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Argon plasma coagulation in the management of gastrointestinal hemorrhage

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INTRODUCTION

Argon plasma coagulation (APC) is a non-contact thermal method of hemostasis. It was introduced as an alternative to contact thermal coagulation (heater probe and bipolar cautery) and to existing non-contact technologies (primarily laser). The theoretical advantages of APC include its ease of application, speedy treatment of multiple lesions in the case of angiodysplasias or wide areas (the base of resected polyps or tumor bleeding), safety due to reduced depth of penetration, and lower cost compared with laser.

This topic will review APC, including how it is used and its efficacy. The general management of adult patients with upper and lower gastrointestinal bleeding, as well as a detailed discussion of angiodysplasia of the gastrointestinal tract are discussed elsewhere. (See "[Approach to acute upper gastrointestinal bleeding in adults](#)" and "[Approach to acute lower gastrointestinal bleeding in adults](#)" and "[Angiodysplasia of the gastrointestinal tract](#)".)

PRINCIPLES AND EQUIPMENT

Contrary to a common misconception, argon plasma coagulation (APC) is **not** a laser. This technology uses argon gas to deliver plasma of evenly distributed thermal energy to a field of tissue adjacent to the probe. A high voltage spark is delivered at the tip of the probe that ionizes the argon gas as it is sprayed from the probe tip in the direction of the target tissue. Argon gas

is non-flammable and inexpensive to refill. It is easily ionized by the 6000 volt peak energy delivered by the tungsten wire that terminates just proximal to the probe tip. This ionized gas or plasma then seeks a ground in the nearest tissue, delivering the thermal energy with a depth of penetration of roughly 2 to 3 mm. The plasma coagulates both linearly and tangentially. By delivering energy to all tissue near the probe tip, APC can be used to treat a lesion around a fold and not clearly in view or a lesion that cannot be positioned directly in front of the endoscope.

A similar technology has been used for many years by surgeons in the operating room, particularly during hepatic surgery, as a means of spray coagulation to control superficial, diffuse bleeding. In the early 1990s, special probes were developed to allow this technology to be applied to flexible endoscopy. The disposable probes are available with diameters of 1.5 mm, 2.3 mm (the most commonly used size), and 3.2 mm. The standard probes are 220 cm long ([picture 1](#)); 300 cm probes can be specially ordered for use during push enteroscopy.

In addition to the probe, the equipment consists of an electrosurgical generator that comes on a cart along with the argon plasma coagulator, a foot pedal, and two tanks of argon gas. Both the argon flow rate and the wattage delivered per pulse are easily adjusted using the control panel. Newer models of this cart include a water pump.

TECHNIQUE

Argon plasma coagulation (APC) is easy to perform and can generally be learned in a few proctored sessions. No special safety precautions are necessary for the operator.

When the endoscopist identifies a lesion suitable for APC, a grounding pad is placed on the patient's thigh or shoulder. The argon gas from one of the tanks is turned on and the generator and coagulator power is switched on. A flow rate (generally 0.8 to 1.0 L/min) of argon is selected. It is important to recognize that, although argon gas only flows through the probe in pulses when the foot pedal is applied, significant insufflation of the bowel lumen can occur with repeated applications unless the gas is suctioned periodically via the endoscope. Continuous suction is not required.

The power setting on the APC2 generator is adjusted based upon the location of the lesion. Lower settings, in the range of 20 to 30 watts, are used in thinner regions of the gastrointestinal tract, such as the colon and small bowel. Higher settings (30 to 40 watts) are used for the thicker-walled stomach and for tumor ablation. Depth of penetration during coagulation depends upon the wattage and the number of pulses at a particular location. Areas of previous

coagulation have greater impedance, so subsequent pulses favor adjacent uncoagulated tissue. However, deeper penetration may occur from extra pulses in the same area.

The electrosurgical generator allows several settings to be pre-programmed. The anatomic location can be selected (eg, right colon, stomach, etc), as well as the intended therapy (eg, soft coagulation, polypectomy, endoscopic mucosal resection). Each pre-programmed function has default power and delivery modes appropriate for the indication. In addition, the endoscopist may manually adjust the settings if desired. We strongly advise all endoscopists to familiarize themselves and their assistants with the use and adjustment of their electrosurgical generators prior to use.

Before use, the apparatus is tested by directing the probe to a special test target that fits into the grounding socket on the generator. Before inserting the probe into the biopsy channel of the endoscope, the operator presses the purge button on the coagulator to prime the probe with argon.

The probe is passed via the endoscope's accessory channel so that the blue tip hovers over the target tissue. A black stripe located a few centimeters proximal to the tip should be visible to ensure that the probe protrudes sufficiently. If the tip of the probe is too close to the endoscope it could result in damage to the scope. Generally, the ionized plasma will only reach tissue if it is fired less than 1 cm from the target. Since the efficiency of APC differs slightly among patients and in different locations within the bowel, we recommend calibrating the coagulator with the first pulse. This is done by intentionally firing a pulse when the probe is too far away from the tissue to deliver any coagulation. The endoscopist fires subsequent pulses while gradually moving the probe closer to the tissue until coagulation occurs. In this way, the endoscopist can identify the furthest possible distance at which APC can be performed for a particular target.

It is important not to fire too close to the target. If the probe touches the mucosa directly when firing, the coagulation is direct rather than via ionizing plasma and a deeper injury, similar to monopolar electrocautery, results. For this reason, we find the calibration technique described above to be particularly helpful in the right colon. In some cases, such as ablation of residual polyp tissue or tumor, deeper coagulation may be desirable. This can be achieved by applying longer periods of APC to a particular area, but care should still be exercised to avoid coming into direct contact with the tissue.

APC may be fired either in a continuous "forced" mode, in which the plasma is delivered as long as the foot pedal is depressed, or in a pulsed mode, in which very short bursts of APC are delivered. Specifically, the following three modes are available on the current VIO 300D/APC 2 system:

- Forced APC is the original continuous delivery mode.
- Pulsed APC fires intermittently and has two pulse speeds: Pulsed Effect 1 with half-second bursts and Pulsed Effect 2 with rapid bursts that occur 16 times per second. The pulsed mode is a particularly useful strategy when only very superficial treatment of an area is desired, as in coagulation of an angiodysplasia.
- Precise APC is a continuous delivery mode, but also offers plasma regulation so that the energy delivery adjusts to become more or less intense as tissue resistance changes. The Precise mode tends to be very homogenous and offers more control over the depth of penetration during APC delivery compared with the other modes.

The probe can be used to coagulate discrete lesions with isolated pulses or may be used to "paint" areas with multiple lesions (eg, in the treatment of gastric antral vascular ectasias or radiation proctopathy). Painting is performed either by dragging the endoscope with the probe in a fixed position or by swinging the probe by deflecting the endoscope tip in a pendulum fashion. Charring of the probe is generally less than is seen with contact thermal devices, but may occur when direct tissue contact is made. Occasionally, [glucagon](#) may be helpful to reduce bowel motility and facilitate treatment of multiple lesions.

Care should be taken to avoid excessive insufflation, particularly in the colon. While there is less smoke generated than with laser therapies, it can still obscure visualization. Intermittent suction serves to prevent over-insufflation while also clearing the field of view.

Superficial ulceration occurs following APC, which typically heals within two to three weeks. Despite theoretical safety advantages due to reduced depth of penetration, all of the complications that have been reported with other thermal hemostasis techniques can occur. (See '[Complications](#)' below.)

USES

The first series of clinical applications of argon plasma coagulation (APC) in gastrointestinal (GI) endoscopy was published in 1994 [1]. Forty-eight of the initial 189 applications were done to control bleeding, either from tumors or from a variety of other sites. While no specific data were provided to assess outcome for GI bleeding, the authors described the technique as successful and without complications. Their largely qualitative description cites facility in treating tangential lesions, lack of smoke, and safety as key advantages compared with other techniques.

Several centers have subsequently reported experience with this technique in the management of GI bleeding [1-8]. However, few randomized comparisons to other hemostasis techniques have been performed. A meta-analysis identified only two randomized trials (with a total of 121 patients) comparing APC with other endoscopic hemostasis interventions (heater probe and injection sclerotherapy) in the treatment of non-variceal upper gastrointestinal bleeding [9]. No significant differences were observed in either study.

A technology assessment report from the American Society for Gastrointestinal Endoscopy concluded that APC was best suited for hemostasis of diffuse superficial vascular lesions, such as gastric antral vascular ectasia syndrome and radiation induced proctopathy, but that there were insufficient comparative data to assess its performance relative to other modalities [10].

Angiodysplasia — The anatomy and superficial location of angiodysplasia make them well suited for APC treatment. Immediate hemostasis rates range from 85 to 100 percent in various reports [5,6,11-14] and treatment can result in long-term control of bleeding [11]. (See ["Angiodysplasia of the gastrointestinal tract"](#).)

Special considerations warrant comment regarding APC for angiodysplasia. Bowel motility can be problematic, particularly in the small bowel. As mentioned above, most authors find that the ease of tangential treatment and decreased smoke are advantages to APC compared with contact techniques ([picture 2](#)). A disadvantage is the inability to irrigate directly through the probe. APC does not work well if the targeted lesion is under water.

A number of recommendations can be made based upon clinical experience:

- Adjust wattage downward for targets with thinner walls.
- Calibrate the optimal distance to avoid undesired contact coagulation. (See ['Technique'](#) above.)
- Treat the center of the angiodysplasia; complete whitening of the area is not always needed and multiple pulses applied to the same tissue may result in unintentional deep penetration.
- Frequently suction gas to avoid over-insufflation, particularly in the colon.
- Avoid getting the probe tip wet. Press the purge button when this happens.
- Wash the lesion to identify the bleeding site, but realize that APC is difficult for lesions that are under a pool of water.

Watermelon stomach/GAVE syndrome — Serial treatments with APC can reduce transfusion requirements and raise hemoglobin in patients with gastric antral vascular ectasia (GAVE) syndrome [15,16]. In most series, the number of sessions required to reduce blood loss was lower than the number of sessions required in published series of treating watermelon stomach using laser and bipolar techniques [17-19]. Most patients required three to four sessions to achieve the desired clinical benefit. However, long-term follow-up data are limited.

Ulcers commonly occur following therapy, although they are rarely symptomatic. At least two weeks should be allowed between treatments to allow ulcers to heal ([picture 3](#)). We also typically place patients on [sucralfate](#) and proton pump inhibitor. Hyperplastic polyp formation following gastric APC has been described [20].

Radiation telangiectasias — A number of methods have been described for controlling bleeding in patients with radiation telangiectasias (also referred to as radiation proctopathy or radiation proctitis), including APC ([picture 4](#)) [21]. (See "[Radiation proctitis: Clinical manifestations, diagnosis, and management](#)".) In a systematic review, the American Society of Gastroenterology found that APC was effective in the treatment of rectal bleeding from radiation telangiectasias [22].

The efficacy of APC has been suggested in several case series and a small randomized trial [4,23-25]. One of the largest reports included 28 patients with persistent bleeding despite medical therapy [4]. The majority of patients had improvements in bleeding and anemia after a median of 2.9 sessions (range 1 to 8). All visible lesions were targeted at each session and follow-up procedures were scheduled in four-week intervals to allow the tissue to heal. The mean hemoglobin rose by 1.2 g/dL and by 1.9 g/dL among individuals presenting with anemia. Some patients experienced post-procedure rectal pain and cramps, but no major complications occurred. Other reports have demonstrated that APC may control bleeding even after unsuccessful treatment using other methods [23,24].

One study that included 50 patients examined the safety and efficacy of a single large-volume APC application for the treatment of chronic radiation proctitis [26]. APC was applied with the goal of ablating all visible telangiectasias during a single endoscopic procedure. Treatment was considered successful if there was no rectal bleeding or only minor, intermittent rectal bleeding following treatment. A single treatment session was successful in 34 patients (68 percent). Fourteen patients (28 percent) were successfully treated after a second session.

Special care is required to avoid spraying too close to the dentate line. 5-ASA suppositories and/or Cortifoam enemas are often used to help treat procedure-induced rectal ulcers, which

occur in more than one-half of patients but are usually asymptomatic [27]. Residual ulcers seen during a follow-up examination should be avoided during subsequent treatment.

A complete bowel lavage is probably safest before each procedure. A potential complication if this is not done is bowel explosion with perforation, presumably due to the accumulation of combustible colonic gas [28]. (See "[Bowel preparation before colonoscopy in adults](#)".)

Piecemeal polypectomy — APC has been used to coagulate the base of large sessile polyps, which can eliminate residual adenomatous tissue and can assist in the control of minor bleeding ([picture 5](#)) [7,29]. A randomized trial suggested that it may decrease recurrence following piecemeal resection of large (>1.5 cm) sessile adenomas that were considered to have been completely removed [30]. (See "[Endoscopic removal of large colon polyps](#)".)

Other methods, such as the use of the snare tip to apply soft coagulation current at the perimeter of laterally spreading lesions following piecemeal resection are commonly used and a large randomized trial is ongoing. The practice of using APC to ablate residual tissue bridges that cannot be removed with a snare during piecemeal resection has been largely supplanted by the newer technique of hot avulsion of the tissue. Hot avulsion is performed by grabbing the non-lifting residual tissue with hot biopsy forceps, tenting it with gentle traction, and applying a second of cutting current to remove the tissue [31]. (See "[Endoscopic removal of large colon polyps](#)", section on 'Treatment of residual adenoma'.)

Tumor debulking and bleeding — APC is widely used as an alternative to laser and bipolar cautery to debulk tumors, to treat tumor ingrowth in stents, and to control generalized bleeding from tumors, although no large series have been published [5,32-35]. Most of the experience with APC has been to debulk tumors and thereby relieve obstruction or dysphagia. APC can also be used to temporarily manage bleeding, although it often does not have long-term benefits. It has an advantage compared with other methods to temporarily control bleeding since it can rapidly coagulate a relatively wide area. However, hemostatic nanopowder is now available and can also be used to control bleeding over a large area. (See "[Overview of the treatment of bleeding peptic ulcers](#)", section on 'Hemostatic sprays'.)

One of the largest series of APC for tumor debulking included 83 patients with inoperable esophageal or gastric cardia cancer [32]. APC achieved recanalization, permitting passage of normal food, in 48 patients (58 percent) after one session and an additional 22 patients (84 percent) after two sessions. The remaining patients had improvement in dysphagia. Perforation occurred in seven patients, all but one of whom were treated conservatively.

Endoscopic mucosal resection or ablation — A newer application of APC, hybrid APC, combines submucosal [saline](#) lift with diffuse tissue ablation at high wattage as an alternative to

mucosal resection or ablation techniques. A special generator delivers a microjet of fluid through a probe that is in direct contact with the mucosa. The hybrid APC probe incorporates this injection capability with standard APC delivery. When used to ablate residual Barrett's mucosa for example, the target area is first lifted by directly touching the probe to the mucosa and depressing a foot pedal. Then APC is delivered just to the area that has been lifted at 60 watts. The coagulated mucosa is then scraped clean with a cap on the tip of the endoscope. Next, a second lift is performed and the area is retreated at 40 watts to ablate the submucosa. The result is a targeted two-layer ablation to a level comparable to that achieved with endoscopic mucosal resection [36,37].

One application of hybrid APC that is being studied is its use in the management of gastrointestinal neoplasia, such as flat dysplasia in patients with Barrett esophagus. Its application in this area will require further prospective evaluation to determine its efficacy, safety, and ease of use [38-43]. Other applications of this technique have been utilized in non-lifting duodenal adenoma tissue and early flat squamous neoplasia in the esophagus. The advantages of APC in this setting (ease of use for superficial lesions, reduced risk of bleeding and perforation) must be weighed against the drawback of lack of histology to confirm negative margins [42] as well as the possibility of incomplete eradication of the lesion.

Another proposed application of hybrid APC is prevention of recurrence following wide piecemeal resection of laterally spreading colonic lesions [44]. Finally, ablation by APC alone has also been applied within the bile duct to try to ablate intraductal papillary neoplasm [45].

Comparisons with other ablation methods, such as radiofrequency ablation and cryotherapy, as well as comparisons with en block mucosal resection and endoscopic submucosal dissection will be needed to pinpoint the optimal applications of hybrid APC in the management of early and superficial neoplasia throughout the GI tract.

Ulcer hemostasis — Endoscopic treatment of serious ulcer bleeding with active spurting or non-bleeding visible vessels is usually accomplished with mechanical or thermal tamponade techniques, with or without [epinephrine](#) injection. (See "[Overview of the treatment of bleeding peptic ulcers](#)".)

There is theoretical concern that firm pressure is an important aspect of contact thermal hemostasis of non-bleeding visible vessels, particularly with a larger diameter. However, one small randomized comparison of 41 patients showed similar rates of hemostasis with use of the heater probe or APC alone for actively bleeding and non-bleeding visible vessels [46]. This finding awaits confirmation by other, larger studies.

APC appears to be effective as part of combination therapy for visible vessels. A randomized trial involving 192 patients found that APC plus [epinephrine](#) injection was as safe and effective as epinephrine injection plus heater probe coagulation in patients with high-risk bleeding peptic ulcers [47].

Weight regain after Roux-en-Y gastric bypass — APC is also being studied to treat patients with a dilated gastrojejunal anastomosis following laparoscopic Roux-en-Y gastric bypass. APC is used to create scarring to narrow the dilated gastrojejunal anastomosis. Several preliminary reports have shown favorable weight loss with this intervention [48,49]. A large multi-center retrospective series examined 217 patients who underwent APC at the gastrojejunal anastomosis [50]. It compared 12-month outcomes in patients treated with low dose APC (45 to 55 Watts) to patients treated with high-dose APC (70 to 80-Watts). The total weight loss was 5.1 percent low dose APC and 9.7 percent for high dose APC. The most common side effect was stenosis of the anastomosis, which occurred in 4.6 percent of patients. There was a trend toward an increased gastrojejunal anastomosis stenosis rate with high-dose APC (7.6 percent versus 3 percent, $P = .06$). The mean number of APC sessions required was 1.4.

In a single-center randomized trial of 40 patients receiving either APC or APC plus full thickness suturing of the anastomosis (FTS-APC), the two groups had similar total weight loss (8.3 percent in the APC alone group and 7.5 percent in the FTS-APC group; $p = 0.71$) [51]. Adverse events were also similar between the groups. If sustained efficacy and low adverse event rates are confirmed in subsequent studies, APC may gain acceptance as a lower cost alternative to endoscopic suture revision of the anastomosis for patients with weight regain after Roux-en-Y gastric bypass. (See "[Bariatric operations: Late complications with subacute presentations](#)", section on 'Failure to lose weight and weight regain'.)

Esophageal varices — Limited preliminary experience suggests a possible role of APC combined with variceal band ligation in the treatment of esophageal varices. (See "[Endoscopic variceal ligation](#)".)

Dieulafoy's lesions — A case series described successful treatment of Dieulafoy's lesions (mainly in the upper gastrointestinal tract) with APC alone [52].

COMPLICATIONS

Argon plasma coagulation (APC) has a theoretical safety advantage over other modalities due to its decreased depth of penetration and the tendency for the ionized arc of electrical current to deflect away from coagulated tissue to surrounding areas. However, like any coagulation

method, serious complications can occur, particularly in the right colon. The perforation rate in one large series was 6 out of 2193 sessions (0.2 percent) in 1062 patients. The authors reported 10 minor complications, most commonly subcutaneous emphysema [3]. Isolated perforations have occurred in other series [2,53].

Other complications that have been observed are asymptomatic and symptomatic pneumoperitoneum and subcutaneous bubbling of gas [54,55]. It is likely that these problems are caused by either over-distension within the cecum or unintentional direct contact of the probe to the thin bowel wall during pulses resulting in deeper monopolar cautery. No treatment is generally required when the subcutaneous bubbling of gas is observed.

A potential complication in patients undergoing colonic procedures who did not receive a full colonic lavage (such as those receiving APC for radiation proctopathy) is bowel explosion with perforation, presumably due to the accumulation of combustible colonic gas [28].

COMPARISONS BETWEEN TECHNIQUES

As mentioned above, few studies have directly compared argon plasma coagulation (APC) to other methods for achieving hemostasis. A systematic review published in 2005 identified only two randomized trials (with only 121 individuals) in non-variceal upper GI bleeding [9]. However, APC is used widely due to its ease of use and perceived safety advantages.

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "[Society guideline links: Gastrointestinal bleeding in adults](#)".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading

level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "[Patient education: Angiodysplasia of the GI tract \(The Basics\)](#)")

SUMMARY AND RECOMMENDATIONS

- **APC versus contact thermal therapies** – Endoscopists experienced with argon plasma coagulation (APC) generally find it helpful for targets that are difficult to reach by direct contact and for treating multiple lesions at the same session. In addition, APC tends to be quicker than contact thermal therapies.

There have been few trials comparing APC to other endoscopic methods used for similar indications. The availability of the necessary equipment and familiarity with specific methods are important considerations when choosing options.

- **Applications** – We suggest APC be used in the following settings (**Grade 2C**):
 - Targeted therapy of isolated angiodysplasia in the colon, small bowel, and stomach.
 - Treatment of gastric antral vascular ectasia.
 - Treatment of radiation telangiectasia (also referred to as radiation proctopathy or radiation proctitis) with significant or symptomatic bleeding.
 - Postpolypectomy for large sessile polyps to fulgurate the base to reduce recurrent adenoma.
 - Ablation of flat residual duodenal or colon polyps in hard to reach locations that cannot be removed with a snare.
 - Treatment of tumor ingrowth into esophageal metal stents.

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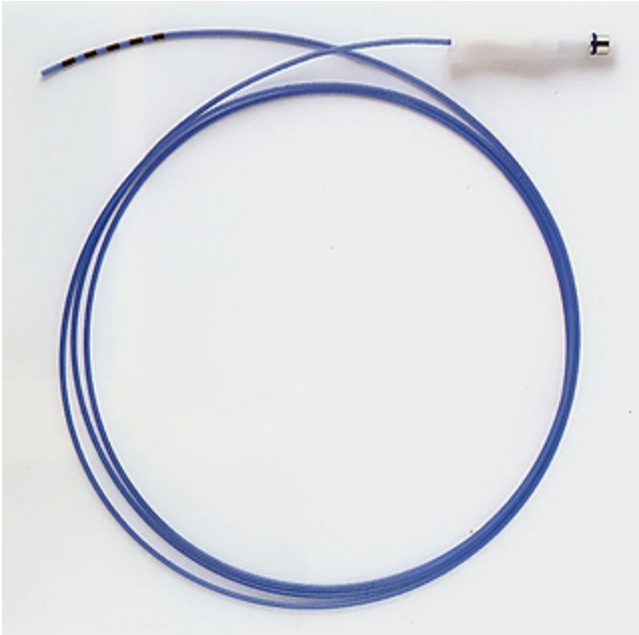
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Topic 2576 Version 20.0

GRAPHICS

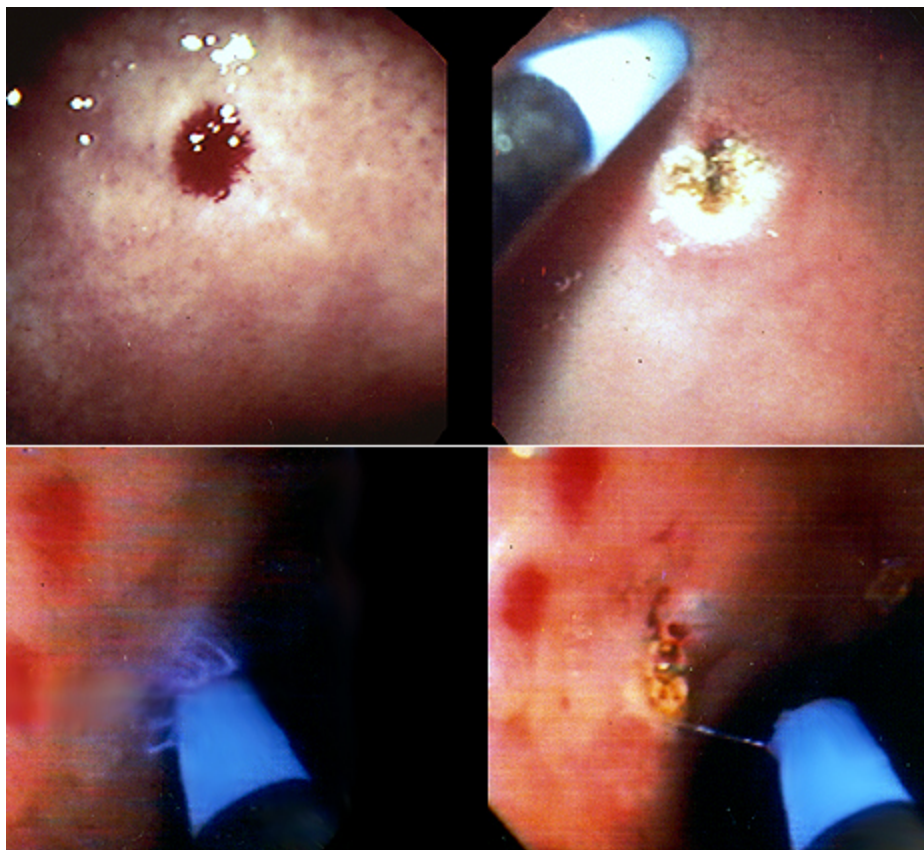
Argon plasma coagulator probe



The disposable probes are available in 1.5 mm, 2.3 mm (the most commonly used size), and 3.2 mm. The standard probes are 220 cm long.

Graphic 72597 Version 1.0

Arteriovenous malformation in the gastrointestinal tract

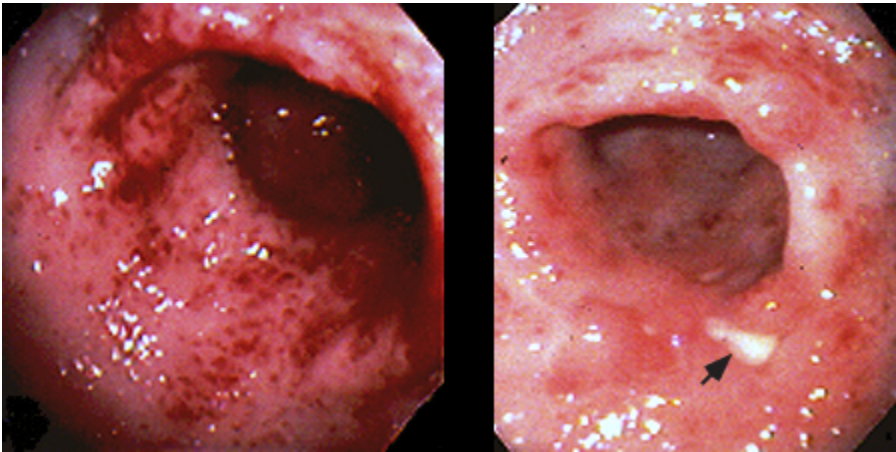


Endoscopic views of arteriovenous malformations being treated with the argon plasma coagulator (APC). The top panels illustrate the appearance before and after APC coagulation. The bottom panels demonstrate the ability of APC to treat lesions tangentially. It is important to see the black portion of the APC catheter prior to initiating coagulation to prevent damage to the endoscope.

Courtesy of Jonathan Cohen, MD.

Graphic 79901 Version 2.0

Gastric antral vascular ectasia syndrome (watermelon stomach)

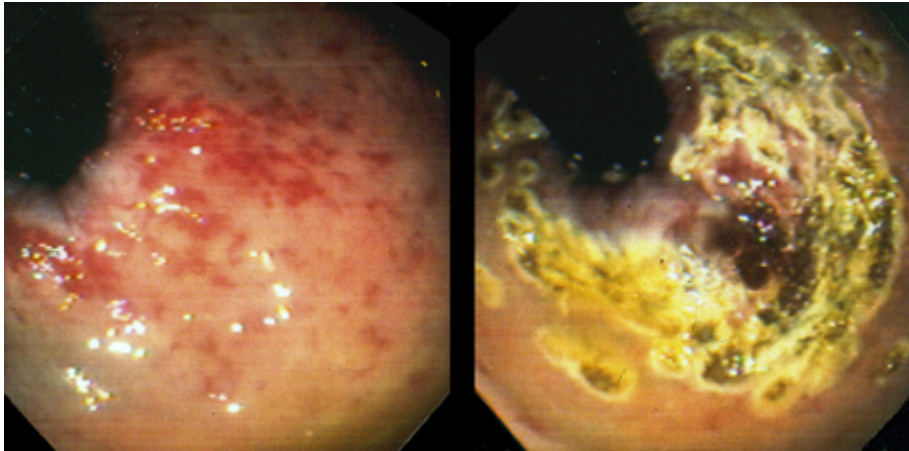


Endoscopy of watermelon stomach before and after argon plasma coagulation (APC). Left panel: Gastric antrum showing hemorrhagic striations that are oozing. Right panel: Marked improvement two weeks following the second APC session. Note the superficial healing ulcer (arrow) resulting from the APC treatment.

Courtesy of Jonathan Cohen, MD.

Graphic 74688 Version 2.0

Radiation telangiectasias

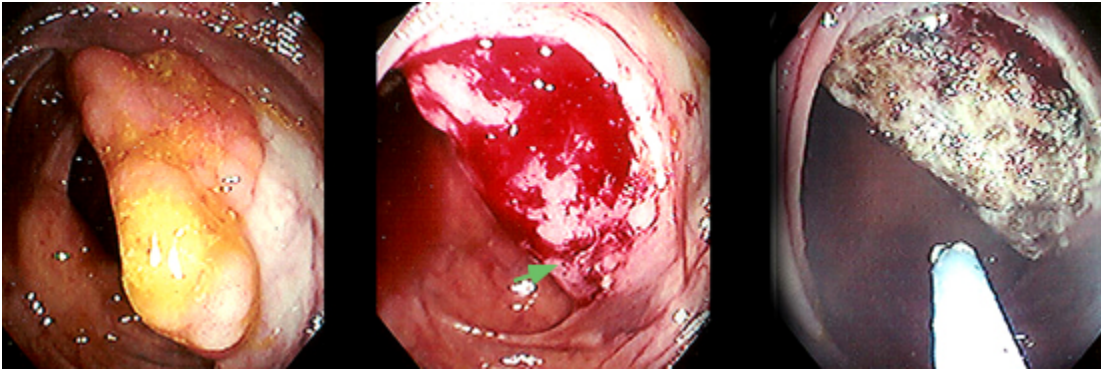


Left panel: Endoscopy shows hemorrhagic areas in the rectum in a patient with radiation telangiectasias and chronic hematochezia. Right panel: The hemorrhagic areas have been treated with argon plasma coagulation.

Courtesy of Jonathan Cohen, MD.

Graphic 64264 Version 2.0

Argon plasma coagulation following colonic polypectomy



Left panel: A large sessile polyp is seen in the sigmoid colon. Middle panel: Following snare excision, the base is oozing blood, and residual adenomatous tissue is visible at the inferior margin (arrow). Right panel: The argon plasma coagulator has been used to fulgurate the base and remaining adenomatous tissue.

Courtesy of Jonathan Cohen, MD.

Graphic 72550 Version 2.0

Contributor Disclosures

Jonathan Cohen, MD Equity Ownership/Stock Options: GI Windows [Magnetic anastomosis]; MD Medical Navigators [Advocacy and consulting]; ROM-Tech, Inc [Joint rehab]; Virtual Health Partners [Obesity]. Consultant/Advisory Boards: Micro-Tech [Endoscopy accessories]; Olympus [Gastrointestinal endoscopy, ERCP, NBI]. Other Financial Interest: Wiley [Textbook royalties]. All of the relevant financial relationships listed have been mitigated. **John R Saltzman, MD, FACP, FACG, FASGE, AGAF** No relevant financial relationship(s) with ineligible companies to disclose. **Anne C Travis, MD, MSc, FACG, AGAF** No relevant financial relationship(s) with ineligible companies to disclose.

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