

## Mucosal ablation devices

*The American Society for Gastrointestinal Endoscopy (ASGE) Technology Committee provides reviews of existing, new, or emerging endoscopic technologies that have an impact on the practice of GI endoscopy. Evidence-based methodology is used, with a MEDLINE literature search to identify pertinent clinical studies on the topic and a MAUDE (Food and Drug Administration Center for Devices and Radiological Health) database search to identify the reported complications of a given technology. Both are supplemented by accessing the "related articles" feature of PubMed and by scrutinizing pertinent references cited by the identified studies. Controlled clinical trials are emphasized, but, in many cases, data from randomized controlled trials are lacking. In such cases, large case series, preliminary clinical studies, and expert opinions are used. Technical data are gathered from traditional and Web-based publications, proprietary publications, and informal communications with pertinent vendors.*

*Technology Status Evaluation Reports are drafted by 1 or 2 members of the ASGE Technology Committee, reviewed and edited by the committee as a whole, and approved by the governing board of the ASGE. When financial guidance is indicated, the most recent coding data and list prices at the time of publication are provided. For this review, the MEDLINE database was searched through April 2008 for articles related to endoscopy by using the keywords electrocoagulation, argon plasma coagulation, laser, cryotherapy, Barrett's esophagus, arteriovenous malformation, gastric antral vascular ectasia, adenoma, mucosal ablation, radiation proctitis, radiofrequency ablation.*

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## BACKGROUND

Mucosal ablation techniques use a variety of devices to destroy the epithelial or mucosal layer of the GI tract, most commonly for the treatment of neoplasia, as a complement to other endoscopic resection techniques, or to treat mucosal vascular lesions that cause chronic blood loss.

Commonly used devices include multipolar electrocautery probes (MPEC) and the argon plasma coagulator (APC). Technologies still available but much less commonly used today include lasers (Nd:YAG and potassium-titanyl-phosphate yttrium aluminum garnet [KTP:YAG]) and heat probes. Recently developed and emerging technologies include radiofrequency balloon-catheter ablation and cryotherapy. Photodynamic therapy (PDT) and EMR are ablative techniques that are the focus of other recent technology status evaluation reports.<sup>1,2</sup>

## TECHNOLOGY UNDER REVIEW

### APC

APC is a noncontact thermal method of tissue coagulation in which argon provides a medium for the delivery of electrical current. Argon gas flows through a flexible catheter that is passed through the working channel of an endoscope. The distal tip of the catheter contains a tungsten electrode. Depression of the foot pedal by the endoscopist triggers a synchronized flow of argon gas and electrical current from the generator. As the argon gas flows over the electrode, it becomes ionized. When the tip of the catheter is in close proximity to tissue with a return electrode (grounding pad placed on the patient), electrical current flows through the arc of ionized argon gas (plasma), which produces tissue coagulation. If the catheter is not near the target tissue (ie, the resistance to electrical current flow is too great), then there is no ignition of the gas, and depression of the foot pedal only results in flow of inert argon gas. The depth of tissue coagulation depends on the flow rate of gas, the power setting on the generator, the duration of application, and the distance from the target tissue.<sup>3</sup> The electrical resistance of the tissue rises as the tissue desiccates and the electrical current flows to adjacent tissues, which limits the depth of injury.<sup>3,4</sup> In vivo studies of porcine colon

**TABLE 1. Mucosal ablation devices**

Company	Generator	Probe diameter	Special features	Length (cm)	Probe price
<b>APC</b>					
ConMed (Billerica, Mass)	\$27,783	7F		220-270	\$2748.90/box of 10
ERBE (Marietta, Ga)	\$16,750	7F, 10F (2.3 mm, 3.2 mm)	Side port and circumferential port available	220	\$1995/box of 10
Canady (Hampton, Va)	\$24,500	4.5F, 7F, 10F	Side fire port available	230-340	\$1550/box of 10
<b>MPEC</b>					
ConMed	\$10,995	7F, 10F		300-350	\$310 each: BICAP Superconductor
Microvasive Endoscopy (Natick, Mass)	\$23,000	7F, 10F		300-350	\$285 each: GoldProbe
		7F, 10F	Probe with injection needle available	210	\$335 each: Injection GoldProbe
Cook Endoscopy (Winston-Salem, NC)		7F, 10F		350	\$271 each: Quicksilver probe
Olympus Endotherapy (Center Valley, Pa)	\$14,330	7F, 10F		350	\$235 each: SolarProbe
<b>Heat Probe</b>					
Olympus Endotherapy	\$9500	7F, 10F	Reusable	230-300	\$530 each: HeatProbe
<b>Radiofrequency ablation</b>					
Barrx Medical (Sunnyvale, Calif)	\$35,000 (HALO <sup>360</sup> )	20F		80	Ablation balloon \$1250; sizing balloon \$350 (both single use)
	\$12,500 (HALO <sup>90</sup> )	9F		160	\$900 each
<b>Cryotherapy</b>					
GI Supply (Camp Hill, Pa)	\$9000	6F	Pressurized CO <sub>2</sub> ; side-port catheters available	200	\$625 for 5 catheters; \$900 per 5 side-port catheters: PolarWand
CSA Medical (Baltimore, Md)	\$39,500	7F	Liquid nitrogen		\$845 each CryoSpray Ablation

revealed that injury to the muscularis propria commonly occurs at usual settings of 20 to 40 W.<sup>5,6</sup> However, another study of ex vivo fresh stomach and esophagus found injury to the muscularis propria in only 3 of 84 samples (3.5%) that used power settings of 40 to 99 W and 1-second to 3-second pulses of therapy.<sup>3</sup>

The available APC systems (ERBE USA [Marietta, Ga], ConMed Electrosurgery [Englewood, Colo] and Canady Technology [Pittsburgh, Pa]) include an electrosurgical generator capable of high-frequency monopolar current, a foot pedal, an argon gas cylinder, a grounding pad, and flexible, single-use delivery probes. A gas-flow meter adjusts to allow argon flow rates of 0.5 to 7 L/min. These generators can also serve as multipurpose electrosurgical

units capable of varying levels of power output with any monopolar or bipolar endoscopic accessory. Probes are composed of Teflon (Dupont, Wilmington, Del), with a ceramic tip that encases the tungsten electrode. They are available in a variety of lengths and widths (Table 1). Probes are available with forward, side, or circumferential ports, which allow forward, tangential, or circumferential applications, respectively.

The flexible probe is passed into the endoscope through the accessory channel. The power setting (W) and the argon flow rate (L/min) must be chosen by the endoscopist based on the location in the GI tract and desired depth of tissue destruction. In general, low-power settings (40 W) and low flow rates (0.8 L/min) are used

for superficial destruction of bleeding lesions and in thinner areas, such as the right side of the colon. Higher power settings (70-90 W) and higher flow rates (1-2 L/min) are used for ablation of neoplastic tissue or in thicker areas, such as the stomach.<sup>7</sup> Higher flow rates result in more rapid gaseous distension of the lumen, and frequent decompression may be required. APC is applied in 0.5-second to 2-second bursts until a white coagulum is seen on the target tissue. The distance the tip of the catheter is held from the tissue varies. One study used a distance of 2 to 8 mm between the probe tip and the tissue,<sup>8</sup> but another study found that, when the probe tip was at a 90° angle from the target, a distance of only 1 mm was required to consistently produce an arc of electricity.<sup>3</sup> When the tip makes contact with the target tissue, it functions as a monopolar probe and can result in deeper injury. In addition, contact of the tip and tissue may result in infusion of submucosal or extraluminal gas. A coagulum may also develop on the catheter tip, which requires periodic removal of the catheter for manual cleaning.

### Multipolar electrocautery

MPEC is a thermal contact method of tissue ablation. MPEC probes have a tip that contains 2 electrodes, which enable completion of an electrical circuit at the working end in contact with the target tissue. As the tissue desiccates, its electrical resistance rises and energy is transferred to adjacent tissues, which helps limit the depth and degree of injury.<sup>9</sup> Probes also have an irrigation port. Equipment includes single-use multipolar or bipolar probes, an electrosurgical generator, a water pump, and a dual foot pedal for coagulation and irrigation. The irrigation channel of the probes can be manually flushed if the water pump is not available. A patient grounding pad is not necessary, because the electrical circuit is completed internally. There are several commercially available single-use MPEC devices in a variety of diameters and lengths (Table 1). An MPEC probe with an injection needle on the tip is also available, which enables injection of saline solution or epinephrine, followed by cautery, without requiring a change of catheter.

The probe is passed through the working channel of an endoscope with an appropriately sized accessory channel. To ablate a wider area with each application, the 10F (3.2 mm) catheter can be used; this catheter can be passed through a therapeutic upper endoscope or a standard colonoscope.

The depth of tissue injury caused by MPEC is a function of the power setting, the duration of application, and the pressure applied to the tissue.<sup>10</sup> A recent study found that, with light pressure and a 2-second duration of application, a 1-mm depth of injury was achieved.<sup>11</sup> Power output is in watts. The maximal power settings are dependent on the generator used but usually do not exceed 50 W. A standard setting is 20 W. In general, for more superficial

lesions and for lesions in thinner areas of the GI tract (eg, right side of the colon), a lower power setting, lower applied pressure, and shorter duration of therapy are recommended compared with the higher power settings and firm coaptive pressure used for treatment of bleeding peptic ulcers.

### Radiofrequency ablation

A novel bipolar device (HALO<sup>360</sup>, Barrx Medical, Inc, Sunnyvale, Calif) was developed specifically for circumferential ablation in the esophagus. The HALO<sup>360</sup> is a balloon that contains 60 separate 250- $\mu$ m electrodes circumferentially oriented on its outer surface; each electrode is separated by a distance of 250  $\mu$ m. Immediately adjacent electrodes function as bipolar devices that deliver heat to the mucosa at a controlled depth. Radiofrequency energy is delivered through the electrodes, which causes superficial tissue destruction circumferentially over a length of 3 cm. Maximal ablation depth by using an energy density of 12 J/cm<sup>2</sup> and 2 applications has been shown to be the muscularis mucosae, with no involvement of the submucosa.<sup>12,13</sup> The HALO<sup>360</sup> system contains a radiofrequency generator with a foot pedal, an esophageal sizing balloon, and ablation balloons in different sizes (diameters 22 mm, 25 mm, 28 mm, 31 mm, and 34 mm, all with balloons 4-cm long and an ablation electrode length of 3 cm). A related device (HALO<sup>90</sup>; Barrx) is designed for focal ablation. The HALO<sup>90</sup> is a rectangular platform on a catheter that mounts onto the tip of a standard endoscope; the catheter runs alongside the endoscope rather than through the channel. The ablation platform is 15  $\times$  20 mm and is covered by an array of 24 electrodes, similar to the HALO<sup>360</sup>. When mounted onto the insertion tube of the endoscope, visualization is preserved.

An initial endoscopy is performed to locate the lesion for ablation, perform a mucolytic wash with N-acetyl cysteine, and place a guidewire up to 0.038 inches in diameter. A 4-cm sizing balloon is then passed into the esophagus over the guidewire and, when activated by a foot pedal, is automatically inflated to a pressure of 4 psi (27.58 kPa) by the generator. The esophageal diameter is measured by the generator by using pressure and volume data. An appropriately sized ablation balloon is selected. The ablation balloon is passed over the guidewire, and the endoscope is passed alongside the catheter for visualization during therapy. The ablation balloon is positioned and inflated with the top end of the balloon extending 1 cm above the proximal extent of the targeted mucosa. High-energy radiofrequency is automatically applied by the generator typically for less than 1 second after depression of a foot pedal. The balloon is moved distally, keeping its most proximal portion in a region that has already been ablated, and creates a zone of overlap to ensure that no areas are missed. This procedure is repeated until the gastroesophageal junction is identified by visualization of the gastric folds. The treated area is typically irrigated and/or

mechanically débrided with a transparent cap on the tip of the endoscope and is then re-treated with a second application of energy to improve the extent of the ablation. Usual settings for ablation are 40 W/cm<sup>2</sup>, for total energy delivery of 12 J/cm<sup>2</sup>. The generator measures tissue impedance and automatically adjusts energy outflow to obtain a uniform depth of tissue destruction throughout the field.

The HALO<sup>90</sup> mounts on the distal tip of the endoscope oriented to the 12-o'clock position of the video image. The esophagus is intubated with the device attached to it, which can be used to ablate focal lesions in the GI tract. The endoscope is positioned to place the targeted lesion at the 12-o'clock position of the endoscopic image, and the tip of the endoscope is deflected upward to bring the platform into contact with the target tissue. Radiofrequency energy is automatically delivered by the generator, as described above. An area of mucosa approximately the size of the ablation platform (15 × 20 mm) is ablated with this device. For focal ablation when using the HALO<sup>90</sup>, the usual protocol is 2 applications of energy to the targeted area, followed by removal of the coagulum from the mucosa, then, in the same session, the area is re-treated with 2 applications to achieve the optimal depth of injury.

### Heat probe

The heat probe is a reusable catheter with a Teflon-coated aluminum cylinder that contains a heated metal coil on the tip. In contrast to MPEC, the mechanism of injury to mucosa is direct heat application rather than electrical current. Coaptive pressure applied by the endoscopist also determines the degree of injury. The catheter is passed through the working channel of the endoscope, and the tip is applied to the target tissue. The catheter has an irrigation port. Application of heat and irrigation is controlled by a foot pedal with a technique similar to MPEC systems. Activation results in delivery of a preset number of joules, the entire amount of energy is delivered to the probe tip, even after release of the foot pedal. One heat probe is commercially available (Heat Probe; Olympus America, Center Valley, Pa).

### Lasers

Lasers are thermal devices that cause tissue destruction by absorption of laser light and have largely been replaced in GI endoscopic applications by other techniques. There are several types of lasers that use different lasing media, including Nd:YAG, KTP:YAG, carbon dioxide (CO<sub>2</sub>) laser, neodymium-holmium, and diode lasers. The depth of penetration of laser light and thermal injury is dependent on the wavelength of the light, the properties of the target tissue, the power setting, and the duration of application.<sup>14</sup> The KTP:YAG laser generates shallow thermal injury relative to the Nd:YAG laser, which can cause much more extensive thermal injury at depths up to 4 to 6 mm.<sup>15</sup> Lasers

can either be contact or noncontact "freebeam" devices. Low-power contact by using a sapphire tip has advantages over the freehand method, including a more controlled application, less charring, and less surrounding edema.<sup>16</sup> In the freebeam mode, a bare laser fiber is passed down the working channel of the endoscope. Fibers are available with the beam pointing forward for head-on applications or to the side pointing tangential application. Activation of the laser is controlled either with a foot pedal or a hand trigger in some models. The laser is cooled with either air or water. In the contact technique, a sapphire tip, which comes in a variety of shapes and sizes, is attached to the end of the laser fiber.

### Cryotherapy

Cryoablation is a noncontact method of causing tissue destruction by application of liquid nitrogen or refrigerated gas onto the target mucosa. Cryotherapy was initially studied by using a cryoprobe (catheter with a cold tip) in the esophagus.<sup>17-19</sup> This method required direct contact of the probe with the mucosa, which caused temporary adhesion of the probe to the tissue and was limited by difficulty in controlling the depth of injury, with a risk of perforation. Prototype devices that use a newer method of spray delivery of liquid nitrogen through a catheter were initially developed, in 1999, for use in the GI tract.<sup>20,21</sup>

There are 2 different devices for cryotherapy in the GI tract. One device (CryoSpray Ablation, CSA Medical Inc, Baltimore, Md) consists of a catheter with an insulating coating, a large console that contains liquid nitrogen, and a foot pedal for release of nitrogen. Because of the insulated coating, the catheter shaft remains at or near ambient temperature, which allows it to maintain pliability. Liquid nitrogen, at -196°C, is released under low pressure (2-3 psi [13.8-20.6 kPa]). A separate orogastric or nasogastric tube placed alongside the endoscope is required to evacuate the expanded cryogenic gas.

The other device that the U.S Food and Drug Administration approved for ablation in the GI tract (Polar Wand; GI Supply, Camp Hill, Pa) was built based on the Joule-Thompson effect, which refers to a drop in temperature of a liquid gas when its pressure drops. In this method, the gas (CO<sub>2</sub>) is contained in a small pressurized canister and delivered to the target tissue by a catheter. The gas remains at or near ambient temperature until it emerges from the end of the catheter, at which point there is a rapid decrease in its pressure associated with a sharp drop in temperature, which results in freezing of the targeted tissue. This portable device includes a small cylinder that contains the CO<sub>2</sub>, which is pressurized to 450 to 750 psi (3.1-5.2 × 10<sup>6</sup> Pa), a 6F, 200-cm-long, single-use catheter (end or side firing), and an evacuation tube that affixes to the tip of the endoscope to suction gas out of the GI tract. Release of the cryogen and simultaneous activation of the evacuation tube is controlled with a foot pedal.

Cryotherapy is performed by passing the catheter through the accessory channel of an endoscope, and the tip of the catheter is held 5 to 10 mm away from the target tissue. The foot pedal is depressed, which triggers release of the cryogen. The cryogen is sprayed onto the target tissue until it turns white, which means that freezing has taken place. This generally occurs after 10 to 15 seconds of application. Results of animal studies demonstrated that this length of application results in injury to the mucosa only.<sup>22</sup> Thawing usually takes place within 10 to 30 seconds. The same area is typically subjected to the freezing-thawing cycle 3 or 4 times to achieve ablation.

## INDICATIONS AND EFFICACY

### Ablation of mucosal vascular lesions

APC is commonly used to treat gastric antral vascular ectasia (GAVE). In multiple nonrandomized studies, endoscopic improvement, as well as a significantly decreased transfusion requirement, is reported in the majority of patients after several treatment sessions.<sup>23-29</sup> Bipolar electrocautery was described in the treatment of GAVE in 2 case reports,<sup>30,31</sup> which reported resolution or improvement of GAVE after several treatment sessions with MPEC. A retrospective study of 32 patients with GAVE or angiodysplasia treated with MPEC, laser, or APC found a reduced or abolished need for transfusions in 76% of patients after 12 months of follow-up.<sup>32</sup> Use of the heat probe to treat GAVE has been described in small series and case reports. Similar to MPEC, improvement or resolution was noted after 1 to 4 treatment sessions.<sup>33-36</sup> A pilot study of 6 patients with GAVE treated with the HALO<sup>90</sup> device showed improved hemoglobin concentrations in all patients after 1 to 3 treatments. Five of 6 patients were no longer transfusion dependent.<sup>37</sup> Multiple nonrandomized studies, which consisted of up to 45 patients, exist that described the use of lasers to treat GAVE. These studies report success rates, including a decreased or abolished need for transfusions, of 61% to 100% after 3 to 6 sessions.<sup>38-43</sup> Lasers have also been found to be efficacious in the treatment of bleeding from arteriovenous malformations (AVM).<sup>44</sup>

A number of studies showed APC to be efficacious in the treatment of radiation proctitis.<sup>45-56</sup> A summary of these nonrandomized trials shows that, with a mean number of treatment sessions that ranged from 1 to 3.7 and a follow-up duration of 10 to 24 months, symptomatic improvement was achieved in 83% to 100% of patients, anemia improved in the majority of patients, and relief from transfusions was achieved in 95% to 100%. Lasers and MPEC were successfully used in the treatment of radiation proctitis in several observational studies.<sup>57-62</sup> As with other techniques, multiple sessions are generally required.

APC has also been used to treat colonic AVMs. A prospective study of 100 patients with lower-GI bleeding

because of AVMs found that after treatment with APC, bleeding ceased in 85% and the transfusion requirement was eliminated in 90% of patients, with a median follow-up of 20 months.<sup>63</sup> Use of a submucosal saline solution injection before treatment of colonic AVM has been reported as a means to reduce the risk of deeper thermal injury when used in the colon.<sup>64</sup> Thermal contact probes and MPEC have also been used successfully in the treatment of colonic AVMs.<sup>65,66</sup>

Limited data exist on the efficacy of cryotherapy for treating mucosal vascular lesions. A study of 26 patients with a variety of bleeding lesions (GAVE, AVMs, radiation proctitis, and radiation gastritis) were treated with cryotherapy, with a mean of 3.6 sessions.<sup>67</sup> These patients had previously undergone treatment with MPEC and heat probe but continued to have bleeding. Cryotherapy with nitrous oxide was efficacious in causing hemostasis in 77% overall, with a follow-up of 6 months. A pilot study, published in abstract form, found that 6 of 9 patients with GAVE treated with cryotherapy had a complete response and 3 of 9 had a partial response.<sup>68</sup>

### Ablation of Barrett's esophagus

All of the modalities discussed in this review have been used to ablate nondysplastic or dysplastic Barrett's esophagus (BE). After the tissue is destroyed, it is replaced by a nondysplastic "neoesophageal" lining, especially if healing occurs in a nonacid environment.<sup>69</sup> The advantage of endoscopic therapy over surgery for BE with high-grade dysplasia (HGD) or early cancer (EC) is that it may provide definitive treatment while avoiding the morbidity and mortality of esophagectomy. However, randomized trials that compared outcomes with endoscopic treatment versus surgery do not exist, and long-term follow-up data are lacking. Concerns with ablation therapy for BE with HGD or EC include the lack of a pathologic specimen, which may preclude adequate staging, especially in ECs, as well as the possibility of "buried glands," a phenomenon in which BE tissue, with or without dysplasia, is hidden beneath the neoesophageal lining. Before deciding on ablative therapy for dysplastic BE or EC, patients must be carefully staged, preferably by a combination of EUS followed by EMR of any visible lesions. Patients who have malignancies that extend deeper than the mucosa are at higher risk for lymph-node metastases<sup>70,71</sup> and should be considered for esophagectomy rather than endoscopic therapy. Other features that make patients suitable for consideration of endoscopic ablation include HGD only, ECs that are less than 2 cm in diameter, moderately or well-differentiated histology, no lymph-node involvement by EUS, and patient willingness to return for frequent surveillance endoscopies after ablation. Because of the low risk of malignant transformation in nondysplastic BE,<sup>72</sup> there is no evidence that ablation should be undertaken in this population.

When endoscopic therapy rather than esophagectomy is decided upon, EMR is often used to endoscopically remove visible dysplastic nodules or EC and provides a pathologic specimen for staging purposes. EMR techniques and devices are reviewed separately,<sup>2</sup> but, for comparison, the procedure was studied in HGD and EC in prospective, observational studies. Local remission rates were >90% for low-risk lesions (limited to mucosa, <2 cm), but recurrence was found in 11% to 14% of patients.<sup>73,74</sup> For lesions that invaded the submucosa or those larger than 2 cm, the local remission rate was only 59%. EMR of the complete segment of BE has also been used to eradicate the remaining at-risk tissue, especially in patients with multifocal HGD. In a study of 41 patients with HGD, 23 of whom had EC, complete EMR resulted in eradication of BE and dysplasia in 76%. However, recurrent BE was seen in 24%, and metachronous cancers were seen in 12.2%.<sup>75</sup> In addition, the rate of stricture formation after circumferential EMR was 17%.

PDT, also discussed in a separate review,<sup>1</sup> was studied extensively in the treatment of BE. Multiple prospective observational trials showed rates of HGD ablation that ranged from 78% to 95%.<sup>76-79</sup> A randomized placebo controlled trial of PDT plus omeprazole versus omeprazole alone for BE with HGD found 77% remission in the PDT group versus 39% in the omeprazole group ( $P < .0001$ ).<sup>80</sup> Five-year follow-up data showed that cancer occurred in 29% in the omeprazole group versus 15% in the PDT group ( $P < .00274$ ).<sup>81</sup> However, buried glands were reported and adenocarcinoma developed beneath the neosquamous lining.<sup>82</sup> In addition, PDT is associated with up to a 36% rate of strictures and causes temporary cutaneous photosensitivity, but, in long-term follow-up, the strictures all responded to endoscopic therapy.<sup>80,81</sup>

Multiple trials showed that it is feasible and safe to eradicate BE with APC, but incomplete eradication is common. Studies that consisted of 7 to 50 patients with nondysplastic BE or low-grade dysplasia (LGD) reported residual BE in 15% to 47% of patients,<sup>83-89</sup> with the largest study reporting residual BE in 68% at 12 months of follow-up.<sup>90</sup> Buried glands were reported in up to 40% of patients,<sup>88</sup> presumably because of the shallow depth of tissue injury. There have been only small series published with the use of APC in HGD or EC. One study of 10 patients (7 HGD and 3 EC) used APC and found that 1 patient had persistent HGD and one progressed to cancer at a mean of 24 months of follow-up.<sup>91</sup> Another series of 3 patients with early adenocarcinoma treated with APC found 1 recurrence during the 2-year follow-up.<sup>92</sup> MPEC has been studied in the ablation of mostly nondysplastic BE tissue. In these nonrandomized studies that consisted of 10 to 52 patients, endoscopic and histologic eradication of BE was achieved in 73% to 81% of patients, with follow-up that ranged from 4 to 53 months.<sup>93-98</sup> The heat probe was studied in ablation of nondysplastic BE in 1 study of 13 patients. At 6 to 36 months of follow-up,

1 patient developed LGD, and, overall, 23% had residual BE.<sup>99</sup>

Several prospective studies examined the use of the radiofrequency balloon ablation device in nondysplastic BE, as well as in HGD. In a dose-response and efficacy study in patients with nondysplastic BE who underwent treatment with the HALO<sup>360</sup>, 70% of 70 patients had complete ablation of BE after 1 year of follow-up.<sup>100</sup> In a multicenter trial, 142 patients with HGD underwent a mean of 1 ablation session with the HALO<sup>360</sup>. Ninety-two patients had at least 1 follow-up biopsy session at a mean follow-up of 12 months. Elimination of HGD was achieved in 90.2%, elimination of all dysplasia in 80.2%, and complete elimination of intestinal metaplasia in 54.3%.<sup>101</sup> There were no buried BE glands and no symptomatic strictures. A prospective study of 11 patients with mostly HGD, some of whom had prior EMR of visible lesions (EC or HGD), found complete eradication of dysplasia and intestinal metaplasia in 100% of patients after a mean of 2 ablation sessions during a median follow-up of 19 months.<sup>102</sup> Some patients underwent up to 3 repeated ablations with the HALO<sup>90</sup> for residual focal disease. A follow-up prospective study of 12 patients with HGD underwent treatment with HALO<sup>360</sup>, followed by HALO<sup>90</sup> as needed for residual disease.<sup>103</sup> Seven patients (58%) had EMR of visible lesions before treatment, with pathology of the resected specimens showing EC ( $n = 2$ ) or HGD ( $n = 5$ ). Most had 1 treatment session and 2 focal ablation sessions, and complete histologic remission (elimination of all dysplasia and BE) was achieved in 91% of patients after a median follow-up of 14 months.

Limited data exist on the efficacy of cryotherapy for ablation of BE. A pilot study of 11 patients with BE, including 5 with LGD and 1 with HGD, showed no dysplasia in any biopsy specimen after treatment at 1 and 6 months.<sup>104</sup> A study of 10 patients with LGD, HGD, or EC who underwent treatment with liquid nitrogen cryotherapy was published in abstract form.<sup>105</sup> At a mean follow-up of 16 months, all dysplasia was eliminated in the patients with dysplasia alone. Another pilot study, published in abstract form, of 32 patients with HGD ( $n = 12$ ) or EC ( $n = 20$ ) showed elimination or downgrading of dysplasia in 89% of patients with HGD and in 66% with EC. No response (defined as no change in pathology or patient proceeded to esophagectomy) was seen in 10% of the patients with HGD and 22% of patients with EC. The mean number of sessions was 4, the length of follow-up has not yet been reported, and 5 patients remain under treatment.<sup>106</sup>

Data on the use of Nd:YAG or KTP:YAG lasers to ablate BE with no dysplasia or only LGD is limited to several small case series of 1 to 11 patients. These series reported complete ablation in 75% to 100% of patients,<sup>69,107-112</sup> although 1 small series reported ablation in 0 of 4 patients.<sup>113</sup> When reported, buried glands were present in 0% to 68% of patients. In patients with HGD or EC,

use of lasers was studied in small case series of 1 to 10 patients, with variable results.<sup>114-117</sup>

### Miscellaneous indications

APC has been used as an ablative therapy for residual neoplastic lesions in the upper-GI and lower-GI tract after snare resection. A retrospective study of 15 patients without polyposis syndromes underwent a mean of 1.8 treatment sessions with APC for duodenal adenomas. The recurrence rate was 39%, with a mean time to recurrence of 14 months. No patients developed cancer, and nearly all were successfully re-treated with APC.<sup>118</sup> In another retrospective series, 30 patients with residual colon polyp after piecemeal resection were treated with APC. On repeated colonoscopy, residual polyp remained in 50% of these patients, but all these residual lesions were amenable to subsequent complete endoscopic resection.<sup>119</sup> APC was also used to debulk tumors of the esophagus in nonoperative candidates for palliation of dysphagia,<sup>120</sup> nonsuperficial colonic tumors, and small tumors of the ampulla.<sup>27,121</sup>

Studies of the use of Nd:YAG laser to ablate large sessile colon polyps, either as the sole treatment or in conjunction with snare polypectomy, reported complete ablation rates in 53% to 94% of patients.<sup>122-129</sup> Lasers and MPEC have been used to palliate bleeding and obstruction in nonoperative patients with GI tumors.<sup>121,130-136</sup> In a series of patients with early gastric tumors treated with laser, complete response was seen in 11 of 13 patients (85%).<sup>137</sup> Laser, APC, and MPEC of ampullary masses were used in patients with and without polyposis syndromes.<sup>138-140</sup> However, resection of ampullary adenoma is generally required for complete removal, because thermal methods may incompletely treat the lesion.

### COMPARATIVE STUDIES

#### Ablation of mucosal vascular lesions

There are no large studies that directly compared these technologies for ablation of vascular lesions.

#### Ablation of BE

APC was compared with PDT in a randomized study of 26 patients with dysplastic BE. At 12 months, dysplasia was eradicated in 67% of patients who had APC versus 77% of patients who had PDT ( $P = .03$ ).<sup>141</sup> APC and MPEC were compared in 2 randomized controlled trials in the ablation of BE. There appear to be no differences in the efficacy of these 2 methods. A randomized trial of 52 patients with BE (nondysplastic or LGD only) who underwent ablation with APC versus MPEC found no statistically significant differences in the rate of successful histologic ablation of BE (81% with MPEC and 65% with APC), although the use of MPEC required fewer treatment sessions.<sup>142</sup> There were no serious adverse events, but transient significant upper-GI symptoms occurred in 13% of patients who

had APC versus 8% of patients who had MPEC. Similarly, a randomized controlled trial of 35 patients with mostly nondysplastic BE who underwent ablative therapy with MPEC versus APC found that, at 2 years of follow-up, complete reversal of BE was maintained in 69% of patients.<sup>97</sup> There was no difference in the ablation rate for APC compared with MPEC. There were no major complications with either treatment.

### EASE OF USE

Contact thermal probes, APC units, and the radiofrequency balloon ablation device are portable, require a standard 110-V electrical outlet, are widely available, and are generally easy to use. Comparative trials that specifically address the ease of use between the ablative methods do not exist. The radiofrequency balloon device and cryotherapy devices can uniformly ablate large surface areas. Compared with other ablative technologies, lasers are expensive and cumbersome to use. They may require a 220-V power source, a continuous gas flow, and a water source for cooling. Other considerations include special safety training, protective eyewear, limited portability, and limited access to the laser area. Many of these obstacles have led to a decline in the use of lasers for mucosal ablation.

### SAFETY

In general, deeper tissue injury increases the risk of complications, such as perforation and stricture formation. A canine model revealed a progression in increased depth of tissue destruction with APC, MPEC, and laser therapy.<sup>143</sup> The radiofrequency balloon catheter appears to cause only superficial destruction; the maximal ablation depth was the muscularis mucosae in 1 study.<sup>144</sup>

Reported complication rates for APC range from 0% to 24%.<sup>84-92</sup> These include pneumoperitoneum, pneumomediastinum, perforation, subcutaneous emphysema, transmural burn syndrome, pain at the site of application, chronic ulceration, luminal distension with argon gas, and stricture. Complication rates may be influenced by the power setting, the distance of the probe tip from the target, and the duration of application.<sup>1</sup> The largest study of APC in the colon (100 patients) reported a 1.7% complication rate, with 1 transient fever and 1 pneumoperitoneum, without evidence of perforation, which was managed conservatively.<sup>63</sup> Case reports exist that describe colonic explosion during APC treatment, generally in a poorly prepared colon.<sup>145,146</sup> Therefore, when APC is used to treat radiation proctitis, a full bowel preparation rather than an enema preparation is advisable.

Complications after use of lasers depend on the site of the application and indication. Perforation is reported in

up to 9%,<sup>137,147,148</sup> and precipitation of bleeding in up to 29%.<sup>149,150</sup> Other complications include stricture formation, fistula, abscess, fever, and pain. Antral hyperplastic polyps, some very large, developed in patients after repeated laser treatment of GAVE.<sup>151</sup> Risks to personnel who use lasers include ocular, skin, and respiratory injury.

The CURE hemostasis research group reported complications after treating colonic angiodysplasia in 7% of patients with the heat probe and 4% with bipolar electrocautery.<sup>152</sup> Perforation after treating lesions in the right side of the colon was reported in 2.5% in 1 study<sup>153</sup>; MPEC should not be applied forcefully in this area.

The radiofrequency balloon ablation catheter appears to be very safe. In postmarketing surveillance of 13,265 procedures performed, 32 adverse events were reported (0.25%). These include 22 strictures (0.17%), 4 perforations (0.04%), and no deaths<sup>154</sup> (D. Utley, MD, personal communication, 2008). No thermal perforations occurred; the few perforations that did occur were thought to be because of technical procedural issues.

Among 46 patients reported on in 3 studies examining cryotherapy, the only reported complication was one case of transient abdominal pain.<sup>67,68,104</sup> A study of the effect of cryotherapy on canine esophagus showed that the depth of injury to the mucosa was limited to 0.5 mm. Twenty-four hours after cryotherapy, the epithelium had sloughed, with preservation of deeper layers.<sup>21</sup> Another study, in porcine esophagus, revealed that, after 15 seconds of cryotherapy application, necrosis was limited to the mucosa.<sup>22</sup> The submucosa was reliably injured after 30 seconds of application, and muscularis propria injury and frank perforation were seen after 45 and 120 seconds of application, respectively. One publication, in abstract form, of 16 patients, reported a gastric perforation in a patient with Marfan syndrome and 3 esophageal strictures required one dilation.<sup>106</sup>

## FINANCIAL CONSIDERATIONS

Prices for various devices are listed in Table 1. Current Procedural Terminology (CPT®)\* codes for mucosal ablation include the following. **43258** for upper-GI endoscopy with ablation of tumor, polyp, or other lesions not amenable to removal by biopsy or snare (eg, treatment of GAVE with APC). **43228** for esophagoscopy with ablation (eg, radiofrequency balloon ablation of Barrett's esophagus).

\* Current Procedural Terminology (CPT®) is copyright 2008 American Medical Association. All Rights Reserved. No fee schedules, basic units, relative values, or related listings are included in CPT. The AMA assumes no liability for the data contained herein. Applicable FARS/DFARS restrictions apply to government use.

However, if it is medically appropriate to examine the stomach and duodenum in the course of performing this procedure, reporting would be with code **43258.45339** for sigmoidoscopy with ablation (eg, treatment of radiation telangiectasia with APC or focal application with radiofrequency device). **45383** for colonoscopy with ablation (eg, treatment of angiodysplasia with APC).

Less commonly used codes, chiefly for balloon (deep) enteroscopy applications, include the following. **44369** with ablation of tumor(s), polyp(s), or other lesion(s) not amenable to removal by hot biopsy forceps, bipolar cautery, or snare technique. With this code, **43235**, diagnostic upper GI endoscopy, if performed and medically necessary the same day, could be separately reported with modifier -59, but Medicare rules would not allow for any additional payment; private payor rules might differ. Alternatively, **43258-59** could also be separately reported the same day, if lesions were sought and treated within the stomach and then further lesions were treated in the jejunum or ileum. In this circumstance, a small further payment would be made for the extra work.

## SUMMARY

APC and MPEC are widely available efficacious methods of treating a variety of superficial bleeding and neoplastic lesions. Use of these methods in the ablation of BE has yielded mixed results, with a very limited number of large series. The radiofrequency balloon ablation device has a very low rate of complications, ablates a large field with uniform depth, and appears efficacious in ablating HGD. The significant risk of recurrent dysplasia after any endoscopic therapy for BE requires close surveillance. Cryotherapy may become a viable alternative method of tissue ablation, but, more data, especially comparative data, are needed. Compared with other ablative techniques, lasers are more difficult to use, have a lower safety threshold, and are now uncommonly used.

*Abbreviations:* APC, argon plasma coagulator; ASGE, American Society for Gastrointestinal Endoscopy; AVM, arteriovenous malformation; BE, Barrett's esophagus; CO<sub>2</sub>, carbon dioxide; EC, early cancer; GAVE, gastric antral vascular ectasia; HGD, high-grade dysplasia; KTP:YAG, potassium-titanium-phosphate yttrium aluminum garnet; LGD, low-grade dysplasia; MPEC, multipolar electrocautery probe; PDT, photodynamic therapy.

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