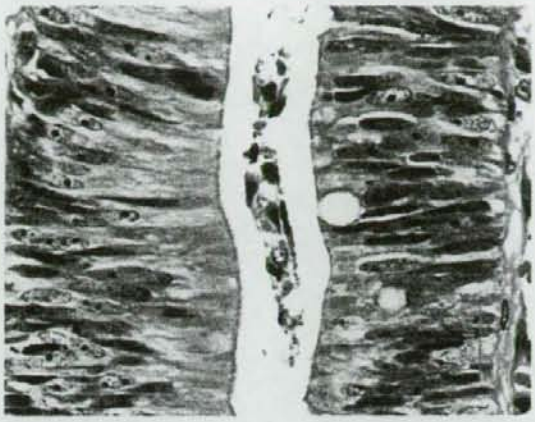
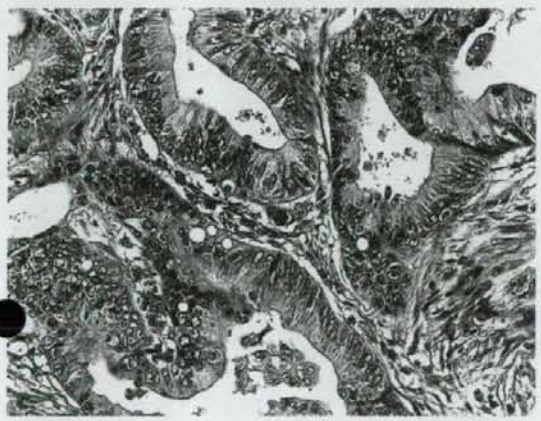
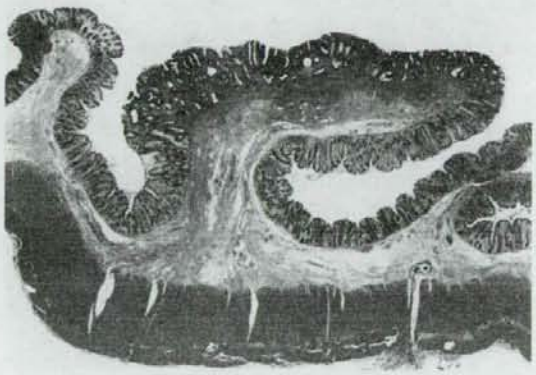
A9. Histopathology of neoplastic lesion, 8 mm, 0-IIa, panoramic view (H&E, orig. mag. × 50).



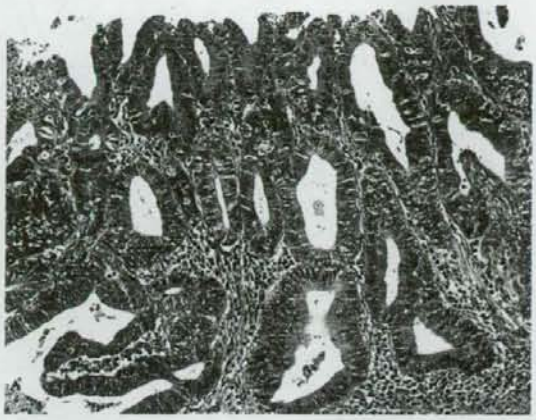
A11. Histopathology of neoplastic lesion, low-grade cell atypia, well-differentiated intramucosal adenocarcinoma; hyperchromatic elongated nuclei in basal arrangement (H&E, orig. mag. × 300).



A10. Same case as in image no. 9. Low-grade cell atypia, well-differentiated adenocarcinoma, no residual adenoma; submucosal invasion (H&E, orig. mag. × 150).

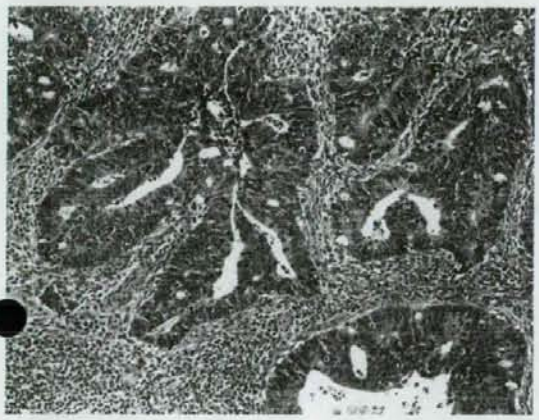


A12. Histopathology of neoplastic lesion, 7 mm, 0-IIa, panoramic view (H&E, orig. mag. × 40).

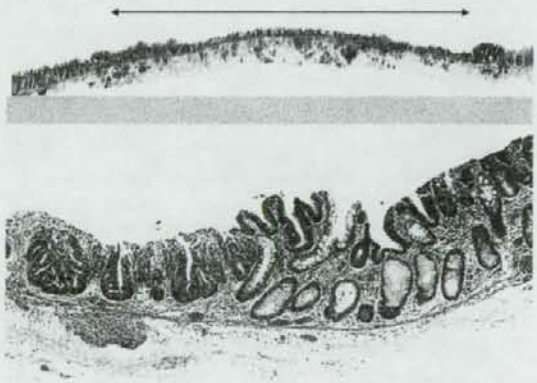


A13. Same case as in image no. 12. High-grade cell atypia, well-differentiated intramucosal adenocarcinoma, no residual adenoma; nuclei up to apical pole of cells (H&E, orig. mag. × 100).

A15. Operative specimen after fixation, mucosectomy; neoplastic lesion 20 mm, 0-IIc.

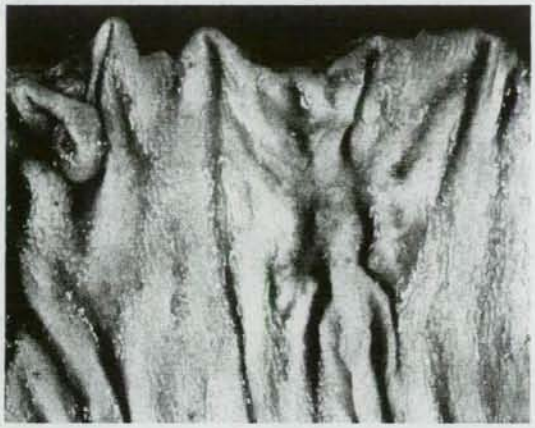


A14. Histopathology of neoplastic lesion, 5 mm, 0-IIa + 0-IIc; high-grade cell atypia, well-differentiated adenocarcinoma, submucosal invasion; no residual adenoma; nuclei up to apical pole of cells (H&E, orig. mag. × 150).

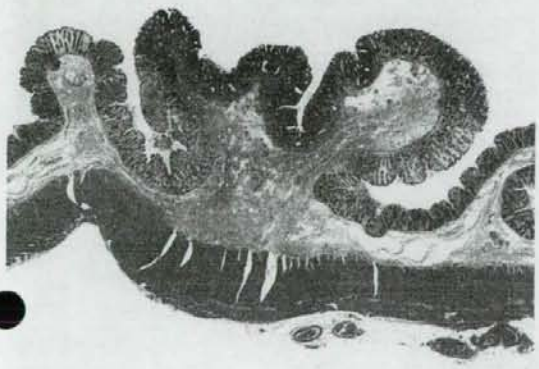


A16. Same case as in image no. 15. Panoramic view, showing a large flat depression (*upper*) (H&E, orig. mag. × 20); well-differentiated intramucosal adenocarcinoma, no residual adenoma (*lower*) (H&E, orig. mag. × 50).

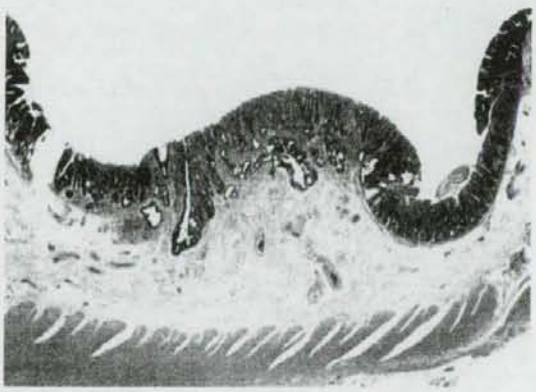
A17. Operative specimen, fresh, neoplastic lesion 7 mm, 0-IIc.



A19. Operative specimen after fixation. Neoplastic lesion, 20 mm, 0-IIc, deep mucosal depression, fold convergence suggestive of invasive cancer.

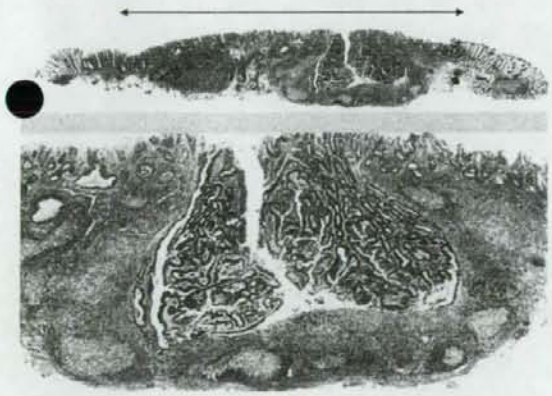


A18. Same case as in image no. 17. Well-differentiated intramucosal adenocarcinoma, no residual adenoma (H&E, orig. mag. × 40).



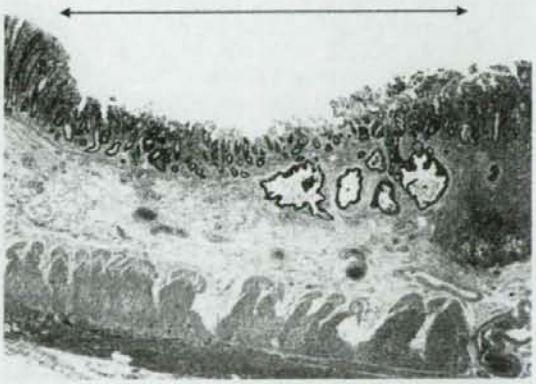
A20. Same case as in image no. 19. Well-differentiated adenocarcinoma, submucosal invasion, no residual adenoma (H&E, orig. mag. × 60).

A21. Operative specimen after fixation, mucosectomy, neoplastic lesion, 20 × 13 mm, 0-IIc.

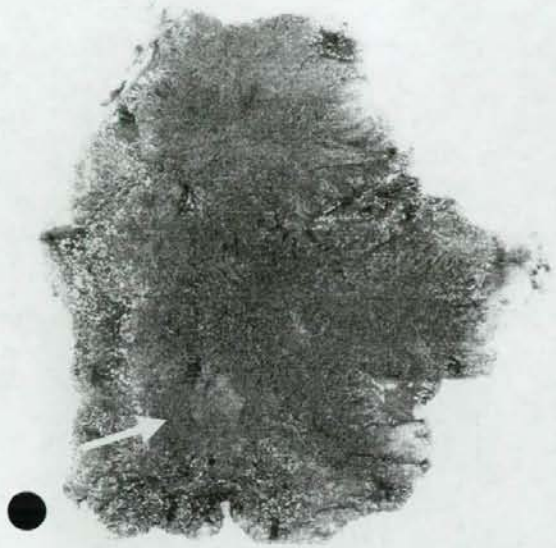


A22. Same case as in image no. 21. Panoramic view, central elevation in a shallow depression (*upper*) (H&E, orig. mag. × 20); well-differentiated adenocarcinoma, submucosal invasion, 1500 μm in depth, no residual adenoma (*lower*) (H&E, orig. mag. × 50).

A23. Operative specimen after fixation, neoplastic lesion, 8 mm, 0-IIc, deep depression; convergence of fold suggestive of invasive cancer.

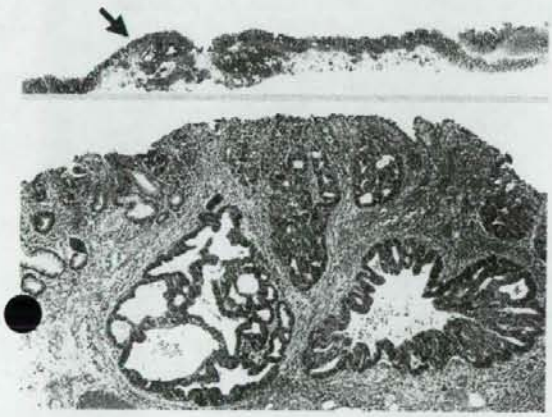


A24. Same case as in image no. 23. Well-differentiated adenocarcinoma, submucosal invasion at the level of the depression, no residual adenoma (H&E, orig. mag. × 60).

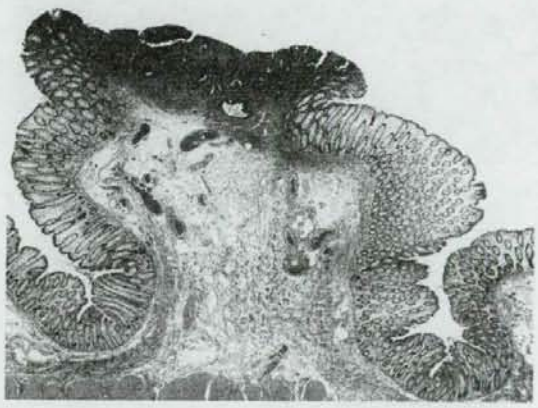


A25. Operative specimen after fixation, mucosectomy, neoplastic lesion, 39 × 33 mm, 0-IIc + IIa, depressed area with a small elevated nodule (*arrow*).

A27. Operative specimen after fixation, neoplastic lesion 5 mm, 0-IIa + IIc.



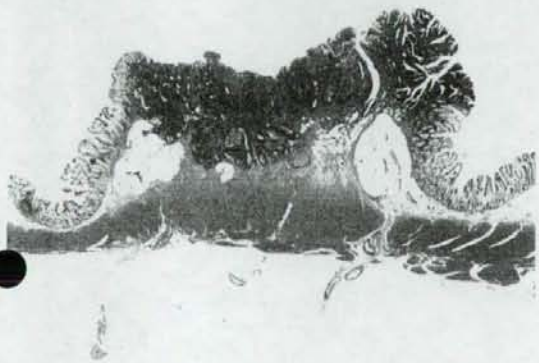
A26. Same case as in image no. 25. Panoramic view of lesion (*upper*) (H&E, orig. mag. × 20); moderately differentiated adenocarcinoma, submucosal invasion, no residual adenoma (*lower*) (H&E, orig. mag. × 50).



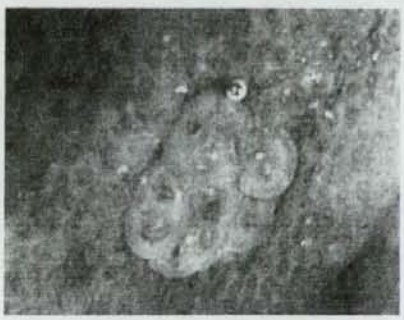
A28. Same case as in image no. 27. Panoramic view of depressed surface of the lesion; well-differentiated adenocarcinoma, submucosal invasion, no residual adenoma (H&E, orig. mag. × 60).

A29. Operative specimen, fresh, neoplastic lesion, 13 mm, 0-IIa + IIc, slightly elevated tumor, with irregular central depression.

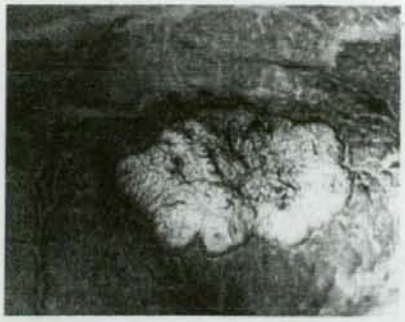
A31. Endoscopy (magnification ×100), chromoscopy with methylene blue 0.01%; ACF nonneoplastic in the rectum; cluster of enlarged crypts.



A30. Same case as in image no. 29. Moderately differentiated advanced adenocarcinoma, massive submucosal invasion that involved muscularis propria, no residual adenoma (H&E, orig. mag. × 40).



A32. Endoscopy (magnification ×100) and NBI; ACF, nonneoplastic; cluster of enlarged crypts; no pericryptic vascular change.

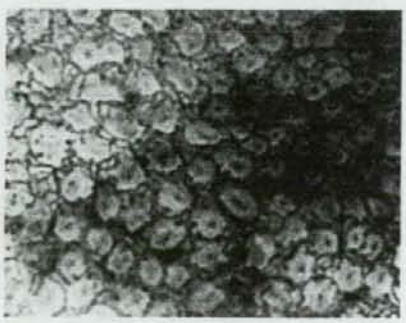


A33. Endoscopy (magnification ×100), chromoscopy with methylene blue 0.01%; ACF, neoplastic; cluster of enlarged, disordered crypts.

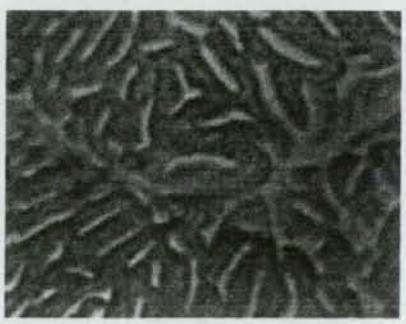
A36. Endoscopy (magnification), chromoscopy with cresyl violet; HP lesion; pit pattern II, star-like crypt openings.

A34. Endoscopy (magnification), chromoscopy with cresyl violet; normal colonic mucosa. Pit pattern I.

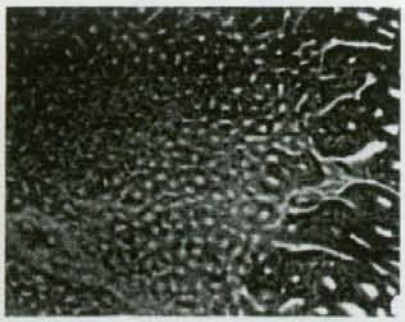
A37. Endoscopy (magnification), NBI; HP lesion; vascular pattern "faint."



A35. Endoscopy(magnification), NBI; normal colonic mucosa; vascular pattern "normal."

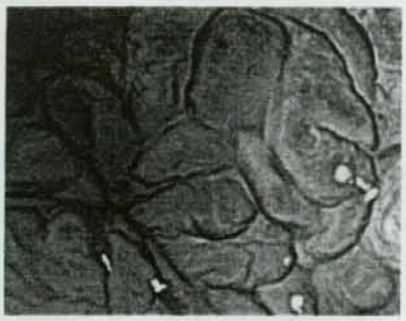


A38. Endoscopy (magnification), chromoscopy with cresyl violet, neoplastic lesion, premalignant; pit pattern IIIL, large crests.

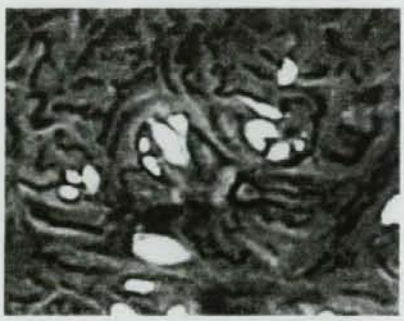


A39. Endoscopy (magnification), chromoscopy with cresyl violet; neoplastic lesion, premalignant; pit pattern IIIS, narrow crypt openings.

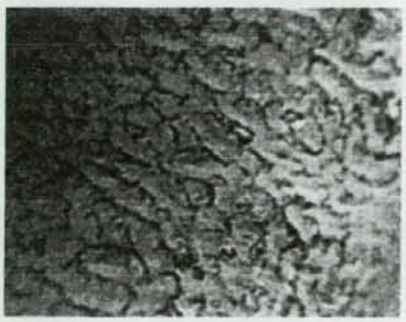
A42. Endoscopy (magnification), chromoscopy with cresyl violet carcinoma; pit pattern Vi, irregular.



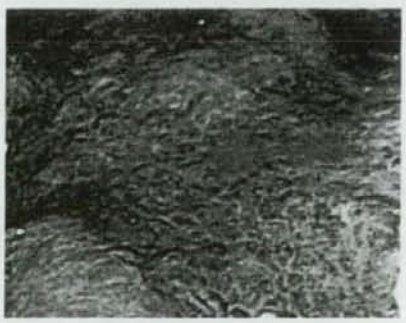
A40. Endoscopy (magnification), chromoscopy with cresyl violet, neoplastic lesion, premalignant; pit pattern IV, branched crests.



A43. Endoscopy (magnification), NBI; carcinoma; vascular pattern "irregular."

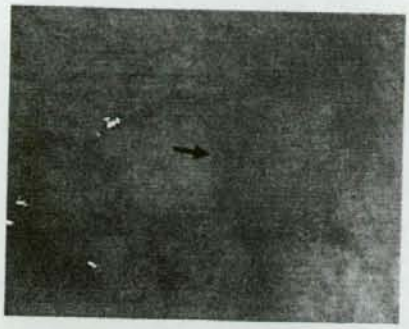


A41. Endoscopy (magnification), NBI; neoplastic lesion, premalignant; vascular pattern "network."

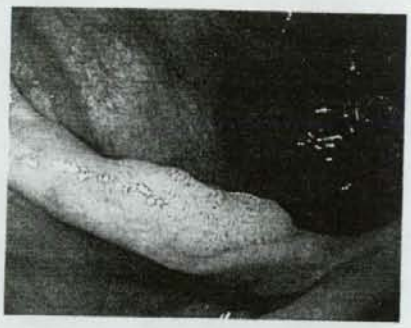


A44. Endoscopy (magnification), chromoscopy with cresyl violet; carcinoma; pit pattern VN, nonstructural.

A45. Endoscopy (magnification), NBI; carcinoma; vascular pattern "sparse."

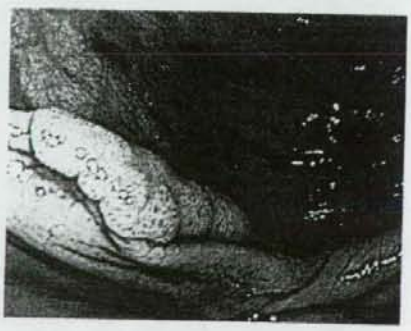


A48. Endoscopy, slightly elevated neoplastic lesion (*arrow*), 0-IIa.

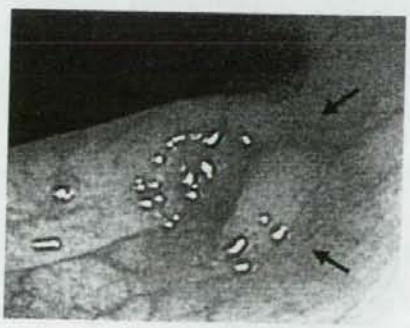


A46. Endoscopy, slightly elevated neoplastic lesion, 0-IIa.

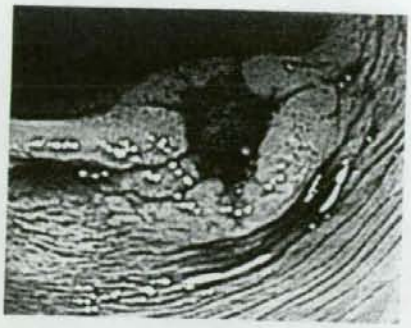
A49. Same case as in image no. 48, chromoscopy with indigo carmine.



A47. Same case as in image no. 46, chromoscopy with indigo carmine.

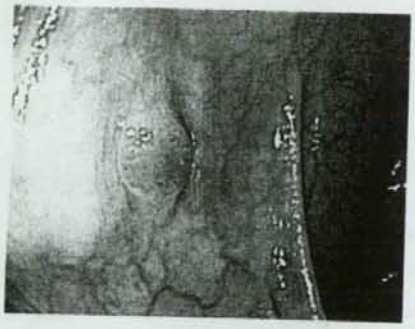


A50. Endoscopy, depressed neoplastic lesion (*arrows*), 0-IIc.

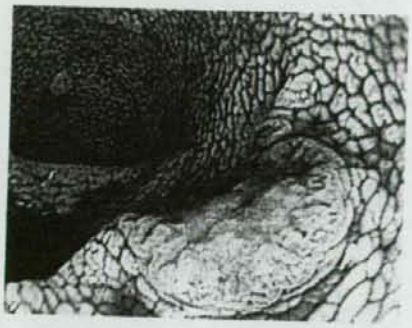


A51. Same case as in image no. 50, chromoscopy with indigo carmine.

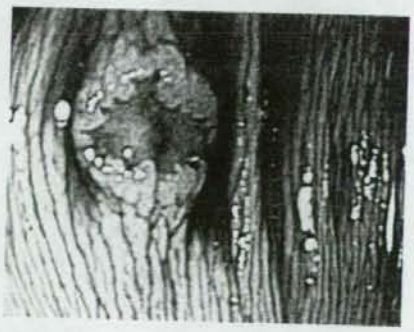
A54. Endoscopy, depressed neoplastic lesion, 7 mm, 0-IIc.



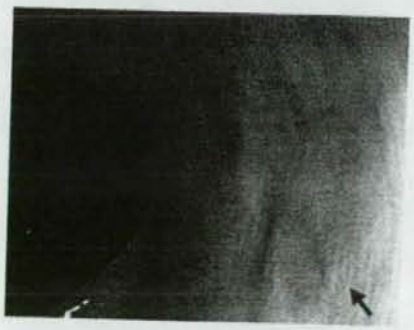
A52. Endoscopy, depressed neoplastic lesion, 4 mm, 0-IIc; the lesion appears as elevated above the surface; can be mistaken for 0-IIa.



A55. Same case as in image no. 54, chromoscopy with indigo carmine.

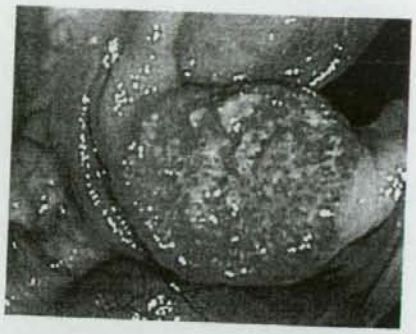


A53. Same case as in image no. 52, chromoscopy with indigo carmine.

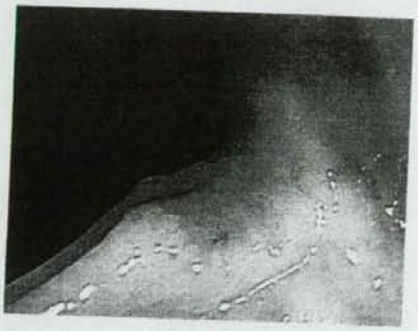


A56. Endoscopy, depressed neoplastic lesion (*arrow*), 4 mm, 0-IIc, intramucosal carcinoma.

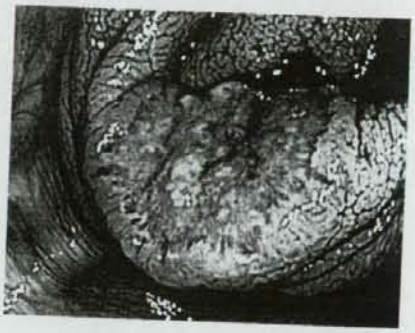
A57. Same case as in image no. 56, chromoscopy with indigo carmine.



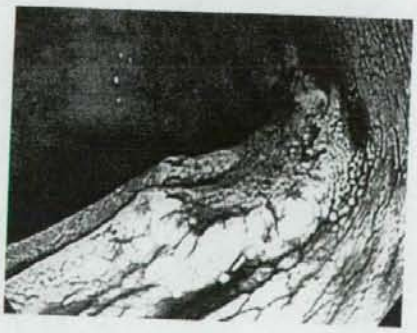
A60. Endoscopy, slightly elevated and depressed neoplastic lesion, 0-IIa + 0-IIc.



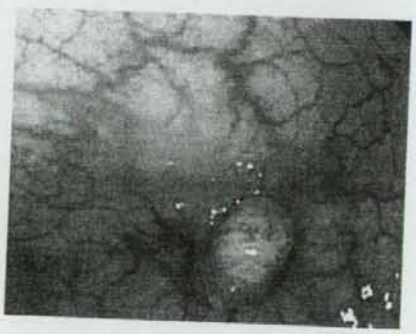
A58. Endoscopy, depressed neoplastic lesion, 7 mm, 0-IIc, carcinoma with submucosal invasion s1.



A61. Same case as in image no. 60, chromoscopy with indigo carmine.

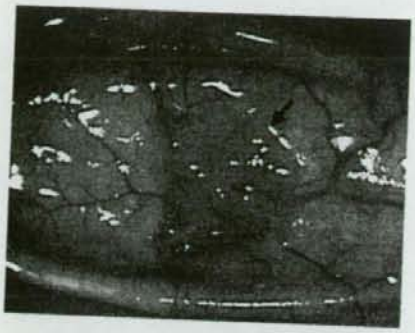


A59. Same case as in image no. 58, chromoscopy with indigo carmine.

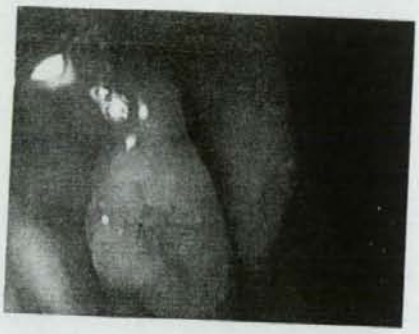


A62. Endoscopy, depressed and polypoid sessile neoplastic lesion, 0-IIc, 0-Is.

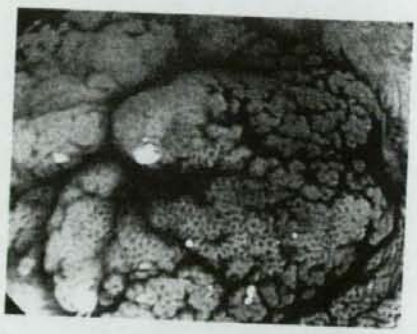
A63. Same case as in image no. 62, chromoscopy with indigo carmine.



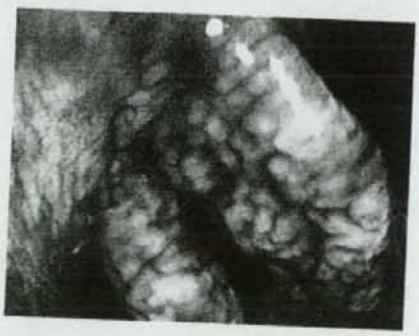
A66. Endoscopy, sessile serrated lesion (*arrow*), 0-IIa.



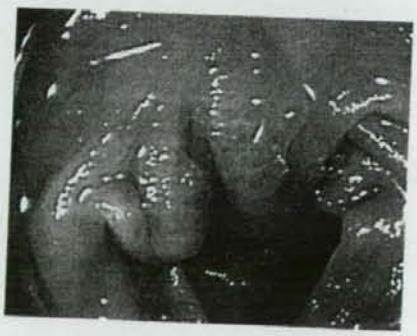
A64. Endoscopy, HP lesion, 0-IIa.



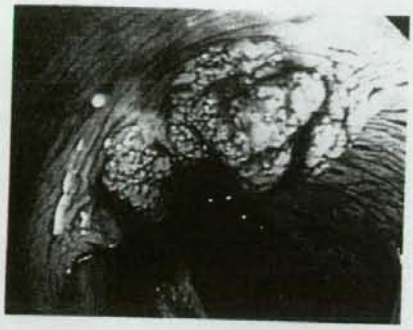
A67. Same case as in image no. 66, chromoscopy with indigo carmine; star-shaped opening of pits in some areas.



A65. Same case as in image no. 64, chromoscopy with indigo carmine.



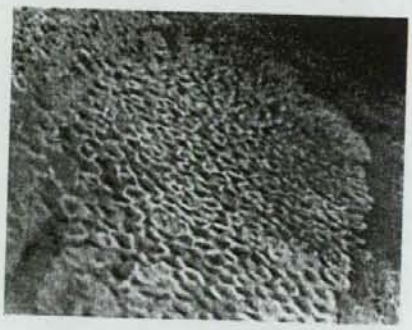
A68. Endoscopy, sessile serrated lesion, 0-IIa.



A69. Same case as in image no. 68, chromoscopy with indigo carmine.

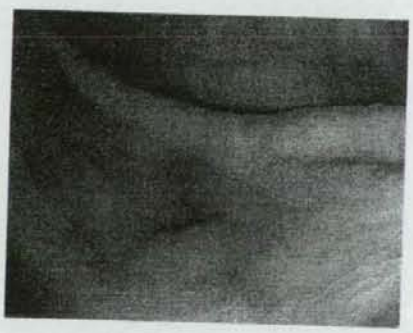
A72. Endoscopy (magnification); ulcerative colitis, quiescent: a flat villous area.

A70. Endoscopy, sessile serrated lesion, with NBI, 0-IIa.

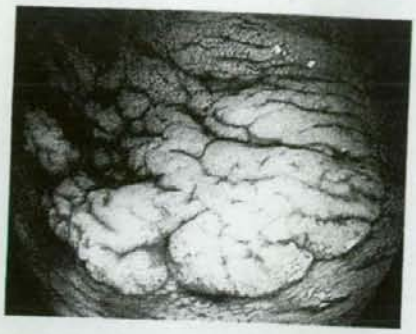


A73. Endoscopy (magnification), chromoscopy with indigo carmine; ulcerative colitis, quiescent; a flat HP lesion with large crypt openings 0-IIb.

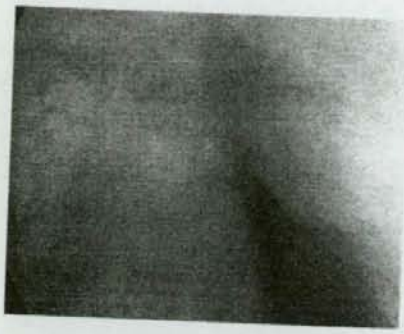
A71. Endoscopy, sessile serrated lesion (*arrow*), with NBI, 0-IIb.



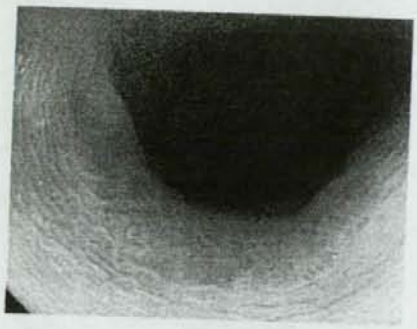
A74. Endoscopy, LST lesion, nongranular, slightly elevated 0-IIa.



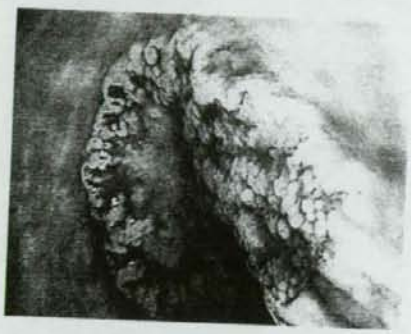
A75. Same case as in image no. 74, chromoscopy with indigo carmine.



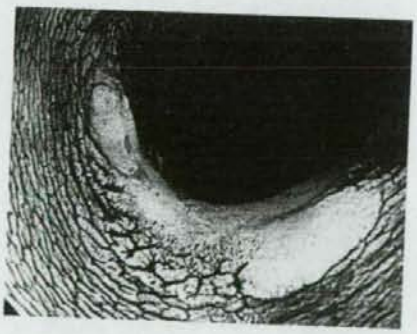
A78. Endoscopy, LST lesion, nongranular, pseudodepressed, 0-IIa + 0-IIc.



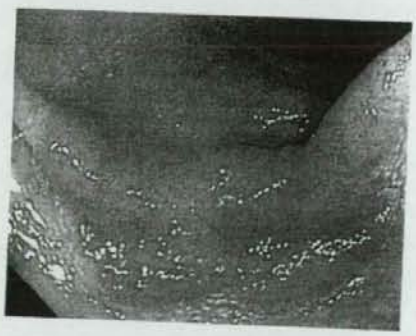
A76. Endoscopy, LST lesion, nongranular, slightly elevated 0-IIa.



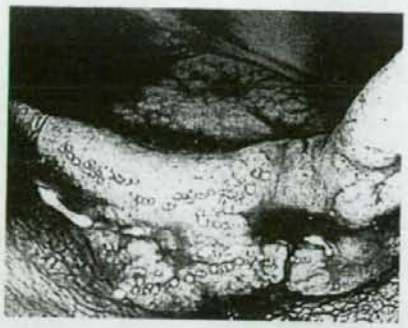
A79. Same case as in image no. 78, chromoscopy with indigo carmine.



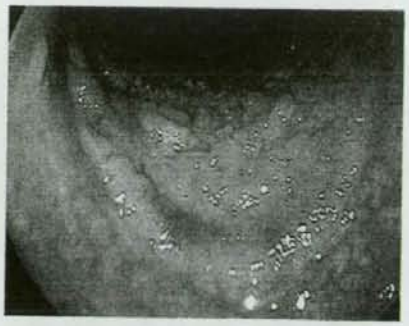
A77. Same case as in image no. 76, chromoscopy with indigo carmine.



A80. Endoscopy, LST lesion, nongranular, slightly elevated 0-IIa.

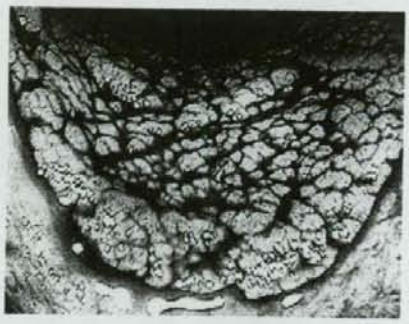


A81. Same case as in image no. 80, chromoscopy with indigo carmine.

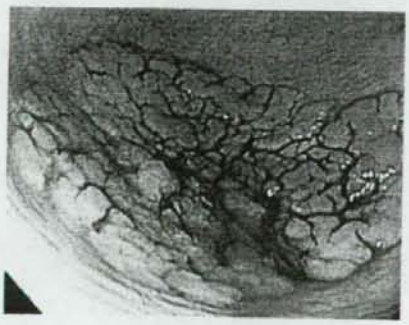


A84. Endoscopy, LST lesion, granular, homogenous, 0-IIa.

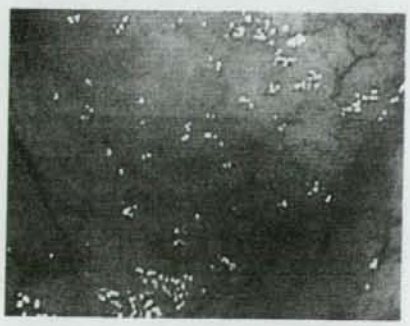
A82. Endoscopy, LST lesion, granular, homogenous, 0-IIa.



A85. Same case as in image no. 84, chromoscopy with indigo carmine.

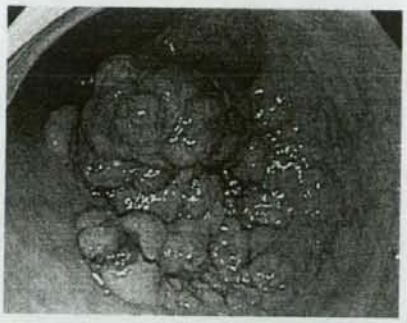


A83. Same case as in image no. 82, chromoscopy with indigo carmine.



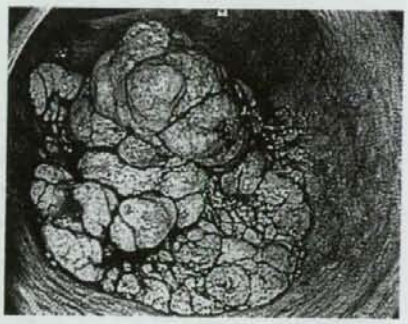
A86. Endoscopy, LST lesion, granular, homogenous, 0-IIa.

A87. Same case as in image no. 86, chromoscopy with indigo carmine.



A89. Endoscopy, LST lesion, granular, mixed type, with irregular and sessile nodules, 0-Is + 0-IIa.

A88. Endoscopy (magnification), NBI; LST lesion, granular, homogenous, 0-IIa, pit pattern type IV.



A90. Same case as in image no. 89, chromoscopy with indigo carmine.

doi:10.1111/j.1440-1746.2008.05635.x

GASTROENTEROLOGY

Detectability of colorectal neoplastic lesions using a narrow-band imaging system: A pilot study

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Key words
colonoscopy, colorectal neoplastic lesion, detection, narrow-band imaging (NBI), screening.

Accepted for publication 21 May 2008.

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Abbreviations: HDC, high definition colonoscopy; HNPCC, hereditary nonpolyposis colorectal cancer; IC, indigo carmine; NBI, narrow-band imaging; NCCH, National Cancer Center Hospital; RCCPS, National Cancer Center Research Center for Cancer Prevention and Screening.

Abstract

Background and Aim: Flat and depressed colorectal neoplastic lesions can be difficult to identify using conventional colonoscopy techniques. Narrow-band imaging (NBI) provides unique views especially of mucosal vascular network and helps in visualization of neoplasia by improving contrast. The aim of this study was to assess the feasibility of using NBI for colorectal neoplasia screening.

Methods: Forty-seven consecutive patients, who underwent high definition colonoscopy (HDC) screening examinations revealing neoplastic lesions, were enrolled in our prospective study. No biopsies or resections were performed during the initial HDC, but patients in whom lesions were detected underwent further colonoscopies using NBI, with the results of the first examination blinded from the colonoscopist. They then received appropriate treatment. We compared diagnostic detection rates of neoplastic lesions for HDC and NBI procedures using total number of all identified neoplastic lesions as reference standard.

Results: Altogether, 153 lesions were detected and analyzed in 43 patients. Mean diagnostic extubation times were not significantly different ($P = 0.18$), but the total number of lesions detected by NBI was higher (134 *vs* 116; $P = 0.02$). Based on macroscopic type, flat lesions were identified more often by NBI ($P = 0.04$). As for lesion size, only flat lesions < 5 mm were detected more frequently ($P = 0.046$). Lesions in the right colon were identified more often by NBI ($P = 0.02$), but NBI missed two flat lesions ≥ 10 mm located there.

Conclusions: Narrow band imaging colonoscopy may represent a significant improvement in the detection of flat and diminutive lesions, but a future multi-center controlled trial should be conducted to fully evaluate efficacy for screening colonoscopies.

Introduction

Early detection and removal of colorectal adenomas have been shown to reduce both the incidence of cancer and cancer-related mortality.[1–3] Colonoscopy is considered to be an effective examination method for the detection of colorectal neoplastic lesions,[1,4] but adenomatous polyps are sometimes missed during routine colonoscopies. Studies using back-to-back examinations have found that the undetected rate for adenomatous polyps was approximately 25%[5,6] and even adenomas greater than 1 cm have been missed.

Recent studies have shown that flat and depressed colorectal neoplasms may contribute to the development of colorectal cancers[7–11] although it is difficult to detect such lesions endoscopically. A need exists for better endoscopic visualization, therefore, especially of flat and depressed colorectal lesions. Endoscopic techniques that improve detection of such adenomas will help maximize effectiveness of colonoscopic examinations in diagnosing colorectal cancers.

Narrow-band imaging (NBI) technology is based on modifying spectral features by narrowing spectral transmittance bandwidth using various optical filters.[12] We first reported that it provided a unique view particularly of the mucosal vascular network and the surface structure.[13] Usefulness of NBI has been reported in endoscopic diagnosis of the gastrointestinal tract,[14–21] oro-hypopharynx[22] and bronchus.[23] In the colorectum, previous research on the usefulness of NBI with magnification for differential diagnosis between neoplastic and non-neoplastic lesions has been conducted,[14–16] but there are only a few reports on its effectiveness in actually detecting neoplastic lesions.[24,25]

The aim of our prospective study was to assess the feasibility of using NBI for colorectal neoplasia screening.

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Methods

Patients and study design

The Research Center for Cancer Prevention and Screening (RCCPS) of the National Cancer Center (NCC), Tokyo, Japan, conducted a prospective cohort study including screening colonoscopy on study participants at baseline.[26] High definition colonoscopies (HDCs) using magnification were performed on patients at RCCPS to detect and diagnose neoplastic lesions, but no treatments or biopsies were performed there because of government insurance-imposed restrictions and the need to comply with existing RCCPS and NCC policies. The RCCPS performs colorectal examinations on patients only for screening purposes in order to detect and diagnose neoplastic lesions so this study utilized the cancer screening and treatment system that had already been developed in close cooperation between RCCPS and the adjacent National Cancer Center Hospital (NCCH).

Subjects found to have neoplastic lesions were enrolled in this study and treated at NCCH. Exclusion criteria included patients with advanced colorectal cancer; genetic syndromes such as hereditary non-polypoid colon cancer (HNPCC) and familial adenomatous polyposis; inflammatory bowel disease; or a previous colonic resection. In addition, patients with polypoid lesions $\geq$ 20 mm in size were excluded because such lesions could be readily identified during intubation prior to NBI so those patients were unsuitable for our purposes in comparing detectability between HDC and NBI. Patients with inadequate bowel preparation also were excluded from this study. A total of 47 consecutive patients with neoplastic lesions 5 mm or larger in size detected at RCCPS, who subsequently were scheduled to undergo removal of such lesions at NCCH, were originally enrolled and informed consent was obtained from all of them prior to their participation in this study.

We compared diagnostic detection rates for neoplastic lesions and extubation times using NBI at NCCH to the initial HDCs performed at RCCPS. Colonoscopies were completed to the cecum at both RCCPS and NCCH on every patient in this study.

NBI system

A medical video endoscopic system (EVIS, Lucera Spectrum, Olympus Optical Co., Tokyo, Japan) equipped with sequential illumination was used for the NBI examinations. The filter wheel in the illumination unit had three optical filters[12–14] so that when those filters were placed in the optical illumination system, they eliminated all illumination wavelengths except for two narrow wavelength bands. The central wavelengths of each band were 415 nm and 540 nm, respectively. Video endoscopic systems with CF-H260AZI magnification colonoscopes (Olympus) were used at both RCCPS and NCCH while the NBI system was used only at NCCH.

Adenomatous lesions including those that were flat and depressed could be seen as dark brown lesions without any dye or staining solution and were easily detected while withdrawing the NBI-equipped colonoscope. Capillary enhancement further contributed to improved visibility with this view.[14–16]

High definition colonoscopy (first examination) at RCCPS

Between December 2004 and November 2005, HDCs with magnification were performed at RCCPS for screening purposes only, by five highly experienced colonoscopists who had been trained and previously performed over 1000 colonoscopies at NCCH. The method of colonoscopic examination and diagnostic procedures followed at RCCPS were virtually identical to those followed at NCCH. All detected lesions were sprayed with 0.4% indigo carmine (IC) dye and then classified into one of the three macroscopic types: flat, polypoid or depressed lesions and diagnosed as either neoplastic or non-neoplastic by chromoendoscopy with magnification using Kudo's classification of pit pattern analysis[27] in which Types I and II are non-neoplastic and Types III_L, III_S, IV and V are neoplastic lesions.[28] Detected lesions were diagnosed using magnification chromoscopy, but no biopsies or resections were performed at RCCPS due to NCC intra-institutional restrictions against such procedures. A stopwatch was used to measure withdrawal time during each examination.

Colonoscopy using NBI (second examination) at NCCH

After their first colonoscopic examinations at RCCPS, patients with detected neoplastic lesions 5 mm or larger in size underwent further colonoscopies at NCCH using NBI during withdrawal examinations, with the results from the initial findings blinded from the performing colonoscopists. The further examinations were performed by three highly experienced, but completely different colonoscopists than at RCCPS. Intubations using HDC were performed and then the colonoscope was changed to NBI mode immediately after reaching the cecum. The study's exclusion criteria included patients with inadequate bowel preparation as determined immediately before their withdrawal examinations using NBI. Three colonic segments (right colon; proximal to the splenic flexure; and left colon and rectum) were examined by NBI during extubation without the colonoscopist having prior knowledge of the results from the first HDC until procedure completion. During each NBI colonoscopy, an independent observer with detailed knowledge of findings from the first HDC including polyp location and type watched the entire procedure.

When undergoing magnification for diagnosis of a detected lesion as either neoplastic or non-neoplastic, the NBI system could be changed to standard mode with the touch of a single button. The independent observer determined whether detected lesions were identical between the two colonoscopies based on RCCPS colonoscopic reports and photographs using the back-to-back method. All identified neoplastic lesions were then removed endoscopically unless the patient requested otherwise.

Withdrawal examination results were compared after completion of each colonic segment observation for matching purposes. If the independent observer determined that a lesion had been missed by NBI, the NBI examination was immediately interrupted and the colonoscope was changed to standard mode to look for the missed lesion in that specific segment to determine whether only HDC could identify that particular lesion.

During the NBI colonoscopy, measurement of withdrawal time was stopped temporarily whenever the colonoscopist performed a

Table 1 Examination technique comparisons: withdrawal time, total lesion number and size

	HDC	NBI	*P*-value
Withdrawal Time (Minutes; Mean ± SD)	12.2 ± 5.4	11.2 ± 4.2	0.18
Total Number of Detected Lesions	116	134	0.02
Size of Detected Lesions (mm; Mean ± SD)	5.5 ± 3.1 (Range: 2–20)	5.3 ± 2.8 (Range: 2–20)	0.89

HDC, high definition colonoscopy; NBI, narrow-band imaging; SD, standard deviation.

therapeutic procedure such as a polypectomy, endoscopic mucosal resection (EMR) or hot biopsy, or searched for a missed lesion using the standard mode. As a result, withdrawal times accurately reflected the actual amount of time spent examining the colonic mucosa for lesions using NBI.

Statistical analysis

Using the total of all detected neoplastic lesions including HDC findings at RCCPS and NBI results at NCCH as the reference standard, we compared diagnostic detection rates for neoplastic lesions and extubation times between HDC and NBI examinations. Statistical comparisons were made for each category of data using chi-square, Mann–Whitney *U* and McNemar's tests.

Results

Of the 47 consecutive patients enrolled in this study within an average of 3.4 months (range: 1–7 months) after their first colonoscopic examinations at RCCPS, we comparatively assessed the accuracy of HDC and NBI systems in 43 of those patients including 33 men and 10 women. Four patients (9%) were excluded because of inadequate bowel preparation prior to their NBI examinations. The independent observer was able to ascertain without discrepancy which lesions were detected at RCCPS, NCCH or both facilities. No invasive cancers were identified in any HDC or NBI examinations. Altogether, 153 identified neoplastic lesions were detected and analyzed with no significant difference in mean diagnostic extubation times (HDC/12.2 ± 5.4 min *vs* NBI/11.2 ± 4.2 min; $P = 0.18$).

Detectability in HDC and NBI examinations

The number of neoplastic lesions detected by NBI was higher than the number of neoplastic lesions detected using HDC (NBI/134 lesions *vs* HDC/116 lesions; $P = 0.02$) although mean size of detected neoplastic lesions was not significantly different (HDC/ 5.5±3.1 mm *vs* NBI/5.3 ± 2.8 mm; $P = 0.89$) (Table 1). Table 2 shows no significant difference in detection rates between the two techniques based on lesion size (< 5 mm, 5–9 mm and ≥ 10 mm in diameter). According to macroscopic type, flat lesions were identified by NBI more often than HDC (flat: NBI/72 lesions *vs* HDC/58 lesions; $P = 0.04$; and polypoid: NBI/62 lesions *vs* HDC/58 lesions; $P = 0.45$), but when lesion size was taken into account, only flat lesions < 5 mm were detected more often by NBI (NBI/44 lesions *vs* HDC/33 lesions; $P = 0.046$) (Table 3). There were no depressed lesions detected by either type of examination. According to location, lesions in the right colon were identified by NBI more often (NBI/87 lesions *vs* HDC/72 lesions; $P = 0.02$) than in the other two colonic locations (Table 2).

Table 2 Detected lesion comparisons: size, macroscopic type and location

	HDC	NBI	*P*-value
Lesion size			
< 5 mm	48	57	0.15
5–9 mm	58	68	0.06
≥ 10 mm	10	9	0.61
Macroscopic type			
Flat Lesion	58	72	0.04
Polypoid Lesion	58	62	0.45
Location			
Right Colon	72	87	0.02
Left Colon	31	36	0.45
Rectum	13	11	> 0.99

HDC, high definition colonoscopy; NBI, narrow-band imaging.

Table 3 Detected lesion comparisons: flat and polypoid lesions by number and size

	HDC	NBI	*P*-value
Total Number of Flat Lesions	58	72	
Number of Lesions			
< 5 mm	33	44	0.046
5–9 mm	22	27	0.27
≥ 10 mm	3	1	0.48
Total Number of Polypoid Lesions	58	62	
Number of Lesions			
< 5 mm	15	13	0.68
5–9 mm	36	41	0.18
≥ 10 mm	7	8	> 0.99

HDC, high definition colonoscopy; NBI, narrow-band imaging.

Among 153 identified neoplastic lesions, 141 were removed endoscopically and histopathological examinations confirmed three intramucosal cancers, 134 tubular adenomas, three hyperplastic polyps and one normal tissue specimen. In terms of the three intramucosal cancers, only one was detected by HDC, but NBI was able to detect all three of them. The positive predictive value for magnification diagnosis of neoplastic lesions was 97.2% (137/141).

Miss rate in HDC and NBI examinations

The overall miss rate using NBI was 12% (19/153). The NBI miss rate was 15% of the 85 flat lesions detected compared to 9% of the 68 polypoid lesions detected, however, there was no significant difference ($P = 0.32$). The NBI miss rates based on lesion size

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were < 5 mm, 16%; 5–9 mm, 8%; and ≥ 10 mm, 18%. The NBI miss rates in individual colonic segments were right colon, 11%; left colon, 15%; and rectum, 14%. None of these differences was significant. In comparison, the HDC miss rate for flat lesions (32%; 27/85) was significantly higher than for polypoid lesions (15%; 10/68) ($P = 0.01$) and HDC missed 33% (20/60) of all flat neoplastic lesions located in the right colon. As for sensitivity, NBI was 88% (134/153) and HDC was 76% (116/153) for total lesions and NBI was 87% (52/60) and HDC was 67% (40/60) for flat neoplastic lesions located in the right colon.

In relation to missed lesions ≥ 10 mm, one polypoid lesion was missed during HDC and two flat lesions were missed during NBI. The missed lesion during HDC was an intramucosal cancer 12 mm in diameter in the left colon while the two flat lesions missed during NBI were located in the right colon. One of these two flat lesions was a tubular adenoma 10 mm in size with low grade atypia and the other one, also a tubular adenoma with low grade atypia, was one of 12 lesions detected in a single patient during HDC examination at RCCPS. A repeat HDC at NCCH after changing to standard mode still could not detect this flat lesion 15 mm in size. It was only after chromoendoscopy was performed that this lesion was detected once again.

Discussion

A number of prospective studies in Western countries previously have indicated both the significant prevalence and the clinicopathological relevance of flat and depressed type colorectal lesions. Such lesions are, however, difficult to detect using HDC, a situation that is all the more significant because both adenomas and carcinomas have a higher malignant potential compared to polypoid lesions of similar size.[7–11]

While the NBI system has been shown to be helpful in visualizing neoplasia by improving contrast and is considered to be a new type of 'optical equipment-based image enhanced endoscopy (IEE)',[21] the feasibility of its use for colorectal screening had not been clarified previously. Since it is important to improve detection of neoplastic lesions, particularly flat and depressed type lesions, we decided to evaluate the effectiveness of colonoscopy examinations using NBI compared to HDC.

In this study, NBI improved detection of neoplastic lesions as well as the detection rate of flat and diminutive lesions particularly in the right colon. Since NBI is a contrast detection method that highlights the mucosal vascular network by narrowing spectral transmittance bandwidth using optical color separation filters, we believed that NBI would be useful specifically for enhancing detection of neoplastic lesions especially flat and diminutive lesions.

Although most flat lesions have been reported to be located in the right colon,[7,8] HDC has a higher miss rate in the right colon compared to the left colon.[29,30] In our study, initial HDCs missed 33% of flat neoplastic lesions in the right colon despite such examinations having been performed by highly skilled endoscopists well versed in the significance of non-polypoid lesions. In comparison, the NBI contrast detection method found many lesions that had been overlooked during HDC. As a result, the detection rate for flat lesions in the right colon for the NBI group showed considerable improvement in comparison to HDC. No significant difference in detection rates between NBI and HDC in the left colon or rectum, however, might have been due to the lower prevalence of flat lesions in those locations.

Diminutive lesions seem to have little clinical significance in Western countries because the majority of polyps 5 mm or smaller are hyperplastic and not thought to confer any increased risk for development of colon carcinoma.[31,32] Flat and depressed lesions, however, are considered to have greater malignant potential compared to polypoid lesions of similar size.[7–11] Since there is a possibility of invasive cancers developing from diminutive flat and depressed lesions, we cannot ignore them.

Recently, the use of NBI in HNPCC patients has been reported to significantly increase the detection of flat and diminutive neoplastic lesions in the proximal colon similar to our results.[25] Flat and small adenomas that are particularly prone to malignant transformation occur with greater frequency in the right colon of HNPCC patients[33,34] so it is feasible that NBI will be used in the future for improved surveillance in such patients.

The mechanism for detection of lesions by NBI depends on angiogenic and vascular morphological changes such as elongation of capillaries and venules and moderate increases in microvascular diameters of neoplastic lesions. It has been reported that angiogenesis is critical to the transition of pre-malignant lesions in a hyperproliferative state to the malignant phenotype[16,35] so NBI is a promising advancement in detection of pre-malignant flat lesions. In this study, NBI missed two flat lesions that were tubular adenomas 15 mm and 10 mm in size both with low grade atypia. This could have been because those lesions might have had poor vascularity. It was not ascertained in our study whether NBI was able to emphasize capillary pattern and surface structure of neoplastic lesions with less angiogenic or vascular morphological changes. It is anticipated that further modification and refinement of the NBI system's optical filters will result in improved visualization of even flat lesions with histopathologically low grade atypia that are the most difficult to detect by HDC.

Pancolonic chromoscopy using an IC diffusion spray catheter during extubation from the cecum, which highlighted subtle mucosal irregularities, has been reported to significantly increase detection of diminutive, flat neoplastic lesions in the right colon similar to our results.[36,37] Brooker's extubation times for the IC group, however, were almost twice as long as for the control group.[36] Subsequently, a considerable amount of 0.5% IC was required (median 68 mL; range: 65–90 mL) as indicated in Hurlstone's report.[37] Our NBI examinations took no longer in terms of withdrawal time compared to HDC. In addition, NBI did not require any specialized colonoscopy techniques, suction time for IC was unnecessary and there was no dye solution cost compared to pancolonic chromoscopy using IC. The simple, one-touch conversion from conventional to NBI mode and back again was shown also to be very useful.

This study had several limitations. All patients had at least one lesion as determined by HDC so it was more likely that additional lesions would be found during NBI examinations in this subset of patients with an increased prevalence for lesions. Although it can be argued that colonoscopists doing NBI withdrawal examinations might have been more careful in their observations so as not to miss any lesions detected during HDC, in fact, there was no significant difference in mean diagnostic extubation times. Since the stated aim of our study was to assess the feasibility of using NBI for the screening of colorectal neoplasia, a controlled trial