Original Article

Clinical Experience and Long-term Outcomes of Radiofrequency Ablation Treatment in Patients with Chronic Radiation Proctitis

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Key Words
Radiation proctitis;
Rectal bleeding;
Radiofrequency ablation

Purpose. Chronic radiation proctitis (CRP) may develop in patients who undergo pelvic radiotherapy. The optimal treatment modality is controversial, and it has several potential side effects. Herein, we report our experience using radiofrequency ablation (RFA) in patients with CRP.
Methods. This was a single-center retrospective study. Between October 2015 and November 2018, 16 patients with CRP and severe rectal bleeding underwent RFA at our institution. The data of these patients, including sex, primary tumor site, symptoms, radiation dosage, and treatment, were collected for analysis.
Results. A total of 16 patients who underwent RFA for CRP at Kaohsiung Chang Gung Memorial Hospital between October 2015 and November 2018 were enrolled in the study. We included 11 (68.7%) men and 5 (31.3%) women. Patient age ranged from 38 to 85 years, with a median of 69.4 years. The primary cancer site was the prostate, cervix, and rectum in nine (56.3%), five (31.3%), and two (12.4%) patients, respectively. All patients received either medical or endoscopic therapy prior to RFA. All patients experienced repeated rectal bleeding, and nine (56.3%) patients required blood transfusion. Most patients (93.7%) underwent RFA only once. One patient (6.3%) underwent a second RFA session due to recurrent hematochezia 16 weeks after the first RFA. The mean hemoglobin level improved from 10.9 ± 2.1 g/dL to 11.2 ± 2.2 g/dL. RFA treatment resulted in discontinuation of blood transfusion in all patients during the follow-up period.
Conclusions. RFA treatment was safe and effective in controlling rectal bleeding in patients with CRP, and can be considered as a first-line endoscopic intervention in selected patients. Further controlled studies are required to confirm these findings.

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Pelvic radiotherapy is a common treatment modality to improve survival in pelvic malignancies. However, radiotherapy causes endothelial dysfunction, microvascular injury with intimal fibrosis, and the development of neovascular lesions. In addition, it carries a risk of pelvic radiation disease. Chronic radiation proctitis (CRP) is a complication of pelvic radiotherapy for malignancy and occurs in 5-20% of pa-

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tients.[1-3] The symptoms of CRP include diarrhea, mucoid discharge, tenesmus, rectal pain, severe rectal bleeding, ulceration, and bowel obstruction. The latency period from radiotherapy to the onset of CRP with rectal bleeding varies from months to years.[4,5] These symptoms resolve spontaneously in many cases, but some patients with persistent rectal bleeding require repeated blood transfusion, which affects the quality of life.[3,4,6,7]

Various treatment options are available for CRP, including medical, endoscopic, and surgical therapy. Medical therapy includes formalin irrigation, topical application, hydrocortisone enema, or hyperbaric oxygen (HBO) therapy. Endoscopic therapy includes argon plasma coagulation (APC) and radiofrequency ablation (RFA).[8-10] However, treatment for CRP remains unsatisfactory with limited evidence. Endoscopic APC is widely used, and currently, it is considered the first-line therapy for CRP. APC uses high-frequency energy transmitted by ionized gas with non-contact electrocauterization and a controllable depth of coagulation (0.5-3 mm) for rapidly controlling rectal bleeding.[9,11,12] However, the use of endoscopic APC is technically challenging, and also has been reported with uncommon complications, including rectal ulcers, strictures, and fistulas in some cases.[9,13]

Endoscopic RFA for the treatment of CRP was first introduced by Zhou et al. and has been shown to effectively control rectal bleeding with a low complication rate.[14] RFA allows focused energy penetration, which restricts damage to the superficial mucosa. In addition, it carries a low risk of ulceration, stricture formation, and stenosis compared to other interventions. With regard to controlling rectal bleeding, RFA has a high success rate with low recurrence and complication rates.[15] However, the experience of RFA treatment for CRP in Taiwan is limited.

Materials and Methods

We retrospectively reviewed the medical records, including long-term outcomes, of 16 patients who underwent RFA for CRP at Kaohsiung Chang Gung Memorial Hospital between October 2015 and November 2018. A total of 16 patients with a history of pelvic radiation and outpatient referrals for intractable rectal bleeding were included. All patients were diagnosed with pelvic malignancies, including cervical, prostate, and rectal cancers, and received pelvic radiotherapy. All patients were treated by a single surgeon and followed-up at our hospital. Patient information, including the age, sex, primary pelvic malignancy, radiotherapy date, period between RFA and onset of CRP, previous treatment with RFA, comorbidities, need for blood transfusion, and post-RFA follow-up data, was collected and analyzed. Successful outcome was defined based on patient satisfaction and endoscopic findings. We used the rectal telangiectasia density grading scale to evaluate CRP severity. The scoring is as follows: Grade 0: normal mucosa; Grade 1: < 10 discrete telangiectasias; Grade 2: single coalescing patch and/or > 10 discrete telangiectasias; Grade 3: ≥ 2 coalescing patches.[16]

All patients underwent standard bowel preparation (sodium picosulfate or polyethylene glycol) prior to RFA. RFA was performed using an RFA probe mounted on the colonoscope at the 12 o'clock position and an electrode array attached to the endoscope paddle with an endoscopic cap (Halo^{90} systems; Covidien GI Solutions, Sunnyvale, California, USA) (Fig. 1A). First, endoscopic inspection was performed to identify bleeding areas from telangiectasia. Next, an electrode-pivoting paddle was applied to the targeted area, and energy was delivered to the electrode with a specific energy generator (HaloFlex system; Covidien). An energy setting of 12-15 J/cm^2 was used for all applications. In general, 1-2 RFA applications were performed per telangiectasia site to achieve adequate ablation (Fig. 1B). After ablation, we would switch to another colonoscope without RFA probe for irrigation and reinserted RFA probe mounted colonoscope for another area for completing adequate hemostasis.

Clinical status, including patient satisfaction, change in hemoglobin (Hb) level, and endoscopic changes, was recorded. We performed colonoscopic examination and checked the Hb level at 1, 3, 6 and 12 months after RFA treatment. Retreatment was performed in patients with continued rectal bleeding and marked anemia after RFA.

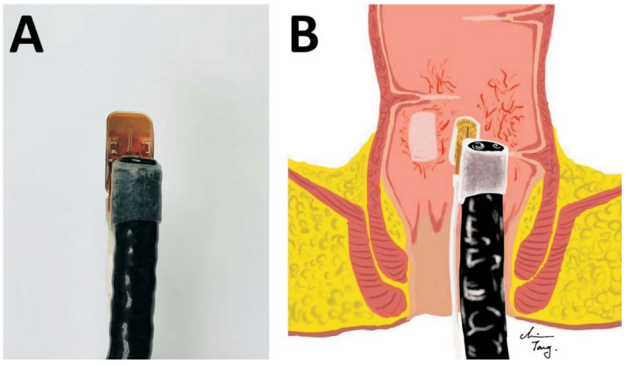

Fig. 1. The Halo^{90} radiofrequency ablation system. A. The Halo^{90} RFA catheter was mounted on a colonoscope at the 12 o'clock position. B. RFA was performed at each telangiectasia site to achieve adequate ablation. RFA, radiofrequency ablation.

Results

A total of 16 patients who underwent RFA for CRP at Kaohsiung Chang Gung Memorial Hospital between October 2015 and November 2018 were enrolled in the study. We included 11 (68.7%) men and 5 (31.3%) women. Patient age ranged from 38 to 85 years, with a median of 69.4 years. The primary cancer site was the prostate, cervix, and rectum in nine (56.3%), five (31.3%), and two (12.4%) patients, respectively. All patients received either medical or endoscopic therapy prior to RFA. All patients experienced repeated rectal bleeding, and nine (56.3%) required blood transfusion. The demographic characteristics of the participants are presented in Table 1. Patient distribution, radiation dosage, period between radiotherapy and onset of CRP, medical therapy prior to RFA, comorbidities, laboratory data including pre-RFA and 6 months post-RFA hemoglobin levels, and the rectal telangiectasia density scores are presented in Table 2.

All RFA procedures were performed by a single surgeon. Most patients received RFA at the outpatient department without admission or anesthesia, except for six patients who were admitted due to personal insurance requirements. Most patients were regularly followed-up at the outpatient department, except three patients who were lost to follow-up after RFA. The endoscopic findings before and after RFA are shown in Fig. 2. Most patients (93.7%) underwent only a single RFA session. One patient (6.3%) underwent a second RFA session due to recurrent hematochezia 16 weeks after the first RFA.

Anal pain was the most common adverse event (50%). Adverse events, including anal pain, tenesmus, hematochezia, and frequent bowel movement, were noted within 1 month after the procedure, and most adverse events subsided spontaneously within 1-3 months. The mean Hb level improved from 10.9 ± 2.1 g/dL to 11.2 ± 2.2 g/dL. Two patients experienced mild stenosis with constipation, which improved after finger dilation. RFA resulted in discontinuation of blood transfusion in all patients during the follow-up period.

Discussion

The optimal treatment for CRP remains controversial. Our retrospective study demonstrated the efficacy and safety of RFA in a long-term follow-up of patients with refractory CRP. Complete resolution of clinical symptoms without major complications was achieved in all patients in this case series. One patient had significant anemia during the follow-up period

Table 1. Demographic characteristics of patients

Variables	Patients (n = 16)	Percentage
Sex		
Male	11	68.7
Female	5	31.3
Primary cancer site		
Prostate	9	56.3
Cervix	5	31.3
Rectum	2	12.4
Prior medical therapy		
Hydrocortisone enema	16	100
Formalin irrigation	1	6.3
Hyperbaric oxygen therapy	1	6.3
Argon plasma coagulation	1	6.3
Anticoagulant use	2	12.5
Blood transfusion	9	56.3
Symptoms		
Bleeding	16	100
Tenesmus	6	37.5
Diarrhea	2	12.5

Table 2. Patient distribution

No	Sex	Age	Primary cancer site	Radiation dose, cGy/fracti on	Onset of CRP after radiation (months)	RTD score	Previous treatment	Co-morbidity	ECOG	Pre-RFA Hb (g/dL)	Post-RFA Hb (6 months, g/dL)	Adverse event after RFA/interval
1	M	60	Rectum	6000/30	12	3	Hydrocortisone enema	COPD, Liver cirrhosis	0	15.1	Lost to follow-up	Lost to follow-up
2	F	84	Cervix	4500/25	11	3	Hydrocortisone enema, APC	ESRD, DM, Hypertension	2	9.4	11.6	Lost to follow-up
3	M	58	Rectum	6000/30	15	3	Hydrocortisone enema	CVA, Infective endocarditis, Hypertension	2	13.4	12.7	Hematochezia/8 weeks
4	M	85	Prostate	6660/37	12	3	Hydrocortisone enema, Formalin irrigation, HBO	Hypertension	0	8.8	4.5	Lost to follow-up
5	M	82	Prostate	7600/38	12	3	Hydrocortisone enema	COPD	0	13.6	12.8	Anal pain, hematochezia/2 weeks
6	M	76	Prostate	7600/38	16	3	Hydrocortisone enema	DM, Hypertension	0	10.4	11.5	Hematochezia/2 weeks
7	M	82	Prostate	7000/35	12	3	Hydrocortisone enema	Hypertension	1	13.8	13.1	Hematochezia/6 months
8	M	74	Prostate	7600/38	4	3	Hydrocortisone enema		0	8.1	11.1	Hematochezia/12 weeks
9	M	69	Prostate	3625/5	9	3	Hydrocortisone enema	Hypertension	0	14.3	14.4	Anal pain, tenesmus, hematochezia/2 weeks
10	F	61	Cervix	5000/25	10	3	Hydrocortisone enema		0	10.6	10.4	Anal pain, tenesmus, hematochezia/2 weeks
11	F	77	Cervix	5000/25	x	3	Hydrocortisone enema	Hepatitis C carrier	0	11.6	11.2	Anal pain/10 days
12	F	47	Cervix	5500/25	10	3	Hydrocortisone enema		0	8.8	9.3	Anal pain, hematochezia
13	F	38	Cervix	Lack	11	3	Hydrocortisone enema		0	8.9	11.4	Anal pain, tenesmus/2 weeks. Anal stenosis/3rd month
14	M	68	Prostate	7600/38	7	3	Hydrocortisone enema	Hypertension	0	12.5	12.2	Anal pain, hematochezia/3 weeks. Anal stenosis/3rd month
15	M	71	Prostate	7600/38	3	3	Hydrocortisone enema	Liver cirrhosis, DM, Hypertension	0	10.3	11.5	Nil
16	M	79	Prostate	7600/38	8	3	Hydrocortisone enema	DM	1	8.8	10.3	Anal pain/4 weeks. Hematochezia/12 weeks

CRP, chronic radiation proctitis; COPD, chronic obstructive pulmonary disease; ESRD, end-stage renal disease; DM, diabetes mellitus; APC, argon plasma coagulation; HBO, hyperbaric oxygen therapy; Hb, hemoglobin; ECOG, Eastern Cooperative Oncology Group performance score; RTD, rectal telangiectasia density.

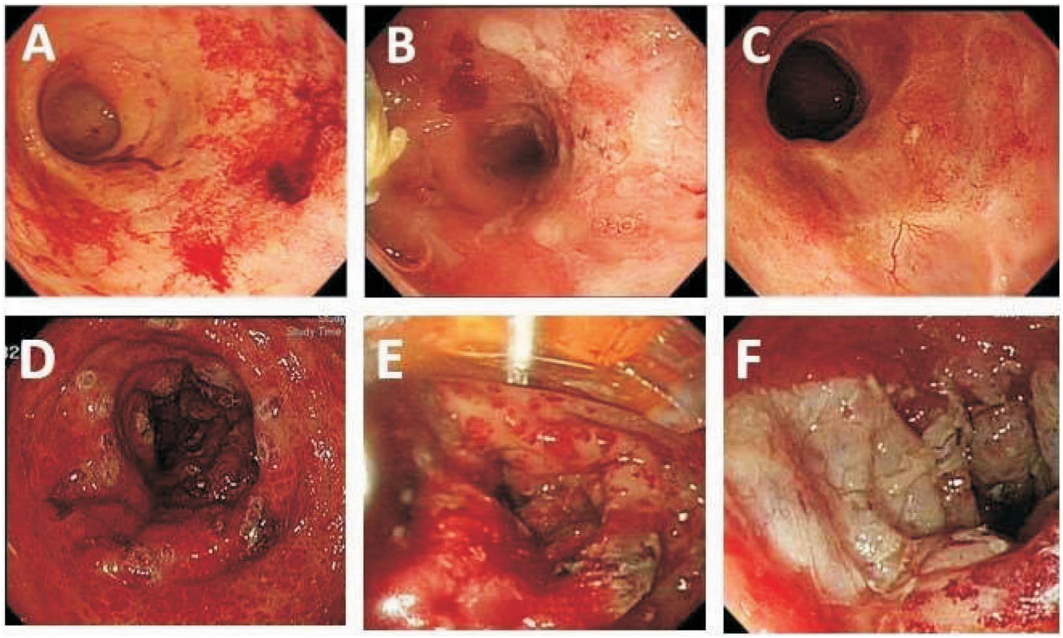

Fig. 2. Endoscopic follow-up after RFA. A. Endoscopic findings before RFA. RTD grade 3 with multiple telangiectasias and rectal bleeding. B. Three months after the RFA treatment. C. One year after RFA treatment. Residual telangiectasia without bleeding or stricture. D. Radiation proctitis after APC treatment. E. Recurrent rectal bleeding as a late complications after APC and treated by RFA. F. Endoscopic findings after RFA. RFA, radiofrequency ablation; RTD, rectal telangiectasia density; APC, argon plasma coagulation.

which was resulted from recurrent prostate cancer with massive hematuria.

CRP symptoms, such as severe bleeding, stricture formation, and bowel obstruction, which are similar to those of acute radiation proctitis, may not become apparent until months to years after the completion of radiotherapy, and the average duration of symptom onset after radiotherapy is approximately 8 to 12 months. Radiotherapy leads to mucosal injuries and compromised blood supply to the rectal wall, which causes full-thickness ischemia and fibrotic changes.[6,7] Several treatments for CRP have been used, including medical interventions such as HBO therapy, and endoscopic, and surgical interventions.[9,10] Medical therapy with 5-aminosalicylic acid-containing medications, steroids, and oral antibiotics may be effective in some cases, but few small trials have shown disappointing results.[17] HBO therapy has shown benefits in some cases. HBO therapy inhibits bacterial growth and preserves marginally perfused tissue. It also results in neovascularization and re-epithelialization.[18]

Endoscopic interventions are considered rescue options for severe bleeding complications and those refractory to medical treatment. The goal of endoscopic intervention is to obliterate mucosal telangiectasias and stop bleeding. APC is recommended as the first-line treatment for bleeding complications in CRP.[11] APC is a non-contact electrocoagulation technique with a controllable depth of coagulation (0.5-3 mm), ease of application, and low cost. Siow et al. reported that 79.1% of patients achieved successful regression of rectal bleeding after 1-2 sessions of APC.[19] The complication rate reported after APC treatment is variable. Anal pain is the most common but minor complication, occurring in 20% of patients, and typically subsided spontaneously. Major complications, including extensive bleeding, necrosis, ulceration, and perforation, are uncommon but have been reported in 10% of patients.[1]

Another endoscopic treatment option is RFA. Unlike the point-to-point approach in APC, RFA allows the treatment of a broader area and avoids deep tissue injury.[14] RFA provides limited and focused energy penetration, restricting damage to the superficial mucosa and muscularis propria, thereby minimizing the risk of ulceration, perforation, and rebleeding. In ad-

dition, RFA leads to squamous re-epithelialization in the rectal mucosa, which may prevent rebleeding and ulceration.[1] McCarty et al. reported that in patients with CRP, RFA is a safe and effective endoscopic treatment with high clinical success rates (99%) and severe complications are rare (0%).[15] However, the RFA procedure needed completed colon preparation, had longer operative time and higher cost then APC, which might influence the patient's preference.

In this study, one (6.2%) patient underwent 2 RFA sessions due to recurrent hematochezia. Rustagi et al. reported that the mean number of RFA sessions was 1.49 (±0.9) in a large cohort.[5] Common adverse events of RFA treatment include anal pain and intermittent hematochezia, but most symptoms subside spontaneously within 10-16 weeks without further interventions.[5,15,20,21] Our results were similar to those of previous studies. Frequent switching and re-insertion of colonoscope and RFA probe mounted colonoscope during procedure might lead to minor anal trauma and was considered as cause of transient anal pain. This might explain the high rate of anal pain in our results. But most patient could tolerate with or without medications. We performed RFA only in patients with previous treatment failure, including medical or APC treatment (Figure 2D, E, F).

Our study had several limitations. First, this retrospective single-arm cohort study lacked a direct comparison with other endoscopic treatments, and all patients had a history of previous treatment, which may have led to a selection bias. Second, we did not have objective data on patient satisfaction and symptomatic improvement, such as the radiation proctitis severity assessment scale scores, which may have resulted in potential subjective bias. In addition, the sample size was small due to the rarity of refractory CRP and treatment cost. However, our results showed the effectiveness and safety of RFA treatment, and were similar to those of previous studies.

Conclusion

In summary, our study revealed that endoscopic RFA for CRP is effective and has fewer major complications than APC. Despite limited evidence, RFA can be considered a first-line endoscopic intervention for CRP in patients with intractable rectal bleeding with broader area when compared to APC. Further controlled studies and follow-up studies are required to compare RFA with other treatment modalities.

Conflicts of Interest

The authors have no conflicts of interest to declare.

References

1. Rustagi T, Mashimo H. Endoscopic management of chronic radiation proctitis. *World J Gastroenterol* 2011;17:4554-62.
2. Weiner JP, Wong AT, Schwartz D, Martinez M, Aytaman A, Schreiber D. Endoscopic and non-endoscopic approaches for the management of radiation-induced rectal bleeding. *World J Gastroenterol* 2016;22:6972-86.
3. Morris KA, Haboubi NY. Pelvic radiation therapy: between delight and disaster. *World J Gastrointest Surg* 2015;7:279-88.
4. Chen MC, Chiang FF, Hsu TW, et al. Clinical experience in 89 consecutive cases of chronic radiation enterocolitis. *J Chin Med Assoc* 2011;74:69-74.
5. Rustagi T, Corbett FS, Mashimo H. Treatment of chronic radiation proctopathy with radiofrequency ablation (with video). *Gastrointest Endosc* 2015;81:428-36.
6. Donaldson SS. Radiation proctitis after prostate carcinoma therapy. *JAMA* 1994;271:819-20.
7. Hayne D, Vaizey CJ, Boulos PB. Anorectal injury following pelvic radiotherapy. *Br J Surg* 2001;88:1037-48.
8. Johnston MJ, Robertson GM, Frizelle FA. Management of late complications of pelvic radiation in the rectum and anus: a review. *Dis Colon Rectum* 2003;46:247-59.
9. Tabaja L, Sidani SM. Management of radiation proctitis. *Dig Dis Sci* 2018;63:2180-8.
10. Castela J, Mao de Ferro S, Ferreira S, Dias Pereira A. Management of severe radiation proctitis with radiofrequency ablation. *GE Port J Gastroenterol* 2019;26:128-30.
11. Sebastian S, O'Connor H, O'Morain C, Buckley M. Argon plasma coagulation as first-line treatment for chronic radiation proctopathy. *J Gastroenterol Hepatol* 2004;19:1169-73.
12. Postgate A, Saunders B, Tjandra J, Vargo J. Argon plasma coagulation in chronic radiation proctitis. *Endoscopy* 2007;39:361-5.
13. Ravizza D, Fiori G, Trovato C, Crosta C. Frequency and outcomes of rectal ulcers during argon plasma coagulation for

chronic radiation-induced proctopathy. *Gastrointest Endosc* 2003;57:519-25.
14. Zhou C, Adler DC, Becker L, et al. Effective treatment of chronic radiation proctitis using radiofrequency ablation. *Therap Adv Gastroenterol* 2009;2:149-56.
15. McCarty TR, Garg R, Rustagi T. Efficacy and safety of radiofrequency ablation for treatment of chronic radiation proctitis: a systematic review and meta-analysis. *J Gastroenterol Hepatol* 2019;34:1479-85.
16. Chi KD, Ehrenpreis ED, Jani AB. Accuracy and reliability of the endoscopic classification of chronic radiation-induced proctopathy using a novel grading method. *J Clin Gastroenterol* 2005;39:42-6.
17. Baum CA, Biddle WL, Miner PB Jr. Failure of 5-aminosalicylic acid enemas to improve chronic radiation proctitis. *Dig Dis Sci* 1989;34:758-60.
18. Alpuim Costa D, Amaro CE, Nunes A, et al. Hyperbaric oxygen therapy as a complementary treatment for radiation proctitis: useless or useful? - A literature review. *World J Gastroenterol* 2021;27:4413-28.
19. Siow SL, Mahendran HA, Seo CJ. Complication and remission rates after endoscopic argon plasma coagulation in the treatment of haemorrhagic radiation proctitis. *Int J Colorectal Dis* 2017;32:131-4.
20. Dray X, Battaglia G, Wengrower D, et al. Radiofrequency ablation for the treatment of radiation proctitis. *Endoscopy* 2014;46:970-6.
21. Eddi R, Depasquale JR. Radiofrequency ablation for the treatment of radiation proctitis: a case report and review of literature. *Therap Adv Gastroenterol* 2013;6:69-76.

原　著

慢性放射性直腸炎病人接受射頻燒灼術治療臨床經驗及長期追蹤

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目的　治療慢性放射性直腸炎的方法目前有不同種治療的方式，本篇研究旨在分享以射頻燒灼術治療慢性放射性直腸炎臨床經驗及長期追蹤。

方法　回溯性分析單一醫學中心自 2015 年 10 月至 2018 年 11 月共 16 位接受射頻燒灼術的慢性放射性直腸炎合併嚴重直腸出血之病患，紀錄及分析病患性別、原發腫瘤位置、症狀、放射線劑量及治療。

結果　病患族群平均年齡為 69.4 歲，含 11 位男性及 5 位女性。原發腫瘤位置依序為攝護腺 9 (56.3%)、子宮頸 5 (31.3%) 以及直腸 2 (12.4%)。所有病患先前已接受過其他藥物或內視鏡治療，後因反覆性直腸出血而求診。有 15 位病患在接受一次射頻燒灼術後症狀得到改善，另一位在接受第二次的射頻燒灼術後症狀也緩解。經治療後可觀察到平均血色素上升，且在血便緩解後所有病人追蹤過程中均不需再接受輸血治療。

結論　放射性直腸炎的病患接受射頻燒灼術可以得到有效且安全的症狀緩解，可以考慮成為針對反覆直腸出血病患的第一線內視鏡治療方式。

關鍵詞　放射性直腸炎、直腸出血、射頻燒灼術。