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Appendix A

Voting Members of the Consensus Group

Joseph Sung (Chair), Murdani Abdullah, Carolyn Aldige, Edgardo Bondoc, Durado Brooks, Jeong-Sik Byeon, Shan-rong Cai, Annie Chan, Francis Chan, Kelvin Cheng, Jessica Ching, Han-mo Chiu, Vui Heng Chong, Khean-Lee Goh, Lawrence KY Ho, Andrew Ip, Yasuo Kakugawa, Wing-man Ko, Ken Koo, Pinit Kullavanijaya, Philip Kwok, James Lau, Rupert Leong, Suet-yi Leung, Wai-keung Leung, Chu-jun Li, Peng Li, David Lieberman, Su-vui Lo, Vivian Lou, Susie Lum, Govind Makharia, Simon Ng, Yasushi Oda, Fei-chau Pang, Rungsun Rerknimitr, Yasushi Sano, Jose Sollano, Ka-fai To, Kelvin Tsoi, Martin Wong, Mei-Yin Wong, Kai-chun Wu, Deng-chyang Wu, Ming-shiang Wu, Eng-kiong Yeoh, Khay-guan Yeoh, Graeme Young, Siu-tsan Yuen, Shu Zheng

Editor's quiz: GI snapshot

ANSWER

From the question on page 1101

During endoscopy, it was found that a wooden toothpick was embedded in the posterior wall of the distal antrum surrounded by a subtle, rounded bulge seen actively to exude a small amount of pus from its centre (fig 1 of the Question). An overtube was placed and a 33 mm long toothpick was recovered. Figure 1 shows the lesion after removal of the stick. In retrospect, the patient had no recollection of having swallowed a toothpick. There was marked diminution of the patient's pain postprocedure. A follow-up abdominal *x* ray and CT scan to rule out perforation and abscess were unremarkable. The patient was admitted to hospital for 1 day, and subsequently discharged in a stable condition.

Clinicians should include inadvertent foreign body ingestion in the differential diagnosis for abdominal pain and gastrointestinal bleed. Patients should be warned of the potential hazards of toothpicks and cocktails sticks, fragments of which may be left in club sandwiches which have been cut in half.

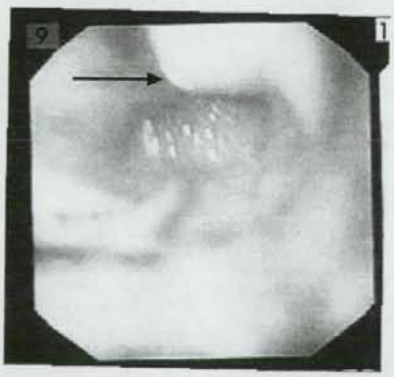

Figure 1 A subtle bulge with pus seen after the removed of the tooth pick from the distal antrum of the stomach.

Patient consent: Patient consent has been received for publication of the case details and the figures in this paper.

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Does Autofluorescence Imaging Videoendoscopy System Improve the Colonoscopic Polyp Detection Rate?—A Pilot Study

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OBJECTIVES: Colonoscopy is considered the gold standard for the detection of colorectal polyps; however, polyps can be missed with conventional white light (WL) colonoscopy. The aim of this pilot study was to evaluate whether a newly developed autofluorescence imaging (AFI) system can detect more colorectal polyps than WL.

METHODS: A modified back-to-back colonoscopy using AFI and WL was conducted for 167 patients in the right-sided colon including cecum, ascending and transverse colon by a single experienced colonoscopist. The patient was randomized to undergo the first colonoscopy with either AFI or WL (group A: AFI-WL, group B: WL-AFI). The time needed for both insertion and examination for withdrawal and all lesions detected in the right-sided colon were recorded.

RESULTS: Eighty-three patients were randomized to group A and 84 to group B. The total number of polyps detected by AFI and WL colonoscopy was 100 and 73, respectively. The miss rate for all polyps with AFI (30%) was significantly less than that with WL (49%) ($P = 0.01$).

CONCLUSIONS: AFI detects more polyps in the right-sided colon compared to WL colonoscopy.

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INTRODUCTION

Colorectal cancer is one of the most common cancers in the world. Early detection and removal of colorectal adenomas have been shown to be the most effective way of colorectal cancer prevention (1, 2). Colonoscopy is considered the gold standard for detection and treatment of colorectal polyps, however, some polyps can be missed during routine colonoscopies. According to the results of back-to-back colonoscopies by Rex *et al.*, the miss rate for adenomas ≥1 cm was 6%, for adenomas 6–9 mm was 13%, and for adenomas ≤5 mm was 27%, respectively (3). Furthermore, there was a trend toward right-sided colorectal adenomas being missed more often than left-sided ones (27% *vs* 21%). As missing adenomas or cancers during colonoscopy would result in increasing the need of surgery and death from colorectal cancers, attempts to reduce this kind of miss rate include pancolonic dye spraying (4, 5), wide angle colonoscopy (6, 7) or cap-fitted colonoscopy (8).

On the other hand, a new prototype of endoscopic autofluorescence imaging (AFI) system has been developed (9). AFI produces real-time pseudo-color images to identify gastrointestinal malignancies (10–13) as well as malignancies of larynx, cervix, lung, and bladder. During AFI colonoscopy, non-neoplastic lesion appears green, while neoplastic lesion has a magenta (reddish purple) image (14, 15). The usefulness of AFI for differential diagnosis between neoplastic and non-neoplastic lesions has been reported (16–21); however, its effectiveness, measured as frequency of detection of colorectal polyps in comparison to conventional white light colonoscopy (WL), has not been investigated enough (22). We therefore conducted this pilot study to evaluate whether AFI can detect more colorectal polyps than WL.

METHODS

Patients

Between June and October 2006, consecutive patients who underwent total colonoscopy using a colonoscope with AFI function were considered eligible for inclusion in the study. This study was conducted prospectively, and our institutional review board approved the study protocol. Written informed consent for examination and treatment were obtained from all of the studied patients prior to the procedures. Patients with previously detected polyps or with a history of surgical resection of the proximal colon (cecum, ascending colon and transverse colon) were excluded from this study. Patients with inflammatory bowel disease (IBD), familial adenomatous polyposis (FAP), or hereditary nonpolyposis colorectal cancer (HNPCC) were also considered ineligible for the study.

Autofluorescence Imaging System (AFI)

The prototype autofluorescence imaging system used in this study (AFI; Olympus Medical Systems Corp., Tokyo, Japan) has a sequential light source (XCLV-260HP) and a high-resolution videoendoscope (XCF-H240FZI) and XCV-260HP video system. AFI equipped two CCDs: One for high-resolution white-light observation and another for autofluorescence observation on the tip of the scope, and they could be easily switched by pushing a button on the scope handle. As shown in Figure 1, AFI composes real-time images from pseudo-colors of autofluorescence (excitation: 390–470 nm, detection: 500–630 nm) and green reflection (G': 540–560 nm) by sequential method in order to represent clear image profiles and to distinguish reduction of autofluorescence by tumor from that by hemoglobin. Furthermore, this AFI videoendoscope is equipped with an accessory channel with an internal diameter of 3.2 mm. The outer diameter of the distal tip of this AFI videoscope is 14.8 mm and also has the function of variable stiffness and magnification (up to ×75 under the WL image).

Endoscopic Procedure

All patients were prepared for colonoscopy by ingesting 2–3 liters of polyethylene glycol-electrolyte solution on the same-day morning. Scopolamine butylbromide (10 mg) was administered intravenously to avoid bowel movement prior to examination for the patients with no contraindication to the use of this agent. Quality of bowel preparation was assessed by the examiner as follows: (a) excellent (near 100% mucosal visualization following suction of fluid residue), (b) good (near 90% mucosal visualization), (c) fair (less than 90% mucosal visualization). Colonoscopic examinations were performed in a modified back-to-back fashion, using WL and AFI in the right-sided colon including cecum, ascending colon, and transverse colon by a single experienced colonoscopist having performed more than 10,000 colonoscopies. Each patient was randomized in one of the following two groups with a computer-generated random number list; group A: after cecal insertion by WL, the colonoscope was withdrawn from the cecum to the splenic flexure with AFI mode, and then re-withdrawing the colonoscope with WL from the cecum to the splenic flexure after reinsertion of the scope to the cecum by WL (AFI-WL); group B: withdrawing the colonoscope in the inverse order of group A (first WL and then AFI; WL-AFI).

All lesions detected during either examination of AFI or WL were removed endoscopically and sent for histological evaluation without exception. All lesions identified on the second examination were considered as lesions missed by the first examination. The location of each lesion was defined according to landmarks including hepatic flexure and splenic flexure. The size of the lesions was estimated using open endoscopic biopsy forceps.

Histopathological Evaluation

Resected specimens were immediately fixed in 10% buffered formalin solution and subsequently stained with hematoxylin-eosin. Experienced gastrointestinal pathologists who were completely blinded to each endoscopic diagnosis evaluated all pathological specimens. Histological diagnoses were determined according to the World Health Organization (WHO) criteria (23).

Statistical Analysis

This study was mainly designed to demonstrate that the colonoscope with AFI has a different reliability than with WL for polyp detection. The design of the study included

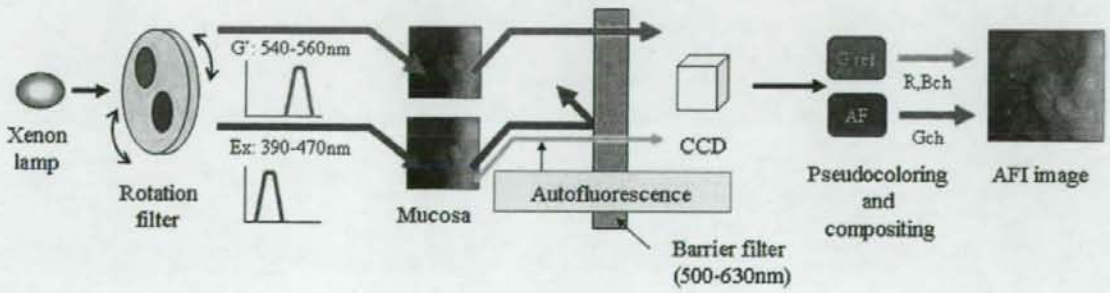

Figure 1. Autofluorescence Imaging (AFI) System.

two independent groups; group A underwent colonoscopy with WL after colonoscopy with AFI, and group B underwent colonoscopy with AFI after colonoscopy with WL.

Nominal and ordinal variables are expressed with frequencies and percentages. Continuous variables are expressed with means and standard deviations. The comparisons of proportions of detected polyps between both groups A (AFI-WL) and B (WL-AFI) in the second exam was carried out with the Kruskal–Wallis test for singly ordered 2×2 table (based on χ^2 distribution with 1 degree of freedom). Proportions between groups on sex, indication for colonoscopy, bowel preparation, location and macroscopic type, size of the lesion, and histopathology were compared with χ^2 test or Fisher's exact test as appropriate. Statistical analysis was conducted with SPSS V. (Chicago, IL), StatXact v. 5.0.3 (Cytel Co., MA), and Statistica v. 5.5 (Tulsa, OK). All statistical tests were 2-sided and significance was defined as $P < 0.05$.

RESULTS

Patient Characteristics and Bowel Preparation

A total of 167 patients were enrolled in this study. The 167 patients included 107 (64%) men, and the mean age was 62.2 ± 9.8 yr. The indications for colonoscopy were polyp surveillance (N = 78), screening (N = 76), abdominal pain/constipation (N = 7), and fecal occult blood test positive (N = 6). The bowel preparation was described as excellent or good in 139 cases (83%) and fair in 28 (17%) (Table 1).

Detected Lesions

Total number of detected and removed lesions by AFI and WL colonoscopy was 100 and 73, respectively. The miss proportion for all polyps with AFI (30%) was significantly less than the miss proportion with WL (49%) ($P = 0.01$). Among all detected polyps, the number of neoplastic lesions detected by AFI and WL colonoscopy was 92 and 69, respectively. Among 66 neoplastic lesions, which were diagnosed in group A, 47 (71%) lesions were detected at the first AFI withdrawal technique (Fig. 2). In contrast, in group B (among 95 neoplastic lesions), only 50 (53%) lesions were recognized at the first WL withdrawal technique, and 45 (47%) lesions were detected by the second AFI examination. Significantly more neoplastic lesions were missed by WL compared with AFI system ($P = 0.02$) (Tables 2 and 3).

Table 1. Patient Characteristics and Indications for Colonoscopy

	Group A (AFI-WL) (N = 83)	Group B (WL-AFI) (N = 84)
Male sex no. (%)	58 (70)	49 (58)
Age* (yr)	62.2 ± 10.2	62.2 ± 9.5
Indication for colonoscopy no. (%)		
Polyps surveillance	42 (51)	36 (43)
Screening	35 (42)	41 (49)
Abdominal pain/constipation	2 (2)	5 (6)
FOBT† (+)	4 (5)	2 (2)
Bowel preparation no. (%)		
Excellent	18 (22)	23 (27)
Good	49 (59)	49 (58)
Fair	16 (19)	12 (14)

*Data presented with mean ± SD.
†Fecal occult blood test.

Characteristics of the Missed Lesions

Characteristics of the missed neoplastic lesions by AFI and WL colonoscopy were flat elevated: 14 (74%) and 39 (87%), small (≤5 mm): 18 (95%) and 41 (91%) and low-grade dysplasia (LGD): 19 (100%) and 45 (100%), respectively (Table 4).

DISCUSSION

In this pilot study, we investigated the utility of a prototype Olympus AFI videoendoscopy system on miss rates during colonoscopy and the efficiency of colonoscopic withdrawal. Based on the results of our study, AFI videoendoscopy system is useful for the detection of colorectal adenomas in the right-sided colon compared to WL conventional colonoscopy. The largest advantage of this system may prove to be the ability to perform faster and more efficient examination without the need for additional attachments to the endoscope and without the time and cost required for dye spraying or infusion. Even though this system is not available in the United States yet, we think it will be available in the near future.

According to the National Polyp Study (NPS), the incidence of colorectal cancer was decreased by endoscopic intervention. In brief, polypectomy during routine colonoscopy has been shown to prevent the development of colorectal cancer, compared with the incidence of it in reference groups. Therefore, colonoscopy is considered as a gold standard for detection and treatment of colorectal adenomas, however, the conventional colonoscopic technique during withdrawal, even if very careful, cannot detect all lesions, especially flat and small depressed ones.

Endoscopic imaging techniques aimed at early detection of colorectal cancer and its precursors have been developed over the last decade. Techniques that improve the detection of mucosal irregularities, such as pancolonic chromoendoscopy, narrow band imaging (NBI), high-resolution imaging, and AFI, have been applied in a variety of clinical situations to enhance the detection of flat and depressed lesions or to enable histopathological diagnosis.

Many authors have reported that chromoendoscopy is helpful for the detection and detailed morphological assessment of flat and depressed colorectal lesions (24–31). Pancolonic chromoscopy using an indigo carmine (IC) diffusion during withdrawal from the cecum, which highlighted subtle mucosal irregularities, has been reported to significantly increase the detection of diminutive, flat neoplastic lesions in the right colon. However, the withdrawal time for the IC

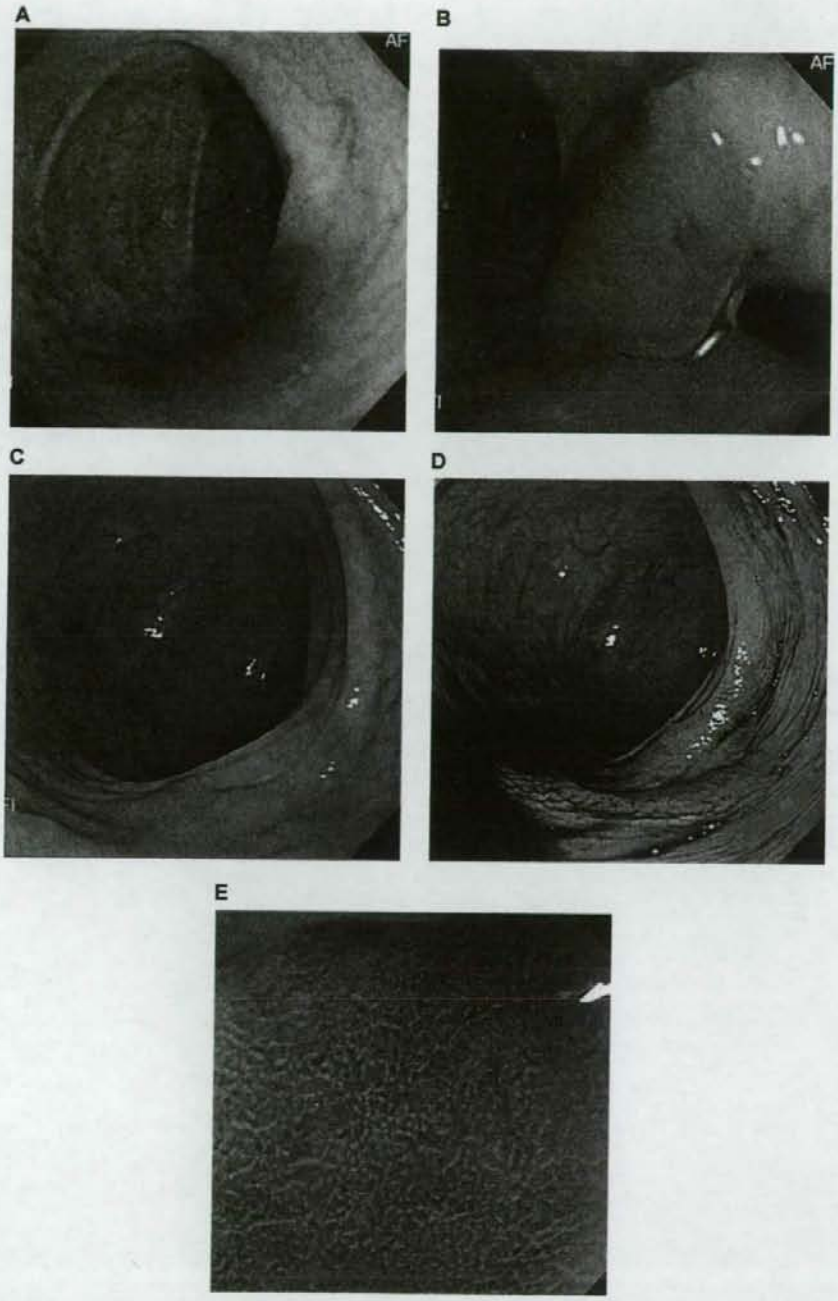

Figure 2. (*A*) A 64-year-old man who enrolled in this study and classified into Group A was referred with positive fecal occult blood test. The lesion was detected in the transverse colon at first AFI examination. (*B*) AFI image revealed a magenta-colored flat elevated lesion, which was macroscopically diagnosed as laterally spreading tumor, non-granular type (LST-NG). The size of the lesion was 20 mm in diameter. (*C*) Conventional (WL) image. (*D*) Chromoendoscopy image (indigo carmine). (*E*) Magnifying view (crystal-violet); Non-invasive (Kudo's type IIIs and IIIL pit) pattern. The final endoscopic diagnosis was HGD without submucosal invasion. We performed endoscopic submucosal dissection (ESD) using B-knife. The final histopathological diagnosis was HGD (intramucosal carcinoma).

Table 2. Detected Lesions in Each Group

	Group A (AFI-WL) (N = 83)		Group B (WL-AFI) (N = 84)		*P*
Total number of lesions (%)					
First exam	AFI	50 (70)	WL	52 (51)	0.01
Second exam	WL	21 (30)	AFI	50 (49)	
Neoplastic lesions (%)					
First exam	AFI	47 (71)	WL	50 (53)	0.02
Second exam	WL	19 (29)	AFI	45 (47)	
Non-neoplastic lesions no. (%)					
First exam	AFI	3 (60)	WL	2 (29)	0.28
Second exam	WL	2 (40)	AFI	5 (71)	

dye spray group was almost twice as long as for the control group (4).

Another technology recently demonstrated to be effective for detecting neoplastic lesions is NBI. The NBI system has been shown to be helpful in visualizing such lesions by improving contrast and is considered to be a new type of optical/digital chromoendoscopy (32, 33). In particular, magnification using NBI colonoscopy for the observation of the presence of "meshed brown capillary vessels" is extremely useful for distinguishing between neoplastic and non-neoplastic lesions without any dye solution. Regarding polyp detection, however, it is controversial at this moment (34). Furthermore, during NBI colonoscopy examinations, intestinal fluid was seen as being reddish in color similar to blood. Therefore, proper bowel preparation is one of the limitations when using this system.

Meanwhile, the feasibility of AFI system use for gastrointestinal (GI) screening and surveillance has not been clarified previously. In 2005, Nakaniwa *et al.* (14) developed and reported a new AFI videoscope system. Images acquired by this new AFI system provided better brightness than old fiberscopic images. From this report, the sensitivity and specificity of differentiating adenomatous and hyperplastic polyps were

Table 3. Clinicopathologic Characteristics of Lesions Detected by AFI and WL Colonoscopy

	AFI	WL	*P*
No. of lesions	100	73	
Location no. (%)			
Cecum	9 (9)	8 (11)	0.31
Ascending	37 (37)	19 (26)	
Transverse	54 (54)	46 (63)	
Macroscopic type no. (%)			
Polypoid	23 (23)	26 (36)	0.07
Flat elevated	77 (77)	47 (64)	
Size no. (%)			
0–5 mm	84 (84)	53 (73)	0.19
6–10 mm	10 (10)	12 (16)	
> 11 mm	6 (6)	8 (11)	
Histopathology no. (%)			
Neoplastic LGD	85 (85)	63 (86)	0.92
HGD	6 (6)	5 (7)	
Inv.ca	1 (1)	1 (1)	
Non-neoplastic	8 (8)	4 (5)	

Table 4. Characteristics of the Missed Neoplastic Lesions by AFI and WL Colonoscopy

	AFI	WL	*P*
No. of lesions	19	45	
Location no. (%)			
Cecum	3 (16)	2 (4)	0.13
Ascending	4 (21)	19 (42)	
Transverse	12 (63)	24 (54)	
Macroscopic type no. (%)			
Polypoid	5 (26)	6 (13)	0.21
Flat elevated	14 (74)	39 (87)	
Size no. (%)			
0–5 mm	18 (95)	41 (91)	0.62
6–10 mm	1 (5)	4 (9)	
Histopathology no. (%)			
LGD	19 (100)	45 (100)	

89% and 81%, respectively. However, there are few prospective studies that have attempted to clarify the usefulness of the adenoma detection rate using AFI system.

In this study, a total of 173 lesions from 167 patients were detected and removed endoscopically. Among these lesions, the number of neoplastic lesion detected by AFI and WL was 92 (92%) and 69 (95%), respectively. In contrast, the number of non-neoplastic lesions recognized as a polyp and removed by AFI and WL colonoscopy was only 8 (8%) and 4 (5%), respectively. The lesions we diagnosed and resected in this study with AFI and WL systems were mostly neoplastic ones. Consequently, our results evaluate the diagnostic yield of adenomatous polyp detection. However, we consider further investigation is necessary to evaluate the efficiency for differential diagnosis with AFI system.

Diminutive flat elevated lesions are thought to be of little clinical significance because such lesions, especially less than 5 mm polyps, are low-grade dysplasia (LGD) in most cases. Meanwhile, depressed lesions are considered to have a high malignant potential compared to polypoid ones in similar size (35–38). In this present study, all detected lesions' macroscopic type was flat elevated or polypoid. Because of low incidence, there were no depressed lesions in this study. However, significantly more small and/or flat neoplastic lesions were detected by AFI compared with WL colonoscopy. Therefore, AFI colonoscopy is considered to be a promising modality to detect small depressed lesions.

There are several limitations in our study. First, we conducted this study using a single experienced colonoscopist. True, our data are precise, but it is uncertain whether it would be available for all examiners. Therefore, additional multicenter studies are necessary to clarify the usefulness of AFI system for all colonoscopists. Another point worth mentioning is that our study was conducted within the limits of the right colon. The higher prevalence of flat and diminutive lesions diagnosed in the right colon may be consistent with Woolfson (39) and Hofstad's (40) description. Furthermore, a higher miss rate of detection has been reported in the right colon compared to the left colon (3). Complete back-to-back colonoscopy may be painful for patients under no sedation.

Therefore, we defined from the cecum to the splenic flexure as the target area in our prospective study. In addition, it is suggested that proper bowel preparation is indispensable to achieve success to detect small colorectal lesions. In this study, the bowel preparation was described as excellent or good in 83% and adequate but imperfect in 17%.

In conclusion, AFI videoendoscopy system is useful for the detection of right-sided colonic polyps, especially flat and/or diminutive adenomatous lesions compared to conventional (WL) colonoscopy. In the near future, multicenter trials should be performed to validate the usefulness of this system.

ACKNOWLEDGMENTS

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STUDY HIGHLIGHTS

What Is Current Knowledge

- Polyps can be missed with conventional white light (WL) colonoscopy.
- Efficacy of autofluorescence imaging (AFI) system is unclear.

What Is New Here

- AFI detects more polyps, especially flat and diminutive lesions, in the right-sided colon than conventional (WL) colonoscopy.
- Prospective multicenter studies are necessary to validate the usefulness of this system.

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CONFLICT OF INTEREST

Even though the prototype autofluorescence imaging scope was provided by Olympus Medical Systems Corp., Tokyo, Japan, this is not a collaborative study. Thus, this study being an absolutely independent investigation, there is neither financial support nor interest from Olympus Corporation.

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ORIGINAL CONTRIBUTIONS

Endoscopy

Efficacy of the Invasive/Non-invasive Pattern by Magnifying Chromoendoscopy to Estimate the Depth of Invasion of Early Colorectal Neoplasms

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OBJECTIVE: During colonoscopy, estimation of the depth of invasion in early colorectal lesions is crucial for an adequate therapeutic management and for such task, magnifying chromoendoscopy (MCE) has been proposed as the best *in vivo* method. However, validation in large-scale studies is lacking. The aim of this prospective study was to clarify the effectiveness of MCE in the diagnosis of the depth of invasion of early colorectal neoplasms in a large series.

METHODS: A total of 4,215 neoplastic lesions were evaluated using MCE from October 1998 to September 2005 at the National Cancer Center Hospital, Tokyo, Japan. Lesions were prospectively classified according to the clinical classification of the pit pattern: invasive pattern or non-invasive pattern. All lesions were histopathologically evaluated.

RESULTS: There were 3,371 adenomas, 612 intramucosal cancers (m-ca), 232 submucosal cancers (sm-ca): 52 sm superficial (sm1) and 180 sm deep cancers (sm 2–3). Among lesions diagnosed as invasive pattern, 154 out of 178 (86.5%) were sm2–3, while among lesions diagnosed as non-invasive pattern, 4,011 out of 4,037 (99.4%) were adenomas, m-ca, or sm1. Sensitivity, specificity and diagnostic accuracy of the invasive pattern to differentiate m-ca or sm1 (<1000 μm) from sm2–3 (≥1000 μm) were 85.6%, 99.4%, and 98.8%, respectively.

CONCLUSION: The determination of invasive or non-invasive pattern by MCE is a highly effective *in vivo* method to predict the depth of invasion of colorectal neoplasms.

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INTRODUCTION

It has been reported that intramucosal colorectal cancers (m-ca) show no lymph node (LN) metastasis (LNM) and are good candidates for endoscopic resection (1, 2). In contrast, submucosal cancers (sm-ca) have approximately 6–12% of LNM, which require surgical resection including LN dissection for curative treatment (3–6). Recently, there is growing evidence supporting the theory that lesions with sm invasion limited to less than 1000 μm (sm1) without lymphovascular invasion and/or poorly differentiated component do not involve LNM (7). Therefore, it is crucial to estimate the depth of invasion of early colorectal neoplasms accurately prior to therapeutic decisions.

Magnifying chromoendoscopy (MCE) has widely demonstrated its effectiveness to differentiate between colorectal neoplastic and non-neoplastic polyps (8–15). In relation to the depth of invasion of colorectal neoplastic lesions, Kudo's classification of colonic crypts suggests that type III and IV pit patterns are found on adenomatous polyps, while type VN is strongly suggestive of sm deep cancers (16–18). In practice, however, there are limitations using only the morphological classification of the pit pattern to discriminate between m-sm1 and sm2 or beyond. MCE with detailed analysis of the pit

pattern has been proposed as the best *in vivo* method to evaluate the depth of invasion, however, validation in large-scale studies is lacking. Herein, we report a clinical classification of the colonic pit pattern, which is useful to determine the proper treatment of colorectal lesions during colonoscopy.

METHODS

Patients

A total of 3,029 consecutive patients diagnosed with a neoplastic colorectal lesion at the National Cancer Center Hospital, Tokyo from October 1998 to September 2005 were enrolled. This study was conducted prospectively, and the study protocol was approved by our institutional review board. Written informed consents for diagnosis and treatment were obtained from all patients prior to the procedures. Exclusion criteria were advanced colorectal cancer, familial adenomatous polyposis (FAP), inflammatory bowel disease (IBD), and hereditary non-polyposis colorectal cancer (HNPCC).

Magnifying Colonoscope

All examinations were performed using magnifying colonoscopes (CF-Q240ZI, PCF-Q240ZI, and CF-200Z, Olympus Optical Co., Tokyo, Japan), which enhance the image up to 80–100 times using a one-touch operation power system. These scopes have equal upward and downward bending range as well as sideways range and biopsy channel diameter but differ minimally in observation range diameters and view angles.

Definition of Terms

1. *Regular pit:* visible crypt orifice independently of shape (Fig. 1A).
2. *Irregular pit*: the orifice of each crypt is indented or jagged (Fig. 1B).
3. *Distorted pit*: the orifice of each crypt cannot be clearly traced, usually seen in desmoplastic areas (Fig. 1C).
4. *Demarcated area*: clearly visualized zone between two morphologically different types of pits, e.g., depression, large nodule, or reddened area (Fig. 1D).

Clinical Classification

1. *Non-neoplastic pattern*: normal mucosa and star-shaped crypts as observed in Kudo's type I or II, respectively (e.g., hyperplastic, juvenile and inflammatory polyps).

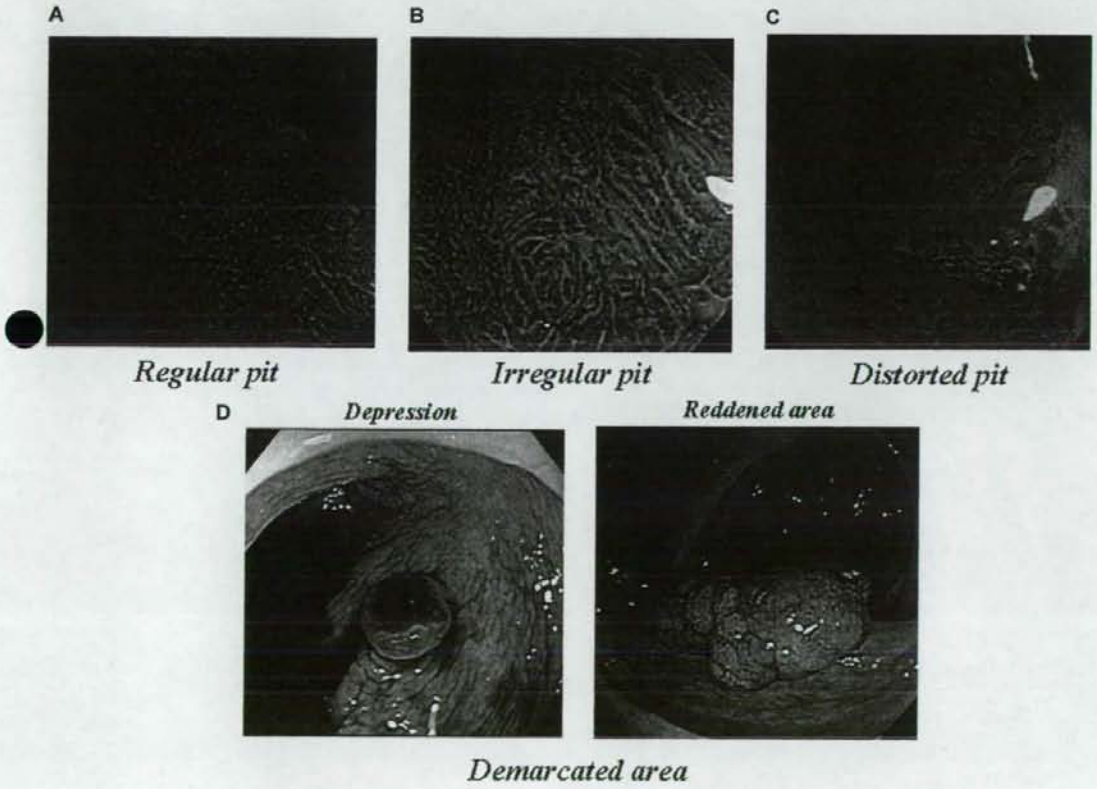

Figure 1. Definition of terms: (A) Regular pit. (B) Irregular pit. (C) Distorted pit. (D) Demarcated area: Depression/Reddened area.

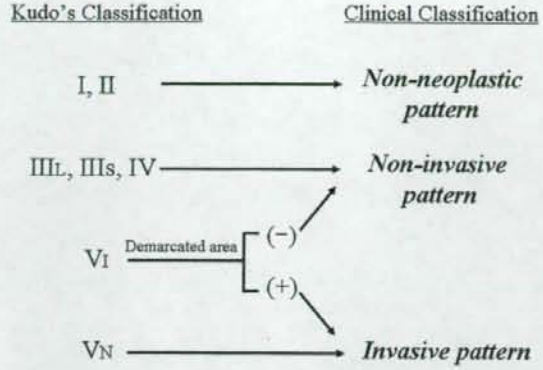

Figure 2. Relationship between Kudo's classification and clinical classification.

2. *Non-invasive pattern*: regular crypts with or without demarcated area or irregular pits without a demarcated area. Usually observed in Kudo's type IIIs, IIIL, IV, and selected cases of VI (e.g., adenomatous polyps, intramucosal, and submucosal superficial cancers), where endoscopic resection is appropriate.
3. *Invasive pattern*: irregular and distorted crypts in a demarcated area as observed in Kudo's type VN and selected cases of VI (e.g., deep submucosal invasive cancers), where surgical resection is the appropriate treatment. Kudo's type VI is observed in both non-invasive and invasive patterns (Fig. 2, 3).

Endoscopic Examination

All patients were prepared for colonoscopy with 2–3 L of polyethylene glycol-electrolyte solution administered on the morning of examination day. Scopolamine butylbromide (10 mg) or Glucagon (0.5 mg) was administered intravenously in patients with no contraindication prior to examination to avoid bowel movement.

All procedures were carried out by experienced examiners who had performed more than 500 colonoscopies per year. When a lesion was detected by conventional view, its surface was washed out with proteinase to remove overlying mucous, after which 0.4% indigo carmine (IC) dye was sprayed to accentuate the contours of the lesions. When a colonoscopist intended to perform chromoendoscopy, a volume of 3 to 5 mL IC dye was flushed through the biopsy channel with 15 mL of air using a 20cc syringe and sprayed directly over the targeted lesion. The pit pattern was evaluated by magnifying view. When high magnification observation with IC dye was not enough for determining the surface structure (pit pattern analysis), 0.05% crystal violet (CV) was applied as a staining method (19). Lesions were evaluated under MCE in real time and categorized as non-neoplastic, neoplastic non-invasive and neoplastic invasive patterns. Those diagnosed as

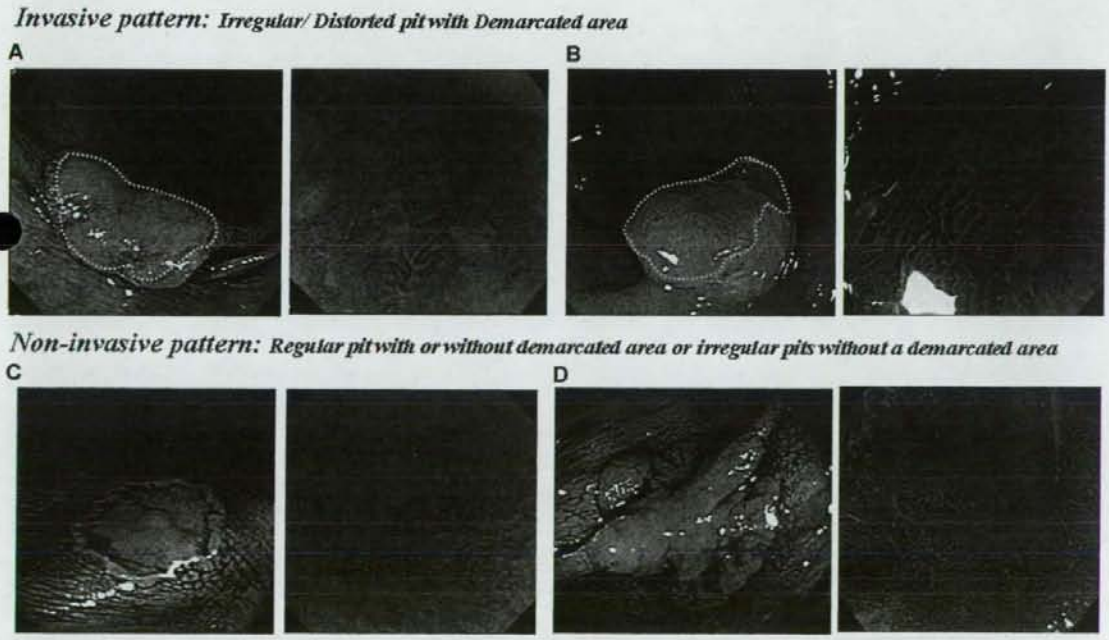

Figure 3. Definition of invasive/non-invasive pattern. Invasive pattern (*A*) Demarcated area (+): Depression, Irregular/distorted pit (*B*) Demarcated area (+): Reddened area, Irregular/distorted pit. Non-invasive pattern (*C*) Demarcated area (+): Depression, Regular pit (*D*) Demarcated area (±), Regular pit.

non-neoplastic were left untreated. If lesions were identified as neoplastic non-invasive lesions (adenomas or m-ca), hot biopsy, snare polypectomy, or endoscopic mucosal resection (EMR) was performed. Lesions <5 mm were resected by coagulation biopsy (hot biopsy), and flat lesions or those >5 mm were treated with loop snare polypectomy or EMR. If lesions were diagnosed as invasive pattern, biopsy specimens were taken and patients were basically referred for surgery. In cases where a polyp was not clearly diagnosed as either hyperplastic polyp (HP) or adenomatous polyp (AP), it was considered as AP and therefore removed for histopathological analysis.

Histopathology

Resected specimens were immediately fixed in 10% buffered formalin solution and subsequently stained with hematoxylin-eosin. Experienced gastrointestinal pathologists blinded to each endoscopic diagnosis evaluated all pathological specimens. Histopathological diagnosis was determined according to the Japanese Research Society for Cancer of the Colon and Rectum (JRSCCR) between 1998 and 2000. Since 2001, lesions were histopathologically evaluated according to JRSCCR and Vienna classification as well (20, 21). Non-pedunculated lesions with a vertical invasion length of less than 1000 μm in the submucosal layer, and pedunculated lesions with head invasion, were classified as submucosal superficial invasive cancer (sm1). Non-pedunculated lesions with invasion of more than 1000 μm and pedunculated lesions with stalk invasion were considered as submucosal deep invasive cancer (sm2–3) (7, 22). Regarding pedunculated lesions, level 2 according to Haggitt's classification (23) was used as the baseline to determine submucosal invasion.

RESULTS

A total of 4,215 neoplastic lesions in 3,029 patients were studied by MCE and removed endoscopically or surgically for analysis. Among lesions endoscopically diagnosed as having an invasive pattern, there were 45 (25.3%) right-sided colon lesions, 53 (29.8%) left-sided lesions, and 80 (44.9%) rectal lesions. On the other hand, among the lesions endoscopically diagnosed as having a non-invasive pattern, there were 2,032 (50.3%) right-sided, 1,475 (36.5%) left-sided and 530 (13.1%) rectal lesions. According to macroscopic type, there were 90 (50.6%) polypoid, 9 (5.1%) flat elevated, and 79 (44.4%) depressed lesions in the invasive pattern group. In contrast, there were 2,700 (66.9%) polypoid, 1,258 (31.2%) flat elevated, and 79 (2.0%) depressed lesions in the non-invasive pattern group (Table 1).

Histopathological analysis revealed adenoma: 3371 (80.0%), intramucosal cancer (m-ca): 612 (14.5%), and submucosal cancer (sm-ca): 232 (5.5%) [sm1: 52 (1.2%), sm2–3: 180 (4.3%)]. Among lesions diagnosed as invasive pattern, 154 out of 178 (86.5%) were submucosal deep invasive cancers (sm2–3), while 4,011 out of 4037 (99.4%) diagnosed as non-invasive pattern were adenomas, m-ca or sm1 (Table 2).

Table 1. Characteristics of Lesions Diagnosed by Magnifying Chromoendoscopy

	Invasive Pattern (n = 178)	Non-Invasive Pattern (n = 4037)
Location—no. (%)		
Right colon*	45 (25)	2032 (50)
Left colon**	53 (30)	1475 (37)
Rectum	80 (45)	530 (13)
Macroscopic type–no. (%)		
Polypoid	90 (51)	2700 (67)
Flat elevated	9 (5)	1258 (31)
Depressed†	79 (44)	79 (2)
Size—no. (%)		
−5 mm	2 (1)	2024 (50)
6–10 mm	30 (17)	1396 (35)
11–20 mm	101 (57)	493 (12)
21 mm−	45 (25)	124 (3)

*Cecum-transverse colon.
**Descending-sigmoid colon.
†IIc, IIa+IIc, Is+IIc.

Diagnostic Accuracy

The calculated sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of the invasive pattern to differentiate m-ca or sm1 (<1000 μm) from sm2–3 ($\geq$1000 μm) were 85.6%, 99.4%, 86.5%, 99.4%, and 98.8%, respectively. Based on the macroscopic appearance, the diagnostic sensitivity of the clinical pit pattern to determine the depth of invasion of polypoid, flat, and depressed lesions was 75.8% (75/99), 85.7% (6/7), and 98.6% (73/74), respectively. Meanwhile, the specificity for polypoid, flat, and depressed lesions was 99.4%, 99.8%, and 92.9%, respectively (Table 3).

Treatment Strategy

Among lesions endoscopically diagnosed as having an invasive pattern, 80.9% (144/178) were treated surgically of which sm2–3 cancer was found in 132 cases (91.7%), and

Table 2. Clinicopathologic Characteristics of Lesions Diagnosed by Magnifying Chromoendoscopy

	Invasive Pattern	Non-Invasive Pattern
No. of lesions	178	4037
Histopathology—no. (%)		
Adenoma	0 (0)	3371 (83)
m-ca	12 (7)	600 (15)
sm-ca	166 (93)	66 (2)
−sm superficial (sm1*)	12 (7)	40 (1)
−sm deep (sm2-3)	154 (86)	26 (0.6)

*sm1: sm <1000 μm.
Sensitivity: 85.6% (15/180).
Specificity: 99.4% (4011/4035).
Positive predictive value (PPV): 86.5% (154/178).
Negative predictive value (NPV): 99.4% (4011/4037).
Accuracy: 98.8% (4165/4215).

Table 3. Diagnostic Sensitivity and Specificity According to Macroscopic Type

	Polypoid	Flat	Depressed	Total
sm deep	75.8% (75/99)	85.7% (6/7)	98.6% (73/74)	85.6% (154/180)
Adenoma m-ca sm superficial	99.4% (2676/2691)	99.8% (1257/1260)	92.9% (78/84)	99.4% (4011/4035)

m-ca or sm1 in 12 cases (8.3%). Thirty-four lesions (19.1%) diagnosed as an invasive pattern were removed endoscopically. Based on lesion size, there were 31 out of 34 (91.2%) small lesions (<20 mm) and 25 out of 34 (73.5%) polypoid lesions. Among these, sm2–3 cancer was found in 22 cases (64.7%), and m-ca or sm1 in 12 cases (35.3%). Among 22 sm2–3 cancers, 15 cases underwent additional surgical treatment and in 7 cases, close follow-up was performed. In contrast, among 4,037 cases diagnosed endoscopically as having a non-invasive pattern, 4,024 (99.7%) were resected endoscopically. The remaining 13 cases (0.3%) were treated surgically. Based on size, there were 8 out of 13 (61.5%) large lesions ≥21 mm and 8 out of 13 (61.5%) polypoid lesions (Fig. 4).

DISCUSSION

This is the first large prospective study to assess the effectiveness of MCE for the endoscopic estimation of the depth of invasion of colorectal neoplasms. MCE is a standardized validated method that facilitates detailed analysis of the morphological architecture of colonic mucosal crypt orifices (pit pattern) in a simple and not time-consuming manner. Despite prospective randomized studies in large reference centers demonstrating the superiority of MCE over conventional colonoscopy, and studies that demonstrated no differences between magnifying and standard colonoscopes in the average time to reach the cecum (11), magnifying endoscopes are still rarely used in endoscopy units. Unrecognized necessity and lack of randomized studies validating the effectiveness of MCE are possible reasons for this. We believe that MCE is an essential armamentarium in gastrointestinal (GI) endoscopy units and that its main clinical significance is the *in vivo* diagnosis of the nature of colorectal lesions, which gives extremely useful information to determine the treatment modality.

The clinical classification of the colonic pit pattern (invasive and non-invasive) using MCE was originally described by Fujii in 1998 with the aim to discriminate between m-sm1 and sm2 or beyond (19). Contrary to the anatomic classification of Kudo *et al.*, the rationale for the clinical classification is based on the identification of irregular or distorted crypts in a demarcated area, (where the orifice of each crypt cannot be traced clearly) which highly suggests that the cancerous lesion is already invading deeply into the sm layer.

Some studies have already reported the clinical usefulness of detailed determination of the V pit pattern using MCE for predicting the depth of invasion of sm neoplasms. Kudo *et al.* reported that 11 of 22 (50%) lesions with a type V pit pattern with a bounded surface were found to be invasive cancers with involvement of the sm layer (16). Other studies have reported a diagnostic accuracy of type V pit for the diagnosis of sm invasive cancer of 85% (81/95) and 79% (11/14), respectively (24, 25). Recently, Ohta *et al.* reported that lesions with high-grade atypia have erosive change in the surface epithelium and histological appearance of a desmoplastic reaction. Due to these histopathological changes, lesions invading deeply into the sm layer usually show a demarcated area on its surface (26). However, protruded type lesions do not often show an invasive pattern, even if they invade deeply into sm. In such cases, it is sometimes difficult to predict the degree of invasion only evaluating the tumor surface. In this study, we found out that the clinical classification of the pit

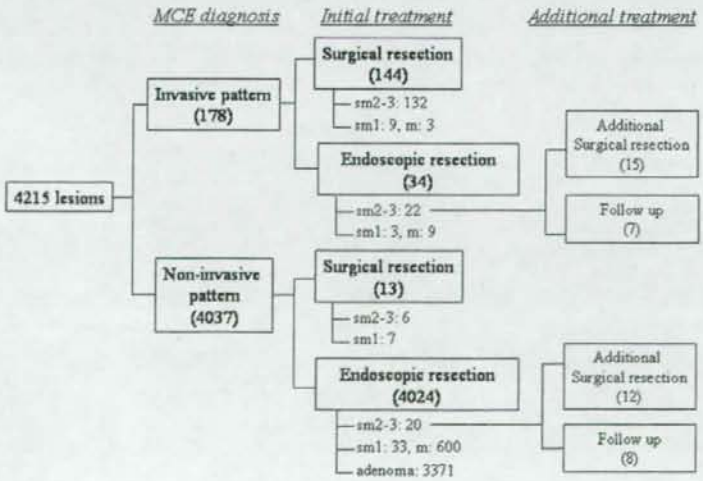

Figure 4. Treatment strategy.

pattern has an overall accuracy of 98.8% suggesting that such invasive pattern is a useful indicator to predict the invasion of sm layer especially sm deep (sm2–3) invasion. Thus, the invasive/non-invasive pit pattern might be used to determine the ideal treatment, either endoscopic resection or surgery. In addition, the diagnostic sensitivity of the clinical pit pattern classification to properly identify the depth of invasion of flat and depressed lesions was superior to that of polypoid lesions (97.5% *vs.* 75.8%). For these former cases, not only MCE but also other predictive factors or diagnostic methods should be considered for diagnosis.

Some authors have reported the usefulness of endoscopic ultrasonography (EUS) particularly the advantages of high frequency ultrasound (HFUS) to diagnose the invasion depth of early colorectal cancer (27–30). Hurlstone *et al.* conducted a study to compare the two modalities (30). According to their result, HFUS was superior to MCE for determination of depth invasion (93% *vs.* 59%, respectively). Meanwhile, Fu *et al.* have recently reported that MCE is as accurate as EUS for preoperative staging of early colorectal cancer (31). Generally, EUS colonoscopes have a rigid tip that makes it difficult to always reach the cecum when compared with conventional ones. Regarding cost-effectiveness and time-consuming issues, EUS is not as good as MCE. Furthermore, Uno *et al.* (32) and Kobayashi *et al.* (33) reported the verification of the "*Non-lifting sign*" as one modality of depth diagnosis for colorectal cancers. In spite of the simplicity of such technique, Kobayashi *et al.* concluded that the "*Non-lifting sign*" could not reliably predict deeper cancerous invasion in comparison with endoscopic diagnosis.

There are some limitations in our study. First, the endoscopic diagnosis using magnification was performed after conventional endoscopic diagnosis which means endoscopists were not blinded to diagnose only with MCE images. Therefore, we could not evaluate how much MCE diagnosis exceeded compared to conventional endoscopic diagnosis. Second, since only neoplastic lesions were included this study, it is difficult to prove the usefulness of MCE as a differential diagnostic modality between neoplastic or non-neoplastic lesions. For such distinction, however, chromoendoscopy with magnification has already been reported to be the most reliable method to determine whether a colorectal lesion is neoplastic or not (12–14). Another point worth mentioning is that all procedures were carried out by experienced examiners. This means that the effectiveness of MCE deserves revalidation studies including ideally general endoscopists. The effort necessary for learning to identify mucosal crypt patterns is important but scarcely studied. Generally, differential diagnosis by MCE is simple and easy to learn compared with depth diagnosis (m/sm1 or sm2–3) for beginners. Togashi *et al.* investigated the efficacy of magnifying colonoscopy in the differential diagnosis of colorectal polyps and also described the learning curve in their study. They reported that a minimum experience of observing 200 lesions with high-magnification was necessary to understand pit pattern diagnosis (9). In addition, we only used the optical zoom (OZ) system, which enables a more precise magnification image than that of the electronic zoom (EZ) system. Except for a small number of institutions, the OZ system is not available in Western countries. In the near future, comparative studies between OZ and EZ should be performed to validate the usefulness of MCE.

In conclusion, the present study suggests that the diagnosis of invasive or non-invasive pit pattern observed by MCE is a highly effective *in vivo* method to predict the depth of invasion of colorectal neoplasms, and consequently a useful tool for endoscopic staging of early colorectal cancers. In the near future, multi-center trials should be performed to validate the usefulness of MCE compared to other modalities (e.g., conventional colonoscopy, EUS, non-lifting sign).

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STUDY HIGHLIGHTS

What Is Current Knowledge

- *In vivo* estimation of the depth of invasion in early colorectal lesions is crucial for an adequate therapeutic strategy.
- Magnifying chromoendoscopy (MCE) has been proposed as the best method. However, there are no large-scale validation studies concerning the clinical classification of the pit pattern.

What Is New Here

- A large prospective study of 4,215 lesions conducted at the National Cancer Center Hospital has demonstrated that the clinical pit pattern (invasive/non-invasive) evaluated by MCE is a highly effective *in vivo* method to predict the depth of invasion of colorectal neoplasms.

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CONFLICT OF INTEREST

This is not a collaborative study. Thus, this study being an absolutely independent investigation, there is neither financial support nor interest from any companies.

Meshed capillary vessels by use of narrow-band imaging for differential diagnosis of small colorectal polyps (CME)

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Background: Although microvascular vessels on the surface of colorectal polyps are observed by narrow-band imaging (NBI) with magnification, its clinical usefulness is still uncertain.

Objective: Our purpose was to evaluate the usefulness of meshed capillary (MC) vessels observed by NBI magnification for differentiating between nonneoplastic and neoplastic colorectal lesions.

Design: Prospective polyp study.

Setting: National Cancer Center Hospital East, Chiba, Japan.

Patients: A total of 702 consecutive patients who underwent total colonoscopy between September and December 2004 were prospectively evaluated. Patients with polyps >10 mm and those with polyps previously evaluated by histologic examination or colonoscopy were excluded.

Intervention: Lesions were classified into 2 groups: polyps with invisible or faintly visible MC vessels as nonneoplastic and polyps with clearly visible MC vessels as neoplastic. Lesions judged as nonneoplastic were subjected to biopsy and those as neoplastic were removed endoscopically. Histologic analysis was performed in all lesions.

Main Outcome Measurement: Visible or invisible surface MC vessels, prediction of histologic diagnosis.

Results: Of 92 eligible patients enrolled in this study, 150 lesions, including 39 (26%) hyperplastic polyps and 111 (74%) adenomatous polyps, were detected. Observation of MC vessels detected 107 of 111 neoplastic polyps and 36 of 39 nonneoplastic polyps. The overall diagnostic accuracy, sensitivity, and specificity were 95.3%, 96.4%, and 92.3%, respectively.

Limitations: MC vessel judgment performed by a single colonoscopist with extensive experience in magnifying NBI.

Conclusion: Observation of surface MC vessels by magnifying NBI is a useful and simple method for differentiating colorectal nonneoplastic and neoplastic polyps. (Gastrointest Endosc 2009;69:278-83.)

Abbreviations: FAP, familial adenomatous polyposis; HNPCC, hereditary nonpolyposis colorectal cancer; IV, intravenously; MC, meshed capillary; NBI, narrow-band imaging.

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See CME section; p. 303.

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Hyperplastic polyps and other nonneoplastic colorectal lesions do not require endoscopic treatment because they are benign and do not have malignant potential.[1,2] In contrast, the adenoma-carcinoma sequence suggests that colorectal cancers develop from adenomatous polyps and, therefore, their removal could prevent colorectal cancers.[3,4] Thus, in vivo distinction of nonneoplastic and neoplastic lesions would greatly increase the efficiency of colonoscopic procedures.[5]

In a hyperproliferative state, angiogenesis is critical to the transition of premalignant lesions to the malignant phenotype.[6,7] Narrow-band imaging (NBI) is an innovative optical technology that provides a unique image that

emphasizes the morphologic and structural character of lesions as well as the surface capillary pattern.

Previously, we described how the presence of "meshed capillary (MC) vessels" by magnifying NBI are arranged in a honeycomb pattern around the mucosal glands constitutes a useful method for differential diagnosis of colorectal lesions without the need for any dye application.[8] Recently, we have proposed the capillary pattern classification (I-III) for distinction of colorectal lesions.[9-11]

The aim of the current study was to prospectively evaluate the usefulness of observing the surface MC vessels to differentiate between nonneoplastic and neoplastic polyps.

Capsule Summary

What is already known on this topic

- Narrow band imaging (NBI) emphasizes the morphologic and structural character of lesions, as well as the surface capillary pattern.

What this study adds to our knowledge

- NBI detected meshed capillary vessels in 107 of 111 neoplastic and 36 of 39 nonneoplastic polyps, for overall diagnostic accuracy, sensitivity, and specificity of: 95.3%, 96.4%, and 92.3%, respectively.

METHODS

Patients

A total of 702 consecutive patients who underwent screening colonoscopy at National Cancer Center East Hospital, Chiba, Japan, between September and December 2004 were analyzed. The study protocol was approved by the institutional review board, and informed consent was obtained from all patients before the examination. Patients with polyps larger than 10 mm, with lesions previously evaluated by histologic examination or colonoscopy, and those with invasive carcinoma were excluded from the study. Patients with inflammatory bowel disease, hereditary nonpolyposis colorectal cancer (HNPCC), and familial adenomatous polyposis (FAP) were also excluded.

Principle of NBI

NBI is based on modification of the spectral features with an optical color separation filter narrowing the bandwidth of spectral transmittance. In this system, the center wavelengths of the dedicated trichromatic optical filters are 540 and 415 nm, with bandwidths of 30 nm.[12,13] By use of this narrow spectrum, the contrast of the capillary pattern in the superficial layer is markedly improved, and thus clear visualization of vascular structures is achieved during endoscopy. The electronic button on the control section of the colonoscope allowed switching between the conventional and the NBI views instantly.[14]

Colonoscopy procedure

Bowel preparation consisted of 2 to 3 L of polyethylene glycol solution in the morning before the procedure, as previously reported.[15] Hyoscine methobromide (10-20 mg given intravenously [IV]) was administered if there were no contraindications, and light sedation with diazepam (3-5 mg IV) was used in selected subjects. The location of lesions was categorized into 2 groups, according to which side of the splenic flexure they were encountered: proximal colon (including the cecum, ascending colon, and transverse colon) and distal colon (including descending colon, sigmoid colon, and rectum). Lesions were classified macroscopically on the basis of the criteria of the Paris classification of superficial GI lesions.[16]

Evaluation of MC vessels

Colonoscopies were carried out by using a magnifying video colonoscope (CF-H260ZI; Olympus, Optical, Tokyo, Japan) with a standard video processor system (EVIS 260, Lucera Spectrum Olympus Optical). Endoscope withdrawal was performed under conventional white light. All lesions detected by conventional colonoscopy were rinsed with water to remove any overlying mucus on the surface and then were examined by magnifying NBI without the use of any dye solution. Once the NBI system was activated through an easy-to-handle, 1-touch electronic bottom, MC vessels were seen as green-brown in color, and the surrounding normal colon mucosa was seen as a yellowish color. The hue of nonneoplastic lesions is very similar to that of normal epithelial layer, whereas the majority of neoplastic lesions appeared brownish. Lesions with invisible or faintly visible MC vessels were categorized as nonneoplastic, and lesions with clearly visible MC vessels were categorized as neoplastic (Fig. 1).[9-11,14] Size was estimated by using the open width of standard, fully opened biopsy forceps as a reference[5] or after removal (hot biopsy or snare polypectomy). Procedures and endoscopic evaluation were performed by an expert colonoscopist with extensive experience in magnification and NBI (Y. S.). Lesions diagnosed as nonneoplastic were subjected to biopsy, and those diagnosed as neoplastic were removed endoscopically without exception.

Endoscopic treatment

Lesions diagnosed as nonneoplastic and advanced carcinomas underwent biopsy. In lesions identified as adenomatous polyps or intramucosal carcinomas (visible MC vessels), hot biopsy, polypectomy, or EMR was performed. Lesions ≤ 5 mm were resected by coagulation biopsy (hot biopsy), and flat lesions or those >5 mm were treated with loop snare polypectomy or EMR.[17,18]

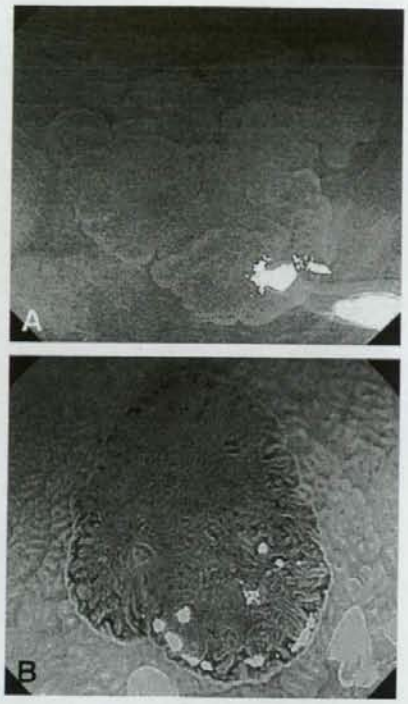

Figure 1. Magnifying endoscopic evaluation of MC vessels with NBI. **A**, Lesions with invisible or faintly visible MC vessels. This lesion was histologically diagnosed as hyperplastic polyp. **B**, Lesions with clearly visible MC vessels. This lesion was histologically diagnosed as adenomatous polyp.

Histopathologic examination

Specimens were fixed in 20% formalin and histologically examined after hematoxylin and eosin staining. Histologic diagnosis was made by a pathologist blinded to the colonoscopic diagnosis at each step. The pathologic definition of the lesions was made on the basis of the Japanese Research Society for Cancer of the Colon and Rectum.[19] Histologically, adenomatous lesions were defined as neoplastic, and other nonepithelial lesions including hyperplastic polyps were defined as nonneoplastic. The accuracy rates of the endoscopic diagnosis was evaluated on the basis of the final pathologic diagnosis.

Statistical analysis

Differences between groups were analyzed with the χ^2 test. Differences with a P value $< .05$ were considered significant.

RESULTS

Clinical data

Of 702 patients recruited for this study, 453 (64%) were found to have no polyps on colonoscopy, 152 (22%) were ineligible on the basis of the exclusion criteria, and in 5 (1%) patients, retrieving the resected specimen was not possible (Table 1). The remaining 92 (13%) patients were enrolled for prospective evaluation. The mean age was 63.6 years (range 36-80 years) with a male/female ratio of 4.7:1. In all examinations, bowel preparation was considered adequate, and colonoscopy was performed up to the cecum. There were no complications during any procedure.

TABLE 1. Patient flow chart

Patient pool (702 patients considered for the study)
Excluded: 453 patients with no polyps found on colonoscopy
Excluded: 68 patient with colorectal lesions with previous evaluation, including histologic examination or colonoscopy
Excluded: 39 patients with invasive carcinoma
Excluded: 41 patients with polyps larger than 10 mm
Excluded: 2 patients with ulcerative colitis (1 with FAP, 1 with HNPCC)
Excluded: 5 patients with polyps that were unretrievable

Clinicopathologic features of the colorectal lesions

A total of 150 lesions including 39 (26%) hyperplastic and 111 (74%) adenomatous polyps were identified, for a ratio of 1.6 lesions per participant. All adenomatous polyps had low-grade dysplasia. Macroscopically, 25 lesions were classified as type 0-Is and 125 as type 0-IIa. The overall prevalence of flat adenomas was 83%. There were no superficial depressed lesions (0-IIc). The mean diameter of the identified lesions was 3.8 mm (range 2-10 mm). On the basis of location, 63 (42%) polyps were distributed in the proximal colon and 87 (58%) in the distal colon. Clinicopathologic features of the colorectal lesions identified in this study are shown in Table 2.

Diagnostic accuracy of MC vessels

The overall diagnostic accuracy of the MC vessels for distinguishing between neoplastic and nonneoplastic lesions was 95.3% (143/150). The diagnostic accuracy for nonneoplastic lesions (negative predictive value) was 90% (36/40), and that for neoplastic lesions (positive predictive value) was 97.3% (107/110). The sensitivity and specificity of MC vessels diagnosis by NBI colonoscopy were 96.4% (107/111) and 92.3% (36/39), respectively (Table 3).

DISCUSSION

To our knowledge, this is the first prospective study on the effectiveness of observing the MC pattern by magnifying NBI for differential diagnosis of < 10 mm colorectal polyps.

TABLE 2. Patient characteristics and clinicopathologic features

No. of patients/lesions	92/150
Sex (male/female)	76/16
Mean age (y [range])	63.6 (36-30)
Macroscopic type*	
0-Is	25
0-IIa	125
Size of resected polyp (mm [range])	3.8 (10)
Location of resected polyp (proximal/distal)	63/87
Histologic findings	
TA with low- and high-grade dysplasia	111
Hyperplastic polyp	39

TA, Tubular adenoma.
*According to the Paris endoscopic classification.[16] Lesion lost after polypectomy.

TABLE 3. MC vessels by NBI and histologic examination

	Neoplastic	Nonneoplastic
MC vessels (+)	107	3
MC vessels (–)	4	36

In 1999, the first prototype of an NBI system was developed at National Cancer Center East Hospital in scientific cooperation with Olympus Corp, Japan. In 2001, we also reported for the first time its clinical usefulness for the diagnosis of lesions in the GI tract.[20] Consequently, in 2004 our first NBI clinical study reported not only equivalent results to chromoendoscopy but also a better visualization of the vascular pattern than that of conventional colonoscopy for the diagnosis of colorectal polyps.[21] After it became commercially available in December 2005, many studies have reported its advantages and effectiveness for the diagnosis of not only lesions within the GI tract[22-25] but also in other organs.[26,27]

This study included only polyps < 10 mm. Although the general consensus is to remove adenomas > 10 mm, there is still no consensus for polyps < 10 mm. Different management strategies include resection, biopsy only, or no treatment. Recently, a rate of up to 7% of colorectal cancers < 10 mm has been reported during screening colonoscopy,[28-30] which warns us to look out for small lesions and, more importantly, to treat them selectively. Herein was found that about 20% (1/5) of screened patients had polyps, most of them neoplastic (73%). This frequency is lower compared with that of other screening studies (1/3, 33%).[5] On the other hand, the frequency of invasive carcinoma (39/702, 5%) was higher than that of a similar screening study (3/500, 0.6%).[5] These results might be explained by the fact that the study was performed in a tertiary referral cancer center. The prevalence of flat neoplastic lesions in this study (125/150, 83%) was higher compared with rates reported in Japan[15] and in Western countries,[31,32] probably because of the advantage of using NBI for screening colonoscopy.

Several investigations had validated our previous results about the equivalency of magnifying NBI and magnifying chromoendoscopy in the evaluation of the colon pit pattern proposed by Kudo et al.[33] These studies have reported sensibilities and specificities ranging from 87% to 99% and from 72% to 94% for magnifying chromoendoscopy and magnifying NBI, respectively.[34-36] Some retrospective/pilot studies have reported the usefulness of microvessels with magnifying NBI colonoscopy.[37,38] However, prospective studies evaluating the surface visibility or invisibility of MC vessels for differential diagnosis of sessile and flat elevated colorectal polyps were absent.

Herein MC vessel evaluation demonstrated high rates of diagnostic accuracy, sensitivity, and specificity for distinction between neoplastic and nonneoplastic lesions (95.3%, 96.4%, and 92.3%, respectively). These data are similar to those of previous reports on magnifying chromocolonoscopy.[21,39,40] However, conventional chromoendoscopy is not globally used and is defined as inconvenient and difficult to reproduce in Western countries.[41] On the basis of the results of this study, we believe that MC vessel evaluation is easier to reproduce, simpler, and faster than conventional chromocolonoscopy. In addition, it seems to be more appealing to Western endoscopists because it offers a short learning curve.

When the NBI results were analyzed, it was found that 4 lesions without MC vessels were misdiagnosed as nonneoplastic lesions. These polyps were histologically diagnosed as adenoma with low-grade dysplasia. One possible explanation for this is that these lesions were diminutive polyps of 3 mm in diameter in which visualization of the MC pattern was not easy. On the other hand, 3 lesions were misdiagnosed as neoplastic (visible MC vessels). These lesions were histologically diagnosed as hyperplastic polyps. Difficulties offered by small polyps when samples are manipulated to reach a proper tissue orientation might explain these results.[42] However, the diagnostic difficulties under NBI observation encountered with small (<3 mm) polyps and atypical hyperplastic polyps, such as sessile serrated polyps, will be investigated in further studies.

Previous studies of patients undergoing colonoscopy have found that small polyps are identified during more than 50% of such examinations.[43] More than 50% of these small polyps are adenomas.[44] Therefore, a key clinical decision in patients with small polyps may depend on determination of the histologic diagnosis. According to the American Society for Gastrointestinal Endoscopy guidelines issued in 2005, every effort should be made during colonoscopy to obtain a tissue diagnosis when