Argon plasma coagulation in chronic radiation proctitis

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Bibliography
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Chronic radiation proctitis is a relatively common late complication of pelvic irradiation. The main symptoms are diarrhea, urgency, tenesmus, and rectal bleeding. While mild cases may settle spontaneously over some months, severe hemorrhagic radiation proctitis may require repeated blood transfusions and is difficult to treat with medical therapy. Argon plasma coagulation (APC) is a noncontact thermal coagulation technique which can be applied endoscopically. A probe passed through the scope delivers a field of argon gas to the mucosal surface where it is ionized by a high voltage filament, resulting in superficial mucosal heating and coagulation of friable blood vessels. The technique reduces rectal bleeding in 80%–90% of cases, and may improve the other troublesome symptoms of diarrhea and urgency. APC is probably less effective in very severe cases of hemorrhagic radiation proctitis; in these cases topical formalin or a combination of APC and topical formalin can be useful. Overall, APC has proved to be a safe and well tolerated technique.

Objectives

Chronic radiation proctosigmoiditis occurs in up to 15% of patients who receive radiation therapy for pelvic malignancies such as cervical or prostatic cancer, or following local radiation treatment for rectal or anal cancer. Symptom onset is usually within the first 2 years after treatment (**Figure 1**). The etiology of radiation proctitis is considered to be chronic mucosal ischemia caused by tissue fibrosis and obliterative endarteritis [1]. Symptoms are often difficult to treat and include diarrhea, rectal bleeding, urgency, tenesmus, rectal strictures, proctalgia, and occasionally fecal incontinence.

In approximately one third of patients the symptoms are mild and settle spontaneously over several months without specific intervention. However a proportion of patients will develop severe hemorrhagic proctitis which is usually refractory to medical therapies such as topical treatment with steroids, 5-aminosalicylic acid (5-ASA), or sucralfate enemas. Other treatment approaches have included hormonal or hyperbaric oxygen therapy, and endoscopic therapy with laser or bipolar heater probes. However, argon plasma coagulation (APC) is now established as an effective treatment for moderate or severe radiation proctitis, reducing rectal bleeding and iron or blood transfusion requirements by cauterizing mucosal telangiectasias. APC may also help to ameliorate symptoms of diarrhea, urgency, and tenesmus [2].

Basic principles

APC is a noncontact thermal coagulation technique which was developed almost 15 years ago by ERBE Medical, Tübingen, Germany. The first experience of its application in flexible endoscopy was published in 1994, and it has since become an established treatment modality in a variety of clinical scenarios [3].

Inert argon gas is pumped at a specified flow rate through a probe which is passed through the endoscope channel. The gas is then ionized by a high voltage current that flows through a tungsten filament at the tip of the probe, which is held just above the mucosal surface (**Figure 2**). The field or "plasma" of ionized gas earths via the nearest mucosal surface, and the circuit is completed via a return plate which is attached to the patient's buttock or thigh. The thermal energy produced heats the surface in a uniform manner to a depth of around 0.5 to 3 mm, and coagulates the superficial blood vessels with limited risk of damage to deeper tissues or of causing perforation.

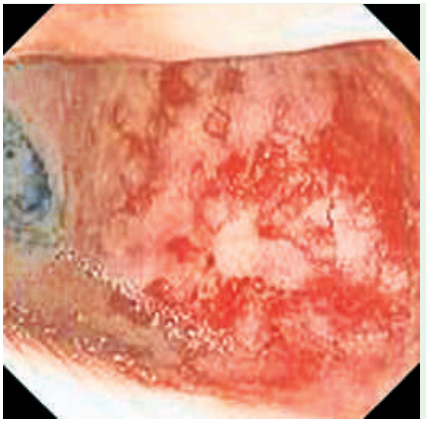

Figure 1 Radiation proctitis.

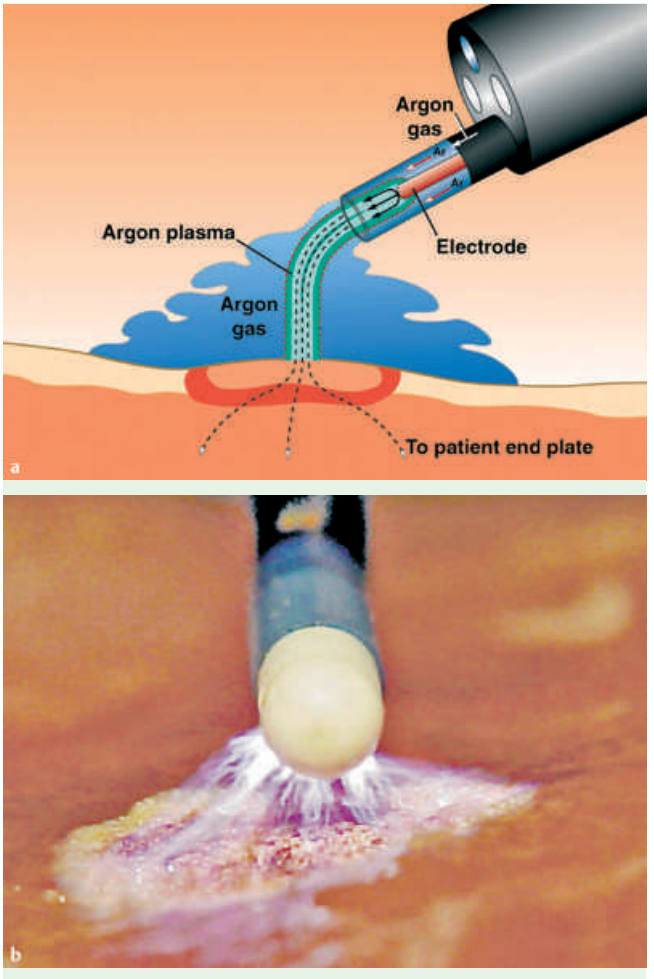

Figure 2 **a,b** Argon plasma coagulation (APC): basic principles.

Figure 3 ERBE VIO 200D Electrosurgical generator.

The wattage can be varied according to the location in the bowel and the depth of penetration or degree of coagulation required [4]. The argon flow rate can also be varied, with higher flow rates producing larger fields of thermal coagulation but also more rapid bowel distension.

Materials used

The APC equipment is stacked into a compact mobile unit, such as the ERBE VIO 200D (ERBE Elektromedizin, Tübingen, Germany). The main components are a high frequency electrosurgical generator, an argon gas delivery system, and two tanks of argon gas that are stored underneath the unit (**Figure 3**). An adhesive return plate (e.g. a Neutral Electrode Safety System, or NESSY, plate 170) is attached to the patient to complete the circuit, and the system is activated by the endoscopist by means of a foot pedal.

The probes are available in different diameters and lengths, but the most commonly used is the disposable 220 cm long, 2.3 mm diameter axial spot beam APC probe (APC 2200A). The probes may be either side- or front-firing depending on the direction in which the argon gas leaves the probe tip.

The controls on the front of the unit allow selection of the argon gas flow rate (L/min) and the wattage to be passed through the tungsten filament. Modern units also provide a choice of different modes of APC: in traditional "forced" APC, a constant wattage is used but the thermal heating varies, depending on the distance from probe to mucosal surface; in "precise" APC, the energy applied is regulated so that a constant level of thermal heat-

ing is applied at the surface irrespective of changes in distance; and in "pulsed" APC, energy is applied in very short precise pulses. The units can also perform basic monopolar and bipolar electrocautery functions.

Description of procedure

It is not necessary to take biopsies to confirm the diagnosis, and treatment can be started at the initial endoscopy on the basis of a typical appearance. However it is mandatory to complete a full colonoscopy to exclude an occult proximal malignancy or an alternate source of bleeding. Because of this, and the potential risk in an unprepared bowel of combustion and colonic explosion, it is imperative that formal bowel preparation is used [5].

Informed consent should cover the risk of bleeding, bowel perforation, and rectal stricturing, and the need for further treatment sessions.

It is standard practice at two of the present authors' hospitals, St. Mark's, London, UK, and The Epworth and Royal Melbourne Hospital, Australia, to document the extent and severity of disease with a standard set of four photographs, of the upper, mid and lower rectum in frontal view, and the rectal ampulla on retroflexion. This allows an objective assessment of improvement after each treatment session. Currently there is no standardized scoring system to grade severity, although such a system might be useful for triaging patients to the most appropriate treatment modality. One suggested example grades hemorrhagic radiation proctitis into mild (grade A), moderate (grade B), or severe (grade C) according to the distribution of telangiectasias, rectal surface area affected, and the presence of fresh blood [6].

Antispasmodics should be used, unless contraindicated, to improve visualization.

The argon flow rate is set at between 1.0 and 1.5 L/min. A voltage of 40 – 50 W should be used, although it can be increased to 60 W for areas of significant hemorrhage. Settings in this range are adequate for successful coagulation but carry less risk of the complications associated with higher power settings. The "precise" APC setting available on new generators provides more controllable thermal heating at the mucosal level, and reduces the risk associated with direct mucosal contact.

The area of mucosa to be treated is located, washed if necessary, and any surface fluid or blood is suctioned. If there is significant hemorrhage, an adrenaline wash can be used to dry up the surface mucosa: 5 ml of 1 : 10 000 adrenaline in 45 ml of normal saline is left in contact with the mucosa for 30 seconds and then suctioned. The probe is purged with argon, tested, and passed through the endoscope until it extends approximately 1 cm from the tip.

The probe should be held just above the mucosal surface but not in contact with it. The most proximal areas are treated first before working distally. Treatment is concentrated on the most prominent telangiectasias in a "spot-weld" fashion, leaving areas of untreated mucosa in between (**Figure 4**). Single or repeat pulses of less than 1 second are used, until the superficial mucosa starts to appear whitish in colour and the bleeding stops. Care should be taken not to overlap or treat a particular area of rectal mucosa repeatedly as this increases the risk for mucosal ulceration that is characteristically slow to heal. The use of adjuvant medical therapies, such as steroids, 5-ASA, and sucralfate enemas, has not been shown to augment the healing process.

Figure 4 Radiation proctitis treated with APC.

Depending on the angulation of the scope and position of the area to be treated, an end-firing or a side-firing probe can be used. Side-firing probes facilitate fulguration of areas behind mucosal folds or sharply angled corners, although for more targeted therapy a forward-firing probe is most useful. The technique can be applied in the retroflex position for areas close to the dentate line, although care must be taken to avoid patient discomfort. In cases where rectal scarring limits APC application through a standard colonoscope, retroflexion with a gastroscope can be helpful.

Each pulse applied during APC introduces argon into the bowel, and periodic suctioning is required to deflate the colon, especially with prolonged treatments.

The aim is to treat all areas of affected mucosa so that there are no visible areas of bleeding or large telangiectasias at the end of the treatment session (**Figure 4**). With extensive or severe disease it is not uncommon to find that the symptoms have not fully resolved after the first session, and a repeat procedure may be necessary after a 2 – 4-week interval. In cases where there is diffuse radiation proctitis, a useful strategy is to apply topical 4% formalin using a swab stick, till the mucosa blanches. The residual visible telangiectasias are then treated with APC.

Limitations and success rate

APC successfully ameliorates rectal bleeding associated with hemorrhagic radiation proctitis in 80% – 90% of cases, and improves symptoms of diarrhea and tenesmus in 60% – 75% of cases [2, 7, 8]. A summary of recent literature is outlined in **Table 1**. Although these goals can usually be achieved in one or two treatment sessions, more resistant cases may necessitate several repeat applications. APC is less effective in very severe cases of radiation proctitis, for instance when more than half of the rectal surface area is involved or when there is fresh surface bleeding [6]. There is evidence supporting the use of topical formalin in severe cases that are refractory to APC [12].

Complications and safety

There are no absolute contraindications to the use of APC. However as with diathermy it is prudent to seek cardiological advice for patients with permanent cardiac pacemakers or implanted cardiac defibrillators. In these cases the return plate should be placed on the buttock or thigh, well away from the implanted

Table 1 Literature on argon plasma coagulation (APC) use in radiation proctitis

Authors (year)	n	% requiring transfusion	Settings	Success rate	Mean no. APC sessions	Complications requiring treatment
Zinicola et al. (2003) [6]	14	21 %	65 W 2.0 L/min	86 %	2.0	None
Ben-Soussan et al. (2004) [5]	27	30 %	40 – 50 W 0.8 – 1.0 L/min	92 %	2.66	1 colonic explosion requiring surgery
Canard J et al. (2003) [9]	30	17 %	30 – 80 W 0.8 – 2.0 L/min	87 %	2.3	1 rectal stricture 1 perforation 1 massive hemorrhage
Tam et al. (2000) [7]	15	20 %	60 W 2.0 L/min	100 %	2.0	2 asymptomatic rectal strictures
Tjandra & Sengupta (2001) [8]	12	33 %	40 W 1.5 L/min	83 %	2.0	None
Silva et al. (1999) [10]	28	53 %	50 W 1.5 L/min	97 %	2.9	None
Sebastian et al. (2004) [4]	25	36 %	30 W 1.5 L/min	76 %	1.0	None
Fantin et al. (1999) [11]	7	–	60 W 3.0 L/min	100 %	2.0	None

device. The current American Society for Gastrointestinal Endoscopy (ASGE) guidelines recommend that patients who are pacemaker-dependent should be driven to automatic pacing with a ring magnet placed over the pacemaker. Patients who are not pacemaker-dependent can be monitored, with a magnet available for continuous pacing if needed. Implanted defibrillators should be deactivated prior to APC and continually monitored until reactivated. In all cases an external cardiac defibrillator should be available.

The usual recommendations for antibiotic prophylaxis apply as there is an increased risk of bacteremia following APC, as there is with diathermy.

Overall the complication rate is low. The commonest procedure-related symptom is of anal or rectal pain, which is most likely to occur following treatment near the dentate line. This is typically mild and self-limiting. Abdominal bloating and cramping, and vagal symptoms related to colonic distension have also been reported. There have been cases of colonic explosion related to APC use when the bowel has not been formally cleansed, and this is therefore a mandatory requirement [5].

Bowel perforation is rare. The largest series to date involved over 1600 applications of APC for a variety of indications in the upper and lower gastrointestinal tract, and reported a perforation rate of 0.31 % [13]. The same series reported intestinal emphysema in 0.46; this phenomenon occurs when direct mucosal contact introduces a submucosal bleb of argon gas. This usually settles spontaneously, but does increase the risk of bowel perforation. Application of APC around radiation-induced rectal strictures may worsen their severity as the treated mucosa heals. Rectovaginal fistulas have also been reported as a rare and late complication.

Indications

Necessary

APC is an effective treatment in patients with rectal bleeding associated with mild to moderate radiation proctitis which has not settled spontaneously or following appropriate medical therapy. The technique may also be successful in cases of more severe radiation proctitis, although success is likely to be more limited, and multiple treatment sessions may be required. APC may ameliorate symptoms of diarrhea, urgency and tenesmus, although with somewhat less success.

Inappropriate

APC is inappropriate where other causes of proctosigmoiditis have not been actively excluded and the diagnosis of radiation proctitis is in any doubt. A full colonoscopy with formal bowel preparation is essential. APC is unlikely to be successful in severe, extensive radiation proctitis although it may ameliorate symptoms to a degree. Multiple, repeated applications in this patient group should be avoided unless there is obvious benefit, and other treatment modalities such as topical formalin therapy should be considered. APC may also be inappropriate in the presence of radiation-induced rectal strictures, and in the presence of rectal fistulae, which may worsen as the treated area heals.

Competing interests: None.

References

1 *Hasleton PS, Carr N, Schofield PF.* Vascular changes in radiation bowel disease. Histopathology 1985; 9: 517 – 534
2 *Sebastian S, O'Connor H, O'Morain C, Buckley M.* Argon plasma coagulation as first-line treatment for chronic radiation proctopathy. J Gastrol Hepatol 2004; 19: 1169 – 1173
3 *Grund K, Storek D, Farin G.* Endoscopic argon plasma coagulation (APC). First clinical experiences in flexible endoscopy. Endosc Surg Allied Technol 1994; 2: 42 – 46
4 *Norton ID, Wang L, Levine SA et al.* Efficacy of colonic submucosal saline solution injection for the reduction of iatrogenic thermal injury. Gastrointest Endosc 2002; 56: 95 – 99
5 *Ben-Soussan E, Antonietti M, Savoye G et al.* Argon plasma coagulation in the treatment of hemorrhagic radiation proctitis is efficient but requires a perfect colonic cleansing to be safe. Eur J Gastroenterol Hepatol 2004; 16: 1315 – 1318
6 *Zinicola R, Rutter M, Falasco G et al.* Haemorrhagic radiation proctitis: endoscopic severity may be useful to guide therapy. Int J Colorect Dis 2003; 18: 439 – 444
7 *Tam W, Moore J, Schoeman M.* Treatment of radiation proctitis with argon plasma coagulation. Endoscopy 2000; 32: 667 – 672
8 *Tjandra JJ, Sengupta S.* Argon plasma coagulation is effective in the treatment of refractory radiation proctitis. Dis Colon Rectum 2001; 44: 1759 – 1765
9 *Canard JM, Vedrenne B, Bors G et al.* Long term results of treatment of hemorrhagic radiation proctitis by argon plasma coagulation. Gastroenterol Clin Biol 2003; 27: 455 – 459
10 *Silva RA, Correia AJ, Dias LM et al.* Argon plasma coagulation therapy for hemorrhagic radiation proctosigmoiditis. Gastrointest Endosc 1999; 50: 221 – 224
11 *Fantin AC, Binek J, Suter WR, Meyenberger C.* Argon beam coagulation for treatment of symptomatic radiation-induced proctitis. Gastrointest Endosc 1999; 49: 515 – 518
12 *Tsujinaka S, Baig MK, Gornev R et al.* Formalin instillation for hemorrhagic radiation proctitis. Surg Innov 2005; 12: 123 – 128
13 *Grund KE, Zindel C, Farin G.* Argon plasma coagulation through a flexible endoscope. Evaluation of a new therapeutic method after 1606 uses. Dtsch Med Wochenschr 1997; 122: 432 – 438