Argon Plasma Coagulation and the Future Applications for Dual-Mode Endoscopic Probes

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Argon plasma coagulation (APC) is a thermoablative technique increasingly being used in endoscopy. Since its introduction, the flexible APC probe has been employed by endoscopists throughout the world. APC has helped change the endoscopic management of many gastrointestinal (GI) diseases, including hemorrhagic proctitis, watermelon stomach, bleeding peptic ulcer, and colonic varices. Endoscopists and surgeons are creatively combining standard and new electrosurgical techniques with APC. For instance, APC used in combination with piecemeal polypectomy, endoscopic mucosal resection, balloon dilatation for strictures, and plasma welding of bleeding vessels after sclerotherapy injection are among the recent innovative techniques reported. Other emerging innovations using APC that are being considered include endoscopic en bloc resection of mucosal and submucosal tumors of the GI tract, endoscopic mucosal resection supplemented with APC for high-grade dysplasia and early GI cancers, endoscopic repair of anastomotic strictures, and welding GI fistula tracts. As such, endoscopists require more efficient and cost-effective multifunctional thermoablative probes. This review discusses the development and the potential application of dual-mode plasma endoscopic probes in fulfilling these emerging needs.

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Hemostasis and tissue destruction are of critical importance when removing abnormal tissue during therapeutic endoscopy. Papp described 3 modes of high-frequency electrocoagulation during surgical procedures: monopolar, bipolar, and fulguration. Monopolar and bipolar electrocoagulation...
Argon Plasma Coagulation continued

are the 2 primary modes of high frequency energy used today during endoscopic therapy. In the monopolar mode, the active electrode is in direct and permanent contact with the patient via an electrode or plate used to collect current over a large area to prevent tissue burns. In the bipolar mode, a pair of active electrodes is attached to the generator, and is connected to the jaws of the forceps, and the tissue between the jaws is coagulated.

The development of a plasma scalpel was introduced in Western medicine 30 years ago. Argon plasma coagulation (APC) is a monopolar thermoablative method of electrocoagulation that has been widely used in general surgery for the last 20 years, and in the specialized fields of laparoscopy, thoracoscopy, and gynecological surgery for more than 10 years. Since Canady’s development of the flexible catheter that allowed the use of APC in endoscopy, numerous applications of APC have been demonstrated in therapeutic endoscopy.

APC has been used to treat many gastrointestinal (GI) diseases (ie, radiation proctitis, Barrett’s esophagus, gastric antral vascular ectasia [GAVE], and treatment of arteriovenous malformations [AVM] throughout the GI tract). Recently, there have been reports of using APC as an adjunct in the endoscopic management of sessile polyps during mucosal resection of neoplastic tissue, and during the management of GI bleeding. However, an optimal single-use device for these complex procedures has not been available before now.

At the present time, 3 single-mode flexible endoscopic APC probes are available in the United States (CANADY TECHNOLOGY, Hampton, VA; CONMED Corporation, Utica, NY; and ERBE Elektromedizin GmbH, Tubingen, Germany). The single-mode flexible endoscopic probes are composed of a handle (proximal connection to the connecting cable), Teflon tubing, a fixed inner tungsten wire within the tube, and with or without a ceramic nozzle tip at the end of the tube. APC probes are available in 3 diameters: 2.3 mm, 3.2 mm, and 1.5 mm.

The APC probes are attached to a high-frequency monopolar electrosurgical generator that delivers an output ranging between 5000 and 6500 V. Gas flow and power range are adjusted between 1.0 L/min to 7 L/min and 0 to 155 W, respectively. APC is activated by a foot switch that synchronizes current with the transfer of an ionized plasma gas across the field to the target tissue (Figure 1).

Dual-mode flexible endoscopic plasma probes are composed of a handle, Teflon tubing, a movable tungsten wire within the tube, and sometimes a ceramic nozzle tip depending on the application. Dual-mode plasma probes are developed to be multifunctional and consist of an APC polypectomy snare, APC sclerosing needle, APC endoscopic mucosal resector, and APC biopsy forceps. The probes allow the endoscopist to combine standard monopolar electrocautery with plasma for thermocoagulation in a polypectomy snare, varix injection, mucosal resection, or biopsy of diminutive polyps as required (Figures 2-7).

Figure 1. Single-mode probe.

Figure 2. A. Handles for dual-mode probes: Canady plasma polypectomy snare, Canady plasma biopsy forceps, Canady plasma sclerosing needle B. Canady plasma dual-mode probes.
What Is Plasma?
Plasma is not a human invention. It is the most common form of matter in the universe (Figure 8). Plasma is considered the fourth state of matter and consists of a collection of freely moving electrically charged particles of electrons and radicals. However, to appreciate the configuration of this fourth state, there must be a basic understanding of the other 3 states of matter: solid, liquid, and gaseous states.

The first state of matter is the solid state. It is configured in a chemical structure of strong, fixed bonds between hydrogen and oxygen molecules. By gradual increases in temperature, the structural bonds between these molecules begin to weaken, separate, and finally free hydrogen and oxygen molecules. These molecular changes cause the transformation of solids (ice) into the second state of matter, the liquid state (water); then the third state, the gaseous state (steam); and finally, the fourth state of matter, the plasma state (Figure 9). Known plasma gases in the earth’s atmosphere are He (helium), Xe (xenon), Ar (argon), Ne (neon), Kr (krypton), and Ra (radon). These are shown in Table 1.

Electrical conduction of the gas occurs when additional energy is supplied, despite the preservation of electrical neutrality. This process occurs when the electrons gain sufficient energy to separate from the gas atoms or molecules. Plasmas are functionally different depending on whether or not they are in a thermal equilibrium. Thermal equilibrium plasmas are typically present in stars, in contrast to nonequilibrium plasmas that do not produce heat overload (low-temperature plasmas).

Low-temperature plasmas are ubiquitous throughout our daily lives. This technology is indispensable in modern material science, microelectronics, nanotechnology, and semiconductor technology. Low-temperature plasma (cold plasma) technology has vast and remarkable biomedical applications. This plasma technology will replace conventional modes of medical treatment in surgery and medicine.

Characteristics of Argon Plasma Coagulation in Clinical Medicine
APC has been demonstrated to be effective in the coagulation of blood vessels and human tissue during surgery. A form of cold plasma technology that is superior to conventional modes of electrosurgery because tissue destruction is greatly reduced, APC is a technological advance compared with radio-frequency (RF) electrosurgery.

APC uses a beam of high purity (99.999%) ionized argon gas to conduct current to the tissue. The argon stream is colorless, odorless, and conducts electrical current to the tissue and vessel walls. Argon, one of the safest gases known, is a noble, inert gas, which will not react with other elements. It will not support combustion and it clears the body in 1 respiratory cycle.

APC functions in a noncontact manner. The electrical current is initiated only when the tip of the handpiece or

When argon plasma coagulation, a form of cold plasma technology, is used in endoscopic surgery, tissue destruction is greatly reduced.

<table>
<thead>
<tr>
<th>Table 1 Noble Gases</th>
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<tr>
<td><strong>He</strong></td>
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<tr>
<td>- From Greek helios for “sun”</td>
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<tr>
<td>- Second most abundant gas in the known universe</td>
</tr>
<tr>
<td>- First noble gas to be discovered by Janssen and Lockyear in 1868</td>
</tr>
<tr>
<td><strong>Xe</strong></td>
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<tr>
<td>- From Greek xenos for “strange”</td>
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<tr>
<td>- Rarest of the stable noble gases in the air</td>
</tr>
<tr>
<td>- Widely used commercially in headlights and lightbulbs</td>
</tr>
<tr>
<td><strong>Ar</strong></td>
</tr>
<tr>
<td>- From Greek argos for “inactive”</td>
</tr>
<tr>
<td>- Third most abundant gas in the earth’s atmosphere</td>
</tr>
<tr>
<td><strong>Ne</strong></td>
</tr>
<tr>
<td>- From Greek neos for “new”</td>
</tr>
<tr>
<td>- Fourth most abundant element in known universe</td>
</tr>
<tr>
<td><strong>Kr</strong></td>
</tr>
<tr>
<td>- From Greek kryptos for “hidden”</td>
</tr>
<tr>
<td>- Sixth in abundance in the Earth’s atmosphere</td>
</tr>
<tr>
<td>- Used in various kinds of lights from flashlights to airport runway lights</td>
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<tr>
<td><strong>Rn</strong></td>
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<tr>
<td>- Radioactive noble gas</td>
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<tr>
<td>- Potential health hazard</td>
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</table>
Table 2

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<tr>
<th>Tissue</th>
<th>Depth of Injury</th>
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<tr>
<td>Kidney</td>
<td>2-4 mm</td>
</tr>
<tr>
<td>Skin flap (Breast tissue)</td>
<td>0.23-0.78 mm</td>
</tr>
<tr>
<td>Stomach</td>
<td>1.0-1.55 mm</td>
</tr>
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Data from Teimourian B et al.17

Table 3

<table>
<thead>
<tr>
<th>Temperature (°C)</th>
<th>Physiological Process</th>
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</thead>
<tbody>
<tr>
<td>Argon Plasma Coagulation</td>
<td>100-110</td>
</tr>
<tr>
<td>Electrocautery</td>
<td>200</td>
</tr>
<tr>
<td>Laser</td>
<td>300-400</td>
</tr>
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<td></td>
<td>500</td>
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Argon plasma coagulation catheter is within 1 cm of the target tissue and produces a homogenous 1 mm to 2 mm well-delineated eschar. This is more effective than standard electrocautery because APC distributes the arc tunnels in a more even pattern, resulting in a uniform depth of penetration to the target tissue. Depth of tissue injury ranges between 0.23 mm and 4 mm (Table 2). Tissue coagulation depths with APC are dependent on the duration of application, power generator output, and distance from the target tissue. The eschar remains firmly attached to the tissue, in contrast to other coagulation modalities where there is an overlying charred layer of coagulated blood. Argon gas is used in this system because it will not oxidize the electrode. Because of the cooling effect of argon gas and because no further conduction of radio-frequency energy into tissue occurs once an eschar forms, the temperature in the tissue being cauterized never exceeds 110°F. This process is thought to minimize tissue destruction and necrosis. In contrast to APC, electrosurgery and lasers use electrical current or light energy to localize heat and thereby achieve hemostasis. Electrocautery and laser technology function by temperature-dependent mechanisms. Tissue temperature increases to 200°F with electrocautery. This results in the boiling of cellular water, the subsequent rupture of cell membranes, and photoevaporation of tissue. With lasers, tissue temperature rises even higher to 300°F to 400°F, at which point carbonization occurs, and 500°F, when combustion occurs (Table 3). This heat is distributed in an uneven fashion and may lead to the damage of adjacent tissue and an unknown depth of tissue injury.

Clinical Application of Dual-Mode Plasma Endoscopic Probes

Large Sessile Polyps

The standard treatment for colorectal polyps is endoscopic polypectomy snare removal. Over the last 2 decades the endoscopic approach of even large sessile adenomas has been established as an alternate option to surgery. The endoscopic technique for large sessile polyps is piecemeal resection; however, recurrence is among the risks.18-26 Laser photoablation27 and hot biopsy forceps28 have been used to eradicate remnant adenomatous tissue after piecemeal polypectomy in an attempt to completely ablate any remaining neoplastic tissue. Drawbacks to lasers are their cost and the potential of full-thickness injury and perforation. Hot biopsy forceps are inadequate to treat large mucosal areas and the depth of tissue injury can be excessive.

![Figure 3. A. 4-cm sessile polyp of transverse colon; B. Polypectomy site after successful plasma resection with Canady polypectomy snare.](image-url)
Figure 4. A. Plasma polypectomy snare around polyp; B and C. Gastric polyp removed with plasma polypectomy snare; D. Residual site after plasma ablation.

Figure 5. A. Circumferential lesion of duodenum; B. Piecemeal resection of the duodenal lesion with plasma polypectomy snare; C. Plasma ablation of the duodenal lesion; D. Residual site after plasma ablation and piecemeal resection.
Argon plasma coagulation is a monopolar thermoablative technique that is suitable to treat large mucosal areas with a predictable depth of tissue injury. Recently, adjunct use of APC after piecemeal polyp resection has been reported to be safe and efficacious. Wahab and colleagues reported that the combination of polypectomy snare resection and APC was effective and safe in the ablation of residual adenomatous tissue throughout the GI tract. Eradication of residual adenomatous tissue after polypectomy with adjunct APC was subsequently reported by Zlatanic, Regula, and Brooker and colleagues. Despite the success of this combination therapy, the use of 2 or separate probes remains costly and a single-use device is intuitively attractive.

Flat Polyps
Early endoscopic treatment of diminutive polyps is not standardized among gastroenterologists. The routine approach to flat small colorectal polyps has been cold and hot forceps, but polypectomy technique is not consistent. A recent survey by the American College of Gastroenterology (ACG) revealed that the method of polypectomy for small polyps (1 to 3 mm) was cold forceps (50.3%) and hot forceps (33.3%). The major disadvantage to the hot and cold biopsy techniques is the residual remnant of the polyp after the procedure. Larger polyps increase the incidence of residual polyp when using cold forceps. Piecemeal resection is often required with the cold forceps. In 16% to 18% of polypectomies using hot biopsy forceps, residual neoplastic tissue was identified in the central portion of the polyp site.

Argon has proven to be safe and efficacious in colon polyp eradication. Wahab and colleagues described the coagulation of multiple gastric polyps. Garcia and colleagues reported the first uncontrolled trial of APC ablation in 22 consecutive patients with colorectal flat or sessile adenomas. In previous reported results of adjunct APC, the authors treated only large sessile polyps.
In Garcia’s report, 11 patients were treated with piecemeal polypectomy and supplemented with APC ablation of residual adenomatous tissue. The other 11 patients with flat adenomas were only treated with APC. The rectum (50%) and cecum (23%) were the most frequent location of the adenomas, with adenomatous tissue size ranging from 20 mm to 40 mm. Complete ablation was obtained in 90.9%, with a recurrence rate of 20% (4) after a mean follow-up period of 16.3 months. Recurrence was not related to previous piecemeal polypectomy. There were no major complications.

Radiation Proctitis

Radiation proctitis is a well-described complication after pelvic radiation. The incidence of chronic radiation proctitis lies in the range between 2% to 20%, and 30% of patients with acute radiation-induced bowel injury develop this condition. Connective tissue fibrosis, obliterative endarteritis with tissue ischemia, and neovascular mucosal lesions are well-described histopathological changes after radiation injury. Early clinical symptoms include tenesmus, and diarrhea with resolution in 2 to 6 months. However, chronic progression of radiation injury results in late complications, which include ulcerations, chronic bleeding, strictures, and fistula formations.

Various nonsurgical treatment modalities have been used with different levels of success. These modalities include topical treatment with formalin solution, sulfasalazine, short-chain fatty acids, corticosteroids, sucralfate enemas, and 5-aminosalicylic acid (5-ASA). Surgical approaches have resulted in significant mortality and morbidity. Endoscopic methods using neodymium:yttrium aluminum garnet (Nd:YAG) laser, and argon lasers, or bipolar electrocoagulation have been used successfully to arrest rectal bleeding.

As a treatment for radiation proctitis, APC was quite effective after failed therapy by Nd:YAG laser, electrocoagulation, heater probe, and endoscopic formalin therapy.

Many authors have reported favorable outcomes in the use of APC for the treatment of radiation proctitis. In the above-mentioned case studies, 210 patients were treated for radiation proctitis by APC. Power setting and gas flow ranged between 40 to 70 W and 0.6 to 3.0 L/min, respectively. Outcome data revealed significant symptomatic relief resulting in decreased transfusion dependency, and improvement in anemia after 2 treatment sessions. APC was also quite effective after failed therapy by Nd:YAG laser, electrocoagulation, heater probe, and endoscopic formalin therapy.

Complications included short-term symptoms like tenesmus, anisimus, and abdominal distension. Long-term complications such as rectal strictures requiring dilation, and rectovaginal fistula were documented in this series. Two patients with a myelodysplastic syndrome developed gram-negative bacteremia. Both patients were regarded as immunocompromised and responded to an appropriate antibiotic regimen. Overall, APC appears to be a safe, effective, coagulative modality for hemorrhagic proctitis and a low-cost alternative to laser therapy.
Vascular Ectasias

GAVE or watermelon stomach is an uncommon but well-described cause of occult GI bleeding. The majority of patients present with iron deficiency anemia. Rider and colleagues were the first to describe this disorder. In 1979, Wheeler and colleagues reported a bleeding vascular lesion of the antrum and in 1984, Jabbari and colleagues termed the phenomenon “watermelon stomach.” He described the endoscopic appearance as longitudinal column vessels traversing the antrum and going across the pylorus. Gostout and colleagues reported that 89% of cases with vascular ectasia present with stripes of ecstatic vascular tissue, and the remaining 11% have diffuse scattered lesions.

Various modalities for treating watermelon stomach are used. In 1979, Wheeler and colleagues believed that partial gastrectomy was the procedure of choice. Several endoscopic treatment options (eg, Nd:YAG laser, bipolar electrocoagulation, sclerotherapy, elastic band ligation) have proven to be effective.

Initial reports stated that APC was effective in the treatment of watermelon stomach. Further non-comparative studies revealed that after 2 to 3 sessions, APC mini-
mized transfusion requirements and significantly improved hemoglobin levels. GAVE was resolved in all patients. A 40% recurrence rate was observed after a mean follow-up of 20 months, but APC was still effective in the recurrence group. Overall APC is effective in controlling bleeding due to watermelon stomach in the majority of patients with low complication rates.

APC has been equally effective in the treatment of AVM of the stomach, small bowel, and colon.16 Despite the success described in this report, there was a 8% recurrence rate over a 6-month follow-up period. Submucosal argon gas and cecal perforation at the treatment site has been reported.15,83 Perhaps submucosal saline solution cushion should be implemented prior to APC therapy to prevent deep tissue injury. Norton and colleagues demonstrated this technique in a porcine model.84 An innovative technique of combining 1% polidocanol and APC to ablate gastric AVM in a patient with Rendu-Osler-Weber disease has been reported.85

Bleeding Peptic Ulcer, Recurrent Esophageal Varices
Upper GI bleeding has a prevalence of approximately 170 cases per 100,000 per year.86 Peptic ulcer disease represents 50% to 70% of acute nonvariceal upper GI bleeding.87,88 Mortality rate89,90 (3.5% to 7%) has remained the same despite innovative technology and advanced training of gastroenterologists.

Recent analysis by the Nonvariceal Upper GI Bleeding Consensus Conference Group91 recommended that no single method of endoscopic thermal coaptive therapy is superior to another. The consensus group reported that individual randomized studies showed no difference in rebleeding rates, surgery, and mortality among thermoablative therapy with heater probe, multipolar electrocoagulation, or Nd:YAG laser when compared with injection therapy.

In a randomized prospective trial, Cipolletta and colleagues92 reported the comparison of APC with heater probe in 41 patients with bleeding peptic ulcers, initial rate of hemostasis, recurrent bleeding, 30-day mortality rate, and emergency surgery. Argon plasma coagulation provided faster hemostasis. However, because of the small sample size, the statistical power of the study was insufficient to conclude a significant P value. In a separate randomized controlled trial, Cipoletta and colleagues93 evaluated APC use in the prevention of recurrent esophageal varices after endoscopic band ligation.

An interim report showed that patients receiving APC exhibited a lower recurrence rate. The sample size, however, was small again, leaving open the question of an adequate statistical evaluation. Nakamura and colleagues94 evaluated a randomized group of patients (n = 60) to endoscopic variceal ligation (EVL), or EVL followed by APC. Recurrence free rate of variceal formation was significantly higher than the patients receiving EVL monotherapy (74.2% vs 49.6%).

Post-treatment fever was significantly greater in the combination group versus monotherapy group (63.3% vs 33.3%). A prospective randomized trial was performed by Chau and colleagues95 comparing patients with actively bleeding ulcers, ulcers with clots, and ulcers with nonbleeding visible vessels. Patients were randomly assigned to epinephrine injection plus heat probe coagulation or epinephrine injection plus APC. They concluded that there was no difference between injection plus heater probe versus epinephrine plus APC.

APC Ablation of Barrett’s Esophagus
Endoscopic thermoablation for Barrett’s epithelium still remains controversial. APC has also been used to treat Barrett’s esophagus. Multiple variables are involved to ascertain the success rate in the treatment of Barrett’s esophagus. For instance,
Argon Plasma Coagulation

continued

Barrett’s segment length, antisecretory regimen used, APC setting, treatment pattern, and surveillance post-treatment all may affect outcome. Van Laethem and colleagues reported a complete eradication of Barrett’s in 61%, whereas Byrne and colleagues reported a success rate of 59.2% using APC. However, microscopic foci of Barrett’s epithelium was identified in up to 50% of the patients.

Morino and colleagues reported an 87% complete macroscopic clearance, whereas 9% of the patients revealed microscopic foci after laparoscopic Nissen fundoplication followed by APC therapy. Variable data are published on the outcome of APC in the treatment of Barrett’s esophagus with high-grade dysplasia or carcinoma in situ. Pereira-Lima and colleagues reported no microscopic recurrence of dysplasia or advancement of malignancy after 10.6 months of follow-up.

APC in Other GI Neoplasias

Combination of APC with other treatment modalities has proved to be a sufficient device for the treatment of GI malignancies. Wahab and colleagues reported using APC in various settings in concert with multiple devices. APC was used in combination with monopolar polypectomy snare in 34 patients who presented with esophageal or gastric cardia malignancies. Savory dilation presented with esophageal or gastric tomy snare in 34 patients who combination with monopolar polypectomy multiple devices. APC was used in combination with different hot biopsy forceps. Canady and colleagues reported using APC on 83 patients with malignant strictures of the esophagus and gastric cardia. APC also has been used for trimming of biliary and GI metallic stents.

Summary

Use of APC via flexible endoscopes is well established throughout the world. Published reports have demonstrated that APC is safe and effective in GAVE, radiation proctitis, angiodyplasia, ablation of colorectal polyps, ablation of residual tissue after polypectomy and mucosectomy, bleeding peptic ulcer and ulcers with high risk of rebleeding, eradication of Barrett’s esophagus, trimming of stents, and for use in opening obstructing GI malignancies.

The expanded use of APC is inevitable because of its ease in learning, mobile apparatus, and low cost. The introduction of dual-mode APC catheters will greatly expand the use of APC beyond its current use.

References


