Blue-light imaging or narrow-band imaging for proximal colonic lesions: a prospective randomized tandem colonoscopy study

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Background and Aims: Blue-light imaging (BLI) is a new image-enhanced endoscopy with a wavelength filter similar to narrow-band imaging (NBI). We compared the 2 with white-light imaging (WLI) on proximal colonic lesion detection and miss rates.

Methods: In this 3-arm prospective randomized study with tandem examination of the proximal colon, we enrolled patients aged ≥40 years. Eligible patients were randomized in 1:1:1 ratio to receive BLI, NBI, or WLI during the first withdrawal from the proximal colon. The second withdrawal was performed using WLI in all patients. Primary outcomes were proximal polyp (pPDRs) and adenoma (pADRs) detection rates. Secondary outcomes were miss rates of proximal lesions found on tandem examination.

Results: Of 901 patients included (mean age, 64.7 years; 52.9% men), 48.1% underwent colonoscopy for screening or surveillance. The corresponding pPDRs of the BLI, NBI, and WLI groups were 45.8%, 41.6, and 36.6%, whereas the corresponding pADRs were 36.6%, 33.8%, and 28.3%. There was a significant difference in pPDR and pADR between BLI and WLI groups (difference, 9.2% [95% confidence interval {CI}, 3.3-16.9] and 8.3% [95% CI, 2.7-15.9]) and between NBI and WLI groups (difference, 5.0% [95% CI, 1.4-12.9] and 5.6% [95% CI, 2.1-13.3]). Proximal adenoma miss rates were significantly lower with BLI (19.4%) than with WLI (27.4%; difference, –8.0%; 95% CI, –15.8 to –.1) but not between NBI (27.2%) and WLI.

Conclusions: Both BLI and NBI were superior to WLI on detecting proximal colonic lesions, but only BLI had lower proximal adenoma miss rates than WLI. (Clinical trial registration number: NCT03696992.) (Gastrointest Endosc 2023;98:813-21.)

Colonoscopy is considered the most sensitive diagnostic tool for detection of colorectal polyps or adenomas. However, missed lesions are not uncommon during colonoscopy, and tandem colonoscopy studies showed that the miss rates for adenomas and serrated polyps were 26% and 27%, respectively.[1,2] Missed lesions during colonoscopy are a main reason for postcolonoscopy colorectal cancer development.[3,4] The reasons for missed lesions could be multiple and related to patient, endoscopist, and technologic factors. Various patient factors such as quality of bowel preparation, patient sex, and underlying risk for colorectal cancer have been suggested.[5,6] Endoscopist factors including colonoscopy

Abbreviations: APC, adenoma per colonoscopy; BBPS, Boston Bowel Preparation Scale; BLI, blue-light imaging; IEE, image-enhanced endoscopy; LED, light-emitting diode; NBI, narrow-band imaging; pADR, proximal adenoma detection rate; PPC, polyp per colonoscopy; pPDR, proximal polyp detection rate; SSL, sessile serrated lesion; WLI, white-light imaging.

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experiences, scope withdrawal time, and baseline adenoma detection rate are also key factors underlying the optimal performance of colonoscopy.[4] Various technologic advances of the endoscopic system have been developed to maximize adenoma detection, particularly with the use of image-enhanced endoscopy (IEE), which enhances the visibility of abnormal mucosal lesions.

Narrow-band imaging (NBI), by using 415- and 540-nm narrow-band illumination, is one of the most widely adopted IEEs. Apart from acting as a virtual chromoendoscopy on lesion characterization, the latest meta-analysis of individual patient data has shown that the use of NBI, particularly the brighter second generation, could enhance adenoma detection rate by 1.28-fold[7] when compared with white-light imaging (WLI). Subgroup analysis showed that NBI detected more nonadenomatous polyps and flat polyps than WLI, making it more useful in the proximal colon.[8]

Blue-light imaging (BLI) is a new IEE that focuses on a short wavelength at 410 nm.[9] There are 2 versions of BLI. The previous version, called blue-laser imaging, used a laser as a light source and was only available in Japan. The current version, as used in this study, uses a light-emitting diode (LED) light source and is widely available in most countries. BLI has been applied to polyp characterization,[10] and a recent Japanese study showed that both blue-laser imaging and BLI were noninferior to NBI in diagnosing colorectal neoplasms, especially for hyperplastic polyps, sessile serrated lesions (SSLs), and low-grade dysplasia.[11] In another Japanese study comparing LED with a laser light source, the LED light source was shown to be noninferior to the laser light source and tended to be brighter during WLI.[12] Furthermore, small randomized controlled studies showed that BLI resulted in a higher rate of adenoma detection[13,14] and lower adenoma miss rates than WLI.[15] As yet, there is no parallel study comparing these 2 competing IEE technologies (NBI and BLI) with conventional WLI on colorectal lesion detection rate or miss rate.

This prospective 3-arm randomized tandem colonoscopy study aimed to compare conventional WLI with NBI or BLI on proximal colonic lesion detection. We also explored the role of these 2 competing technologies on the miss rates of proximal colonic lesions during tandem examination.

METHODS

Study design and patients

This is an investigator-initiated 3-arm randomized tandem colonoscopy study comparing the adenoma detection rate and miss rate of BLI or NBI with WLI in the proximal colon. The study was approved by the Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster (UW 18-420) and was registered with clinicaltrials.gov (NCT03696992). All authors had access to the study data and reviewed and approved the final manuscript.

The study was conducted at the Endoscopy Center of the Queen Mary Hospital of Hong Kong. We included consecutive patients, aged ≥40 years, who were scheduled to have colonoscopy for screening and surveillance as well as for symptoms. Patients aged <40 years were not included because the prevalence of colonic lesions is expected to be low in these younger patients, and there was no upper age limit for enrollment. Patients were also excluded if they were unable to provide written informed consent; had undergone previous colorectal resection; or had a personal history of colorectal cancer, inflammatory bowel disease, familial adenomatous polyposis, Peutz-Jeghers syndrome, or other polyposis syndromes. Patients who were considered unsafe for polypectomy, including patients with bleeding tendency and those with severe comorbid illnesses, were also excluded.

Randomization and masking

Eligible patients were asked to provide written informed consent for participation in this study on the day of colonoscopy. They were then randomly assigned to 3 different groups in a 1:1:1 ratio to undergo tandem examination of the proximal colon with NBI followed by WLI, BLI followed by WLI, or WLI followed by WLI (Fig. 1). Randomization was carried out by computer-generated random sequences and stratified according to indications of colonoscopy (symptomatic vs screening/surveillance) and endoscopist experience (experienced vs trainees). A research assistant not involved in this study kept all randomization codes, which were placed in individual opaque envelope. The envelope was opened to disclose the assigned examination sequences once consent was obtained from the patient. Patients were blinded to the group assignment.

Tandem examination

Patient preparation for colonoscopy followed usual hospital practice. Colonoscopy was performed with the patient under conscious sedation with intravenous midazolam and pethidine. Procedures were performed by either experienced endoscopists with at least 5 years of experience in colonoscopy (n = 9) or gastroenterology fellows with at least 12 months of independent colonoscopy experience including IEE training (n = 6). High-definition colonoscopes were used including the CF-HQ290L/I with the EVIS- EXERA 290 video system (Olympus Optical, Tokyo, Japan) for the NBI group and the EC-760ZP-V/L with the ELUXEO 7000 endoscopic system (Fujifilm Co, Tokyo, Japan) for the BLI group. Both systems were used for patients assigned to the WLI group.

During the colonoscopy, the assigned colonoscope was first advanced to the cecum under WLI. The proximal colon, defined as the segments from the cecum to the splenic flexure, was examined by the assigned examination

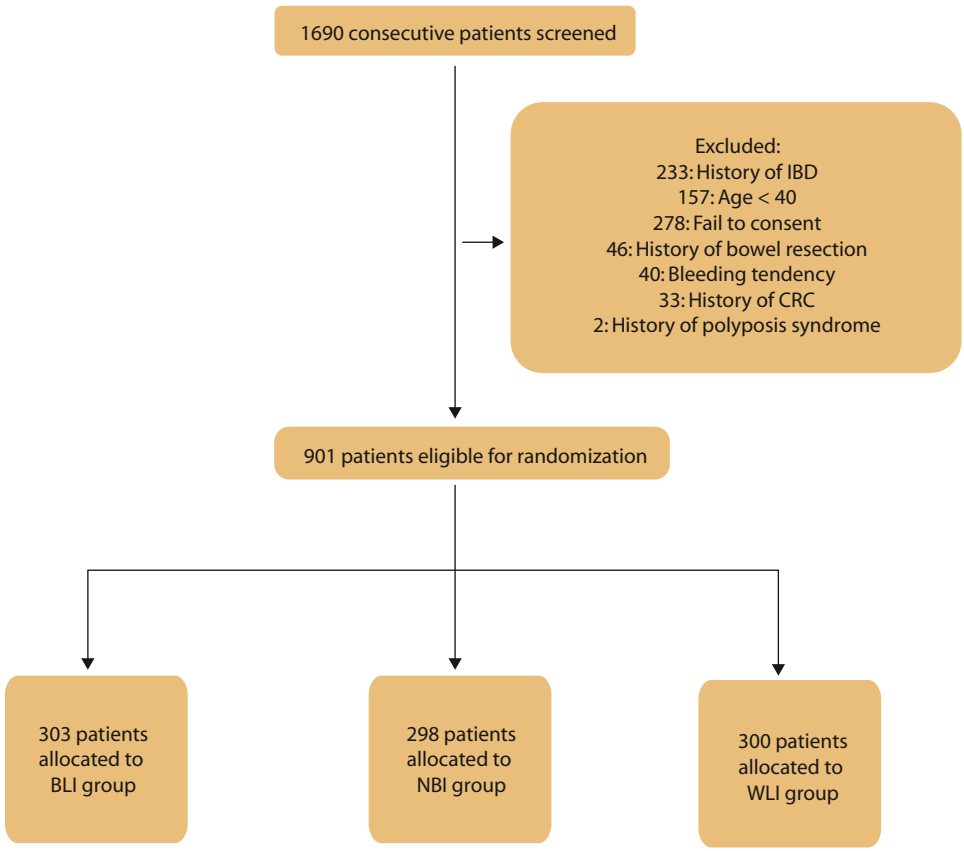

Figure 1. Patient flow in the trial. *IBD*, Inflammatory bowel disease; *CRC*, colorectal cancer; *BLI*, blue-light imaging; *NBI*, narrow-band imaging; *WLI*, white-light imaging.

mode of NBI, BLI, or WLI during the first withdrawal (Fig. 2). The time of the first withdrawal to the splenic flexure (minus the polypectomy site) was kept to a minimum of 4 minutes as reported previously.[4] The splenic flexure was identified by the sharp bend after the transverse colon and with external indentation of the abdominal wall. The location of the splenic flexure was gently marked by a small biopsy forceps or by creating a suction artifact as a landmark for subsequent tandem examination. The Boston Bowel Preparation Scale (BBPS) score of the proximal colon during the first-pass examination was used to evaluate the quality of bowel preparation. All polyps, except very large lesions that would require prolonged endoscopic intervention or malignant-looking lesions (in which a biopsy sample would be taken), were removed during the first withdrawal. The size (measured with open biopsy forceps), location, and morphology (as described in Paris classification) of all polyps detected were recorded by an independent researcher.

Immediately after the first withdrawal to the splenic flexure, the same colonoscope was reintroduced to the cecum for the second examination of the proximal colon by the same endoscopist. The second examination of the proximal colon was performed under WLI in all 3 groups. Any additional polyps or adenomas detected on the second examination was also removed, labeled separately, and sent for histologic examination. The distal colon, from the splenic flexure to the rectum, was examined once by WLI after the tandem examination of the proximal colon by the same endoscopist.

Advanced adenomas were defined as adenomas $\geq$10 mm with villous histology in 25%, high-grade dysplasia, or the presence of carcinoma. An SSL was defined according to the World Health Organization classification, which included traditional serrated adenoma, sessile serrated adenoma with or without cytologic dysplasia, and hyperplastic polyp.[16]

Outcomes

The primary outcome of this study was proximal adenoma detection rates (pADRs) and proximal polyp detection rates (pPDRs) during the first examination of the proximal colon with WLI compared with BLI or NBI. pADRs and pPDRs were defined as the proportion of patients with at least 1 proximal adenoma or polyp, respectively, detected during the first examination.

Secondary outcomes were the proximal adenoma miss rate, proximal polyp miss rate, proximal SSL miss rate, proximal advanced adenoma miss rate, and the number of polyps per colonoscopy (PPCs) or adenomas per colonoscopy

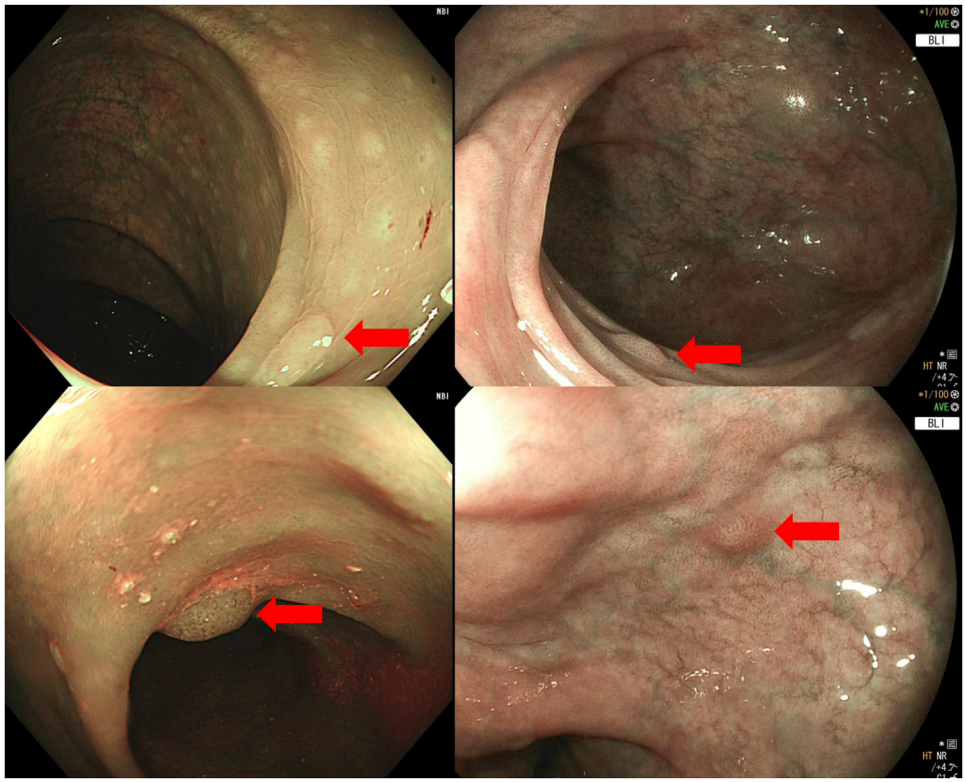

Figure 2. Small colorectal polyps as detected by narrow-band imaging (*left*) and blue-light imaging (*right*). *Arrows* indicate location of polyps.

(APCs) detected in the proximal colon during the first and second examinations. Miss rates were defined as the number of histologically confirmed lesions of interest detected during the second examination divided by the total number of histologically confirmed lesions of interest detected in both examinations.[17] We also compared the detection and miss rates of advanced adenomas and SSLs.

Sample size estimation

Because there is no direct comparison between the 2 IEE modalities, we hypothesized that BLI and NBI are comparable and are both superior to WLI on proximal adenoma detection. With the assumptions that the pADR of NBI or BLI would be about 30%[18] and the difference between NBI or BLI and WLI was 10%,[19-21] 280 patients were needed in each study arm to achieve a power of 80% and a 2-sided significance level of 5%. Allowing for 5% of patients to have incomplete tandem examinations or inadequate bowel preparation, a minimum of 884 patients would need to be enrolled.

Statistical analysis

The primary analysis was based on an intention-to-treat analysis. Continuous variables are presented as mean (standard deviation) and were compared using nonparametric bootstrap t tests.[22] Categorical variables are presented as frequencies and percentages and were compared using the χ^2 test or Fisher exact test or nonparametric bootstrap t test when applicable.[22] $P \leq .025$ was considered to be statistically significant after adjustment with Bonferroni correction for the comparison between WLI and BLI or NBI.

Asubgroup analysis was performed according to quality of bowel preparation and indications of colonoscopy as screening, surveillance, or symptomatic. Because the mean BBPS score of all patients was 7.3, we chose to use a BBPS score of 7 and 8 as cutoff values.

RESULTS

Patient characteristics

Between November 2018 and February 2022, 901 patients were enrolled and randomized, with 303, 298, and 300 patients in the BLI, NBI, and WLI arms, respectively (Fig. 1). The mean age of the entire cohort was 64.7 years (standard deviation, 10.0), and 477 patients (52.9%) were men. Four hundred thirty-three patients (48.1%) underwent colonoscopy for screening or surveillance, whereas the remaining 51.9% underwent colonoscopy for symptoms. Seven patients had incomplete colonoscopy (2 in the BLI group, 3 in the NBI group, and 2 in the WLI group), and all randomized patients were included in the intention-to-treat analysis. The baseline characteristics of patients and colonoscopies are shown in Table 1.

TABLE 1. Patient baseline characteristics (intention to treat)

	Blue-light imaging (n = 303)	Narrow-band imaging (n = 298)	White-light imaging (n = 300)	All (n = 901)
Mean age, y (SD)	64.8 (10.4)	64.5 (10.0)	64.7 (9.8)	64.7 (10.0)
Male sex	155 (51.1)	157 (52.7)	165 (55.0)	477 (52.9)
Experienced endoscopist	127 (41.9)	125 (41.9)	129 (43.0)	381 (42.3)
Indication for colonoscopy				
Screening/surveillance	151 (49.8)	136 (45.6)	146 (48.6)	433 (48.1)
Symptomatic	152 (50.1)	162 (54.3)	154 (51.3)	468 (51.9)
Mean Boston Bowel Preparation Scale score				
Right-sided colon (SD)	2.1 (.6)	2.1 (.6)	2.2 (.6)	2.1 (.6)
Transverse colon (SD)	2.5 (.6)	2.5 (.6)	2.6 (.5)	2.5 (.6)
Left-sided colon (SD)	2.6 (.6)	2.6 (.6)	2.6 (.5)	2.6 (.6)
Total (SD)	7.1 (1.5)	7.3 (1.4)	7.4 (1.3)	7.3 (1.4)
Mean cecal intubation time, min (SD)	7.7 (.3)	8.1 (.3)	7.9 (.3)	7.9 (.2)
Mean first withdrawal time from cecum to splenic flexure, min (SD)	5.3 (.2)	5.1 (.2)	4.7 (.2)	5.0 (.2)
Mean second withdrawal time from cecum to splenic flexure, min (SD)	2.2 (.2)	2.4 (.2)	2.2 (.2)	2.3 (.1)
Mean withdrawal time from splenic flexure to rectum, min (SD)	3.7 (.2)	4.0 (.2)	3.7 (.2)	3.8 (.1)

Values are n (%) unless otherwise defined.
SD, Standard deviation.

The polyp and adenoma detection rate of the entire colon when counting the first-pass examination only was 64.3% and 51.3%, respectively. Advanced adenomas and SSLs were detected in 14.1% and 23.3% of patients based on first-pass examination of the entire colon.

Proximal colonic lesion detection

During the first-pass examination of the proximal colon, the highest polyp and adenoma detection rates were noted in the BLI group and the lowest detection rates in the WLI group (Table 2). The respective pPDRs and pADRs of the BLI group were 45.8% (95% CI, 43.2-48.2) and 36.6% (95% CI, 34.7-39.0), which was significantly higher than those in the WLI group (pPDR vs pADR: 36.6% [95% CI, 34.7-39.0]; difference, 9.2% [95% CI, 3.3-16.9; $P = .027$] vs 28.3% [95% CI, 26.0-30.7]; difference, 8.3% [95% CI, 2.7-15.9; $P = .006$]). The NBI group also had significantly higher pPDRs (41.6% [95% CI, 39.3-44.3] vs 36.6%; difference, 5.0% [95% CI, 1.4-12.9]; $P = .045$) and pADRs (33.8% [95% CI, 31.5-36.2] vs 28.3%; difference, 5.6% [95% CI, 2.1-13.3], $P = .025$) than the WLI group.

The detection rates of advanced adenomas in the BLI, NBI, and WLI groups were 8.6% (95% CI, 7.3-10.0), 6.7% (95% CI, 5.3-8.1), and 4.7% (95% CI, 3.7-5.7), respectively. There was a significant difference in the advanced adenoma detection rate between the BLI and WLI groups (difference, 3.9%; 95% CI, 1.2-7.5; $P = .04$) but not between the NBI and WLI groups (difference, 2.0%; 95% CI, –0.6 to 5.7; $P = .318$). For SSLs, the corresponding detection rates for the BLI, NBI, and WLI groups were 12.2% (95% CI, 10.6-14.2), 11.7% (95% CI, 10.1-13.1), and 9.3% (95% CI, 8.0-10.7), with no significant differences between WLI and BLI or NBI .

The PPCs, APCs, and advanced adenomas per colonoscopy detected in the proximal colon by BLI were significantly higher than those detected by WLI (PPC: $1.10 \pm .10$ vs $.73 \pm .08$, $P = .003$; APC: $.79 \pm .09$ vs $.52 \pm .06$, $P = .006$; advanced adenomas per colonoscopy: $.09 \pm .02$ vs $.05 \pm .01$, $P = .040$). The PPCs and APCs detected in the proximal colon by NBI were also significantly higher than WLI (PPC: $.92 \pm .08$ vs $.73 \pm .08$, $P = .048$; APC: $.65 \pm .07$ vs $.52 \pm .06$, $P = .049$). However, there was no significant difference in advanced adenomas detected per colonoscopy between the NBI and WLI groups (Table 2).

A subgroup analysis was performed according to quality of bowel preparation and indications of colonoscopy. BLI and NBI were only found to be superior to WLI on pPDRs and pADRs in patients with BBPS scores ≥ 7 but not in patients with BBPS scores <7 (Supplementary Table 1, available online at www.giejournal.org). Similar findings were observed with a BBPS cutoff score of 8 (Supplementary Table 1). Moreover, BLI and NBI were significantly better than WLI (in both pPDRs and pADRs) in subgroups of symptomatic patients only but not in patients who underwent screening or surveillance colonoscopy (Supplementary Table 2, available online at www.giejournal.org).

Proximal colonic missed lesions

A second examination of the proximal colon was performed with WLI in all 3 study arms. The proximal polyp miss rates in the BLI, NBI, and WLI groups were 20.3% (95% CI, 14.6-24.8), 26.6% (95% CI, 22.1-32.9), and 26.3%

TABLE 2. Proximal colonic lesion detection rates

				Difference (%)		*P* value	
	BLI (n = 303)	NBI (n = 298)	WLI (n = 300)	BLI-WLI	NBI-WLE	BLI vs WLE	NBI vs WLE
Detection rate in the proximal colon during the first examination							
Proximal polyp, %	45.8 (43.2-48.2) (n = 139)	41.6 (39.3-44.3) (n = 124)	36.6 (34.7-39.0) (n = 110)	9.2 (3.3-16.9)	5.0 (1.4-12.9)	.027	.045
Proximal adenoma, %	36.6 (34.3-39.3) (n = 111)	33.8 (31.5-36.2) (n = 101)	28.3 (26.0-30.7) (n = 85)	8.3 (2.7-15.9)	5.5 (2.1-13.3)	.006	.025
Proximal advanced adenoma, %	8.6 (7.3-10.0) (n = 26)	6.7 (5.3-8.1) (n = 20)	4.7 (3.7-5.7) (n = 14)	3.9 (1.2-7.5)	2.0 (–.6 to 5.7)	.04	.32
Proximal sessile serrated lesion, %	12.2 (10.6-14.2) (n = 37)	11.7 (10.1-13.1) (n = 35)	9.3 (8.0-10.7) (n = 28)	2.9 (–.4 to 7.8)	2.4 (–1.2 to 7.4)	.43	.47
Mean no. of lesions per colonoscopy in the proximal colon during the first examination							
Polyp	1.10 (.10)	.92 (.08)	.73 (.08)	.37 (.18-.63)	.19 (.15-.40)	.003	.048
Adenoma	.79 (.09)	.65 (.07)	.52 (.06)	.27 (.13-.47)	.13 (.01-.30)	.006	.049
Advanced adenoma	.09 (.02)	.07 (.01)	.05 (.01)	.04 (.01-.08)	.02 (–.01 to .06)	.04	.11
Sessile serrated lesion	.18 (.03)	.15 (.02)	.13 (.03)	.05 (–.01 to .13)	.02 (–.03 to .10)	.32	.23

Values in parentheses are 95% confidence intervals or standard deviation unless otherwise defined.
BLI, Blue-light imaging; *NBI*, narrow-band imaging; *WLI*, white-light imaging.

(95% CI, 20.4-29.9), respectively, whereas the corresponding proximal adenoma miss rates were 19.4% (95% CI, 16.6-22.8), 27.2% (95% CI, 21.8-35.2), and 27.4% (95% CI, 23.1-29.7). The BLI group had a significantly lower miss rate than the WLI group for adenomas (difference, –8.0%; 95% CI, –15.8 to –.1; $P = .02$) but not for polyps (difference, –6.0%; 95% CI, –10.9 to 1.1; $P = .08$). However, there was no significant difference between the use of NBI and WLI on proximal polyp or adenoma miss rates (Table 3).

The miss rates of proximal advanced adenomas in the BLI, NBI, and WLI groups were 13.3% (95% CI, 5.6-24.2), 23.0% (95% CI, 9.1-46.0), and 22.5% (95% CI, 5.9-41.1), respectively. Furthermore, the corresponding miss rates for proximal SSLs were 28.0% (95% CI, 19.5-39.2), 29.7% (95% CI, 18.7-41.7), and 20.8% (95% CI, 9.9-33.0). No significant differences in the miss rates of proximal advanced adenomas and SSLs were observed between BLI or NBI and WLI.

The mean numbers of missed proximal PPCs in the BLI, NBI, and WLI groups were .28, .33, and .26, whereas the mean numbers of missed proximal adenomas in the 3 groups were .19, .24, and .20, respectively (Table 3). There was again no significant difference between groups.

Because 2 systems of WLI were used in this study, we also compared the performance of the 2 WLI systems in the proximal colon. There was no significant difference between the Olympus and Fujifilm WLI systems in terms of polyp and adenoma detection rates (Supplementary Table 3, available online at www.giejournal.org). Moreover, the number of lesions detected in the distal colon by WLI in the BLI and NBI groups was comparable (Supplementary Table 4, available online at www.giejournal.org). The total numbers of proximal colonic lesions detected after tandem examinations are shown in Supplementary Table 5 (available online at www.giejournal.org).

DISCUSSION

To our knowledge, this is the first study to prospectively evaluate the performance of 2 competing IEE technologies (NBI and BLI) with conventional WLI on proximal colonic lesion detection and miss rates using a tandem colonoscopy approach in a single randomized trial setting. We found that both BLI and NBI were superior to WLI on detection of proximal polyps and adenomas, particularly BLI ,which had the highest pADR and pPDR. Furthermore, we found that BLI had a lower adenoma miss rate than WLI but not between NBI and WLI.

A pooled meta-analysis showed that the use of NBI could improve the adenoma detection rate.[7] Although BLI uses a light filter of similar wavelengths as NBI, it is anticipated that a similar performance could be achieved when BLI is applied to colorectal polyp and adenoma detection. Although a previous randomized controlled trial from Japan also demonstrated the superiority of BLI to WLI on polyp detection,[15] so far no study has compared these 2 similar modalities in the same trial setting. Although this study was not designed to directly comparing BLI with NBI, our findings could provide some insights into the performance of these 2 competing IEE technologies when applied to polyp or adenoma detection. In fact, there was a numerically higher pADR and pADR as well as a

TABLE 3. Proximal colonic lesions miss rates

		NBI	WLE	Difference (%)		*P* value	
	BLI (n = 303)	NBI (n = 298)	WLI (n = 300)	BLI-WLE	NBI-WLE	BLI vs WLE	NBI vs WLE
Miss rate in the proximal colon during the second examination							
Proximal polyp, %	20.3 (14.6-24.8) (n = 85)	26.6 (22.1-32.9) (n = 99)	26.3 (20.4-29.9) (n = 78)	−6.0 (−10.9 to 1.1)	.3 (−5.1 to 10.7)	.08	.45
Proximal adenoma, %	19.4 (16.6-22.8) (n = 58)	27.2 (21.8-35.2) (n = 73)	27.4 (23.1-29.7) (n = 59)	−8.0 (−15.8 to −.1)	−.2 (−6.7 to 14.2)	.02	.44
Proximal advanced adenoma, %	13.3 (5.6-24.2) (n = 4)	23.0 (9.1-46.0) (n = 6)	22.2 (5.9-41.1) (n = 4)	−8.9 (−27.1 to 10.0)	.8 (−21.6 to 29.6)	.21	.47
Proximal sessile serrated lesion, %	28.0 (19.5-39.2) (n = 21)	29.7 (18.7-41.7) (n = 19)	20.8 (9.9-33.0) (n = 10)	7.2 (−6.7 to 23.9)	8.9 (−6.1 to 25.5)	.17	.18
Mean no. of missed lesions per colonoscopy in the proximal colon during the second examination							
Polyp	.28 (.04)	.33 (.04)	.26 (.04)	.02 (−.06 to .13)	.08 (−.01 to .19)	.71	.23
Adenoma	.19 (.03)	.24 (.03)	.20 (.03)	−.01 (−.08 to .08]	.04 (−.03 to .16)	.92	.37
Advanced adenoma	.01 (.007)	.02 (.008)	.01 (.007)	.00 (−.01 to .02)	.01 (−.01 to .03)	.99	.52
Sessile serrated lesion	.07 (.01)	.06 (.02)	.03 (.01)	.04 (−.01 to .07)	.03 (−.01 to .07)	.10	.16

Values in parentheses are 95% confidence intervals or standard deviation unless otherwise defined.
BLI, Blue-light imaging; *NBI*, narrow-band imaging; *WLI*, white-light imaging.

higher number of proximal lesions detected in the BLI group than in the NBI group. Moreover, our tandem examination showed that BLI had a significantly lower miss rate of adenomas than WLI, but this difference was not found between NBI and WLI, as more lesions were removed on the first-pass examination by BLI. Although there was larger difference between BLI and WLI than between NBI and WLI, this could account for the significant difference in miss rate between BLI and WLI as more lesions were removed on the first-pass examination by BLI.

The reasons for the favorable trend of BLI over NBI remains uncertain, and we speculate that it is from the brighter LED light source of the BLI system,[11] because other parameters, including the wavelength of the optical filter and image resolution, are generally comparable between the 2 systems. The brighter light source could facilitate lesion detection after the application of an optical filter of NBI or BLI, which could dim the endoscopic image. In keeping with this, a meta-analysis showed that the second generation of NBI (EVIS EXERA 290) with a brighter light source was better than WLI for colorectal adenoma detection but not the first generation of NBI.[7] There is a newer version of the Olympus endoscopy system based on an LED light source (EVIS X1 Video System). A Japanese study showed that the new system with NBI could identify the brown slits of adenoma with a high accuracy of 96.3%.[23] It remains to be determined whether the new generation of NBI with an LED light source will outperform the second-generation NBI. Apart from BLI, the Fujifilm system has another mode of IEE called the linked-color imaging, which emphasizes red mucosal color detection. In our previous randomized controlled trial,[24] we showed that NBI was significantly better than linked-color imaging in detecting colorectal polyps (71.3% vs 55.9%) and serrated lesions (34.6% vs 22.1%).

It is important to note, however, that at least 20% of proximal adenomas were missed across all different imaging modalities including NBI and BLI, which were picked up on tandem examination by WLI only. This observation was compatible with a previous meta-analysis that up to 26% of adenomas were missed in the entire colon on tandem examination.[1] Surprisingly, we found that up to 23% of proximal advanced adenomas and 29.7% of proximal SSLs, both more advanced lesions, could be missed by NBI. Similarly, BLI missed 13.3% of advanced adenomas and 28% of SSLs. Despite the low number of actual lesions missed (mean of .01-.02 per patient or 1-2 per 100 patients), the consequences can be considerable because the risk of progression to cancer of these proximal lesions could be higher than nonadvanced adenomas.

Together, these findings suggest that other measures in addition to IEE are needed to reduce the miss rate. As shown in this study, repeat examination, even with WLI, could pick up >20% of these missed lesions. Numerous studies determined the role of computer-assisted detection in increasing polyp and adenoma detection.[25,26] However, most existing commercially available computer-assisted detection models were built on WLI, and further studies are needed to determine whether there is incremental benefit of the combined use of computer-assisted detection and IEE. Despite the application of these technologic advancements, missed lesions remain a major issue because they can contribute to postcolonoscopy colorectal cancer.[1,3]

The strength of this study is that, to our knowledge, it is the first industry-independent study to compare WLI with 2 different IEE technologies (BLI and NBI) in the same trial setting. Although studies have reported the use of BLI on detection of colonic lesions,[13-15] few studies used this new version of BLI with an LED light source, and there is a paucity of high-quality data. We also included patients undergoing colonoscopy for broad indications rather than limited to screening colonoscopy alone as well as endoscopists of variable experience to simulate the real-world scenario. The tandem design further enables the determination of both detection and miss rates of these 2 competing IEE technologies.

One important assumption of this study was that there is no difference in the performance of the 2 white-light systems on detecting colonic lesions. In response to that, we performed further subgroup analysis to compare the proximal adenoma and polyp detection rates of the 2 systems and found no significant difference between 2 WLI systems (Supplementary Table 3). Moreover, the distal colonic findings, which were all performed by WLI, were similar between the BLI and WLI group (Supplementary Table 4), suggesting that the 2 WLI systems are largely comparable.

Although the quality of bowel preparation is another important determinant for polyp or adenoma detection, particularly during IEE, we showed that BLI and NBI performed better in patients with higher BBPS scores (>7). This observation was compatible with a previous study[27] that found patients assigned to the NBI group with good bowel preparation had a significantly higher detection rate of adenomas and polyps when compared with those with fair bowel preparation. In that study, they defined good bowel preparation as having no more than liquid residue that could be aspirated to achieve near 100% visualization.

This study has several limitations. First, this is a single-center study, and about 50% of patients underwent colonoscopy for symptoms, which may have a higher lesion detection rate. Although these symptomatic patients were not found to have higher pADRs or pPDRs, a significant difference between WLI and BLI or NBI was only found in this group (Supplementary Table 2). However, we could not exclude the possibility of statistical underpowering in the other 2 subgroups. Second, most of our patients were of Chinese ethnicity, but the overall adenoma detection rate of the entire colon was 40% in this study, and the recent incidences of colorectal cancer in Hong Kong are very comparable with many Western countries.[28] Third, tandem colonoscopy was limited to the proximal colon only rather than the entire colon. Although no evidence shows that the beneficial effect of IEE is limited to the proximal colon, missed proximal lesions are suspected to be the main culprit of postcolonoscopy interval cancers.[5,6] Hence, this study focused on the detection and miss rates of proximal colonic lesions. Fourth, a second examination was performed by WLI in all patients by the same endoscopist without crossover. This was to ensure the standardization of the second examination, which aimed to identify missed lesions in the absence of potential enhanced detection by IEE. However, the possibility of nonblinding of the same endoscopist during the second examination and the potential inferior performance of WLI could not be eliminated. Fifth, despite the 3-arm design, the sample size estimation was based on the difference between WLI and NBI or BLI rather than between NBI and BLI. Hence, this study was not powered to compare the difference between NBI and BLI on colonic lesion detection. Because of the anticipated enhanced performance of both BLI and BLI, this direct comparison would require a huge sample size to achieve, which may not carry any major clinical relevance because of the subtle difference between the 2 modalities as shown in this study. Finally, we did not attempt to apply 2 different IEE systems in the same patient because this would require the deployment of 2 different endoscopic systems in the same endoscopy room for a single patient, which would pose major logistic challenges to the execution of this study involving more than 900 patients. The need of repeated insertion of 2 different colonoscopes to the same patient would also potentially increase discomfort and total procedure time, which may not be acceptable by patients.

In conclusion, the results from this 3-arm randomized controlled study showed that both BLI and NBI are superior to WLI on detection of proximal colonic lesions. BLI, but not NBI, had a lower adenoma miss rate in the proximal colon than WLI. Although both NBI and BLI could enhance proximal colonic lesion detection, they still missed at least 20% of proximal colonic adenomas and about 30% of proximal SSLs. Other innovations are therefore necessary to address the issue of missed proximal colonic lesions in addition to the application of IEE.

DISCLOSURE

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REFERENCES

1. Zhao S, Wang S, Pan P, et al. Magnitude, risk factors, and factors associated with adenoma miss rate of tandem colonoscopy: a systematic review and meta-analysis. Gastroenterology 2019;156:1661-74.

2. Rex DK, Ahnen DJ, Baron JA, et al. Serrated lesions of the colorectum: review and recommendations from an expert panel. Am J Gastroenterol 2012;107:1315-29; quiz 4, 30.
3. Cheung KS, Chen L, Seto WK, et al. Epidemiology, characteristics, and survival of post-colonoscopy colorectal cancer in Asia: a population-based study. J Gastroenterol Hepatol 2019;34:1545-53.
4. Jung Y, Joo YE, Kim HG, et al. Relationship between the endoscopic withdrawal time and adenoma/polyp detection rate in individual colonic segments: a KASID multicenter study. Gastrointest Endosc 2019;89:523-30.
5. Cheung D, Evison F, Patel P, et al. Factors associated with colorectal cancer occurrence after colonoscopy that did not diagnose colorectal cancer. Gastrointest Endosc 2016;84:287-95.
6. Anderson R, Burr NE, Valori R. Causes of post-colonoscopy colorectal cancers based on World Endoscopy Organization system of analysis. Gastroenterology 2020;158:1287-99.
7. Atkinson NSS, Ket S, Bassett P, et al. Narrow-band imaging for detection of neoplasia at colonoscopy: a meta-analysis of data from individual patients in randomized controlled trials. Gastroenterology 2019;157:462-71.
8. Laiyemo AO, Doubeni C, Sanderson AK 2nd, et al. Likelihood of missed and recurrent adenomas in the proximal versus the distal colon. Gastrointest Endosc 2011;74:253-61.
9. Bisschops R, Hassan C, Bhandari P, et al. BASIC (BLI Adenoma Serrated International Classification) classification for colorectal polyp characterization with blue light imaging. Endoscopy 2018;50:211-20.
10. Neumann H, Neumann Sen H, Vieth M, et al. Leaving colorectal polyps in place can be achieved with high accuracy using blue light imaging (BLI). United Eur Gastroenterol J 2018;6:1099-105.
11. Higurashi T, Ashikari K, Tamura S, et al. Comparison of the diagnostic performance of NBI, laser-BLI and LED-BLI: a randomized controlled noninferiority trial. Surg Endosc 2022;36:7577-87.
12. Yoshida N, Hayashi Y, Kashida H, et al. Images of laser and light-emitting diode colonoscopy for comparing large colorectal lesion visibility with linked color imaging and white-light imaging. Dig Endosc 2022;34:1413-21.
13. Ang TL, Li JW, Wong YJ, et al. A prospective randomized study of colonoscopy using blue laser imaging and white light imaging in detection and differentiation of colonic polyps. Endosc Int Open 2019;7:E1207-13.
14. Ikematsu H, Sakamoto T, Togashi K, et al. Detectability of colorectal neoplastic lesions using a novel endoscopic system with blue laser imaging: a multicenter randomized controlled trial. Gastrointest Endosc 2017;86:386-94.
15. Shimoda R, Sakata Y, Fujise T, et al. The adenoma miss rate of blue-laser imaging vs. white-light imaging during colonoscopy: a randomized tandem trial. Endoscopy 2017;49:186-90.
16. Nagtegaal ID, Odze RD, Klimstra D, et al. The 2019 WHO classification of tumours of the digestive system. Histopathology 2020;76:182-8.
17. Wallace MB, Sharma P, Bhandari P, et al. Impact of artificial intelligence on miss rate of colorectal neoplasia. Gastroenterology 2022;163:295-304.
18. Inoue T, Murano M, Murano N, et al. Comparative study of conventional colonoscopy and pan-colonic narrow-band imaging system in the detection of neoplastic colonic polyps: a randomized, controlled trial. J Gastroenterol 2008;43:45-50.
19. Leung WK, Lo OS, Liu KS, et al. Detection of colorectal adenoma by narrow band imaging (HQ190) vs. high-definition white light colonoscopy: a randomized controlled trial. Am J Gastroenterol 2014;109:855-63.
20. Ikematsu H, Saito Y, Tanaka S, et al. The impact of narrow band imaging for colon polyp detection: a multicenter randomized controlled trial by tandem colonoscopy. J Gastroenterol 2012;47:1099-107.
21. Rex DK, Clodfelter R, Rahmani F, et al. Narrow-band imaging versus white light for the detection of proximal colon serrated lesions: a randomized, controlled trial. Gastrointest Endosc 2016;83:166-71.
22. Dwivedi AK, Mallawaarachchi I, Alvarado LA. Analysis of small sample size studies using nonparametric bootstrap test with pooled resampling method. Stat Med 2017;36:2187-205.
23. Toyoshima O, Nishizawa T, Yoshida S, et al. Brown slits for colorectal adenoma crypts on conventional magnifying endoscopy with narrow band imaging using the X1 system. World J Gastroenterol 2022;28:2748-57.
24. Leung WK, Guo CG, Ko MKL, et al. Linked color imaging versus narrow-band imaging for colorectal polyp detection: a prospective randomized tandem colonoscopy study. Gastrointest Endosc 2020;91:104-12.
25. Repici A, Badalamenti M, Maselli R, et al. Efficacy of real-time computer-aided detection of colorectal neoplasia in a randomized trial. Gastroenterology 2020;159:512-20.
26. Wang P, Liu X, Berzin TM, et al. Effect of a deep-learning computer-aided detection system on adenoma detection during colonoscopy (CADe-DB trial): a double-blind randomised study. Lancet Gastroenterol Hepatol 2020;5:343-51.
27. East JE, Ignjatovic A, Suzuki N, et al. A randomized, controlled trial of narrow-band imaging vs high-definition white light for adenoma detection in patients at high risk of adenomas. Colorectal Dis 2012;14:e771-8.
28. Hong Kong Cancer Registry, Hospital Authority. Available at: https://www3.ha.org.hk/cancereg/. Accessed May 3, 2023.

SUPPLEMENTARY TABLE 1. Proximal colonic lesion detection rates according to bowel preparation quality

				Difference (%)		*P* value	
	BLI	NBI	WLI	BLI- WLE	NBI-WLE	BLI vs WLE	NBI vs WLE
Boston Bowel Preparation Scale score <7							
No. of patients	118	102	92				
Proximal polyp, %	55.1 (51.7-58.4) (n = 65)	47.1 (43.1-51.0) (n = 48)	47.8 (43.5-52.1) (n = 44)	7.3 (–1.8 to 16.1)	–.7 (–10.2 to 7.6)	.15	.44
Proximal adenoma, %	44.1 (39.8-47.4) (n = 52)	39.2 (35.3-43.1) (n = 40)	40.2 (35.9-44.5) (n = 37)	3.9 (–4.8 to 12.6)	–1.0 (–10.0 to 8.8)	.28	.46
Mean no. of lesions per colonoscopy in the proximal colon during the first examination							
Polyp	1.32 (.18)	1.13 (.16)	1.04 (.18)	.28 (–.06 to .60)	.09 (–.31 to .40)	.15	.36
Adenoma	.99 (.15)	.80 (.13)	.77 (.14)	.22 (–.02 to .51)	.03 (–.22 to .27)	.12	.43
Boston Bowel Preparation Scale score ≥7							
No. of patients	185	196	208				
Proximal polyp, %	40.0 (36.8-43.2) (n = 74)	38.8 (35.7-41.8) (n = 76)	31.7 (28.8-34.1) (n = 66)	8.3 (2.5-13.8)	7.1 (1.0-13.1)	.040	.045
Proximal adenoma, %	31.9 (29.2-35.1) (n = 59)	31.1 (28.5-33.7) (n = 61)	23.1 (20.7-25.5) (n = 48)	8.8 (3.4-14.2)	8.0 (2.7-13.6)	.024	.032
Mean no. of lesions per colonoscopy in the proximal colon during the first examination							
Polyp	.96 (.12)	.80 (.09)	.59 (.08)	.37 (.17-.57)	.21 (.06-.36)	.004	.038
Adenoma	.66 (.10)	.58 (.08)	.41 (.06)	.25 (.10-.41)	.17 (.05-.29)	.015	.037
Boston Bowel Preparation Scale score <8							
No. of patients	154	139	126				
Proximal polyp, %	49.3 (46.1-52.6) (n = 76)	43.8 (40.3-47.5) (n = 61)	46.0 (42.1-50.0) (n = 58)	3.3 (–4.7 to 10.7)	–2.2 (–9.7 to 5.7)	.28	.38
Proximal adenoma, %	39.6 (36.3-42.8) (n = 61)	34.5 (31.7-37.4) (n = 48)	38.9 (35.7-42.9) (n = 49)	.7 (–6.5 to 8.4)	–4.4 (–11.8 to 3.1)	.44	.24
Mean no. of lesions per colonoscopy in the proximal colon during the first examination							
Polyp	1.16 (.15)	.99 (.13)	.94 (.13)	.22 (–.03 to .45)	.05 (–.19 to .29)	.14	.40
Adenoma	.86 (.12)	.68 (.11)	.68 (.10)	.18 (–.03 to .38)	.001 (–.19 to .20)	.15	.48
Boston Bowel Preparation Scale score ≥8							
No. of patients	149	159	174				
Proximal polyp, %	42.2 (38.9-45.6) (n = 63)	39.6 (36.4-43.4) (n = 63)	29.9 (27.0-32.7) (n = 52)	12.3 (5.6-19.6)	9.7 (3.0-17.0)	.009	.022
Proximal adenoma, %	33.6 (30.2-36.9) (n = 50)	33.3 (30.2-36.4) (n = 53)	20.7 (17.8-23.6) (n = 36)	12.9 (6.4-18.8)	12.6 (6.8-19.2)	.003	.005
Mean no. of lesions per colonoscopy in the proximal colon during the first examination							
Polyp	1.05 (.14)	.86 (.10)	.57 (.09)	.48 (.25-.71)	.29 (.11-.46)	.001	.021
Adenoma	.72 (.12)	.63 (.10)	.40 (.07)	.32 (.16-.51)	.23 (.08-.37)	.010	.016

Values in parentheses are 95% confidence intervals or standard deviation.
BLI, Blue-light imaging; *NBI*, narrow-band imaging; *WLI*, white-light imaging.

SUPPLEMENTARY TABLE 2. Proximal colonic polyp and adenoma detection rates according to indications of colonoscopy

				Difference (%)		*P* value	
	BLI	NBI	WLI	BLI - WLE	NBI-WLE	BLI vs WLE	NBI vs WLE
Screening							
No. of patients	100	83	85				
Proximal polyp, %	49.0 (45.0-53.0) (n = 49)	45.8 (41.0-49.6) (n = 38)	45.9 (41.2-50.6) (n = 39)	3.1 (–6.1 to 12.0)	–.1 (–9.6 to 10.5)	.34	.50
Proximal adenoma, %	40.0 (36.0-44.0) (n = 40)	38.6 (34.9-43.3) (n = 32)	37.6 (32.9-41.2) (n = 32)	2.4 (–6.7 to 11.4)	.1 (–8.6 to 9.3)	.38	.50
Surveillance							
No. of patients	51	53	61				
Proximal polyp, %	52.9 (47.1-58.8) (n = 27)	50.9 (45.3-56.6) (n = 27)	41.0 (36.0-47.5) (n = 25)	11.9 (–.1 to 25.0)	9.9 (–2.2 to 22.9)	.10	.15
Proximal adenoma, %	41.2 (35.3-47.1) (n = 21)	39.6 (34.0-45.3) (n = 21)	37.7 (32.8-42.6) (n = 23)	3.5 (–8.9 to 15.2)	1.9 (–9.4 to 14.1)	.37	.37
Symptomatic							
No. of patients	152	162	154				
Proximal polyp, %	41.4 (38.2-44.7) (n = 63)	36.4 (33.3-39.5) (n = 59)	29.9 (26.6-33.1) (n = 46)	11.5 (3.8-18.1)	6.5 (.3-13.9)	.022	.049
Proximal adenoma, %	32.9 (29.6-36.2) (n = 50)	29.6 (26.5-32.7) (n = 48)	19.5 (16.9-22.0) (n = 30)	13.4 (7.5-20.0)	10.1 (3.9-16.0)	.002	.012

Values in parentheses are 95% confidence intervals.
BLI, Blue-light imaging; *NBI*, narrow-band imaging; *WLI*, white-light imaging.

SUPPLEMENTARY TABLE 3. Proximal colonic lesion detection and miss rates by WLI Olympus vs WLI Fujifilm

	WLI Olympus (n = 159)	WLI Fujifilm (n = 141)	*P* value
Detection rate in the proximal colon during the first examination			
Proximal polyp, %	34.0 (30.8-37.1) (n = 54)	39.7 (36.2-43.3) (n = 56)	.14
Proximal adenoma, %	27.0 (23.9-30.2) (n = 43)	29.8 (26.2-32.6) (n = 42)	.28
Mean no. of lesions per colonoscopy in the proximal colon during the first examination			
Polyp	.65 (.10)	.82 (.12)	.15
Adenoma	.49 (.08)	.55 (.09)	.28

Values in parentheses are 95% confidence intervals or standard deviation.
WLI, White-light imaging.

SUPPLEMENTARY TABLE 4. Number of lesions detected in the distal colon by white-light imaging

	BLI (n = 303)	NBI (n = 298)	WLI (n = 300)
Polyp	205	209	192
Adenoma	117	124	118
Advanced adenoma	23	24	26
Sessile serrated lesion	66	60	59

BLI, Blue-light imaging; *NBI*, narrow-band imaging; *WLI*, white-light imaging.

SUPPLEMENTARY TABLE 5. Total number of lesions found in proximal colon after each examination

	BLI (n = 303)	NBI (n = 298)	WLI (n = 300)
On first examination			
Proximal polyp	334	273	219
Proximal adenoma	240	195	156
Proximal advanced adenoma	26	20	14
Proximal sessile serrated lesion	54	45	38
On second examination (white-light imaging)			
Proximal missed polyp	85	99	78
Proximal missed adenoma	58	73	59
Proximal missed advanced adenoma	4	6	4
Proximal missed sessile serrated lesion	21	19	10
Proximal polyp detected	419	372	297
Proximal adenoma detected	298	268	215
Proximal advanced adenoma detection detected	30	26	18
Proximal sessile serrated lesion detection detected	75	64	48

BLI, Blue-light imaging; *NBI*, narrow-band imaging; *WLI*, white-light imaging.