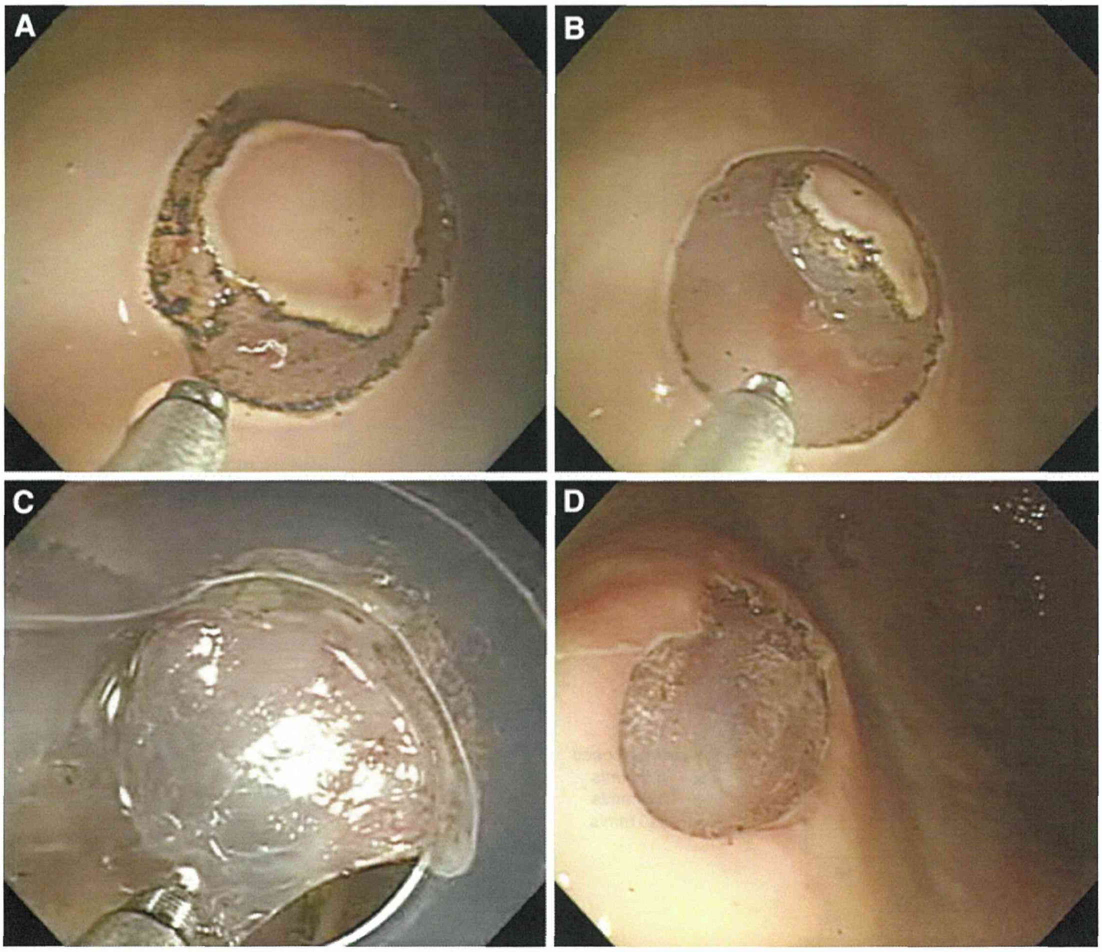

Fig. 6 Endoscopic view of ESD using a CO_2 laser. **A** Circumferential mucosal incision. **B**, **C** Submucosal dissection. **D** Artificial ulcer produced by laser ESD

addition, no muscular damage was detected (Fig. 5B). These results suggest that ESD using a CO_2 laser is feasible.

Living porcine study

The *ex vivo* study suggested that ESD using a CO_2 laser is a feasible method. To verify the feasibility and safety of this method in vivo, a living porcine model study was performed (Fig. 6A–D). The median procedure time from the circumferential mucosal dissection to the end of the submucosal dissection was 22.3 min. Little hemorrhaging occurred during the circumferential mucosal dissection or submucosal dissection, and the hemorrhaging that did occur was arrested immediately with CO_2 laser irradiation. The procedures were accomplished without any complications, such as perforations or serious bleeding. During the circumferential mucosal dissection, smoke and fragment splattering temporarily reduced the endoscopist's visibility. However, the smoke and fragments were successfully suctioned using an accessory channel, and the lens of the endoscope was cleaned, thereby recovering visibility. The incision edge was sharp and clear on the endoscopic view. During the submucosal dissection, no smoke or fragment splattering occurred. Specimens of the resected mucosa were collected, and the surface and edge of the ulcers produced by ESD were smooth. The heat damage caused by the incision and dissection was not extensive so it was possible to histologically evaluate the resected mucosa (Fig. 7A, B). The muscularis propria was not damaged by the laser irradiation (Fig. 7C, D). These findings indicate that ESD using a CO_2 laser is a feasible and safe method.

Discussion

Endoscopic submucosal dissection has been widely performed, not only for early gastric cancer, but also for superficial cancers in other parts of the gastrointestinal tract, such as esophageal cancer and colorectal cancer.

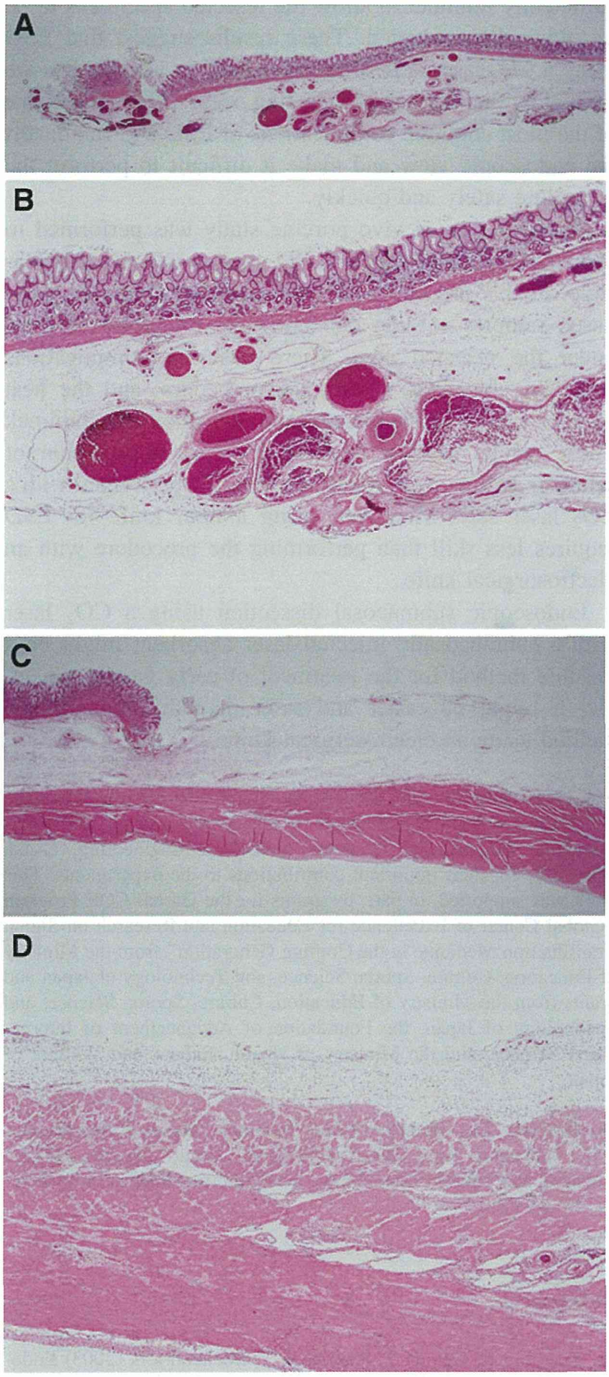

Fig. 7 **A**, **B** Histological findings of the resected lesion and ESD resected site. **C**, **D** Histological findings of the laser ESD site. Enough of the submucosa remained free of heat damage to allow submucosal invasion and lymphovascular invasion to be evaluated (**A**, **B**). No muscular damage was detected at the ESD resection site (**C**, **D**)

However, ESD requires a great deal of endoscopic skill, and the procedure takes a long time. In addition, ESD carries a high risk of perforation and bleeding [4]. ESD is usually performed with an electrosurgical knife. It is difficult to make incisions with electrosurgical knives without appropriate traction; therefore, skill is required to move the knife in the appropriate direction. Thus, to broaden ESD it is necessary to develop simple methods for mucosal incision and submucosal dissection. We hypothesized that laser irradiation might be a suitable alternative to using electrosurgical knives in ESD, because it can be used to make incisions and induce coagulation regardless of the skill of the operator. If the target can be directly viewed, then only the laser beam has to be in contact with the target, rather than the device itself, which is required for procedures performed with electrosurgical knives.

CO_2 lasers have been widely used in various surgical procedures in the otorhinolaryngology, dermatology, and oral surgery fields [12–14]. However, there have been few reports about CO_2 laser treatment involving the gastrointestinal tract, because the endoscopic use of CO_2 lasers in gastrointestinal procedures is limited by the lack of an efficient delivery system. Until recently, due to the wavelength characteristics of CO_2 lasers articulated arms with mirrors or lenses attached to them and optical fibers that were hard to pass through gastrointestinal endoscope channels were the only devices that could be used to perform CO_2 laser treatment in the gastrointestinal tract. However, flexible optical fibers that can be passed through gastrointestinal endoscope channels have since been developed for CO_2 lasers [18], so it has become possible to use CO_2 lasers for endoscopic procedures in the gastrointestinal tract. Anandasabapathy et al. [19] described the endoscopic ablation of the esophagus using a CO_2 laser in an in vivo porcine model. In this study, we have developed a safe ESD procedure involving the use of a CO_2 laser.

In standard ESD procedures, a solution is injected into the submucosa to lift it in order to ease its resection, to keep it a suitable distance from the muscularis propria, and to protect the muscularis propria from thermal and mechanical injury, thereby decreasing the risk of perforation. Compared with most other lasers, a large amount of the energy produced by CO_2 lasers is absorbed by water and soft tissue [17]. It was hypothesized that if a solution that could absorb the energy of CO_2 lasers could be injected into the submucosa, the energy of the CO_2 laser would be immediately absorbed, and hence, would not reach the muscularis propria. Previous studies have demonstrated that injecting a light absorbent solution into the submucosa and using a laser whose energy is specifically absorbed by the solution protects the muscularis propria from laser irradiation. In dogs that underwent laparotomy, Hayashi et al. [20] reported that when diode laser ablation was performed after the injection of indocyanine green (ICG) solution into the submucosa, the ablation did not extend beyond the proper muscularis propria of the gastric wall. In clinical practice, endoscopic laser treatment involving the injection of ICG solution for early gastric cancer has been reported [21]. In these reports, an 805-nm laser and ICG solution were used. The energy of the 805-nm laser was strongly absorbed by the ICG solution, which has a specific absorption spectrum peak at a wavelength of 805 nm. CO_2 lasers are capable of precisely cutting tissue whilst causing limited injury to the surrounding tissue [12–14], because their energy is strongly absorbed by water and protein and hardly penetrates deeper tissues [15]; thus, CO_2 lasers are suitable for making sharp incisions. In this study, we used a CO_2 laser and saline, which is widely used in standard ESD procedures, as a CO_2 laser absorbent.

To provide proof of concept for CO_2 laser-based ESD, we performed an *ex vivo* study to investigate whether injecting a light absorbent solution into the submucosa would prevent the muscularis propria from being injured by laser irradiation. First, a preliminary study was performed to determine the optimal laser output power level for ESD. Then, to determine the appropriate incision speed, we measured the speed of the mucosal incisions produced during the resection of a porcine stomach with an electrosurgical knife. As a result, we found that the mean incision speed was ~1.0 mm/s (data not shown). Next, we performed a mucosal incision experiment in which a porcine stomach was resected using a CO_2 laser. Based on the abovementioned results, the mucosal incision speed was set to 0.5, 1.0, or 2.0 mm/s and the output power was set to 6.0, 8.0, or 10.0 W during this experiment. In the group in which no laser absorbent was injected into the submucosa, when an output power of 6.0 W was employed the ablation did not reach the submucosa at an incision speed of 2.0 mm/s (the fastest incision speed), but it did reach the muscularis propria when an incision speed of 1.0 mm/s was used, and the incision penetrated all of the layers at a speed of 0.5 mm/s (the slowest incision speed). On the other hand, in the group in which saline was injected into the submucosa, the ablation stopped in the submucosa when output powers of 6.0, 8.0, and 10.0 W were employed together with a 0.5 mm/s incision speed, and furthermore, the ablation did not reach the muscularis propria or injure the muscularis propria when an output level of 12 W was used. These results showed that the saline injected into the submucosa absorbed the energy of the laser and prevented the muscularis propria from being injured.

Next, to investigate whether CO_2 laser-based ESD is feasible, an *ex vivo* study was performed. A resected porcine stomach was subjected to five ESD procedures involving a CO_2 laser. Based on the results of the preliminary study, the output power of the laser was set at 10 W. All of the procedures were accomplished without perforation or damaging the muscularis propria, and visual evaluations of each resection site were performed after the procedure. The heat damage caused by the laser was sufficiently minimal to allow the resected specimens to be histologically evaluated. These results suggest that ESD using a CO_2 laser is feasible. However, *ex vivo* studies are limited by the fact that no bleeding occurs. Bleeding is one of the most common complications of ESD and can distort the endoscopic view and make it difficult to perform the procedure safely and quickly.

Therefore, an in vivo porcine study was performed to further investigate whether ESD using a CO_2 laser is feasible. In this procedure, we were able to obtain mucosal tissue samples without damaging the muscularis propria under the resected area. There were no complications (including bleeding) during the procedure, and the heat damage caused by the incision and dissection was minimal. These results suggest that the submucosal injection of saline or sodium hyaluronate makes ESD performed with a CO_2 laser safe. Moreover, using a laser knife for ESD requires less skill than performing the procedure with an electrosurgical knife.

Endoscopic submucosal dissection using a CO_2 laser with a submucosally injected laser absorbent might be a feasible method for the treatment of early gastric cancer, and it might be easier and safer than the conventional method using an electrosurgical knife.

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Disclosures Drs. Daisuke Obata, Yoshinori Morita, Rinna Kawaguchi, Katsunori Ishii, Hisanao Hazama, Kunio Awazu, Hiromu Kutsumi, and Takeshi Azuma have no conflicts of interest or financial ties to disclose.

References

1. Soetikno R, Gotoda T, Nakanishi Y, Soehendra N (2003) Endoscopic mucosal resection. Gastrointest Endosc 57:567
2. Korenaga D, Haraguchi M, Tsujitani S, Okamura T, Tamada R, Sugimachi K (1986) Clinicopathological features of mucosal carcinoma of the stomach with lymph node metastasis in eleven patients. Br J Surg 73:431–433
3. Tanabe S, Koizumi W, Mitomi H, Nakai H, Murakami S, Nagaba S, Kida M, Oida M, Saigenji K (2002) Clinical outcome of endoscopic aspiration mucosectomy for early stage gastric cancer. Gastrointest Endosc 56:708–713
4. Ono H, Kondo H, Gotoda T, Shirao K, Yamaguchi H, Saito D, Hosokawa K, Shimoda T, Yoshida S (2001) Endoscopic mucosal resection for treatment of early gastric cancer. Gut 48:225

5. Ohkuwa M, Hosokawa K, Boku N, Ohtu A, Tajiri H, Yoshida S (2001) New endoscopic treatment for intramucosal gastric tumors using an insulated-tip diathermic knife. Endoscopy 33:221–226
6. Fujishiro M (2006) Endoscopic submucosal dissection for stomach neoplasms. World J Gastroenterol 12:5108
7. Hirao M, Masuda K, Asanuma T, Naka H, Noda K, Matsuura K, Yamaguchi O, Ueda N (1988) Endoscopic resection of early gastric cancer and other tumors with local injection of hypertonic saline-epinephrine. Gastrointest Endosc 34:264–269
8. Toyonaga T, Nishino E, Hirooka T, Dozaiku T, Sugiyama T, Iwata Y, Ono W, Ueda C, Tomita M (2005) Use of short needle knife for esophageal endoscopic submucosal dissection. Dig Endosc 17:246–252
9. Oyama T, Kikuchi Y (2002) Aggressive endoscopic mucosal resection in the upper GI tract-hook knife EMR method. Minim Invasive Ther Allied Technol 11:291–296
10. Strauss R, Fallon S (2004) Lasers in contemporary oral and maxillofacial surgery. Dent Clin N Am 48:861
11. Patel C (1964) Selective excitation through vibrational energy transfer and optical maser action in N_2–CO_2. Phys Rev Lett 13:617–619
12. Strong M, Jako G (1972) Laser surgery in the larynx. Early clinical experience with continuous CO_2 laser. Ann Otol Rhinol Laryngol 81:791
13. Anderson R, Parrish J (1983) Selective photothermolysis: precise microsurgery by selective absorption of pulsed radiation. Science 220:524
14. Brugmans M, Kemper J, Gijsbers G, van der Meulen F, van Gemert M (1991) Temperature response of biological materials to pulsed non-ablative CO_2 laser irradiation. Lasers Surg Med 11:587–594
15. Burke L, Rovin R, Cerullo L, Brown J (1985) Thermal effects of the Nd:YAG and carbon dioxide lasers on the central nervous system. Lasers Surg Med 5:67–71
16. Kotlow LA (2004) Lasers in pediatric dentistry. Dent Clin N Am 48:889–922
17. LeCarpentier G, Motamedi M, McMath L, Rastegar S, Welch A (1993) Continuous wave laser ablation of tissue: analysis of thermal and mechanical events. IEEE Trans Biomed Eng 40:188–200
18. Shi Y, Wang Y, Abe Y, Matsuura Y, Miyagi M, Sato S, Taniwaki M, Uyama H (1998) Cyclic olefin polymer-coated silver hollow glass waveguides for the infrared. Appl Opt 37:7758–7762
19. Anandasabapathy S, Maru D, Klumpp S, Uthamanthil R, Borne A, Bhutani M (2009) Novel endoscopic application of a new flexible-fiber CO_2 laser for esophageal mucosal ablation in a porcine model. Endoscopy 41:138–142
20. Hayashi T, Arai T, Tajiri H, Niwa H (1997) Enhanced diode laser ablation using submucosal injection of indocyanine green solution: part II; irradiation to resected porcine gastric wall and canine gastric walls under laparotomy. Gastroenterol Endosc 39:1753–1765
21. Kawaguchi A, Nagao S, Takebayashi K, Higashiyama M, Komoto S, Hokari R, Miura S (2008) Long-term outcome of endoscopic semiconductive diode laser irradiation therapy with injection of indocyanine green for early gastric cancer. J Gastroenterol Hepatol 23:1193–1199

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Evaluation of the Bending Loss of the Hollow Optical Fiber for Application of the Carbon Dioxide Laser to Endoscopic Therapy

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ABSTRACT

Since carbon dioxide laser is excellent for incision, hemostasis, coagulation, and vaporization of soft tissues, it has been widely applied in clinical treatments as the laser knife. In these days, flexible thin hollow optical fibers transmitting mid-infrared light have been developed, and the application of carbon dioxide laser to endoscopic therapy has become possible. However, it is expected that the irradiation effect is influenced by the change in the laser power at the tip of the hollow optical fiber due to the change in the transmittance by the bending loss. The purpose of this research is to quantitatively evaluate the change in the output power and therapeutic effect by bending the hollow optical fiber in a gastrointestinal endoscope. The change in the transmittance of the hollow optical fiber due to the insertion of the fiber into the endoscope and bending of the head of the endoscope was measured. Then, the relationship between the irradiated laser power and the incision depth for a porcine stomach was investigated. As the results, the most significant decrease in the transmittance of the hollow optical fiber was caused by the insertion of the fiber into the instrument channel of the endoscope, and bending of the head of the endoscope with the angle of 90° decreased the output laser power and incision depth by 10% and 25%, respectively. Therefore, it was confirmed that the bending loss of the hollow optical fiber due to the bending of the head of the endoscope had no significant influence on the endoscopic therapy using the carbon dioxide laser.

Keywords: Hollow Optical Fiber; Carbon Dioxide Laser; Bending Loss; Endoscopic Therapy

1. Introduction

Since carbon dioxide laser with the wavelength of 10.6 μm is absorbed strongly by water, which is contained about 70% in biological soft tissues, it is excellent in incision, hemostasis, coagulation, and vaporization of the soft tissues [1,2]. In fact, carbon dioxide laser is widely efficient for medical field, e.g., plastic surgery, cosmetic surgery, otolaryngology, and dentistry. Even in the endoscopic surgery, carbon dioxide laser had various promising application, so that many researchers developed new techniques for clinical treatment [3,4]. At the same time, several kinds of optical fibers transmitting mid-infrared light have been developed. These optical fibers are classified broadly into three categories, *i.e.*, glasses composed of fluoride or oxide, special glasses such as chalcogenide, and polycrystalline materials such as metal halide [5]. However, these optical fibers have problems in terms of the mechanical and chemical properties, toxicity, manufacturing cost, etc. Therefore, they could not be used for medical purposes. Recently, hollow optical fibers with a dielectric coating made of cyclic olefin polymer (COP) inside a cylindrical metal waveguide have been developed as shown in **Figure 1** [6]. Since the core of the hollow optical fibers is air or other gases with a high transmittance at the wavelength of the carbon dioxide laser, extremely low absorption loss could be obtained [7]. Because the reflection loss at the end surface of the fiber and related damage do not occur, the hollow optical fibers are suitable to transmit high-power lasers. In addition, the hollow optical fiber shown in **Figure 1** can simultaneously transmit carbon dioxide laser and visible aiming laser. Although it is possible to enhance the reflectance of the inner surface to nearly 100% by designing the COP layer thickness according to the wavelength of the transmitting laser light, the leaking loss to the outside of the fiber can not be eliminated in principle. Therefore, by bending the hollow optical fiber, the transmittance decreases due to the increase in the number of reflection per unit length and decrease in the reflectance in the fiber. When the hollow optical fiber is used in a clinical treatment with an endoscope, it is inferred that output laser power and therapeutic effect are changed due to the change in the transmittance of the hollow optical fiber caused by the bending of the endoscope. The purpose of this research is to quantitatively evaluate the change in the output laser power and therapeutic effect caused by bending the hollow optical fiber in a gastrointestinal endoscope.

2. Materials and Methods

2.1. Transmittance of the Hollow Optical Fiber with Bending of the Endoscope

In this research, a carbon dioxide laser system modified from a commercial laser system for dental treatment and so on (COM-2, J. Morita Manufacturing Corp., Kyoto, Japan) was used. The laser was operated in the continuous wave mode, and the maximum output power of the laser oscillator was 30 W. Two types of the hollow optical fiber (J. Morita Manufacturing Corp.) listed in **Table 1** were used to deliver the carbon dioxide laser through a gastrointestinal endoscope (GIF-2T200, Olympus Corp., Tokyo, Japan) shown in **Figure 2**. A laser power meter (30-A-BB-18, Ophir Optronics, Israel) was used to measure the laser power.

The carbon dioxide laser, the visible aiming laser with a wavelength of 650 nm, and air were simultaneously transmitted through the hollow optical fiber. Input and output powers of the hollow optical fibers were measured under four different conditions as shown in **Figure 3**, and each condition was described as follows:

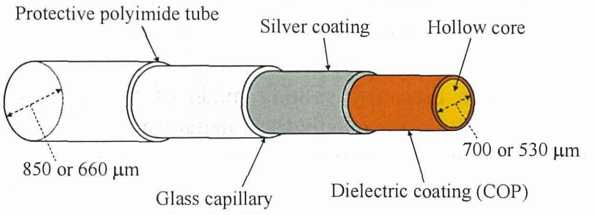

Figure 1. Schematic of the hollow optical fiber used in this research.

Table 1. Specifications of the hollow optical fibers.

	Outer diameter (μm)	Inner diameter (μm)	Length l (cm)
L-1	850	700	250
L-2	850	700	260
S-1	660	530	260

I. The hollow optical fiber was kept straight without insertion to the endoscope.
II. The hollow optical fiber was inserted into the endoscope, and endoscope was kept straight.
III. In addition to the condition II, the middle part of the endoscope was gradually bent 90° with a radius r_1 = 50 cm.
IV. In addition to the condition III, the head of the endoscope was steeply bent 90° with a radius r_2 = 5 cm.

2.2. Dependence of the Output Laser Power and Incision Depth on the Bending of the Head of the Endoscope

By assuming the case where the endoscope is used in transoral surgery, the middle part of the endoscope was bent 90° with a radius r_1 = 50 cm, and the tip of the hollow optical fiber L-1 was bent with various angles and radii r_2 as listed in **Table 2**. To avoid the accidental damage to the endoscope due to the break of the hollow optical fiber during laser irradiation, the fiber was ejected about 15 cm from the head of the endoscope, and only the fiber was bent by using in-house guide plates made of foamed polystyrene in order to simulate the bending conditions of the head of the endoscope.

A segment of a porcine stomach was set on a motorized linear stage (SGSP20-20, SIGMA KOKI Co., Ltd., Tokyo, Japan) and moved at a constant speed of 1.0 mm/s during laser irradiation for a time of 20 s. The car-

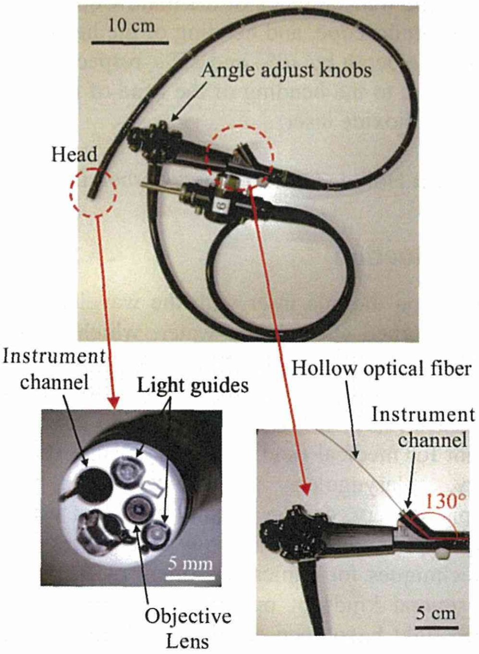

Figure 2. The photographs of the endoscope and its head and instrument channel. The hollow optical fiber is steeply bent 130° just after the insertion to the instrument channel.

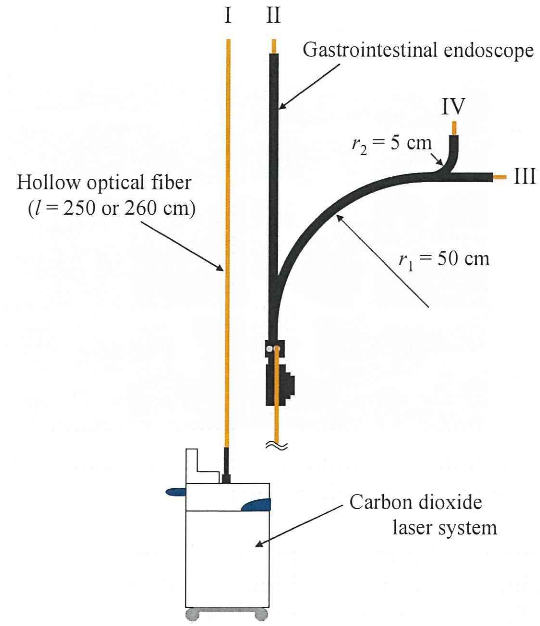

Figure 3. Schematics of the measurement of the transmittance of the hollow optical fibers for various bending conditions.

bon dioxide laser was irradiated vertically to the surface of the mucosa from a distance of 2 mm. The setting power of the carbon dioxide laser system was set at 3, 5, and 8 W, and laser power transmitted through the hollow optical fiber was measured under each condition. To simulate the *in vivo* environment, the sample surface was kept wet by pouring saline on the sample at a rate of 120 mL/h using a micro syringe pump (IC3100, AS ONE, Osaka, Japan). After laser irradiation, each sample was stored at −80˚C and was sliced to a thickness of 10 μm by using a cryostat microtome (CM1850, Leica Microsystems, Wetzlar, Germany) at a temperature of −20˚C. Then, each sample section attached onto a glass slide was stained with hematoxylin and eosin (HE) staining and observed using a high-resolution slide scanner (NanoZoomer 2.0 RS, Hamamatsu Photonics K. K., Shizuoka, Japan).

3. Results and Discussion

3.1. Transmittance of the Hollow Optical Fiber with Bending of the Endoscope

Table 2. Conditions for the measurement of the dependence of the output laser power and incision depth on the bending of the head of the endoscope.

Bending angle (˚)	0	30	60	90
Bending radius r_2 (cm)	-	11.0	7.0	5.0

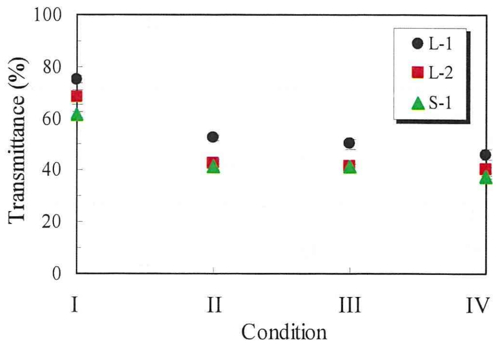

Figure 4. Transmittance of the hollow optical fibers under each condition.

Figure 4 shows the transmittance of the hollow optical fibers under each condition. When the hollow optical fiber was inserted into the instrument channel of the endoscope (from the condition I to II), the transmittance of the fiber L-1, L-2, and S-1 decreased by 29%, 28%, and 24%, respectively. On the other hand, the transmittance was not significantly decreased by the bending of the endoscope. When the bending of the endoscope was changed from the condition II to IV, the transmittances of the fibers L-1, L-2, and S-1 decreased by 7, 3, and 4%, respectively. Therefore, it was found that the decrease in the transmittance of the hollow optical fiber due to the insertion into the instrument channel was the most dominant loss in the hollow optical fibers. It is suggested that these results are caused by the steep bending of 130˚ just after the insertion into the instrument channel as shown in **Figure 2**.

3.2. Dependence of the Output Laser Power and Incision Depth on the Bending of the Head of the Endoscope

Figure 5 shows the relationships between the bending angle of the tip of the hollow optical fiber and the output laser power. The output laser power gradually decreased with the increase in the bending angle of the tip of the hollow optical fiber, and the output laser power at 90˚ was about 10% lower than that for 0˚.

Figure 6 shows the photomicrographs of the cross sections of the HE stained porcine stomach samples after laser irradiation with each condition. **Figure 7** shows the relationships between the bending angle of the tip of the hollow optical fiber and the incision depth measured from the photomicrographs of the sample shown in **Figure 6**. The incision depth under each condition decreased by up to 25% compared to that for 0˚ with an exception for the condition of 8 W at 90˚. Therefore, it was confirmed that the bending loss of the hollow optical fiber due to the bending of the head of the endoscope had no significant influence on the endoscopic therapy using the carbon dioxide laser.

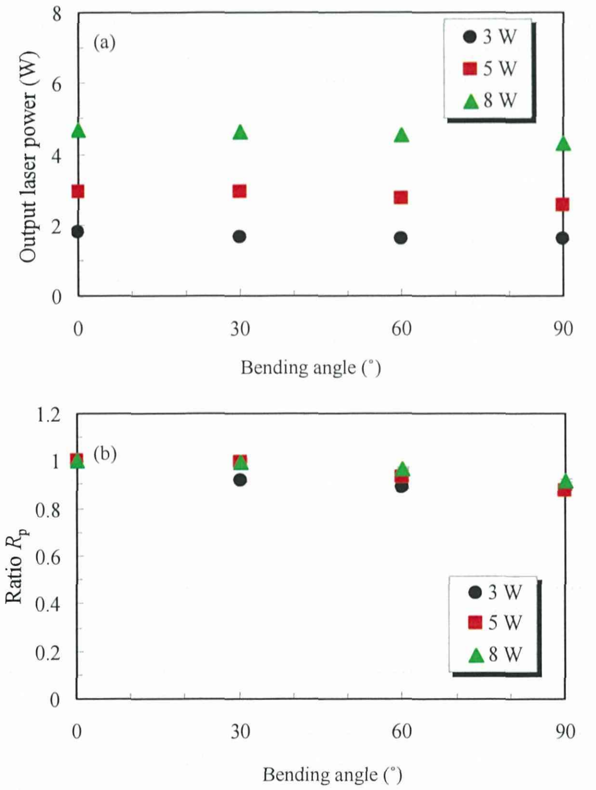

Figure 5. The relationships between (a) the bending angle of the head of the endoscope and the output laser power and (b) the bending angle and the ratio R_p of the output laser power to that for 0°.

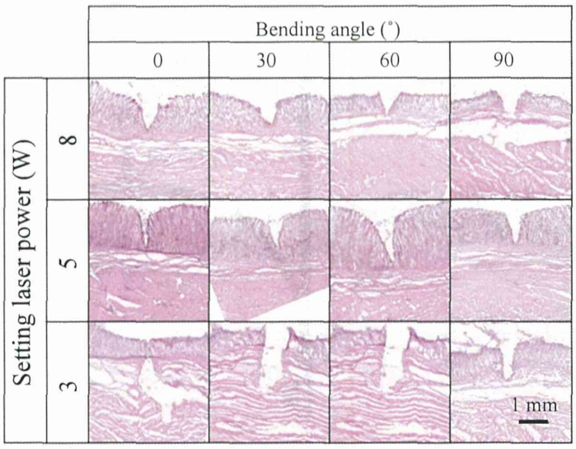

Figure 6. Photomicrographs of the HE stained samples after laser irradiation with each condition.

The mechanism of the vaporization of the biological soft tissue by a laser knife is described as follows: When the biological soft tissue absorbs the laser, the temperature of the tissue quickly rises within a time of microseconds. Since the boiling point of water is 100°C, water in tissue is immadiately vaporized and the volume is expanded by continuously making water in the tissue over 100°C. Then, cell membrane and organelle fragment are vaporized. In our experiment, laser was linerly scanned with a speed of 1.0 mm/s, incision was performed using the vaporization. In order to describe the reltionship between the irradiated laser energy density and the incision depth, the steady-state model has been proposed [8,9]. This model was developed for continuous ablation process using a continuous wave or pulsed laser with microseconds or longer pulse width. In the steady-state model, the relational expression between the incision depth δ (mm) and the irradiated laser energy density Φ_0 (J/mm^2) is given by

$$\delta = \frac{\Phi_0 - \Phi_{\text{th}}}{\rho h_{\text{abl}}}, \tag{1}$$

where $\rho = 1.02 \times 10^{-3}$ g/mm^3 is the density of biological soft tissue composed of water of 70%, and the ablation enthalpy h_{abl} (J/g) and the ablation threshold energy density Φ_{th} (J/mm^2) are defined as follows:

$$h_{\text{abl}} = C\Delta T + L,$$

$$\Phi_{\text{th}} = \frac{\rho h_{\text{abl}}}{\mu_a},$$

where $C = 3.45$ J/(g·K) is the heat capacity, $\Delta T = 63.0$ K is the temperature rise to the boiling point of water, $L = 2.58 \times 10^3$ J/g is the heat of vaporization, and $\mu_a = 6.15 \times 10^2$ mm^{-1} is the absorption coefficient of the porcine mucosa at the wavelength of 10.6 μm [10-12]. In **Figure 8**, the dots show the relationship between the irradiated laser energy density and the incision depth obtained from the results in **Figures 5** and **7**, and the solid line represents the theoretical values estimated using Equation (1). The laser beam diameter at the surface of the porcine stomach mucosa was measured for the fiber L-1 by using knife-edge method and was about 710, 712, 772, and 740 μm at the bending angle of 0°, 30°, 60°, and 90°, respectively. The laser beam diameter was increased with the increase in the bending angle, because the beam spread angle from the exit of the hollow optical fiber was increased with the increase in the bending angle due to the conversion of the propagation mode from the low-order modes to the high-order modes in the hollow optical fiber.

From the results in **Figure 8**, it was found that both the experimental and theoretical values have similar correlations between the irradiated laser energy density and the incision depth. However, the theoretical values were about 1.5 times higher than the experimental values. It is inferred that the principal factor for this difference is the uncertainty in the physical values used in the model calculations, e.g., the density of biological soft tissue, ablation enthalpy, and the heat capacity. Since these values

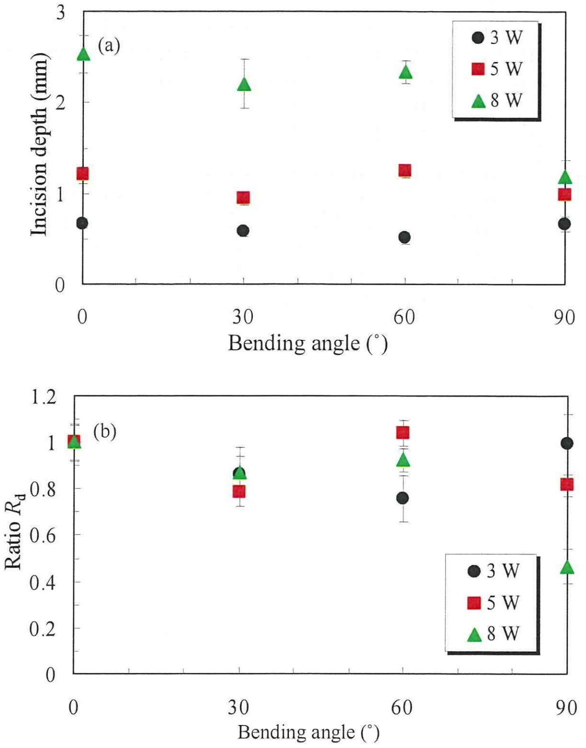

Figure 7. The relationships between (a) the bending angle of the tip of the hollow optical fiber and incision depth and (b) the bending angle and the ratio R_d of the incision depth to that for 0°.

were taken from the literatures, some values might not be suitable for the porcine stomach sample used in this research.

4. Conclusion

The change in the output power of the carbon dioxide laser and therapeutic effect by bending the hollow optical fiber inserted in a gastrointestinal endoscope was quantitatively evaluated. The change in the transmittance of the hollow optical fiber due to the insertion of the fiber to the endoscope and bending of the head of the endoscope was measured. Then, the relationship between the irradiated laser power and the incision depth of a porcine stomach was investigated. As the result, the greatest decrease of the transmittance of the hollow optical fiber was caused by insertion of the fiber into the instrument channel of the endoscope, and bending of the head of the endoscope with the angle of 90° decreased the output laser power and incision depth by no more than 10% and less than 25%, respectively. Therefore, it was confirmed that the bending loss of the hollow optical fiber due to the bending of the head of the endoscope had no significant influence on the endoscopic therapy using the carbon dioxide laser.

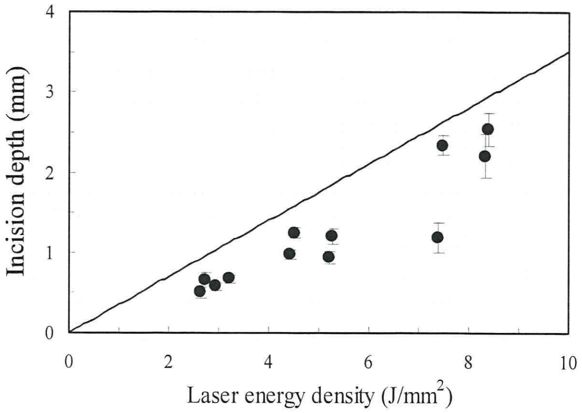

Figure 8. The relationships between the incision depth and irradiated laser energy density, where the solid line shows the theoretical values estimated with the steady-state model.

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REFERENCES

[1] J. T. Walsh and T. F. Deutsch, "Er:YAG Laser Ablation of Tissue: Measurement of Ablation Rates," *Lasers in Surgery and Medicine*, Vol. 9, No. 4, 1989, pp. 327-337. doi:10.1002/lsm.1900090404

[2] J. T. Walsh, T. J. Flotte, R. R. Anderson and T. F. Deutsch, "Pulsed CO_2 Laser Tissue Ablation: Effect of Tissue Type and Pulse Duration on Thermal Damage," *Lasers in Surgery and Medicine*, Vol. 8, No. 2, 1988, pp. 108-118. doi:10.1002/lsm.1900080204

[3] K. Ishii, S. Watanabe, D. Obata, H. Hazama, Y. Morita, Y. Matsuoka, H. Kutsumi, T. Azuma and K. Awazu, "Selective Mucosal Ablation Using CO_2 Laser for the Development of Novel Endoscopic Submucosal Dissection: Comparison of Continuous Wave and Nanosecond Pulsed Wave," *Proceedings of SPIE*, Vol. 7562, 2010, Article ID: 75620Q. doi:10.1117/12.842426

[4] S. R. Browd, J. Zauberman, M. Karandikar, J. G. Ojemann, A. M. Avellino and R. G. Ellenbogen, "A New Fiber-Mediated Carbon Dioxide Laser Facilitates Pediatric Spinal Cord Detethering," *Journal of Neurosurgery*: *Pediatrics*, Vol. 4, No. 3, 2009, pp. 280-284. doi:10.3171/2009.4.PEDS08349

[5] Y. Matsuura, "Basics of Optical Fibers for Medical Applications," *The Journal of Japan Society for Laser Surgery and Medicine*, Vol. 31, No. 4, 2011, pp. 407-412 (in Japanese).

[6] Y. Abe, Y. W. Shi, Y. Matsuura and M. Miyagi, "Flexible Small-Bore Hollow Fibers with an Inner Polymer Coating," *Optics Letters*, Vol. 25, No. 3, 2000, pp. 150-152. doi:10.1364/OL.25.000150

[7] Y. Matsuura, "Basics of Hollow Optical Fiber," *Medical Photonics*, No. 2, 2010, pp. 11-15 (in Japanese).

[8] A. Vogel and V. Venugopalan, "Mechanisms of Pulsed Laser Ablation of Biological Tissues," *Chemical Reviews*, Vol. 103, No. 2, 2003, pp. 577-644. doi:10.1021/cr010379n

[9] M. H. Niemz, "Laser-Tissue Interactions: Fundamentals and Applications," Springer, Berlin, 1996, pp. 58-87. doi:10.1007/978-3-662-03193-3

[10] B. Choi and A. J. Welch, "Analysis of Thermal Relaxation during Laser Irradiation of Tissue," *Lasers in Surgery and Medicine*, Vol. 29, No. 4, 2001, pp. 351-359. doi:10.1002/lsm.1128

[11] V. Venugopalan, N. S. Nishioka and B. B. Mikic, "Thermodynamic Response of Soft Biological Tissues to Pulsed Infrared-Laser Irradiation," *Biophysical Journal*, Vol. 70, No. 6, 1996, pp. 2981-2993. doi:10.1016/S0006-3495(96)79868-5

[12] D. Obata, Y. Morita, R. Kawaguchi, K. Ishii, H. Hazama, K. Awazu, H. Kutsumi and T. Azuma, "Endoscopic Submucosal Dissection Using a Carbon Dioxide Laser with Submucosally Injected Laser Absorber Solution (Porcine Model)," *Surgical Endoscopy*, 2013, in Press. doi:10.1007/s00464-013-3029-x