NEW METHODS & MATERIALS

Complete ablation of esophageal epithelium with a balloon-based bipolar electrode: a phased evaluation in the porcine and in the human esophagus

Robert A. Ganz, MD, David S. Utley, MD, Roger A. Stern, PhD, Jerome Jackson, MS, Kenneth P. Batts, MD, Paul Termin, DVM, PhD

Background: **The aim of this study was to evaluate the endoscopic and the histologic effects of a balloon-based bipolar radiofrequency electrode for ablation of porcine and human esophageal epithelium.**

Methods: **All procedures were performed with a balloon-based, bipolar radiofrequency system that creates a circumferential, thin-layer epithelial ablation zone within the esophagus. In Phase I, multiple ablations were created in 10 farm swine, followed by acute euthanasia and histologic assessment for completeness of epithelial removal and ablation depth. In Phase II, multiple ablations were created in 19 farm swine, with varying power and energy density, followed by endoscopy at 2 and 4 weeks to assess stricture formation. In Phase III, 3 ablations were created in 12 farm swine, with varying energy density (5, 8, 10, 12, 15, or 20 J/cm^2) at 350 W. Animals were euthanized at 48 hours. Histologic examination determined the percentage of epithelium removed and the ablation depth. In Phase IV, 3 patients underwent esophageal epithelial ablation before esophagectomy, creating separate lesions proximal to the tumor. Completeness of epithelial ablation and ablation depth was quantified histologically.**

Results: **In Phase I, complete removal of esophageal epithelium was achieved at energy density settings of 9.7 to 29.5 J/cm^2. In Phase II, 9.7 and 10.6 J/cm^2 produced no stricture, whereas more than 20 J/cm^2 produced a stricture in every case. In Phase III, 8-20 J/cm^2 resulted in 100% epithelial ablation. Five and 8 J/cm^2 spared the muscularis mucosae, whereas 10 J/cm^2 caused injury to the muscularis mucosae but preserved the submucosa. In Phase IV, histologic examination demonstrated full-thickness epithelial removal in areas of electrode contact. Ablation extended only to the muscularis mucosae, without injury to submucosa.**

Conclusions: **In the porcine and the human esophagus, circumferential, full-thickness ablation of epithelium without direct injury to the submucosa is possible and was well tolerated. In all cases, depth of ablation was linearly related to energy density of treatment.**

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Current affiliations: Abbott-Northwestern Hospital, Gastroenterology, Minneapolis, Minnesota, BARRx, Inc., Sunnyvale, California, Abbott-Northwestern Hospital, Hospital Pathology Associates, Minneapolis, Minnesota, Lincoln Associates, Research Pathology, St. Paul, Minnesota.

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Reprint requests: Robert A. Ganz, MD, Abbott-Northwestern-Gastroenterology, Abbott-Northwestern Hospital, Chicago Ave. and 26th St., Minneapolis, MN 55407.

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Between 1% and 2% of adults in the United States have Barrett's esophagus.[1] In these patients, the normal squamous epithelium of the distal esophagus has been replaced by specialized intestinal metaplasia (IM)—a response to GERD-related chronic injury and inflammation.[2] The incidence of esophageal adenocarcinoma in patients with IM is 30 to 125 times greater (5 cases/1000 patient years) than that of the general population.[1,3] Current management of IM includes an antisecretory regimen for GERD symptoms and prevention of erosive esophageal injury, although it is recognized that such therapy neither eliminates nor reduces the extent of IM.[4]

A number of endoluminal modalities have been evaluated for the ablation of IM (with and without dysplasia), including multipolar electrocoagulation,[5] argon plasma coagulation,[6] laser photoablation,[7] and photodynamic therapy.[8] Although there are reports of success for each of these techniques, most studies describe nonuniform ablation that can potentially result in persistent IM (surface and subsquamous) or excessively deep ablation, resulting in stricture and, rarely, perforation. The reason(s) for ablation treatment failure is not entirely clear but possible contributing causes include the operator-dependent nature of many of these hand-held, hand-aimed devices, the large surface area that requires treatment, the necessity for multiple ablation sessions, and the inherent need for a physician-determined visual end point for the ablation.

The present multiphase study evaluated the effect of a novel, balloon-based bipolar radiofrequency (RF) electrode on esophageal epithelium. Phases I to III were conducted in a stepwise manner in the porcine esophagus to determine the treatment settings (energy density) necessary to fully ablate the esophageal epithelium, the relationship between energy density dose and stricture formation rate, and the histologic depth of ablation associated with each treatment setting. In Phase IV, the following were evaluated: technical performance, patient tolerance, histologic depth of ablation, and percentage of the surface area ablated in human esophageal

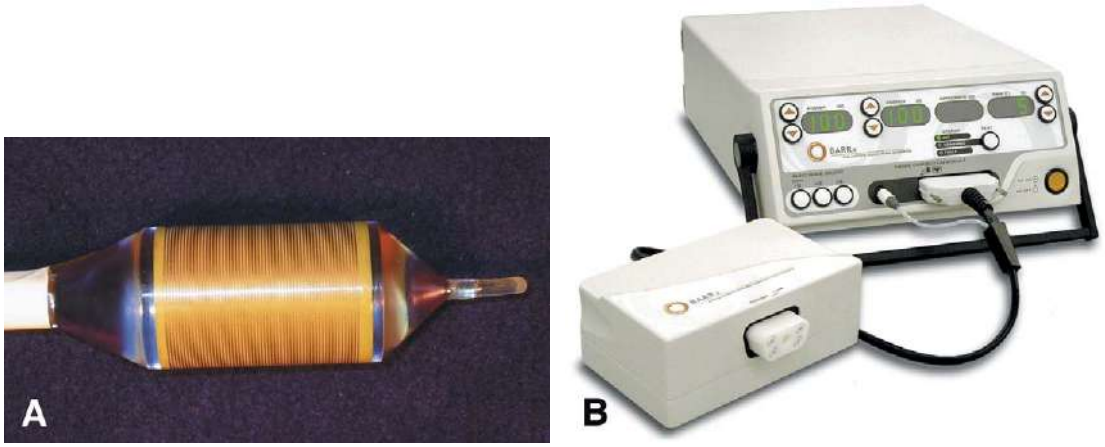

Figure 1. Esophageal epithelium ablation system. **A,** Balloon-based bipolar RF electrode (fully inflated). **B,** Automated RF generator.

epithelium 1 to 2 days before scheduled esophagectomy. Data from the present study were used for planning subsequent clinical trials of this technique in patients with IM.

MATERIALS AND METHODS

The system used for all procedures (Stellartech Research Coagulation System, manufactured for BARRx, Inc., Sunnyvale, Calif.) consists of an array of sizing balloons used to determine the inner diameter of the targeted portion of the esophagus (18-34 mm), an array of balloon-based bipolar RF electrodes (Fig. 1A) to ablate the epithelium (18-34 mm), and a RF generator designed specifically for use with this device (Fig. 1B). The balloon-based electrode is 3 cm in length and incorporates multiple, tightly spaced, bipolar electrodes that alternate in polarity. Total electrode length is 3 cm, and the electrode surface area varies according to the outer diameter of the balloon. Total energy in joules (J) delivered to the tissue is controlled by the generator and is determined by the balloon size (electrode surface area), thereby allowing the energy delivered to be standardized (energy density, J/cm^2). The RF generator delivers the preselected amount of energy in an automated manner in less than 1 second at 350 W.

Phase I

An acute porcine feasibility study (Phase I) was performed in an AAALAC (Association for Assessment and Accreditation of Laboratory Animal Care) accredited facility (HealthPartners Research Foundation, Minneapolis, Minn.) under an approved Institutional Animal Care and Use Committee (IACUC) protocol. Ten farm swine (18-22 kg) were fasted (12 hour) and then were sedated by intramuscular injection of tiletamine (5 mg/kg) and zolazepam (5 mg/kg), followed by endotracheal intubation. Anesthesia was maintained with intermittent intravenous boluses of pentobarbital. All animals underwent endoscopy, followed by introduction of an 18-mm bipolar balloon electrode (sizing balloons were not available for Phase I or II). Ablations were performed by positioning the balloon electrode in the esophagus under endoscopic guidance, inflating the balloon to 7 to 10 psi, so that the electrode contacted the esophageal wall, and delivering RF energy via the RF generator. Automated energy delivery was actuated by a single depression of a button on the generator. Multiple (3-4) ablations (each 1 cm in length) were performed in each esophagus, with varying power (W) and energy density (J/cm^2) between sites. All animals were euthanized immediately, and the esophagus was removed. Each ablation site was evaluated grossly and histologically to determine the treatment settings (power and energy density) that resulted in complete removal of epithelium. Depth of injury was not assessed.

Phase II

Nineteen farm swine (mean 21.3 kg) were prepared, and endoscopy was performed with the animals under anesthesia, as in Phase I (same facility and approved protocol). Multiple, separate circumferential ablations (2-4 per animal, depending on anatomy, each 3 cm in length) were created proximal to the gastroesophageal junction (GEJ) by using different combinations of power (range 60-375 W) and energy density (range 9.7-29.5 J/cm^2) settings. After treatment, the animals were monitored until they were able to ambulate and then they were allowed to have water and pig chow ad libitum. No antisecretory regimen was used.

All animals underwent endoscopy at 2 weeks, and ablation zones were graded by a single investigator (R.A.G.) as follows: 0, normal; 1, visible effect of ablation (i.e., color change neosquamous re-epithelialization) without stricture; 2, mild stricture; 3, moderate stricture; 4, severe stricture (unable to pass endoscope). Animals with at least one grade 3 or 4 ablation zone were euthanized.

Animals with grade 0 to 2 ablation zones underwent endoscopy at 4 weeks and then were euthanized. The results of endoscopic ablation zone grading (last grade available, 2 or 4 weeks) were further summarized for each energy density setting.

At the time of euthanasia, the esophagus was immediately removed, fixed in formalin, and subsequently sectioned transversely. Sections were stained with H&E for histologic evaluation. For each energy density and power setting, depth of ablation was assessed as epithelium, lamina propria, muscularis mucosae, submucosa, or muscularis propria.

Phase III

Phase III of this study was conducted at a preclinical contract research laboratory (Lychron, LLC, Mountain View, Calif.). The Phase III protocol was approved by Lychron's internal IACUC, which is governed, bound, and/or directed by the U.S. Department of Agriculture, the U.S. Food and Drug Administration, the U.S. Drug Enforcement Administration, the Office of Laboratory Animal Welfare, and the Animal Welfare Act.

Twelve male farm swine (50-60 kg) were fasted for 12 hours and then were sedated by intramuscular injection of ketamine (15 mg/kg), followed by endotracheal intubation and inhalation anesthesia (2%-3% isofluorane). All animals underwent endoscopy and sizing of the inner diameter of 3 separate regions within the esophagus (5, 10, and 15 cm proximal to the GEJ). The sizing procedure began with the introduction of a 25-mm sizing balloon "along-side" the endoscope. The balloon was positioned under direct vision and then inflated to 7 psi (0.5 atmosphere). This pressure was selected because it is adequate to expand the electrode in subsequent procedure steps, yet low enough to mitigate against perforation and mucosal injury. After inflation, balloon fit was assessed by observation for gaps around the balloon (too small) or unfolded areas of the balloon material (too large). Further, contact of the balloon with the esophageal wall was assessed by looking through the clear balloon material; visible water or fluid collections suggested that the balloon was undersized. As necessary, larger or smaller sizing balloons then were used to achieve a proper fit. By using an appropriately sized bipolar balloon electrode, 3 separate, circumferential ablations (each 3 cm in length) were created at the specified sites. In an effort to bracket the settings, based on the results of Phases I and II that resulted in complete removal of epithelium without stricture, 6 treatment groups were created (two animals each). In each group, a different energy density (5, 8, 10, 12, 15, or 20 J/cm^2) was used at a fixed power of 350 W. All animals underwent endoscopy followed by euthanasia (by intravenous injection of potassium chloride) at 48 hours. Endoscopic photographs were obtained immediately after treatment and again at 48 hours. The esophagus was removed immediately after sacrifice, opened longitudinally, photographed, and affixed to cork. After fixation in formalin, full-thickness sections were obtained from each ablation zone (3 transverse, 2 longitudinal, and 1 non-ablated control) and stained with H&E. Thus, 18 sections were obtained per animal (216 sections in total).

Histologic evaluation was performed in a blinded manner to determine the following: (1) completeness of epithelial ablation (percentage of surface area of epithelium removed per ablated specimen) and (2) depth of thermal injury (tissue layer depth). Surface area ablation was determined by histologically quantifying the linear measurement of the luminal surface of each section as having either "present" or "absent" epithelium (184 specimens) and then by calculating the percentage of the epithelium that was absent (ablated). Thinned, but present, epithelium was counted as present (non-ablated).

Maximum depth of injury was noted for each histologic specimen by examining each tissue layer (epithelium, lamina propria, muscularis mucosa, submucosa, and muscularis propria) for signs of thermal damage (i.e., coagulum, absent nuclei, darkened cytoplasmic staining for myocytes, lymphocyte infiltration).

Phase IV

Eligible patients were those scheduled to undergo total esophagectomy for adenocarcinoma. Exclusion criteria were the following: prior radiation therapy and ablative/resective esophageal procedures. All patients consented to undergo endoscopy with ablation of two or 3 separate regions of esophageal epithelium 24 to 48 hours before surgery. Phase IV of the study was performed at a single center (Abbott-Northwestern Hospital, Minneapolis, Minn.). The protocol was approved by the institutional review board of that hospital.

The location of the tumor was identified during endoscopy. The esophageal body was sized as described in Phase III. An appropriately sized balloon-based bipolar RF electrode was introduced, positioned visually at 5 cm proximal to the tumor, and inflated to 7 psi. Energy was delivered at 260 to 350 W and either 10 or 12 J/cm^2. One or two additional sites were treated in each patient, each separated by at least 1 cm linearly.

After the procedure, patients were monitored in the post-treatment recovery unit until awake and alert with stable vital signs. They were instructed to observe a diet in compliance with their planned esophagectomy over the next 24 to 48 hours. They were to inform the physician in case of chest pain, dysphagia, odynophagia, or other adverse symptom before surgery. Patients were not provided with prophylactic antibiotics or narcotic medication. Esophagectomy was performed 24 to 48 hours after the ablation procedure.

At surgery, the esophageal adventitia and mediastinum were inspected for thermal injury and inflammation. Each esophagectomy specimen was opened longitudinally and fixed in formalin. Longitudinal sections were obtained from each ablation zone, followed by the preparation of glass slides stained with H&E. Completeness of epithelial ablation (percentage of surface area removed), depth of ablation (defined as depth of necrosis), and the presence and the extent of any accompanying non-lethal

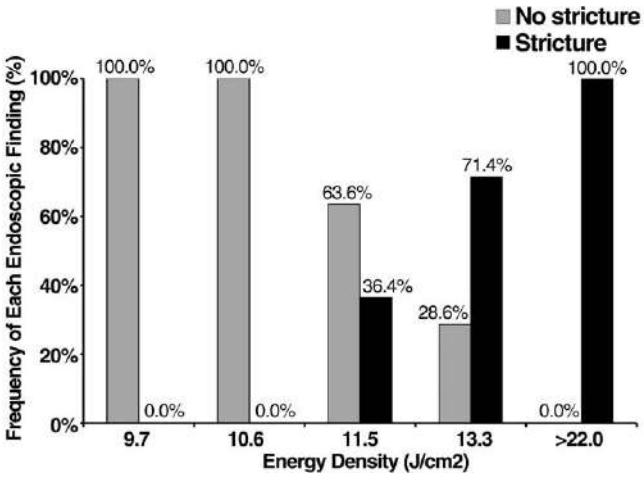

Figure 2. Energy density (J/cm^2) group plotted against frequency of esophageal stricture at final endoscopy (Phase II). "No Stricture" includes normal or color change findings (Grades 0-1). "Stricture" includes mild, moderate, and severe grades (Grades 2-4). The ">22 J/cm^2 group" includes those areas treated at 22.1, 26.5, and 29.5 J/cm^2 settings.

inflammation were assessed histologically for each energy density setting.

RESULTS

Phase I

Acutely, ablation zones were white and circumferential in appearance on endoscopic and gross examination. As energy density was increased, the ablation effect was visibly more complete. However, altering the power did not have the same effect. Complete removal of esophageal epithelium (gross and histologic) was achieved at power settings of 60 to 375 W, combined with energy density settings of 9.7 to 29.5 J/cm^2. Energy density settings less than 9.7 J/cm^2 resulted in incomplete epithelial removal.

Phase II

Acutely, the endoscopic findings after ablation were similar to those of Phase I. There was no perforation, death, or other serious adverse event related to the ablation procedure, although there was one anesthesia-related (pentobarbital) death immediately after the 2-week endoscopy. A mean animal body mass increase was noted from baseline (21.3 kg) to 2 weeks (25.0 kg). Animals surviving to 4 weeks continued to gain weight (from 25.0 to 30.2 kg). All 19 animals were available for evaluation at 2 weeks; 9 were available at 4 weeks, because of early euthanasia of animals with high-grade stricture (n = 9) and the death of one animal because of anesthesia.

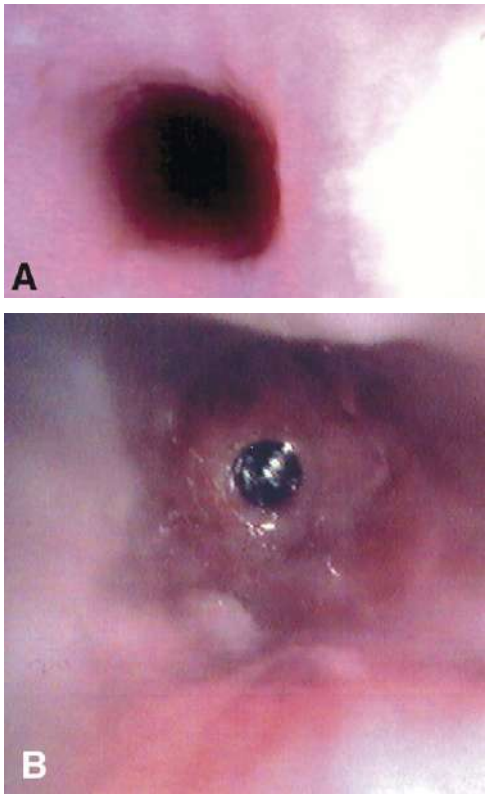

Figure 3. A, Endoscopic view (Phase II) of ablation site at 4 weeks after treatment with 9.7 J/cm^2, showing healed epithelium and no stricture. **B,** Endoscopic view (Phase II) of ablation site at 2 weeks after treatment with 29.5 J/cm^2, showing severe stricture (Grade 4).

At 2 weeks, all ablation zones (n = 48) were grossly evident as either healed epithelium, ulceration, or stricture. As energy density increased, the grade and the frequency (Fig. 2) of stricture also increased. At the lowest energy density settings (9.7 and 10.6 J/cm^2), there were no strictures in 20 treated regions and histology revealed mild inflammation with no injury to the submucosa or the muscularis propria. In these animals, the epithelium was fully healed (Fig. 3A) and there was no evidence of buried epithelial cells beneath neosquamous epithelium. At intermediate energy densities (11.5 and 13.3 J/cm^2), 9 of the 18 ablation zones were completely free of stricture (Grade 0-1) and those strictures that occurred were predominantly mild or moderate (Grade 2-3). There was moderate inflammation within the submucosa but no injury to the muscularis propria. High energy densities (>22 J/cm^2) resulted in severe stricture (Grade 4, Fig. 3B) at 2 weeks in all animals, with evidence of damage to the muscularis propria and esophageal edema. Although the frequency and the severity of stricture formation increased with increases in energy density, variations

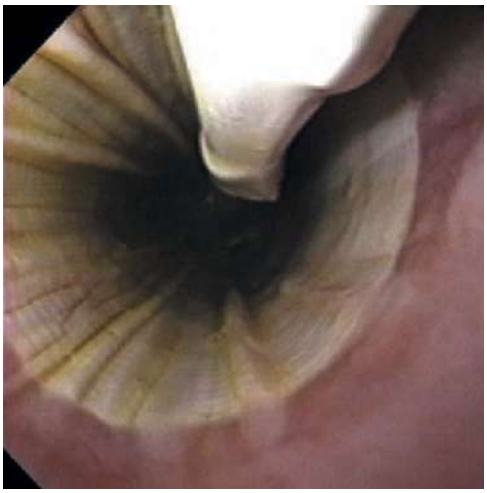

Figure 4. Endoscopic view (Phase III) showing acute appearance of ablation zone in porcine esophageal body (12 J/cm^2).

in power (by comparing groups treated at <175 W vs. those treated at >300 W) did not change either outcome.

Phase III

There was no perforation, death, or other serious adverse event related to the ablation procedure. Total procedure time was less than 30 minutes; the actual ablation portion of the procedure required 2 to 3 minutes. Immediately after treatment, the epithelium appeared uniformly blanched at all settings above 5 J/cm^2, with more pronounced gross whitening of epithelium at the highest doses (Fig. 4). At the 48-hour endoscopy, there was evidence in all animals of tissue injury within the ablation zones. As energy density increased, the depth of injury noted at the 48-hour endoscopy and on gross examination of the specimens also increased (Fig. 5A to D). At surgical harvest of the esophageal specimens, the adventitia was normal in the 3 lowest energy density groups (5, 8, and 10 J/cm^2) and there was no edema. The 12 J/cm^2 group had mild edema of the esophageal wall, corresponding in linear location to the 3 endoluminal ablation zones. In the 15 and 20 J/cm^2 groups of animals, there was moderate esophageal edema and induration but no evidence of transmural thermal injury (i.e., no coagulation of adventitia). In one animal in this group (20 J/cm^2), there was a small reactive effusion that was limited to the periesophageal space.

The lowest energy dose (5 J/cm^2) resulted in the full-thickness epithelial removal of 63.3% of the ablation zone surface area and thinned the remaining epithelium, most commonly to one to two remaining basal cell layers. Energy density settings of 8 J/cm^2 and higher resulted in complete elimination (100%) of epithelium in all specimens (Fig. 6).

There was a histologically observable relationship between energy density and maximum ablation depth, with the lowest energy density settings causing the most limited and superficial injury. At 5 and 8 J/cm^2, thermal injury was limited to the epithelium and the lamina propria, with complete sparing of the muscularis mucosae (Fig. 6). At 10 J/cm^2, the injury extended to the muscularis mucosae but spared the submucosa. At 12 J/cm^2, there was lymphocytic infiltration of the most superficial portion of the submucosa but minimal thermal injury. At the highest settings, 15 and 20 J/cm^2, there was evidence of muscularis propria injury, together with significant lymphocytic infiltrate into the completely ablated submucosa, supporting the surgical findings at harvest in these groups.

Phase IV

Three patients (3 men, age 55-70 years) were enrolled, each of whom had adenocarcinoma of the GEJ. All procedures were performed with the patients under conscious sedation (midazolam, mean 7 mg; fentanyl, mean 158 μg). RF energy delivery time for each ablation zone was less than 1 second. Total procedure room time used for each patient was 60, 26, and 27 minutes, respectively.

Endoscopy immediately after ablation revealed uniform, circumferential ablation zones in Patients 002 and 003 (Fig. 7). In Patient 001, however, tumor-related esophageal dilatation prevented adequate contact of the balloon electrode with the entire inner circumference of the esophagus. Therefore, only 50% of the circumference of the esophagus in this patient appeared to have been treated on postablation endoscopy, an observation corroborated by the histologic findings.

There were no acute complications, specifically, no bleeding, mucosal injury, or perforation, nor was there any device malfunction. One patient (Patient 003) treated at the 12 J/cm^2 setting had mild esophageal discomfort (described as "spasm") 4 hours after treatment. This was relieved with an orally administered mixture of antacid and lidocaine. None of the other patients reported chest pain, dysphagia, fever, or abdominal pain. At esophagectomy, the surgeon reported no evidence of pleural effusion, esophageal edema, perforation, or adventitial injury in any patient.

Histologic examination revealed that, for all specimens, the depth of ablation was the lamina propria or the muscularis mucosae; necrosis beyond the

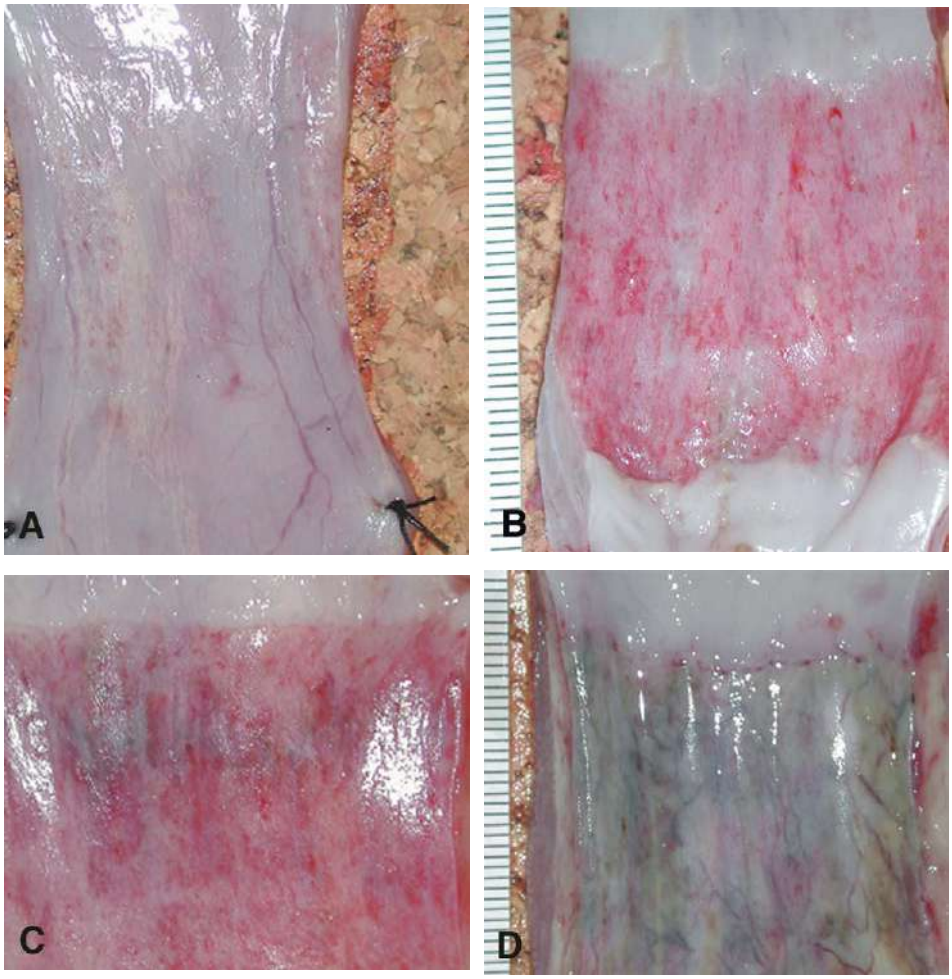

Figure 5. Gross esophageal specimens (Phase III), demonstrating the visible dose-response of increasing energy density. **A,** 5 J/cm^2. **B,** 10 J/cm^2. **C,** 12 J/cm^2. **D,** 20 J/cm^2.

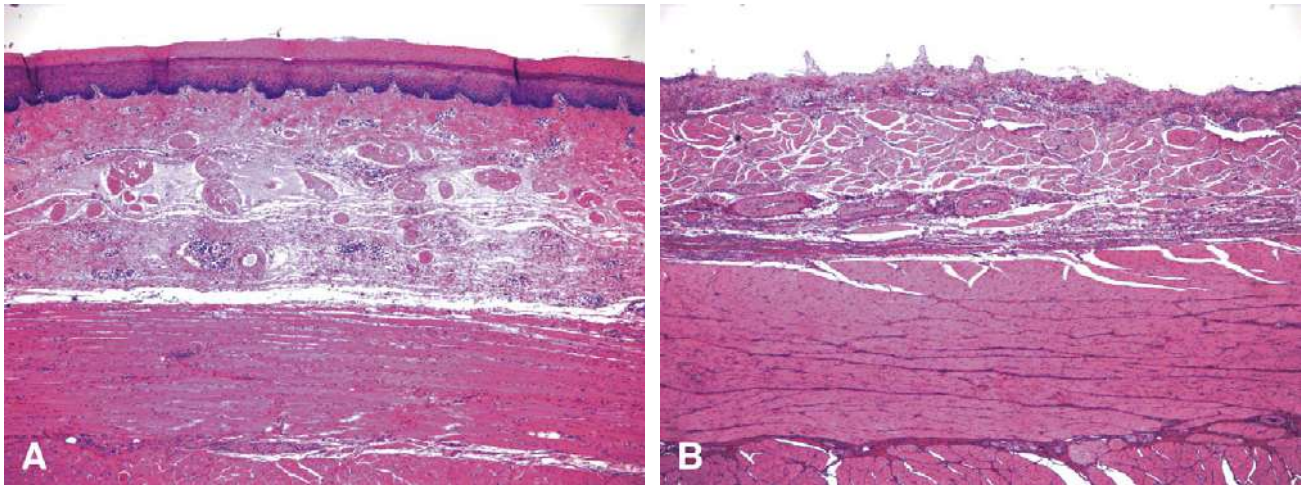

Figure 6. A, Photomicrograph of porcine nonablated esophagus (H&E, orig. mag. ×40). **B,** Photomicrograph of porcine esophagus at 48 hours after ablation with 5 J/cm^2, showing absence of epithelium with intact lamina propria and muscularis mucosae (H&E, orig. mag. ×40).

Table 1. Summary of phase IV results

Patient	Total ablation zones	Tumor-related esophageal dilatation	Adventitial injury noted at surgery	Energy density treated region (J/cm^2)	Epithelial ablation (% surface area)	Histologic ablation depth
001	3	Yes	No	10	50	LP/MM
				10	50	LP/MM
				10	50	LP/MM
002	2	No	No	10	75	LP/MM
				12	75	MM
003	2	No	No	10	95	LP/MM
				12	95	MM

LP, Lamina propria; *MM*, muscularis mucosae.

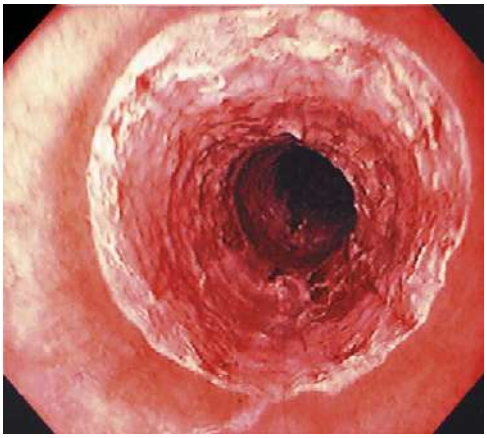

Figure 7. Endoscopic view (Phase IV) showing acute appearance of ablation zone in human esophagus (12 J/cm^2).

muscularis mucosae was not present, and the submucosa and the muscularis propria appeared viable in all cases (Table 1). In most sections, intact submucosal glands were identified, further confirming the absence of significant injury to the submucosa.

The percentage of mucosal ablation ranged from 50% (Patient 001, because of poor contact) to 75% (Patient 002) to 95% (Patient 003). Except in Patient 001, residual mucosa was in the form of small islands, with severe injury, the fate of which could not be determined. These findings suggest that energy densities of both 10 and 12 J/cm^2 are adequate to fully ablate the epithelium and that any nonablation was caused by inadequate electrode contact in specific areas.

DISCUSSION

A number of endoluminal techniques for the ablation of IM have been studied. The majority use hand-held, hand-aimed ablative devices, such as argon plasma coagulation, multipolar electrocoagulation, and laser photoablation. Thus, they place the burden of positioning and aiming the device, as well as the determination of the dose of ablative energy, upon the endoscopist. The most commonly used treatment end point is a visible change in the color of the tissue or "coagulation." Although there are selected reports of successful, durable elimination of IM by using these techniques, most include occurrences of excessively deep ablation (with stricture formation) and irregular ablation (resulting in residual or buried glands).[9]

Effective and safe endoluminal ablation of esophageal epithelium, whether squamous, as in the present study, or IM in patients with Barrett's esophagus, requires a uniform delivery mechanism and extremely precise control of ablation depth. These objectives are difficult and perhaps impossible to consistently achieve with existing ablative methods. The present study evaluated a balloon-based bipolar electrode and RF generator designed to overcome the shortcomings of current endoscopic ablation techniques. To achieve uniform ablation, the balloon-based device temporarily flattens the esophageal folds and allows for application of a standardized pressure against the esophageal wall. To control ablation depth, the design incorporates an array of closely spaced bipolar electrode pairs. The narrow spacing of these electrodes, as assessed by finite element modeling and bench experimentation, limits the depth of RF heating. Finite element analysis is a technique for mapping electrical field and heating characteristics. Lastly, it is essential that an endoscopist not be required to rely on visual evidence of heat-related changes in the epithelium as the end point for ablation. An RF system, such as that evaluated in this study, must be automated and capable of delivering a precise and repeatable amount of energy to each unit of surface area (J/cm^2) to avoid unintended deep tissue injury. To illustrate this concept, the delivery of the proper amount of RF energy (J/cm^2) to a 3-cm-long circumferential segment of esophagus takes approximately

800 milliseconds. Varying this time exposure by even 20% could result in excessively deep ablation and subsequent stricture formation. Thus, automation is mandatory.

The current study evaluated a balloon-based bipolar RF electrode system in a multiphased manner, transitioning from the porcine to the human esophagus. The study sought to determine the technical feasibility, tolerance, ablation depth, completeness of surface ablation, and stricture formation rate related to the procedure. Phase I, an acute feasibility study in the porcine esophagus, determined that the esophageal epithelium can be ablated completely with energy density settings of 9.7 J/cm^2 and higher.

Phase II, a longer duration study of the porcine esophagus, assessed the relationship of energy density and stricture formation at 2 and 4 weeks. Low energy density settings (9.7 and 10.6 J/cm^2) resulted in no stricture formation and no submucosal injury, whereas higher settings (>22 J/cm^2) resulted in stricture formation and submucosal injury in all cases. The frequency and the severity of stricture formation were directly related to the energy density dose administered but not to the power.

Phase III, a long-term study of the porcine esophagus, was designed to determine the completeness of epithelial ablation and the depth of ablation, as determined histologically, for a broad range of energy densities (5-20 J/cm^2). Settings of 8 J/cm^2 and higher ablated all treated epithelium surface. Histologic ablation depth results corroborated observations made in Phase II, namely that low energy settings (5-10 J/cm^2) did not cause injury to the submucosa.

Phase IV was a subacute evaluation of the procedure in human esophagus 24 to 48 hours before esophagectomy. Energy densities of 10 and 12 J/cm^2 were selected, because these settings uniformly resulted in ablation to the level of the muscularis mucosae and the superficial submucosa in Phase III, a depth believed by us to be optimal for ablating IM. In the human esophagus, these settings resulted in complete ablation of the squamous epithelium (provided there was good contact between the electrode and the target tissue) that did not penetrate deeper than the muscularis mucosae. The latter was considered by us to be the most favorable feature of the balloon-based bipolar electrode RF ablation technique.

Although the depth of ablation appears fairly uniform, the completeness of surface ablation observed in Phase IV deserves further study. Technical issues relating to sizing of the esophageal lumen and proper fit of the balloon electrode are clearly important, as evidenced by the incomplete ablation in Patient 001 because of incomplete electrode contact. With experience, the degree of ablation was as high as 95% (Patient 003) and the residual epithelium was severely injured. A second immediate application of energy (i.e., 10 J/cm^2 delivered twice) may also serve, in future studies, to eliminate any residual epithelium.

One disadvantage, inherent to all phases of the study, was the use of squamous epithelium as a surrogate for IM. Although the thickness of squamous epithelium and non-dysplastic IM do not differ significantly, according to Ackroyd et al.,[10] it is possible that IM is more resistant to RF ablation, given its higher content of both intra- and extracellular mucin. If so, a slightly higher energy density will be necessary to fully ablate IM in future human trials.

In conclusion, this study demonstrated that complete ablation of esophageal epithelium is possible with the balloon-based bipolar electrode, while avoiding injury to the submucosa. It is important that ablation techniques preserve the muscularis mucosae, because this assures preservation of the submucosa. The submucosal gland ductal epithelium may play a role in repopulation of squamous mucosa in this porcine model, as well as the replacement of ablated IM with neosquamous epithelium in humans, just as epidermal adnexal ductal epithelium repopulates the epidermis after a split-thickness skin graft is harvested.

In our opinion, the key advantages of our balloon-based system are its ease of use, the ability to create a circumferential ablation zone in less than 1 second, the automated nature of the energy delivery, which mitigates operator variability, and the relative absence of significant post-treatment discomfort compared with other ablative techniques. Most importantly, however, ablation depth is uniform, given the control of energy density afforded by the marriage of a balloon and a bipolar electrode array. With experience and the further acquisition of data regarding energy dosing and electrode fit, near-total or even 100% ablation of epithelium should be achievable. The safety and the dosimetry data obtained in the present multiphase trial has permitted the design and the commencement of multiple human clinical trials in which this ablative technique is being evaluated in patients with IM, with and without dysplasia.

DISCLOSURE

Robert A. Ganz, MD, holds an equity position in the company, BARRx, Inc., that sponsored this clinical study. David S. Utley, MD, is an employee of the sponsoring company. Roger A. Stern, PhD, and Jerome Jackson are consultants to the sponsoring company.

Preclinical work was performed at two animal research facilities: HealthPartners Research Foundation, Minneapolis, Minnesota, and Lychron, LLC, Mountain View, California.

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CASE STUDY

Palliation of patients with malignant gastroduodenal obstruction with self-expanding metallic stents: the treatment of choice?

Andrew P. Holt, MBChB, MRCP, Minesh Patel, MBChB, MRCP, Mohammed M. Ahmed, MBChB, BSc, MD, FRCP

Background: **Gastroduodenal obstruction is a common preterminal event for patients with gastric and pancreatic cancer who often undergo palliative surgical bypass. Endoscopic palliation with self-expanding metallic stents has emerged as a safe and an effective alternative to surgery, but experience with the technique remains limited.**
Methods: **Twenty-eight patients hospitalized with GI obstruction because of incurable gastric or pancreatic cancer were recruited for a prospective study of palliation with self-expanding metallic stents. Complications and clinical outcomes were assessed.**
Observations: **Stent insertion was technically successful in 26 patients. Thereafter, 24 patients resumed an adequate liquid or semisolid diet. Stent insertion facilitated hospital discharge for 20 patients. Occlusion of the stent because of tumor ingrowth occurred in 3 patients, but there was no complication related to stent insertion or the stent itself.**
Conclusions: **Endoscopic placement of a self-expanding metallic stent is a simple, effective means of palliation for patients with malignant gastroduodenal obstruction.**

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Current affiliations: Liver Transplant and Hepato-biliary Unit, Queen Elizabeth Hospital, Birmingham, United Kingdom, Department of Gastroenterology, Good Hope Hospital, Sutton Coldfield, United Kingdom.

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Reprint requests: Dr. Mohammed M. Ahmed, Department of Gastroenterology, Good Hope Hospital, Rectory Rd., Sutton Coldfield, B75 7RR, UK.

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The terminal stages of pancreatic and gastric cancer often are dominated by symptoms of gastroduodenal obstruction. Palliative treatment of this distressing condition, characterized by hyperemesis, dehydration, and starvation, is difficult. Laparoscopic gastroenterostomy is useful but has a high morbidity, and its effectiveness often is limited because of the poor physical condition of the patient.[1-3] Self-expanding metal stents (SEMS), inserted under endoscopic and fluoroscopic guidance, have been used with success in these patients, providing simple, safe, and effective palliation. A 4-year, single-center experience with the use of SEMS to palliate patients hospitalized with gastroduodenal obstruction because of inoperable gastric and pancreatic cancer is reported.

PATIENTS AND METHODS

Twenty-eight patients were hospitalized with unresectable gastric or pancreatic cancer and symptoms of gastroduodenal obstruction. Written informed consent was obtained from patients for participation in a prospective study of palliative gastroduodenal stent insertion, and a consensus for the inclusion of each patient was