

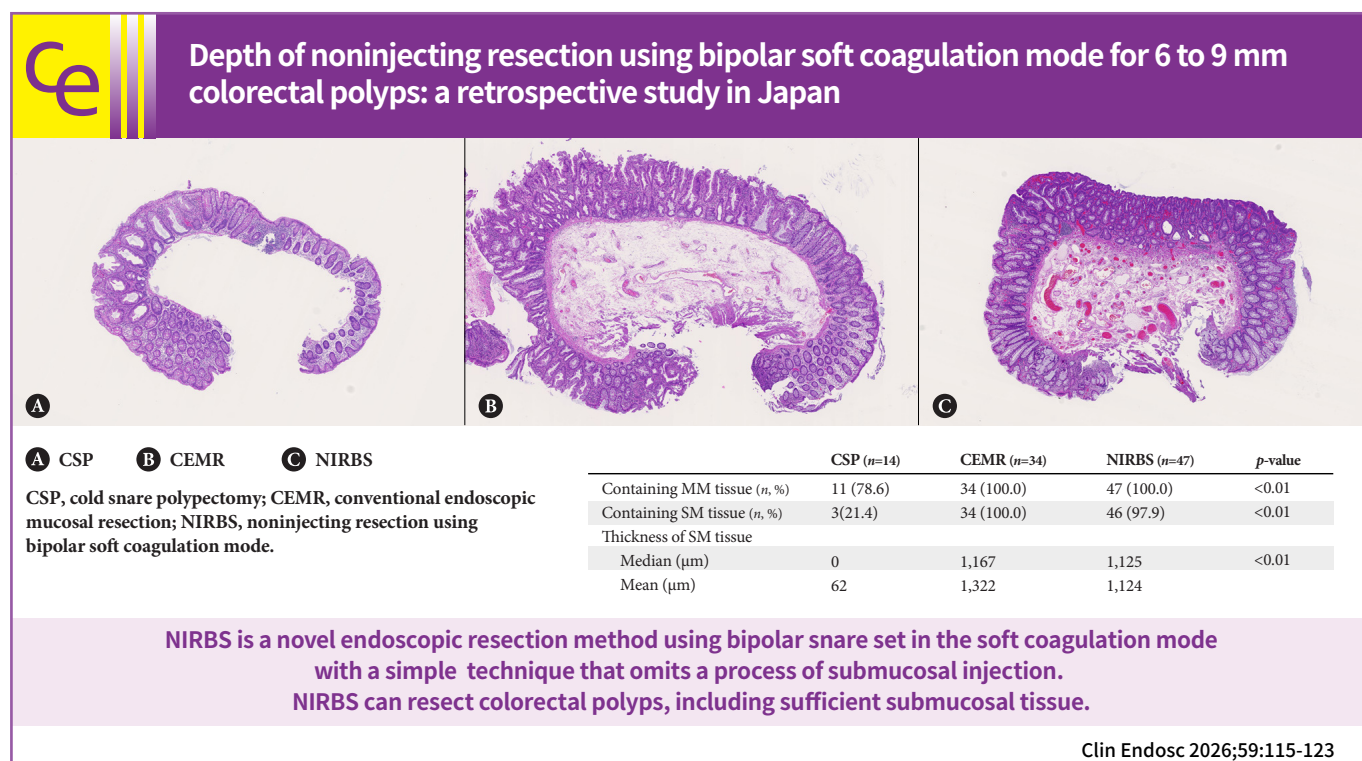


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Depth of noninjecting resection using bipolar soft coagulation mode for 6 to 9 mm colorectal polyps: a retrospective study in Japan

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Background/Aims: Endoscopic resection of colorectal polyps reduces mortality from colorectal cancer. We report here a novel resection method, known as noninjecting resection using bipolar soft coagulation mode (NIRBS), and assess its feasibility. This study aimed to compare the resection depth achieved with NIRBS to those achieved with cold snare polypectomy (CSP) and conventional endoscopic mucosal resection (CEMR).

Methods: Patients with 6 to 9 mm colorectal polyps underwent endoscopic resection at Hoshigaoka Medical Center between October 2023 and January 2024. We analyzed the thickness of resected submucosal tissue following the use of NIRBS, CSP, and CEMR.

Results: We identified 95 polyps, including adenomas and serrated lesions. The proportions of specimens containing submucosal tissue were 21.4%, 100.0%, and 97.9% in CSP, CEMR, and NIRBS, respectively. The median submucosal tissue thickness for CEMR and NIRBS was 1,167 and 1,125 μm , respectively, which was significantly greater than 0 μm for CSP. For NIRBS, the median thickness was 1,140 and 1,017 μm for the expert and non-expert endoscopists, respectively.

Conclusions: The depth of submucosal resection with NIRBS exceeded 1,000 μm regardless of endoscopist experience. NIRBS can be a useful resection method for patients with colorectal polyps, including those with non-submucosally invasive carcinomas.

Keywords: Bipolar snare; Endoscopic mucosal resection; Polyp; Polypectomy; Soft coagulation mode

INTRODUCTION

Colorectal cancer (CRC) is the third most common cancer and second leading cause of cancer-related mortality worldwide.¹ Most cases of CRC develop through the adenoma–carcinoma sequence.² Endoscopic resection of colorectal polyps reduces the development of CRC and prevents CRC-related mortality.^{3,4} Cold snare polypectomy (CSP) is recommended for the removal of colorectal polyps <10 mm in size, whereas conventional endoscopic mucosal resection (CEMR) is typically used for polyps 10 mm or larger.⁵ Advantages of CSP include less effort and fewer complications; however, CSP provides only superficial resection, which may increase the risk of residual lesions or recurrence if high-grade adenomas or carcinomas are present.^{5–8} Although CEMR achieves deeper submucosal (SM) resection compared to CSP, its use can be inconvenient because of the requirement for SM injection.⁹ The ideal method for the resection of colorectal polyps would combine the simplicity and safety profile of CSP with the ability of CEMR to achieve adequate vertical margins and SM tissue resection. Tokuhara et al.¹⁰ introduced a novel endoscopic resection method, noninjecting resection using bipolar soft coagulation mode (NIRBS), and evaluated its feasibility. NIRBS is designed to achieve SM tissue resection using a bipolar snare with the soft coagulation mode, simplifying the procedure by eliminating the need for SM injection. NIRBS is fundamentally different from conventional hot snare polypectomy (CHSP), which utilizes a monopolar snare and forced coagulation mode in the electrosurgical generator.^{9,10} In a series of 746 polyps (mean diameter, 4.5 mm; range, 1–35 mm), NIRBS was associated with a delayed bleeding rate of only 0.27% and no reported cases of perforation.¹⁰

More than 90% of all colorectal polyps are less than 10 mm in size.^{11,12} The cancer prevalence is 0.32% to 0.46% for polyps of 5 mm or smaller and 3.3% to 3.7% for those measuring 6 to 9 mm.^{13,14} High-grade adenomas measuring 6 to 9 mm account for 12.3% of polyps in this size range.¹⁴ Therefore, polyps measuring 6 mm or larger should be carefully assessed for the presence of high-grade adenomas or carcinoma. When early cancer or high-grade adenoma is suspected, CEMR is the commonly adopted technique. NIRBS provides complete resection for patients with early cancer, as all 37 early cancers in one study had negative tumor margins; however, the depth of resection achieved with NIRBS remains unclear.¹⁰ Thus, this study aims to investigate the resection depth of NIRBS compared with that of CSP or CEMR.

METHODS

This study included all consecutive colorectal polyps that were endoscopically resected at Hoshigaoka Medical Center between October 2023 and January 2024. We included 203 patients (716 polyps), and data were collected and analyzed in October 2024. We analyzed only 6 to 9 mm polyps to compare the resection depths when using CSP, CEMR, and NIRBS. The exclusion criteria were histopathological findings other than adenoma and serrated polyps (including sessile serrated lesions and hyperplastic polyps), polyps that could not be precisely assessed histologically, inflammatory bowel disease, or familial adenomatous polyposis. Lesions with irregular surfaces or distorted vessel patterns were resected using CEMR or NIRBS, whereas all methods were used for lesions with regular surfaces and vessel patterns, according to the endoscopist's preference. [Figure](#)

1 shows the case selection and allocation processes used in the study.

All patients underwent standardized bowel preparation before colonoscopy. The administration of antithrombotic drugs was continued or discontinued in accordance with Japanese guidelines for endoscopy with antithrombotic drugs.^{15,16} We used standard colonoscopes (CF-XZ1200I, CF-EZ1500DI, or PCF-H290ZI; Olympus Co.). NIRBS used a bipolar electrosurgical snare (26 mm Dragonare; Zeon Medical Co.), whereas CSP and CEMR used a monopolar electrosurgical snare (15 mm Snare Master Plus; Olympus Co.). The mucosa was screened during the withdrawal period to detect polyps. The locations, sizes, and morphologies of the polyps were recorded. Each polyp was then captured using a snare appropriate for the chosen resection method. For CSP, the polyps were resected without SM injection or electrocautery. For CEMR, the polyps were removed using snare electrocautery (VIO3 Endocut Q effect 2 and forced coagulation effect 4.5; ERBE) after SM injection below the polyp. For NIRBS, the polyps were resected using snare electrocautery (VIO3 soft coagulation effect 3.3; ERBE) without SM injection.¹⁰ The resected polyps were suctioned and retrieved for histological assessment. The resected specimens were fixed in 10% formalin on a plate without pinning and examined using hematoxylin and eosin staining. Six endoscopists performed the polypectomies. Expert endoscopists had at least 10 years of

experience, whereas non-expert endoscopists had less than 10 years of experience. Non-expert endoscopists had no previous experience with NIRBS. Histopathologists evaluated the resected specimens based on the Japanese classification of colorectal carcinomas.¹⁷ The resection depth from the muscularis mucosa (MM) to the vertical resection margin of the SM tissue was measured at the center of each specimen (Fig. 2). The measurements were performed by a single experienced histopathologist who was blinded to patient details. We also evaluated whether the resected specimens contained MM or SM tissue. Additionally, we retrospectively examined cases of early cancer resected using NIRBS during the same period, regardless of polyp size, to confirm whether NIRBS can ensure a therapeutically sufficient resection depth.

Adverse events occurring after endoscopic resection of colorectal polyps were also assessed. Delayed bleeding was defined as a large volume of bloody stool after resection that required endoscopic hemostasis, according to previous studies.⁶ Postpolypectomy syndrome was defined as a localized inflammatory response with abdominal pain, rebound tenderness, fever, leukocytosis, and elevated C-reactive protein levels after resection.

Fisher's exact test was used to compare categorical data. Continuous data were compared between two groups using the Mann-Whitney *U*-test. The Kruskal-Wallis and Steel-Dwass tests were used for comparisons among the three groups. Mul-

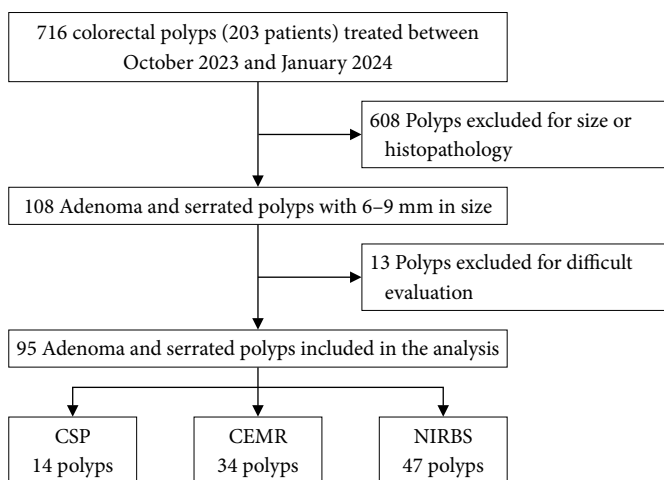


Fig. 1. Flow diagram of the study enrollment. The analysis included 95 adenomas and serrated polyps measuring 6 to 9 mm. Fourteen, 34, and 47 polyps were resected using CSP, CEMR, and NIRBS, respectively. CSP, cold snare polypectomy; CEMR, conventional endoscopic mucosal resection; NIRBS, noninjecting resection using bipolar soft coagulation mode.

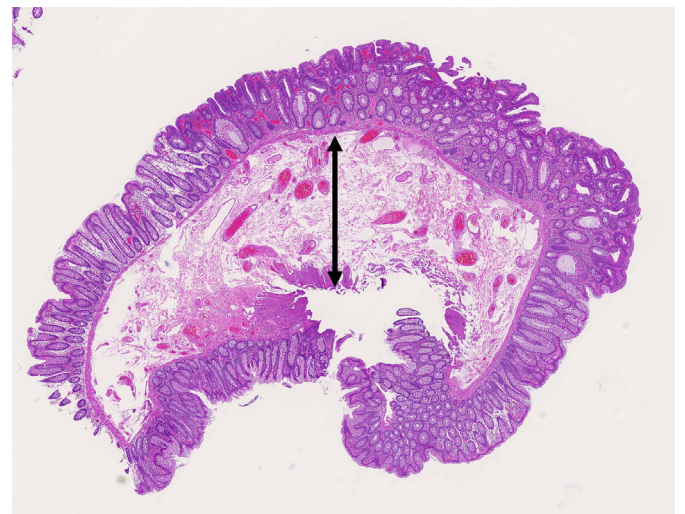


Fig. 2. Measurement method for the resection depth of the submucosal layer. The resection depth from the muscularis mucosa to the vertical resection margin of the submucosal tissue was measured at the center of each specimen. The double-headed arrow indicates the submucosal layer resection depth.

multiple logistic regression analysis was used to evaluate variables related to the containment rate of SM tissue. Statistical significance was set at $p < 0.05$. JMP Pro 17 statistical software (SAS Institute) was used for statistical analyses.

Ethical statements

This study was approved by the Hoshigaoka Medical Center Research Ethics Committee (approval No. 2450). All participants provided informed consent. All procedures involving human participants were conducted in accordance with the institution's ethical standards, the 1964 Helsinki Declaration, and its later amendments or comparable ethical standards.

RESULTS

We resected 108 adenomas and serrated polyps measuring 6 to 9 mm between October 2023 and January 2024. Thirteen polyps were uninterpretable because of destruction caused by suction retrieval or inadequate sectioning. We finally included 95 adenomas and serrated polyps for analysis. Fourteen, 34, and 47 polyps were resected using CSP, CEMR, and NIRBS, respectively (Fig. 1).

Patient characteristics are shown in Table 1. The median ages of patients in the CSP, CEMR, and NIRBS groups were 74, 64, and 71 years, respectively. The anticoagulant and antiplatelet drug usage rates were 9.1%, 16.7%, and 8.8% for the CSP, CEMR, and NIRBS groups, respectively. The median number

of resected polyps per patient was one for each method. Many polyps were found in the right colon across all groups. The median resected polyp sizes were 6 mm for CSP and 7 mm for both CEMR and NIRBS. Histologically, most polyps showed a protruding morphology and were adenomas with low-grade dysplasia. None of the resection methods resulted in delayed bleeding, perforation, or postpolypectomy syndrome.

The histopathological findings are shown in Figure 3. The resected specimens obtained by CSP contained MM, but not SM tissue. By contrast, specimens obtained by CEMR and NIRBS contained both MM and SM tissue. Table 2 shows the histopathological resection depths obtained using CSP, CEMR, and NIRBS. The percentage of specimens containing MM tissue was 78.6% for CSP and 100% for both CEMR and NIRBS. The percentages of specimens containing SM tissue were 21.4%, 100.0%, and 97.9% for CSP, CEMR, and NIRBS, respectively ($p < 0.01$). The median thicknesses of the SM tissue were 0 μm , 1,167 μm , and 1,125 μm for CSP, CEMR, and NIRBS ($p < 0.01$), respectively (Fig. 4). Table 3 presents the results of single and multiple logistic regression analyses comparing factors associated with SM tissue containment between CSP and NIRBS. Only NIRBS was identified as a significant factor in multivariate analysis. Univariate analysis revealed that both polyp size and NIRBS were associated with SM tissue containment.

Expert and non-expert endoscopists resected 19 and 28 polyps measuring 6 to 9 mm, respectively (Table 4). The percentage of specimens containing MM tissue was 100% for both

Table 1. Characteristics of the participants

Characteristic	CSP	CEMR	NIRBS	<i>p</i> -value
Age (median, yr)	74	64	71	0.11
Sex: male/female	9/2	9/9	25/9	0.14
Use of anticoagulant and antiplatelet drugs (n, %)	1 (9.1)	3 (16.7)	3 (8.8)	0.75
Median removed polyps per patient (range)	1 (1–2)	1 (1–5)	1 (1–4)	0.17
Total removed polyps	14	34	47	
Location				0.65
Right colon	7	22	28	
Left colon	7	12	19	
Polyp size (mm)	6	7	7	0.15
Morphology				0.81
Protruded type	11	29	38	
Superficial type	3	5	9	
Histology				0.08
Adenoma with low-grade dysplasia	11	29	45	
Serrated polyp	3	5	2	

CSP, cold snare polypectomy; CEMR, conventional endoscopic mucosal resection; NIRBS, noninjecting resection using bipolar soft coagulation mode.

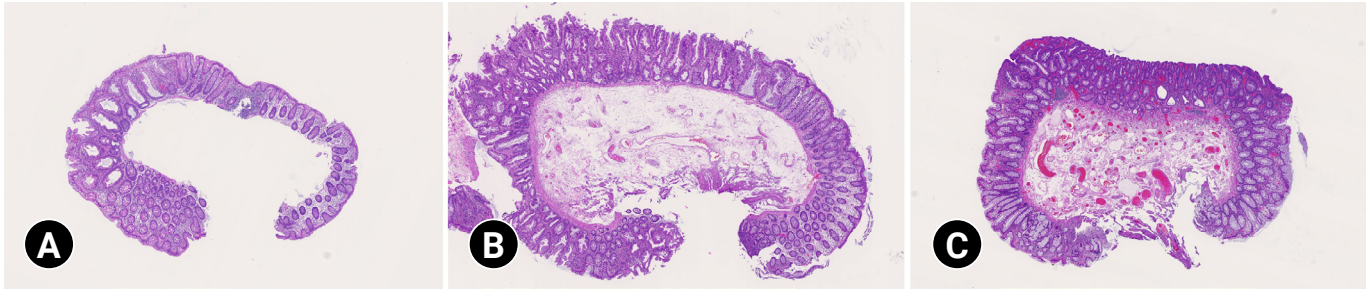


Fig. 3. Histopathological findings. Representative images of polyps resected using cold snare polypectomy (A), conventional endoscopic mucosal resection (B), and noninjecting resection using the bipolar soft coagulation mode (C) (hematoxylin and eosin stain, $\times 4$).

Table 2. Comparison of resection depth using CSP, CEMR and NIRBS

	CSP (n=14)	CEMR (n=34)	NIRBS (n=47)	p-value
Containing MM tissue (n, %)	11 (78.6)	34 (100.0)	47 (100.0)	<0.01
Containing SM tissue (n, %)	3 (21.4)	34 (100.0)	46 (97.9)	<0.01
Thickness of SM tissue				
Median (μm)	0	1,167	1,125	<0.01
Mean (μm)	62	1,322	1,124	

CSP, cold snare polypectomy; CEMR, conventional endoscopic mucosal resection; NIRBS, noninjecting resection using bipolar soft coagulation mode; MM, muscularis mucosa; SM, submucosa.

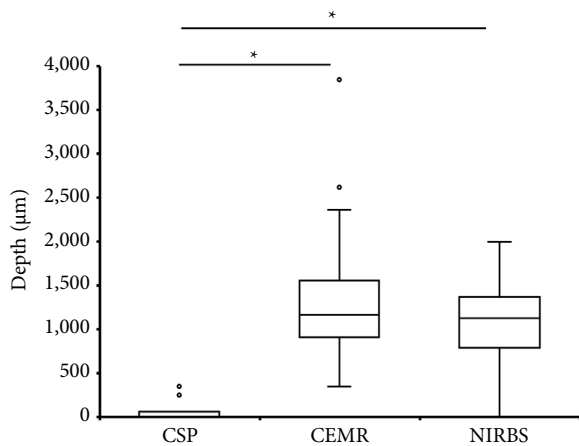


Fig. 4. Comparison of the resection depths using CSP, CEMR, and NIRBS. The median thicknesses of the submucosal tissue were 1,167 and 1,125 μm in CEMR and NIRBS, respectively, which were significantly greater than 0 μm in CSP. CSP, cold snare polypectomy; CEMR, conventional endoscopic mucosal resection; NIRBS, noninjecting resection using bipolar soft coagulation mode. * $p < 0.01$.

endoscopist groups, whereas the percentage containing SM tissue was 100.0% and 96.4% for expert and non-expert endoscopists, respectively. One specimen resected by a non-expert endoscopist with NIRBS on their second procedure lacked SM

tissue. The median thicknesses of SM tissue were 1,140 μm for expert endoscopists and 1,017 μm for non-expert endoscopists ($p = 0.87$).

Table 5 shows the characteristics of all early cancers resected using NIRBS between October 2023 and January 2024. The median size of the cancers was 14 mm (range, 4–20 mm), and 75% exhibited a protruding morphology. The resected SM tissue's median thickness was 1,896 μm . All tumors were resected with sufficient margins (Fig. 5).

DISCUSSION

Snare electrocautery is used to resect tumors in the digestive tract, including SM tissue. CEMR is the gold standard; adequate mucosal lift below the target polyp by SM injection facilitates grasping the polyp with a snare and may reduce perforation risk by thickening the SM layer. By contrast, a disadvantage of SM injection is that snaring the lesion becomes more difficult because of excessive mucosal swelling when appropriate uniform swelling cannot be achieved.¹⁸ Operators also require skill and longer procedure time to effectively perform SM injection. Underwater endoscopic mucosal resection (EMR), which fills the luminal space with fluid instead of SM injection, has

Table 3. Analyses for the containment rate of submucosal tissues among CSP and NIRBS

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	<i>p</i> -value	OR (95% CI)	<i>p</i> -value
Location				
Right colon	1		1	
Left colon	0.68 (0.19–2.44)	0.56	0.58 (0.05–6.53)	0.65
Polyp size	3.52 (1.13–10.92)	0.02	4.29 (0.31–57.60)	0.27
Morphology				
Protruded	1		1	
Superficial type	1.28 (0.24–6.80)	0.77	6.37 (0.001–982.83)	0.67
Histology				
Adenoma	1		1	
Serrated polyp	0.32 (0.04–2.21)	0.25	0.64 (0.0001–3,618.7)	0.92
Treatment				
CSP	1		1	
NIRBS	168.66 (15.97–1,780.6)	<0.01	149.22 (10.50–2,119.3)	<0.01

CSP, cold snare polypectomy; NIRBS, noninjecting resection using bipolar soft coagulation mode; OR, odds ratio; CI, confidence interval.

Table 4. Comparison of resection depth between expert and non-expert endoscopists

	Expert (<i>n</i> =19)	Non-expert (<i>n</i> =28)	<i>p</i> -value
Containing MM tissue (<i>n</i> , %)	19 (100.0)	28 (100.0)	1.00
Containing SM tissue (<i>n</i> , %)	19 (100.0)	27 (96.4)	1.00
Thickness of SM tissue			
Median (μm)	1,140	1,017	0.87
Mean (μm)	1,121	1,126	

MM, muscularis mucosa; SM, submucosa.

emerged as an alternative method.¹⁹ Underwater EMR is expected to improve the *en bloc* resection rate by facilitating floating techniques and reduce thermal injury to surrounding tissue because of the heat sink effect. However, this method requires more effort and time for water immersion, which can sometimes be difficult for non-expert endoscopists. CHSP is a simple method involving grasping target polyps without SM injection and resecting them using snare electrocautery. CHSP can be used to resect polyps including SM tissue. The mean depths of resected SM tissue were 1,720 μm in a porcine model and 933 μm in humans.^{20,21} However, CHSP causes thermal degeneration in the deep submucosa and muscularis propria.²² Necrosis and inflammation of the muscularis propria occurred in 2% and 12%, respectively, and transmural subserosal inflammation was seen in 10% of animal experiments.²⁰ Therefore, resection methods without SM injection must address the issue of vertical thermal damage that can lead to perforation and postpolypectomy syndrome.

We took two approaches to reduce complications during endoscopic resection using snare electrocautery. First, a bipolar snare was used. Monopolar snares have been used in most procedures. In 1979, the first use of a bipolar snare for endoscopic resection was reported.²³ Electric current flows from the snare toward the sheath electrode, thus avoiding current flow through the colorectal wall.^{23,24} Moreover, lower energy is required when using a bipolar snare compared to a monopolar snare.²⁵ These mechanisms lead to less thermal degeneration of the surrounding tissue and a reduced risk of perforation. Tucker et al.²⁵ reported that bipolar snare polypectomy caused an average depth of damage to the underlying gastric wall of only 32%, whereas monopolar snare polypectomy caused an average depth of damage of 69%. Second, the setting mode of the electrosurgical generator was changed. The current should be minimal enough to facilitate cutting of the SM tissue but not the muscularis propria. The electric voltage in the NIRBS mode was approximately one-fourth of that in the conventional bipolar forced coagulation mode.¹⁰ Additionally, the soft coagulation mode had less heat spread than the forced coagulation mode. These approaches enable safer snare electrocautery without SM injection, thereby reducing the risk of vertical thermal injury.

The vertical margin of endoscopic resection using the snare in CSP was superficial with few SM tissues, whereas CEMR specimens contained sufficient SM tissue.^{9,21,26} The median thickness of SM tissue in CSP was 0 to 76 μm for polyps ≤9 mm.^{9,21,26} The resection depths in this study were similar to

Table 5. Cases of early cancer resected by NIRBS

	Age (yr)	Sex	Location	Polyp size (mm)	Morphology	Histology	Depth of tumor invasion	Lymphatic and venous invasion	Horizontal and vertical margin	Thickness of SM tissue (μm)
1	74	Female	Transverse colon	4	Superficial type	Tub2	Mucosa	No	No tumor	1,158.79
2	81	Male	Descending colon	20	Protruded type	Tub1	Mucosa	No	No tumor	2,634.84
3	80	Male	Sigmoid colon	16	Protruded type	Tub1	Mucosa	No	No tumor	3,976.62
4	81	Male	Sigmoid colon	13	Protruded type	Tub1	Mucosa	No	No tumor	449.66

NIRBS, noninjecting resection using bipolar soft coagulation mode; SM, submucosa; tub1, well differentiated tubular adenocarcinoma; tub2, moderately differentiated tubular adenocarcinoma.

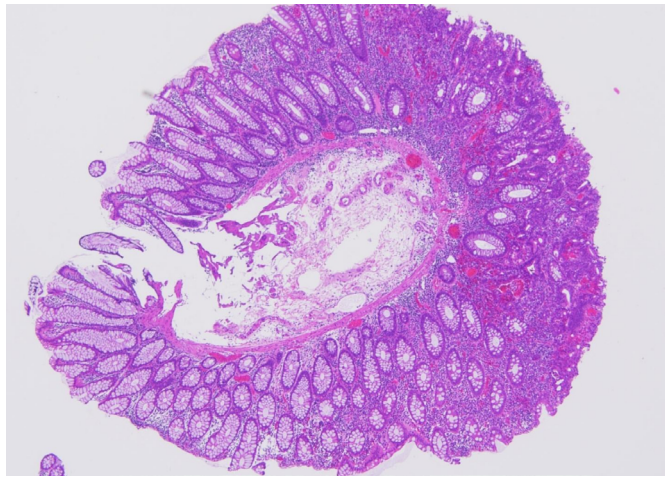


Fig. 5. Histopathological findings of an early cancer resected by non-injecting resection using bipolar soft coagulation mode (hematoxylin and eosin stain, ×40).

those reported previously. This study showed that the resection depth of NIRBS specimens was greater than that of CSP and was not significantly different from that of CEMR. Almost all NIRBS specimens contained SM tissue, except for one case in which a non-expert endoscopist performed NIRBS for the second time, indicating the potential of NIRBS to improve the weakness of CHSP, in which 17% to 18.5% of resected specimens contained no SM tissue.^{9,21} This study showed that the median depths of SM tissue were 1,192 and 1,137 μm in CEMR and NIRBS, respectively; however, SM injection in CEMR may artificially increase the apparent resection depth because the injected fluid thickens the SM layer.²⁷ NIRBS requires no SM injection and may represent the true SM resection depth. Resected specimens containing ≥1,000 μm of SM tissue are necessary because a SM invasion depth ≥1,000 μm is an indication for additional treatment after endoscopic resection.²⁸ Similar to CEMR, NIRBS also contained >1,000 μm of SM tissue. Thus, both CEMR and NIRBS are suitable for resecting high-grade

dysplasia and early cancer, for which tumor-free vertical margin resection is desirable.

Differences in resection depth among endoscopists should be clarified to confirm the reliability of snare-based resection methods. The resection depth by non-expert endoscopists was shallower than that by expert endoscopists in CEMR, indicating that the CEMR technique may be affected by the endoscopists' experience.²⁷ The median resection depths using NIRBS were 1,017 and 1,140 μm for non-expert and expert endoscopists, respectively. In contrast to CEMR, our results showed no significant difference in the resection depth of NIRBS according to the endoscopist's experience. NIRBS enables reliable resection, including that of SM tissue, even when performed by inexperienced endoscopists from the early stages of its introduction.

This study has several limitations. First, it was a single-center study; second, the resection method was selected based on each endoscopist's preference. Our resection depth results for CSP and CEMR were similar to those of previous reports.^{9,21,27} Therefore, we believe that our endoscopists had standard skills for endoscopic resection of colorectal polyps, but selection bias remains. Third, all polyps were retrieved by suction and fixed in formalin without stretching. Thirteen polyps could not be assessed pathologically because of destruction during the suction retrieval process or because they were not cut vertically.

In conclusion, NIRBS is a simple method for resecting colorectal polyps, including SM tissue. The SM layer resection depth in NIRBS is >1,000 μm, regardless of endoscopist experience. NIRBS can be a useful resection method for all colorectal polyps, including those with non-SM invasive cancers.

Conflicts of Interest

The authors have no potential conflicts of interest.

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None.

Author Contributions

Conceptualization: YW; Data curation: YW, MT; Formal analysis: YW, MT; Investigation: YW, MT, IT; Methodology: YW, MT; Project administration: YW; Resources: YW; Validation: HidN, HirN, YS; Writing–original draft: YW; Writing–review & editing: all authors.

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