—Original—

Comparison of Linked Color Imaging and White Light Imaging Colonoscopy for Detection of Colorectal Adenoma Requiring Endoscopic Treatment: A Single-Center Randomized Controlled Trial

Shu Tanaka[1], Jun Omori[2], Aitoshi Hoshimoto[2], Takayoshi Nishimoto[2], Naohiko Akimoto[2], Atsushi Tatsuguchi[2], Shunji Fujimori[3] and Katsuhiko Iwakiri[2]

[1]Department of Gastroenterology, Nippon Medical School Tama Nagayama Hospital, Tokyo, Japan
[2]Department of Gastroenterology, Nippon Medical School Hospital, Tokyo, Japan
[3]Department of Gastroenterology, Nippon Medical School Chiba Hokusoh Hospital, Chiba, Japan

Background: Linked color imaging (LCI) improves detection of colorectal neoplastic lesions during colonoscopy. However, polyps <5 mm in diameter often do not require resection, and the benefits of LCI are unclear for detection of colorectal polyps ≥5 mm that are indicated for endoscopic resection in clinical practice. This randomized controlled trial compared rates of detection of adenoma polyps, stratified by size, for LCI and white light imaging (WLI).

Methods: We compared ADR(5 mm-) and PDR(5 mm-), which were defined as the proportion of patients with at least one adenoma or polyp with a diameter of 5 mm or larger in the LCI and WLI groups. Moreover, we estimated ADR and PDR for diameters between 5 and 10 mm (ADR(5-9 mm), PDR(5-9 mm)) and for diameters larger than 10 mm (ADR(10 mm-), PDR(10 mm-)).

Results: Data from 594 patients (LCI, n=305; WLI, n=289) were analyzed. ADR(5 mm-) and PDR(5 mm-) were significantly higher in the LCI group than in the WLI group (ADR(5 mm-): P=0.016, PDR(5 mm-): P=0.020). In the assessment of adenoma and polyp size, ADR(5-9 mm) and PDR(5-9 mm) were significantly higher in the LCI group than in the WLI group, although no significant differences were seen in ADR(10 mm-) and PDR(10 mm-) between these groups.

Conclusions: Polyps ≥5 mm, which are indicated for endoscopic treatment, were more easily visualized with LCI mode than with WLI mode. The improvement in detection rate was obvious for polyps <10 mm, which are easier to miss. (J Nippon Med Sch 2023; 90: 111–120)

Key words: linked color image, adenoma detection rate, polyp detection rate, 5 mm, colonoscopy

Introduction

Colorectal cancer (CRC) has a good prognosis when detected and treated early. Several studies reported a 5-year survival rate of 60-80% for patients with stage II or better colorectal cancer and no lymph node or distant metastasis[1–4]. Furthermore, the National Polyp Study in the United States found that endoscopic removal of adenomatous polyps reduced the risk of death from colorectal cancer[5]. Thus, early detection and treatment are much more effective for CRC than for several other carcinomas.

Colonoscopy is the gold standard for detection of CRC and adenomas, its precursor lesions. However, studies have reported a substantial adenoma miss rate of 20-26%[6]. The adenoma detection rate (ADR) is considered to be the primary quality indicator in CRC prevention, because of its association with the risk of interval cancer, and each 1.0% increase in ADR was associated with a 3.0% decrease in the risk of cancer and a 5.0% decrease in the CRC mortality rate[7]. Several studies have shown improvements in ADR with cap-assisted endoscopy, image-enhanced colonoscopy, and narrow-band imaging (NBI)[8–14]. In 2012, a novel endoscopic system (LASEREO;

Correspondence to Shu Tanaka, MD, PhD, Department of Gastroenterology, Nippon Medical School Tama Nagayama Hospital, 1–7–1 Nagayama, Tama, Tokyo 206–8512, Japan
E-mail: tanashu@nms.ac.jp
https://doi.org/10.1272/jnms.JNMS.2023_90-117
Journal Website (https://www.nms.ac.jp/sh/jnms/)

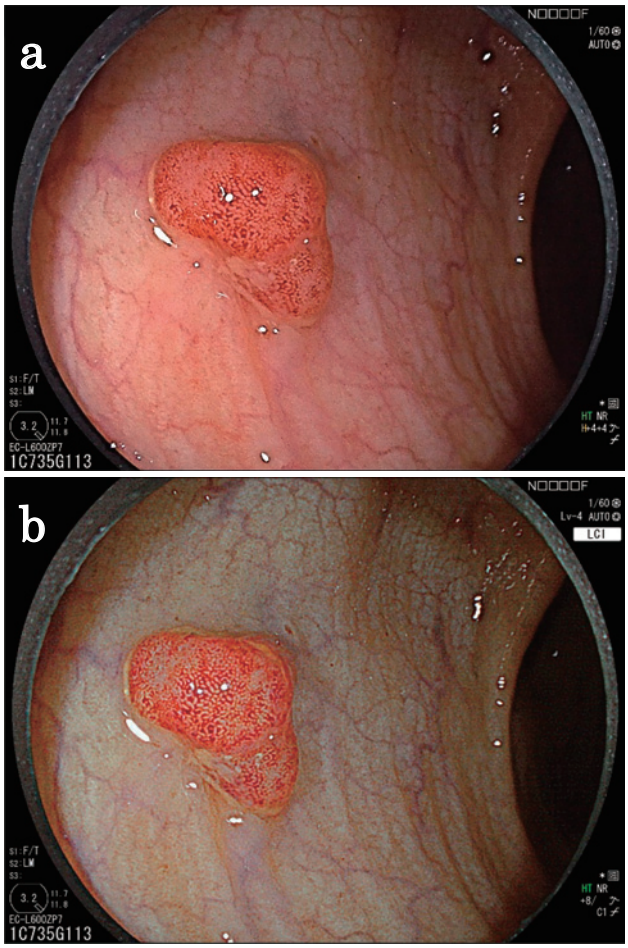

Fig. 1 A representative adenomatous polyp
a: white light imaging, b: linked color imaging

Fujifilm Co, Tokyo, Japan) was developed. It uses a semiconductor laser light source that combines two types of lasers to achieve a narrow-band light observation function, blue laser imaging (BLI)[15–19], which improved detection of minute changes on the surface of the mucosa and polyp visibility[20,21]. In 2014, linked color imaging (LCI) was developed as a novel image-enhanced endoscopic system that enhances slight color differences in the red region of the mucosa. The acquired color information is reallocated to differentiate colors that are similar to the mucosal color, resulting in additional image processing that enhances color separation. LCI visualizes red lesions as even redder and white lesions as whiter. The difference in color between a colon polyp and the surrounding mucosa is increased, resulting in easier polyp recognition (**Fig. 1**). Several recent studies reported that LCI mode improved visibility and detection of colorectal polyps as compared with white light imaging (WLI) mode[22]. Other studies reported that LCI increased visibility of colorectal flat lesions and improved the detection rate for these lesions. It is likely that ADR is improved by using LCI mode during total colonoscopy[23]. Similar results were reported for sessile serrated lesions (SSL). A recent prospective randomized controlled trial (RCT) concluded that LCI was the most sensitive mode for SSL detection among WLI, BLI, BLI-bright, and LCI mode[24]. In addition, multiple studies reported that LCI mode was better for detecting flat and very small lesions.

Small polyps (<5 mm in diameter) are not usually resected in practice, as they rarely increase in size or change morphologically even after 2-3 years. Those that do change have a low rate of progression to colorectal cancer (0.03-0.05%). However, complications occur in 0.7% of polypectomy cases. When we consider the benefit-risk ratio, removing all polyps <5 mm would not justify the increase in risk for healthy people and impose unnecessary costs on society[25,26]. Conversely, polyps ≥5 mm are more likely than smaller polyps to be associated with carcinoma[27,28]. Since it is often difficult to classify polyps ≥5 mm as adenoma or cancer morphologically, they are strongly indicated for endoscopic resection[29,30]. Thus, polyps ≥5 mm are commonly removed endoscopically. Polyps ≥10 mm are rarely missed during colonoscopy; one study reported a miss rate of 2.1% for adenomas ≥10 mm[6]. Therefore, we assumed that increasing the detection rate for adenomatous polyps with diameters of 5-10 mm, which are associated with increased risk of developing cancer and are likely to be missed, would effectively increase the ADR while lowering the risk of cancer. However, the clinical usefulness of LCI for detecting colorectal polyps ≥5 mm that are indicated for endoscopic resection is unknown. This study investigated whether LCI mode improves the detection rate of colorectal polyps indicated for endoscopic treatment, by comparing the ADR for polyps with a diameter ≥5 mm (ADR(5 mm-)), and the mean number of adenomas ≥5 mm per patient, between LCI and WLI. In addition, we evaluated detection rates, in relation to size, for diameters of 5-10 mm and ≥10 mm.

Materials and Methods

Study Design

This study was a prospective single-center RCT.

Patients

A total of 646 patients underwent total colonoscopy at Nippon Medical School Hospital between January 2018 and July 2019. Nine endoscopists (five experts and four trainees) performed the colonoscopies. We defined an expert as an endoscopist with >5 years of colonoscopy experience and a trainee as an endoscopist who had per-

Table 1 Gloucester Comfort Score

Score	Scale	Descriptor
1	No	No discomfort-resting comfortably throughout
2	Minimal	One or two episodes of mild discomfort, well tolerated
3	Mild	More than two episodes of mild discomfort, adequately tolerated
4	Moderate	Significant discomfort, experienced several times during the procedure
5	Severe	Extreme discomfort, experienced frequently during the procedure

Table 2 The Boston Bowel Preparation Scale

Score	Description
0	Unprepared colon segment with mucosa not seen because of solid stool that cannot be cleared.
1	Portion of mucosa of the colon segment seen, but other areas of the colon segment are not well seen because of staining, residual stool, and/or opaque liquid.
2	Minor amount of residual staining, small fragments of stool, and/or opaque liquid, but mucosa of the colon segment is seen well.
3	Entire mucosa of the colon segment seen well, with no residual staining, small fragments of stool, and/or opaque liquid.

formed at least 500 colonoscopies but had <5 years of experience.

Patients aged 20 to 80 years (410 men, 236 women) were enrolled in this study if they had been scheduled for colonoscopy for one of the following indications: a positive fecal immunochemical test (FIT), screening, hematochezia, abdominal symptoms, bowel movement disorder, and polyp surveillance. Exclusion criteria included polyposis syndromes, inflammatory bowel disease, previous total or partial colonic resection, history of colonoscopy during the previous 2 years, possible colonic stricture, and acute abdominal pain or severe inflammation. Patients in poor general condition (for whom colonoscopy was considered a high-risk procedure), those unable to provide informed consent, and those for whom coloscopy was contraindicated, as determined by the physician in charge, were also excluded. Written informed consent was obtained from each patient before the procedure. This study was approved by the medical ethical committees of Nippon Medical School (approval number 229005).

Randomization and Masking

Computer generated block randomization was used to allocate eligible patients (n=594) at a ratio of 1:1 to the LCI group or WLI group before colonoscopy (open-label). Randomization was stratified by using an electronic information collection system (EDC: electric data capture). All data, including the findings of clinical examinations, were collected electronically and managed by EDC from the onset of the study.

Endoscopic Procedure

All patients underwent standard bowel preparation comprising oral intake of 2 L of transparent fluid and 2 L of hypertonic polyethylene glycol solution at home. EC-L 600ZP7 (LASEREO, Fujifilm Co) scopes and CO_2 insufflation were used for all colonoscopies. Antispasmodics (butylscopolamine or glucagon) were administered to most patients, and some colonoscopies were performed under conscious sedation with intravenous midazolam or flunitrazepam, at the discretion of the endoscopist. In the WLI group, cecal intubation and withdrawal of the scope were performed in WLI mode during the full procedure, and cecal intubation and withdrawal of the scope were all performed in LCI mode in the LCI group.

All polyp features detected during colonoscopy, including site, estimated size, and morphology, were reported by each endoscopist. Polyp size was estimated by experience and the discretion of the endoscopist. Morphology was recorded on the basis of Paris Endoscopic Classification. All polyps ≥5 mm in diameter were retrieved endoscopically and analyzed histopathologically. The degree of patient discomfort was estimated by using the Gloucester Comfort Score, which ranges from no discomfort (1) to severe discomfort (5) (**Table 1**)[31]. Bowel cleanliness was judged with the Boston Bowel Preparation Scale (BBPS), with scores ranging from 3 (complete segment without feces, good visualization) to 0 (solid feces, not evaluable) (**Table 2**)[32]. All colonoscopies were performed by endoscopists who had an experience of at least 500 colonoscopies. All patients were independently evaluated

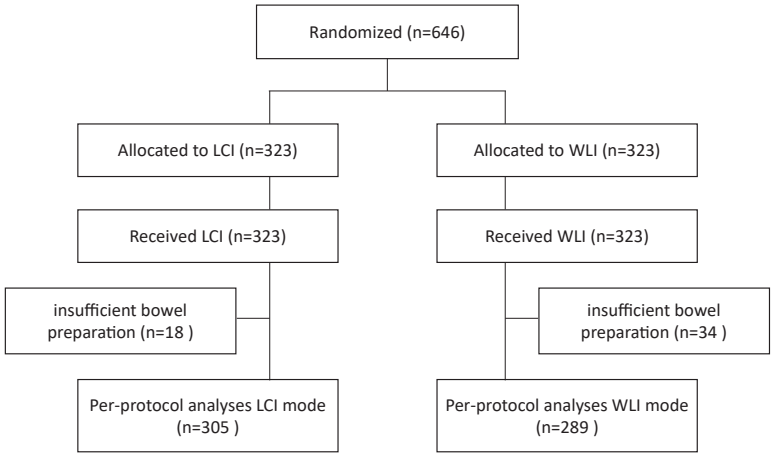

Fig. 2 Flowchart of study design
LCI: linked color imaging, WLI: white light imaging

for adverse events at 2 weeks after colonoscopy.

Outcomes

The primary outcome was ADR, defined as the proportion of patients with at least one adenoma measuring ≥5 mm in diameter (ADR(5 mm-)), and PDR was defined as the proportion of patients with at least one polyp measuring ≥5 mm in diameter (PDR(5 mm-)). In addition, we calculated ADR(5 mm-) and PDR(5 mm-) separately for experts and trainees. Similarly, the total number of adenomas ≥5 mm per patient (APC: adenomas per colonoscopy) and total number of all polyps ≥5 mm per patient (PPC: polyps per colonoscopy) were compared between the two groups. We also calculated ADR, PDR, APC, and PPC for adenomas and polyps with diameters of 5-10 mm (ADR(5-9 mm), PDR(5-9 mm)) and diameters ≥10 mm (ADR(10 mm-), PDR(10 mm-)) in both groups. As a secondary outcome, we compared polyp morphology and site in both groups. We also evaluated cecal intubation rate, cecal intubation time, withdrawal time (which is observation time in cases without polyp detection), bowel preparation (BBPS), patient discomfort (Gloucester Comfort Scale), and complications.

Sample Size Calculation and Statistical Analysis

There are no reports of ADR for polyps ≥5 mm, so the evidence is unclear. However, a previous study of LCI for all adenomas reported an ADR of 34-56% in an LCI group and 26-43% in a WLI group[33]. On the basis of previous studies, we assumed an ADR(5 mm-), ie, the ADR for lesions ≥5 mm, of about 20% for the WLI group and about 35% for the LCI group. To demonstrate a 10% increase with a 5% significance level and 80% power using a two-sided test and an allocation ratio of 1:1, 600 patients would be required. Accordingly, we set an enrollment goal of 650 patients.

All patients who successfully underwent complete colonoscopies were assessed in the per-protocol analysis as the target population, after excluding those with incomplete colonoscopies due to stricture or poor bowel preparation. Patients for whom insertion to the cecum was impossible or with a poorly prepared bowel (BBPS score <2) were also excluded. A P value of <0.05 was considered statistically significant. We analyzed outcomes by using Fisher's exact test and the Mann-Whitney U test as the nonparametric statistical method. Analyses were performed with SPSS statistical software package version 25 (IBM Co., New York, NY, USA).

Results

Patient Characteristics

A total of 646 consecutive patients satisfied the inclusion criteria, and all these patients consented to participate in the study. Among this initial pool of patients, 52 (LCI group, n=18; WLI group, n=34) were excluded from the study because of poor bowel preparation (BBPS 0 or 1), and the remaining 594 patients (LCI group, n=305; WLI group, n=289) were enrolled in the study (**Fig. 2**). No significant difference was seen in mean age or gender between the LCI group and WLI groups. The most common indication for colonoscopy was a positive FIT result, and no significant difference was seen between groups; the LCI group consisted of 217 patients (71.7%) and the WLI group of 214 patients (74.0%) (**Table 3**).

Polyp and Adenoma Detection Rates in the LCI and WLI Groups

ADR(5 mm-) was significantly higher in the LCI group than in the WLI group (35.1% vs 26.0%, P=0.016). Simi-

Table 3 Baseline demographic characteristics of patients

	LCI mode (n=305)	WLI mode (n=289)	*p* value
Age	53.9 (22-79)	52.2 (22-79)	*n.s.*
Males	194/305 (63.6%)	177/289 (61.2%)	*n.s.*
Colonoscopy indication			
FIT (+)	217 (71.1%)	214 (74.0%)	*n.s.*
screening ※	43 (14.1%)	36 (12.5%)	*n.s.*
hematochezia	23 (7.5%)	20 (6.9%)	*n.s.*
abdominal symptoms	11 (3.6%)	6 (2.1%)	*n.s.*
bowel movement disorder	6 (2.0%)	10 (3.5%)	*n.s.*
polyp surveillance	5 (1.6%)	3 (1.0%)	*n.s.*

※screening: high tumor marker, preoperative exam, staging (other malignancies), anemia, body weight loss, malignancy check

Table 4 Rates of polyp and adenoma detection in the LCI and WLI groups

	LCI mode (n=305)	WLI mode (n=289)	*p* value
Adenomas			
ADR (5 mm)	35.1% (107/305)	26.0% (75/289)	0.016
APC (5 mm)	0.61 (187/305)	0.46 (134/289)	0.023
All Polyps			
PDR (5 mm)	39.3% (120/305)	30.1% (87/289)	0.020
PPC (5 mm)	0.78 (237/305)	0.53 (154/289)	0.016

ADR (5 mm): Proportion of patients with at least one adenoma ≥5 mm
APC (5 mm; adenomas per colonoscopy): Total number of adenomas ≥5 mm per patient
PDR (5 mm): Proportion of patients with at least one polyp ≥5 mm
PPC (5 mm; polyps per colonoscopy): Total number of polyps ≥5 mm per patient

larly, PDR(5 mm-) was significantly higher in the LCI group than in the WLI group (39.3% vs 30.1%, P=0.020) (**Table 4**). In addition, the APC and PPC were significantly higher in the LCI group than in the WLI group (APC: 0.61 vs 0.46, P=0.023; PPC: 0.78 vs 0.53, P=0.016) (**Table 4**).

Polyp and Adenoma Detection, in Relation to Size, in the LCI and WLI Groups

We analyzed ADR and PDR in relation to size for adenomas and polyps measuring 5-10 mm (ADR(5-9 mm), PDR(5-9 mm)) and ≥10 mm (ADR(10 mm-), PDR(10 mm-)). ADR(5-9 mm) and PDR(5-9 mm) were significantly higher in the LCI group than in the WLI group (ADR(5-9 mm): 29.5% vs 14.9%, P<0.001, PDR(5-9 mm): 33.4% vs 18.3%, P<0.001), although no statistically significant difference was found in ADR(10 mm-) or PDR(10 mm-) between the two groups (**Table 5**).

Polyp and Adenoma Detection Rates in the LCI and WLI Groups, for Experts and Trainees

We evaluated the clinical utility of LCI by calculating ADR(5-9 mm) and PDR(5-9 mm) rates for experts and trainees in each group. Data for both expert and trainee colonoscopists showed a significant difference in ADR(5-9 mm) and PDR(5-9 mm) detection rates between the LCI and WLI groups (**Table 6**).

Polyp Morphology and Site in the LCI and WLI Groups

Morphologically, 0-Is polyps were significantly more frequently detected in the LCI group (p<0.001) than in the WLI group, and 0-IIa polyps tended to be more often detected in the LCI group. Regarding site, polyps were detected significantly more frequently in the transverse colon (P=0.02) and sigmoid colon (P=0.031) in the LCI group (**Table 7**).

Other Colonoscopy Results

The cecal intubation rate was 100% in both groups. Mean cecal intubation time was 7.2 ± 5.8 minutes in the LCI group and 7.0 ± 5.2 minutes in the WLI group, a nonsignificant difference. Similarly, mean withdrawal time, defined as observation time in cases without polyp

Table 5 Polyp and adenoma detection rates, according to size, in the LCI and WLI groups

	LCI mode (n=305)	WLI mode (n=289)	*p* value
Adenomas size (total)			
5-9 mm			
ADR (5-9 mm)	29.5% (90/305)	14.9% (43/289)	<0.001
APC (5-9 mm)	0.46 (139/305)	0.19 (56/289)	<0.001
10 mm-			
ADR (10 mm-)	10.8% (33/305)	15.9% (46/289)	*n.s.*
APC (10 mm-)	0.16 (48/305)	0.27 (78/289)	*n.s.*
All Polyps size (total)			
5-9 mm			
PDR (5-9 mm)	33.4% (102/305)	18.3% (53/289)	<0.001
PPC (5-9 mm)	0.58 (176/305)	0.23 (67/289)	<0.001
10 mm-			
PDR (10 mm-)	12.4% (38/305)	17.6% (51/289)	*n.s.*
PPC (10 mm-)	0.2 (61/305)	0.3 (87/289)	*n.s.*

ADR (5-9 mm): Proportion of patients with at least one adenoma between 5 and 10 mm
ADR (10 mm-): Proportion of patients with at least one adenoma more than 10 mm
APC (5-9 mm): Total number of adenomas between 5 and 10 mm per patient
APC (10 mm-): Total number of adenomas more than 10 mm per patient
PDR (5-9 mm): Proportion of patients with at least one polyp between 5 and 10 mm
PDR (10 mm-): Proportion of patients with at least one polyp more than 10 mm
PPC (5-9 mm): Total number of polyps between 5 and 10 mm per patient
PPC (10 mm-): Total number of polyps more than 10 mm per patient

Table 6 Polyp and adenoma detection rates in the LCI and WLI groups for experts and trainees

	LCI mode (n=305)	WLI mode (n=289)	*p* value
Expert endoscopist	192	190	
Adenomas (5-9 mm)			
ADR (5-9 mm)	28.6% (55/192)	15.3% (29/190)	0.002
All Polyps (5-9 mm)			
PDR (5-9 mm)	33.3% (64/192)	17.9% (34/190)	0.001
Trainee endoscopist	113	99	
Adenomas (5-9 mm)			
ADR (5-9 mm)	31.0% (35/113)	14.1% (14/99)	0.005
All Polyps (5-9 mm)			
PDR (5-9 mm)	33.6% (38/113)	19.2% (19/99)	0.020

detection, was 9.3 ± 3.2 minutes in the LCI group and 9.3 ± 3.4 minutes in the WLI group, a nonsignificant difference. Furthermore, neither bowel preparation (BBPS) nor patient discomfort (Gloucester Comfort Scale) significantly differed between groups. CO_2 insufflation was used during all colonoscopies, and no complications occurred during any colonoscopy (**Table 8**).

Discussion

To our knowledge, this is the first study to compare the sensitivity of LCI colonoscopy to that of WLI colonoscopy for the detection of polyps ≥5 mm. In this single-center RCT, we analyzed the detection rate for polyps ≥5 mm and found that, as compared with WLI mode, LCI mode yielded a significantly higher PDR(5 mm-) (9.2%: 39.3% vs 30.1%, P = 0.018) and ADR(5 mm-) (9.1%: 35.1% vs 26%, P = 0.016).

A number of novel colonoscopy technologies have recently been developed to improve detection of adenomas and reduce miss rates. Gralnek et al. found that the adenoma miss rate was significantly lower for patients in a full-spectrum endoscopy group than for those in a stan-

Table 7 Polyp morphology and site in the LCI and WLI groups

	LCI mode (n=305)	WLI mode (n=289)	*p* value
All polyps morphology (total)	237	154	
Is	93	32	<0.001
Isp	58	61	0.826
Ip	27	29	0.622
IIa	57	24	0.069
other	2	8	
	LCI mode (n=305)	WLI mode (n=289)	*p* value
All polyps location (total)	237	154	
C	11	10	0.746
A	31	22	0.663
T	49	25	0.02
D	30	18	0.326
S	91	57	0.031
R	25	15	0.556

C: cecum
A: ascending colon
T: transverse colon
D: descending colon
S: sigmoid colon
R: rectum

Table 8 Colonoscopy results

	LCI mode (n=305)	WLI mode (n=289)	*p* value
Caecal intubation rate (%)	100.0	100.0	*n.s.*
Caecal intubation time (min)	7.2 ± 5.8	7.0 ± 5.2	*n.s.*
Withdrawal time (min)	9.3 ± 3.2	9.3 ± 3.4	*n.s.*
Boston Bowel Preparation Scale (0, 1, 2, 3)	2.3 ± 0.4	2.9 ± 0.3	*n.s.*
Gloucester Comfort Scale (1, 2, 3, 4, 5)	1.4 ± 0.7	1.1 ± 0.3	*n.s.*
CO_2 insufflation (%)	100.0	100.0	*n.s.*
Adverse Event (%)	0	0	*n.s.*

dard forward-viewing endoscopy group: 7% vs 41%[34]. Leufkens et al. reported that the ADR was higher for The Third Eye Retroscope, which visualizes areas behind folds, than for standard colonoscopy[35]. Halpen et al. found that a novel balloon colonoscopy technique detected significantly more adenomas than standard colonoscopy and missed fewer adenomas (44.7% vs 7.5%, p=0.0002)[36]. In 2012, the endoscopic system LASEREO (Fujifilm Co, Tokyo, Japan) was developed. It has four endoscopic observational modes (WLI, BLI-Bright, BLI, and LCI) and was designed for use in diagnosis and treatment, as well as for polyp detection. Yoshida et al. suggested that BLI magnification via this laser source could predict histopathological diagnosis and invasion depth of colorectal neoplasms[17,18,21]. In addition, in a multicenter RCT, BLI was better than WLI in detecting adenomatous lesions[20]. LCI is better for unmagnified observation, because it enhances slight color differences in the red region of the mucosa. This color information is reallocated to differentiate colors that are similar to those of the mucosa. A previous study using LCI reported a significant increase in overall polyp detection rate[22]. Because LCI often generates a bright field of view, it can produce differences in color contrast between polyps and surrounding vessels, leading to evaluation of a suspicious area noted in a distant view and, potentially, to easier detection of polyps. Suzuki et al. reported that LCI increased the visibility of colorectal flat lesions and enhanced the detection rate for these lesions[23]. A review of several studies concluded that polyp and adenoma detection rates were significantly higher for LCI than for WLI[33].

The value of the sensitivity of polyp detection in colonoscopy depends on the size of the target lesion. Al-

though the sensitivity of the ADR for adenomas ≥10 mm is 79-100%[37,38], the sensitivity of the ADR for lesions <10 mm is only 75-85%[37]. However, detection rates may be increased if devices and image quality are improved. In a previous report, the adenoma miss rate varied in relation to lesion size, as follows: adenomas >10 mm, 2.1%; 5-10 mm, 13%; and <5 mm, 26%. In other words, adenomas >10 mm were seldom missed[6]. Polyps <5 mm rarely grow or show morphological changes, even after 2-3 years of observation, and seldom develop into colorectal cancer (0.03-0.05%). Because the rate of adverse events after polypectomy is 0.7%, removal of all polyps <5 mm may not be warranted.

In contrast, it is strongly recommended that polyps ≥5 mm undergo endoscopic resection[29,30]. In a report from the United Kingdom, the relative risk of malignancy or severe dysplasia in adenomas, as compared with polyps <5 mm, was 7.2 for polyps measuring 6-10 mm and 12.7 for polyps measuring 11-20 mm. Thus, it is critically important to remove all polyps ≥5 mm[29]. In sum, increasing the rate of detection of adenomas ≥5 mm, which have the highest risk of cancer, and of adenomas <10 mm, which are likely to be missed, may decrease the risk of interval cancer.

In this study, we compared detection rates for polyps ≥5 mm in LCI and WLI groups, namely, ADR(5 mm-), PDR(5 mm-), APC, and PPC. The detection rate was significantly higher in the LCI group than in the WLI group. In addition, analysis of detection rates, stratified by polyp size, for LCI and WLI showed a significantly higher detection rate for polyps with a diameter of 5-9 mm-which are often missed during routine colonoscopy-in the LCI group than in the WLI group. Therefore, LCI might substantially reduce the miss rate for these lesions.

Polyp miss rates during endoscopy might be attributable to lack of colonoscopist experience, and we believe that an improvement in the detection rate for inexperienced colonoscopists must be lead to decrease the overall miss rates of adenoma and interval CRC. Therefore, we evaluated success in detecting polyps among trainees, defined as endoscopists who had performed at least 500 colonoscopies but had <5 years of experience, and experts (those with >5 years of experience). We found that ADR(5-9 mm) and PDR(5-9 mm) were significantly higher with LCI mode than with WLI mode for both experts and trainees. Consequently, LCI mode may be a valuable diagnostic tool for all colonoscopists, regardless of years of endoscopic experience.

With regard to polyp morphology, the detection rate for 0-Is polyps, as well as for 0-IIa polyps, was significantly higher in the LCI group. Other studies have confirmed that flat lesions are easier to detect by LCI than by WLI[22,23]. Regarding polyp site, significantly more polyps were detected in the transverse colon and sigmoid colon in the LCI group than in the WLI group. A similar tendency was observed in other sites except the cecum, suggesting we might detect substantial differences in the number of polyps at all sites if we were to expand the pool of patients. Although many polyps were detected in the transverse colon and sigmoid colon in this study, we cannot explain the significant difference in T/C and S/C between LCI and WLI.

Regarding secondary outcomes, the LCI and WLI groups had similar cecal intubation rates, cecal intubation times, and observation times. No adverse events were recorded in either group. Therefore, colonoscopy in LCI mode can be performed as quickly and safely as WLI mode by any endoscopist, regardless of experience.

The limitations of this study were its single-center design and the fact that endoscopists were not blinded to patient group allocation. However, when polyp size was limited to ≥5 mm, the ADR(5 mm-) was satisfactory, at 26%, even in the WLI group-well above the established threshold for ADR. The APC in the WLI group was high, at 0.46; thus, endoscopist bias was unlikely.

In conclusion, LCI mode improved visibility, even for polyps measuring 5-9 mm, which are indicated for endoscopic treatment and likely to be missed. This improvement in detection rates did not depend on endoscopist experience. Thus, the present novel LCI detection system for endoscopy improves ADR and detects more adenomatous lesions ≥5 mm, as compared with WLI mode, which may ultimately reduce the rate of interval cancer.

Conflict of Interest: The authors declare no conflicts of interest.

References

1. Ukegjini K, Zadnikar M, Warschkow R, Müller S, Schmied BM, Marti L. Baseline mortality-adjusted survival in colon cancer patients. Langenbecks Arch Surg. 2016;401:633−41.
2. Lips DJ, Koebrugge B, Liefers GJ, et al. The influence of micrometastases on prognosis and survival in stage I-II colon cancer patients: the Enroute plus sign in circle Study. BMC Surg. 2011;11:11.
3. Buchwald P, Hall C, Davidson C, et al. Improved survival for rectal cancer compared to colon cancer: the four cohort study. ANZ J Surg. 2018;88:E114−7.
4. Nissan A, Protic M, Bilchik AJ, Howard RS, Peoples GE, Stojadinovic A. United States Military Cancer Institute

Clinical Trials Group (USMCI GI-01) randomized controlled trial comparing targeted nodal assessment and ultrastaging with standard pathological evaluation for colon cancer. Ann Surg. 2012;256:412–27.
5. Winawer SJ, Zauber AG, Ho MN, et al. Prevention of colorectal cancer by colonoscopic polypectomy. The National Polyp Study Workgroup. N Engl J Med. 1993;329:1977–81.
6. van Rijn JC, Reitsma JB, Stoker J, Bossuyt PM, van Deventer SJ, Dekker E. Polyp miss rate determined by tandem colonoscopy: a systematic review. Am J Gastroenterol. 2006;101:343–50.
7. Corley DA, Jensen CD, Marks AR, et al. Adenoma detection rate and risk of colorectal cancer and death. N Engl J Med. 2014;370:1298–306.
8. Kim SY, Park HJ, Kim HS, et al. Cap-assisted chromoendoscopy using a mounted cap versus standard colonoscopy for adenoma detection. Am J Gastroenterol. 2020; 115:465–72.
9. 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.
10. 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.
11. 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.
12. East JE, Suzuki N, Stavrinidis M, Guenther T, Thomas HJ, Saunders BP. Narrow band imaging for colonoscopic surveillance in hereditary non-polyposis colorectal cancer. Gut. 2008;57:65–70.
13. Ogiso K, Yoshida N, Siah KT, et al. New-generation narrow band imaging improves visibility of polyps: a colonoscopy video evaluation study. J Gastroenterol. 2016; 51:883–90.
14. Horimatsu T, Sano Y, Tanaka S, et al. Next-generation narrow band imaging system for colonic polyp detection: a prospective multicenter randomized trial. Int J Colorectal Dis. 2015;30:947–54.
15. Togashi K, Nemoto D, Utano K, et al. Blue laser imaging endoscopy system for the early detection and characterization of colorectal lesions: a guide for the endoscopist. Therap Adv Gastroenterol. 2016;9:50–6.
16. Kaneko K, Oono Y, Yano T, et al. Effect of novel bright image enhanced endoscopy using blue laser imaging (BLI). Endosc Int Open. 2014;2:E212–9.
17. Yoshida N, Yagi N, Inada Y, et al. Ability of a novel blue laser imaging system for the diagnosis of colorectal polyps. Dig Endosc. 2014;26:250–8.
18. Yoshida N, Hisabe T, Inada Y, et al. The ability of a novel blue laser imaging system for the diagnosis of invasion depth of colorectal neoplasms. J Gastroenterol. 2014;49: 7390.
19. Osawa H, Yamamoto H. Present and future status of flexible spectral imaging color enhancement and blue laser imaging technology. Dig Endosc. 2014;26(Suppl 1):105–15.
20. 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.
21. Yoshida N, Hisabe T, Hirose R, et al. Improvement in the visibility of colorectal polyps by using blue laser imaging (with video). Gastrointest Endosc. 2015;82:542–9.
22. Min M, Deng P, Zhang W, Sun X, Liu Y, Nong B. Comparison of linked color imaging and white-light colonoscopy for detection of colorectal polyps: a multicenter, randomized, crossover trial. Gastrointest Endosc. 2017;86: 724–30.
23. Suzuki T, Hara T, Kitagawa Y, et al. Linked-color imaging improves endoscopic visibility of colorectal nongranular flat lesions. Gastrointest Endosc. 2017;86:692–7.
24. Fujimoto D, Muguruma N, Okamoto K, et al. Linked color imaging enhances endoscopic detection of sessile serrated adenoma/polyps. Endosc Int Open. 2018;6:E322–34.
25. Gschwantler M, Kriwanek S, Langner E, et al. High-grade dysplasia and invasive carcinoma in colorectal adenomas: a multivariate analysis of the impact of adenoma and patient characteristics. Eur J Gastroenterol Hepatol. 2002;14: 183–8.
26. Bretagne JF, Manfredi S, Piette C, Hamonic S, Durand G, Riou F. Yield of high-grade dysplasia based on polyp size detected at colonoscopy: a series of 2295 examinations following a positive fecal occult blood test in a population-based study. Dis Colon Rectum. 2010;53:339–45.
27. O'Brien MJ, Winawer SJ, Zauber AG, et al. The National Polyp Study. Patient and polyp characteristics associated with high-grade dysplasia in colorectal adenomas. Gastroenterology. 1990;98:371–9.
28. Sakamoto T, Matsuda T, Nakajima T, Saito Y. Clinicopathological features of colorectal polyps: evaluation of the 'predict, resect and discard' strategies. Colorectal Dis. 2013;15:e295–300.
29. Aldridge AJ, Simson JN. Histological assessment of colorectal adenomas by size. Are polyps less than 10 mm in size clinically important? Eur J Surg. 2001;167:777–81.
30. Ahlawat SK, Gupta N, Benjamin SB, Al-Kawas FH. Large colorectal polyps: endoscopic management and rate of malignancy: does size matter? J Clin Gastroenterol. 2011; 45:347–54.
31. Dyson JK, Mason JM, Rutter MD. Prior hysterectomy and discomfort during colonoscopy: a retrospective cohort analysis. Endoscopy. 2014;46:493–8.
32. Lai EJ, Calderwood AH, Doros G, Fix OK, Jacobson BC. The Boston bowel preparation scale: a valid and reliable instrument for colonoscopy-oriented research. Gastrointest Endosc. 2009;69:620–5.
33. Shinozaki S, Kobayashi Y, Hayashi Y, et al. Colon polyp detection using linked color imaging compared to white light imaging: Systematic review and meta-analysis. Dig Endosc. 2020;32:874–81.
34. Gralnek IM, Siersema PD, Halpern Z, et al. Standard forward-viewing colonoscopy versus full-spectrum endoscopy: an international, multicentre, randomised, tandem colonoscopy trial. Lancet Oncol. 2014;15:353460.
35. Leufkens AM, DeMarco DC, Rastogi A, et al. Effect of a retrograde-viewing device on adenoma detection rate during colonoscopy: the TERRACE study. Gastrointest Endosc. 2011;73:480–9.
36. Halpern Z, Gross SA, Gralnek IM, et al. Comparison of adenoma detection and miss rates between a novel balloon colonoscope and standard colonoscopy: a randomized tandem study. Endoscopy. 2015;47:238–44.
37. de Zwart IM, Griffioen G, Shaw MP, Lamers CB, de Roos A. Barium enema and endoscopy for the detection of colorectal neoplasia: sensitivity, specificity, complications and its determinants. Clin Radiol. 2001;56:401–9.

38. Graser A, Stieber P, Nagel D, et al. Comparison of CT colonography, colonoscopy, sigmoidoscopy and faecal occult blood tests for the detection of advanced adenoma in an average risk population. Gut. 2009;58:241–8.

(Received, August 24, 2022)
(Accepted, November 10, 2022)