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Flexible CO₂ laser and submucosal gel injection for safe endoluminal resection in the intestines

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Abstract

Background—The CO₂ laser's unique wavelength of 10.6 μ m has the advantage of being readily absorbed by water but historically limited it to line-of-sight procedures. Through recent technological advances, a flexible CO₂ laser fiber has been developed and holds promise for endoluminal surgery. We examined whether this laser, along with injection of a water-based gel in

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the submucosal space, will allow safe dissection of the intestines and enhance the potential of this tool for minimally invasive surgery.

Methods—Using an ex vivo model with porcine intestines, spot ablation was performed with the flexible CO₂ laser at different power settings until transmural perforation. Additionally, excisions of mucosal patches were performed by submucosal dissection with and without submucosal injection of a water-based gel.

Results—With spot ablation at 5 W, none of the specimens was perforated by 5 min, which was the maximum recorded time. The time to perforation was significantly shorter with increased laser power, and gel pretreatment protected the intestines against spot ablation, increasing the time to perforation from 6 to 37 s at 10 W and from 1 to 7 s at 15 W. During excision of mucosal patches, 56 and 83% of untreated intestines perforated at 5 and 10 W, respectively. Gel pretreatment prior to excision protected all intestines against perforation. These specimens were verified to be intact by inflation with air to over 100 mmHg. Furthermore, excision of the mucosal patch was complete in gel-pretreated specimens, whereas 22% of untreated specimens had residual islands of mucosa after excision.

Conclusion—The flexible CO₂ laser holds promise as a precise dissection and cutting tool for endoluminal surgery of the intestines. Pretreatment with a submucosal injection of a water-based gel protects the intestines from perforation during ablation and mucosal dissection.

Keywords

Ablation; Carbon dioxide laser; Colorectal malignancy; Dissection; Gastrointestinal surgery

Lasers are among the most advanced tools available in the surgical armamentarium. The carbon dioxide (CO₂) laser was originally developed in 1963 by Dr. Kumar Patel, who was subsequently awarded the National Medal of Science for its discovery and impact on industrial, scientific, defense, and medical applications. It is a powerful laser with a high efficiency of energy output that has so far been adopted in dermatologic surgery, neurosurgery, and head and neck surgery.

Fundamental to the CO₂ laser's physical properties is its unique wavelength of 10.6 μm, a relatively long wavelength that lies on the infrared part of the light spectrum. Historically, this long wavelength limited the CO₂ laser to line-of-sight delivery with rigid articulated arms. Not only was this cumbersome for the surgeon to maneuver, but the straight system also restricted the angle at which the laser could be pointed toward its target. Such shortcomings precluded the widespread use of the CO₂ laser in minimally invasive surgery.

Recent technological advances are shifting the paradigm as the CO₂ laser can now be transmitted through a flexible fiber. The innovation of photonic bandgaps to guide light led to the development of an omnidirectional mirror that can be tailored for light of any wavelength [1]. What followed was the design of a hollow flexible fiber with alternating layers of glass and polymer to establish a photonic bandgap and effectively transmit the laser beam [2]. Thus, the flexible fiber essentially acts as a rolled-up mirror that can reflect and direct the CO₂ laser.

Numerous advantages are offered by this advanced technology. Because of its flexibility and small fiber diameter of 1.8 mm, the flexible CO₂ laser fits into ports and can now be used in endoscopy and laparoscopy. It can be adopted for surgical procedures via an approach that decreases postoperative pain, shortens hospital stay, and reduces time to return to normal activity. Furthermore, the flexible CO₂ laser may now reach areas like the luminal surface of the intestine, once inaccessible to the previous rigid articulated system; hence, its potential use is expanding into the field of gastrointestinal surgery. With the CO₂ laser beam being

only 315 μm in spot size as it exits the flexible fiber, the CO_2 laser is suitable for microsurgery where fine control of dissection and ablation is necessary. While the width of thermal injury to neighboring tissue is on the scale of millimeters with the Nd:YAG laser and electrocautery, the CO_2 laser exerts minimal collateral damage on the scale of only micrometers, which promotes rapid wound healing [3].

What particularly interests our lab is the efficient absorption of the CO_2 laser by water. This is the basis of our belief that water may be used as a protective shield against this laser. By interposing a water-based substance between the target and adjacent structures, those structures may be protected and spared from bystander injury. In this study we propose that the flexible CO_2 laser may be a valuable surgical tool for the intestines in endoscopy and laparoscopy, and that pretreatment with a water-based gel can protect the intestines from perforation.

Methods

Flexible CO_2 laser and gel pretreatment

The flexible CO_2 laser fiber (OmniGuide, Cambridge, MA) comprised a hollow fiber of dielectric layers that had a 1.8-mm outer diameter and was 1.5 m long, with a beam spot size of 315 μm upon exiting the fiber. Helium flowed through the hollow core of the fiber at 2.6 ml/s to keep it cool, and the fiber was attached to the NovaPulse CO_2 laser (Lumenis, Santa Clara, CA) (Fig. 1), which was used on continuous wave mode at different power levels.

In each experiment, intestines were divided into untreated and gel-pretreated groups. For the latter, 1 ml of a water-based gel made from water, 0.9% sodium chloride, and 15 g/l of gelatin was injected into the submucosa via a 25-gauge needle before laser ablation or dissection.

Spot ablation

This research on ex vivo intestines harvested from Yorkshire pigs was carried out with approval from the Institutional Animal Care and Use Committee at Memorial Sloan-Kettering Cancer Center. To test the threshold at which the flexible CO_2 laser can achieve transmural ablation of the intestines, a spot ablation experiment was performed. The intestines were opened longitudinally and laid flat on top of a wire rack with the mucosal side up. Receipt paper, known to turn brown instantaneously when burned by the CO_2 laser, was placed below the rack on the table. With the flexible fiber held perpendicular and as close as possible to the mucosa without touching it, laser ablation was performed and focused on a single spot until the laser had burned through the intestines, as signaled by the immediate appearance of a brown spot on the receipt paper underneath. The time to such perforation was recorded, and increasing power levels of 5, 10, and 15 W were tested. Specimens subsequently underwent histologic examination with hematoxylin and eosin (H&E) staining.

Mucosal dissection

Intestines were divided into segments and turned inside out to expose the mucosal surface. A square of 1×1 cm was marked by lightly scoring the mucosa with the CO_2 laser and was then dissected out at low and medium power levels of 5 and 10 W. The intestinal segment was turned inside out again so that the mucosal surface was back on the luminal side. With the mucosal dissection centered in the middle, a 10-cm length was measured and one end was tied off. On the other end, the intestine was closed with silk ties around a tube that led to a 717–100G manometer (Fluke, Everett, WA) and a bulb pump. The intestines were submerged in water and insufflated with air to a minimum pressure of 100 mmHg to check

for microperforations which would be indicated by bubbles in the water. Specimens were then stained with H&E for histologic evaluation.

Results

Spot ablation

During spot ablation, 12 intestinal specimens were tested at each of the laser power settings of 5, 10, and 15 W, with half the specimens receiving gel pretreatment and half remaining untreated. At 5 W, the flexible CO₂ laser had not burned through any intestines when the maximum recorded time of 300 s or 5 min was reached. However, at 10 W, the laser burned through the untreated specimens in a mean time of just 6.33 s (SD = 3.20), but took longer to burn through the gel-pretreated intestines with a mean time of 36.6 s (SD = 5.50). At the highest power tested of 15 W, the flexible CO₂ laser burned through all intestines more rapidly, with a mean time of 1.33 s (SD = 0.52) in untreated intestines and 6.83 s (SD = 2.79) in gel-pretreated specimens. Thus, the threshold for transmural ablation of the intestines by the flexible CO₂ laser was significantly lowered by higher laser power ($p < 0.001$) and raised by gel pretreatment ($p < 0.001$) (Fig. 2).

Although both untreated and gel-pretreated intestines were not perforated at 5 W, the two groups of intestines demonstrated significant histologic differences on H&E staining. Gel pretreatment created a chemical and physical barrier within the intestinal wall that limited thermal injury to the layers above it while leaving the layers below unharmed (Fig. 3). While four of six untreated intestines had thermal injury extending full thickness to the serosa, only two of six gel-pretreated specimens had any thermal injury beyond the submucosa; in those two cases, the gel was injected below the submucosal space into the muscularis so thermal injury was only to the superficial muscularis propria above the gel barrier.

Mucosal dissection

Nine and ten intestinal specimens underwent mucosal dissection at 5 W without and with gel pretreatment, respectively. An additional six specimens in each group were tested at 10 W. Inadvertent perforation occurred during mucosal dissection in untreated intestines, with an incidence of 56% at 5 W and 83% at 10 W. On the other hand, none of the gel-pretreated intestines were perforated after mucosal dissection, not even at 10 W of laser power (Table 1). Moreover, gel pretreatment not only protected the intestines from perforation but also facilitated the dissection process by separating and elevating the layer to be removed (Fig. 4). When reviewed under the microscope, it was found that there were islands of residual mucosa in 22% of the untreated intestines that underwent dissection at 5 W; in contrast, the mucosal removal was complete in gel-pretreated specimens (Fig. 5).

Discussion

This is the first study, to our knowledge, on the efficacy of the use of the flexible CO₂ laser on the intestines. Our study demonstrates that it is indeed a novel and valuable surgical tool for ablation and dissection. During spot ablation, the CO₂ laser was safe at 5 W. With an increase of laser power to 10 and 15 W came a decrease in the threshold to transmural ablation and perforation. Beyond being a thermal scalpel, the flexible CO₂ laser has the precision for fine dissection. In contrast to the previous rigid articulated system, which required multiple adjustments, our experience was that the flexible CO₂ laser fiber was lightweight and granted freedom of movement in direction and angle to carefully excise the thin intestinal mucosa.

The safety and utility that we found with the flexible CO₂ laser are supported by preliminary animal studies in head and neck surgery, neurosurgery, and gastroesophageal surgery. The

flexible CO₂ laser demonstrated consistency in the shape and size of the created lesion, greater depth of penetration with increased laser power, limited width of collateral injury, and complete or near-complete healing within a week [4, 5]. Furthermore, bleeding during laser dissection is minimal with the CO₂ laser [3, 6] as the laser may be retracted from the tissue for a wide superficial coagulative effect. In addition, the gas flow down the hollow fiber not only keeps the fiber cool but also evacuates smoke and debris from the field of view. From laryngectomy [7] to bronchoscopic ablation [8], gastric incisions, esophageal and gastric mucosal resections [9], and esophageal ablation [10], the flexible CO₂ laser has demonstrated a great deal of potential.

Transitioning to humans, the potential of the flexible CO₂ laser has been realized with success in both diagnostic and therapeutic procedures. Its clinical utility is extensive, from biopsy of an anatomically difficult vocal cord lesion [11] to resection of tumors at the base of the tongue, palate, tonsil, and supraglottic larynx [12, 13], partial laryngectomy [11], stapedotomy [14], resection of intracranial neoplasms [15], and spinal cord detethering [16]. Most importantly, there were no adverse events or postoperative complications for the patient. Furthermore, the safety of operating around vital nerve structures was tested and ensured by measuring the air bone gap after stapedotomies and performing electromyographic stimulation of the spinal cord nerve roots. These experiences illustrate the versatility of the flexible CO₂ laser and its suitability for fine delicate procedures.

The flexible CO₂ laser is also feasible for minimally invasive surgery. No difference in tissue response was found between the flexible CO₂ laser fiber bent to 90° and the straight laser fiber [3]. In porcine studies, the flexible CO₂ laser has been used via upper endoscopy to perform circumferential ablation of the esophagus, achieving a depth of ablation to the muscularis mucosa and submucosa layers [10], as well as mucosectomy of 2-cm segments in the esophagus and stomach with minimal damage to the muscularis propria [9]. The flexible CO₂ laser also has been effective in natural orifice transluminal surgery (NOTES) to cauterize and control bleeding at a splenic biopsy site [9], and case reports in patients have shown that the flexible CO₂ laser placed on the robotic arm of a da Vinci robot can successfully resect oropharyngeal and supraglottic laryngeal tumors [12, 13]. Furthermore, at Memorial Sloan-Kettering, we are in the process of developing a surgical laser microscanner to guide endoscopic laser therapy with fine remote control (patent pending; Publ. No. WO/2011/032165).

A unique finding in our study is that based on the principle that the CO₂ laser is inherently absorbed by water, pretreatment with a water-based gel injected into the submucosa protected the intestines from perforation. This was evident during spot ablation where gel pretreatment raised the threshold to perforation, and during mucosal dissection where it prevented any perforation of the intestines from occurring. In contrast to water in the liquid state leaking away as soon as an outlet was created, water in a gel state maintained its bleb form after injection and kept the mucosa raised, even as a patch of mucosa was being dissected out. This made it an effective shielding barrier. In addition, one of the most concerning findings was the discovery of islands of mucosa left behind after mucosal dissection in untreated specimens. This has severe implications when considering the consequences of residual microscopic disease in oncologic surgery, and further argues for the use of gel pretreatment where the excision of the mucosal patches in gel-pretreated specimens was clean and thorough. Pretreatment with a water-based gel thus is an excellent adjunct for flexible CO₂ laser surgery for safety, ease, and completeness of dissection.

The results of our study hold promise for the clinical use of the flexible CO₂ laser and pretreatment with a water-based gel for endoluminal resection of the intestines. This advanced technology is remarkable for its thin flexible design, which makes it amenable to

minimally invasive surgery; its safety, which is bolstered by water-based gel pretreatment; and its maneuverability and precision for fine delicate procedures.

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Fig. 1.
Flexible CO₂ laser fiber setup

Fig. 2. Threshold to perforation with spot ablation. The threshold for the flexible CO₂ laser to achieve transmural ablation of the intestines was lowered by increased laser power and raised by gel pretreatment

Fig. 3. Histological sections of untreated (**A**) and gel-pretreated (**B**) intestines after spot ablation. The barrier formed by gel pretreatment limited thermal injury from the flexible CO₂ laser at 5 W. Vertical bars indicate depth of thermal injury as characterized by tissue fragmentation and increased staining intensity. Asterisk indicates gel that was injected for pretreatment. Scale bar = 500 μm. H&E stain

Fig. 4.
Separation and elevation of the mucosa by gel pretreatment

Fig. 5. Histological sections of untreated (**A, C**) and gel-pretreated (**B, D**) intestines after mucosal dissection. Islands of mucosa can be left behind in untreated specimens but not with gel pretreatment. Arrows indicate residual islands of mucosa and submucosa, and asterisk indicates gel injected for pretreatment. Scale bar = 1 mm in **A** and **B** and 200 μm in **C** and **D**. H&E stain

Table 1Flexible CO₂ laser dissection of the mucosa with and without gel pretreatment

	Perforation at different laser power	
	5 W	10 W
Untreated intestines	5/9 (56%)	5/6 (83%)
Gel-pretreated intestines	0/10 (0%)	0/6 (0%)

The flexible CO₂ laser can be used for mucosal dissection of the intestines with a lower incidence of perforation with gel pretreatment