Thieme

Additional 30-second observation of the right-sided colon for missed polyp detection with linked color imaging compared with narrow band imaging

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ABSTRACT

Background and study aims We previously demonstrated the efficacy of an additional-30-seconds (Add-30 s) observation with linked color imaging (LCI) or narrow band imaging (NBI) of the cecum and ascending colon (right-sided colon) after white light imaging (WLI) observation for improving adenoma detection rate (ADR) by 3% to 10%. We herein compared Add-30 s LCI with Add-30 s NBI in a large number of cases.

Patients and methods We retrospectively collected 1023 and 1011 cases with Add-30 s LCI and NBI observation for right-sided colon in 11 affiliated institutions from 2018 to 2022 and propensity score matching was performed. Add-30 s observation was as follows. First observation: WLI observation of the right-sided colon as first observation. Second observation: Reobservation of right-sided colon by Add-30 s LCI or NBI. The comparison of the mean numbers of adenoma + sessile serrated lesions (SSLs) and adenomas per patient (MASP and MUTYH-associated polyposis) were analyzed in the Add-30 s LCI/NBI groups. The increase in right-sided ADR was also analyzed in the groups.

Results Among 748 matched cases in the Add-30 s LCI/NBI groups, the MASP and MAP were 0.18/0.19 ($P=0.54$) and 0.14/0.15 ($P=0.70$). Among experts, they were 0.17/0.22 ($P=0.16$) and 0.15/0.21 ($P=0.08$). Among non-experts, they were 0.13/0.12 ($P=0.71$) and 0.12/0.07 ($P=0.04$). The right-sided ADRs of the first + second observations in the LCI and NBI groups were 32.2% and 28.9% ($P=0.16$) and the increase of ADRs were 7.5% and 7.2% ($P=0.84$).

Conclusions In right-sided colon, the detection of adenoma/SSL did not differ between Add-30 s LCI and NBI. Both of them significantly increased ADR.

Introduction

Removal of colorectal adenomas by colonoscopy is known to reduce the morbidity and mortality of colorectal cancer (CRC) [1, 2]. However, according to a systematic review, the rate of missed polyps in patients who received white light imaging (WLI) observation during colonoscopy was 15% to 32% [3]. The risk factors for missed polyps are reported to include poor bowel preparation, right-sided colon (ascending colon and cecum), flat morphology, small polyp, and sessile serrated lesions (SSLs) [4].

Various image-enhanced endoscopies (IEEs) have been developed to prevent missed polyps. The laser endoscope (LASER-EO; Fujifilm, Tokyo, Japan) was developed in 2012 and allows blue laser imaging (BLI) and linked color imaging (LCI) as a type of narrow band light observation [5]. Furthermore, a light-emitting diode (LED) endoscope system (ELUXEO; Fujifilm) has been available since 2016 throughout the world, including in the United States and Europe [6]. This system enables blue light imaging (which is also called BLI) and LCI to be performed with multilight technology. Many randomized controlled trials (RCTs) have shown the efficacy of polyp detection, including adenoma and SSLs with LCI, for both laser and LED systems [7, 8, 9, 10, 11, 12].

Narrow band imaging (NBI), which also improves polyp visibility and detection, has been available since 2006 [13]. Thus, a recent systematic review showed that the efficacy of NBI for improving the adenoma detection rate (ADR) was only achieved with the best bowel preparation [14]. Whether NBI or LCI is better for improving ADR is an important issue for endoscopists. In one RCT, the polyp detection rate (PDR) with NBI was significantly higher than that with LCI [15]. However, the observational time (min) for NBI was significantly longer than that for LCI. Another recent RCT showed that observation time was not significantly different between NBI and LCI, and there was no difference in the SSL detection rate and ADR between NBI and LCI [16]. Thus, the observation time may be related to lesion detection and it cannot be controlled in a clinical study. In addition, lesion detection is related to many other factors, including bowel preparation and endoscopist skill, which are sometimes difficult to control even in RCTs.

We previously reported the efficacy of an additional-30-seconds (Add-30 s) observation with LCI or NBI after the first WLI observation on the right-sided colon for improving ADR in two observational studies [17, 18]. Add-30 s LCI and NBI increased the ADR by 10.7% and 3.9%, respectively. In addition, we recently reported a RCT to analyze Add-30 s NBI and texture color and enhancement imaging (TXI) for right-sided colon; NBI and TXI increased the ADR by 10.2% and 10.5%, respectively (P = 0.81) [19]. In the Add-30 s observation, the second observational time was accurately determined to be 30 seconds and residual liquid was removed during the first WLI observation. Thus, the two modalities can be compared under the same conditions including time and bowel preparation.

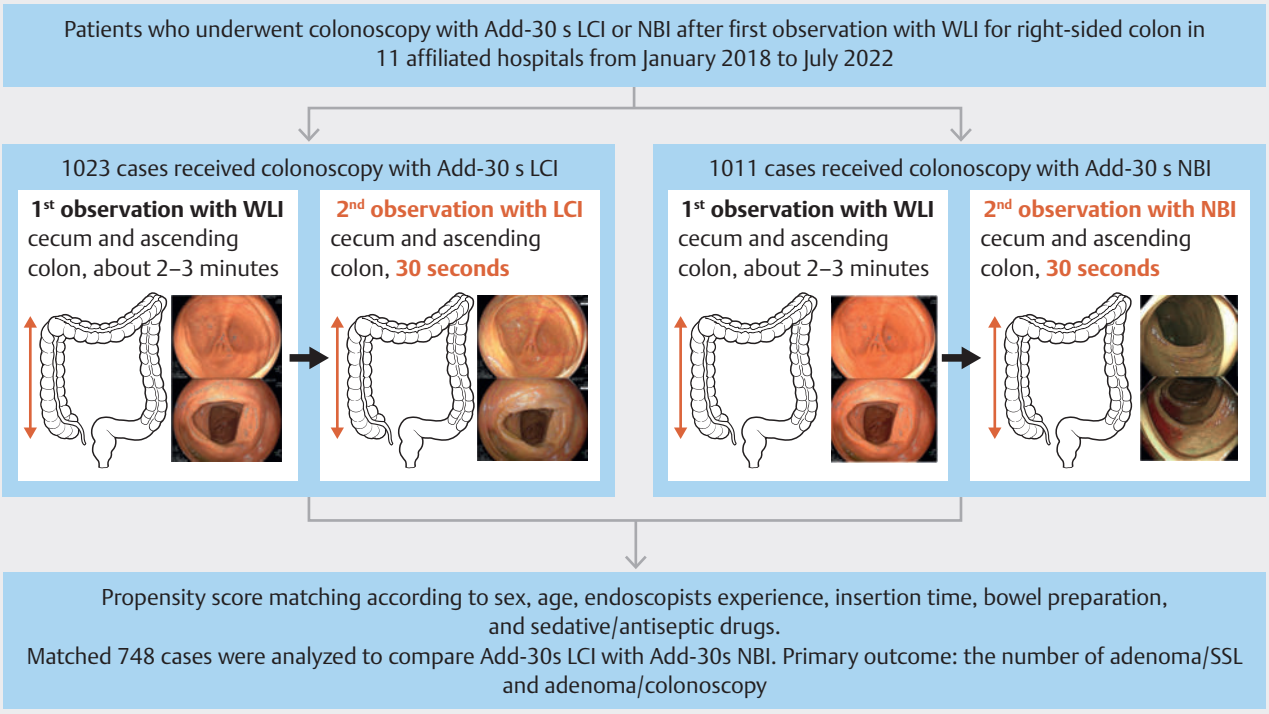
In this study, we aimed to compare Add-30 s LCI with Add-30 s NBI for detection of missed adenomas and SSL among a large number of real-world colonoscopies.

Patients and methods

We retrospectively reviewed patients who underwent colonoscopy with Add-30 s LCI or NBI after first WLI observation for right-sided colon in 11 affiliated hospitals from January 2018 to July 2022 (▶ **Fig. 1**) [17, 18, 19]. The study period was selected because of the need to collect more than 1000 cases for each observation according to sample size calculation. The 11 affiliated hospitals were Kyoto Prefectural University of Medicine, North Medical Center, Kyoto Prefectural University of Medicine, Kyoto Kuramaguchi Medical Center, Kyoto Kujo Hospital, Tomie Clinic, Nishijin Hospital, Nara City Hospital, Ayabe City Hospital, Japanese Red Cross Kyoto Daiichi Hospital, Aiseikai Yamashina Hospital, and Saiseikai Suita Hospital. Inclusion criteria were total colonoscopy for: 1) detailed examination of various symptoms (e. g., abdominal pain, constipation, anemia, and hematochezia); 2) surveillance after polyp or cancer resection; 3) screening; and 4) positive fecal occult blood. We excluded patients with recurrent lesions after previous endoscopic resection, lesion resected using EMR/ESD on the day, T1–T4 CRC, inflammatory bowel syndrome, or various polyposis syndromes. We also excluded patients who underwent surgery of the cecum or ascending colon. Colonoscopies were performed by eight experts and 22 nonexperts. During the study period, all endoscopists were motivated to perform Add-30 s LCI or NBI to prevent missed polyps [17, 18]. Then, collected cases with Add-30 s LCI (1023 cases) or Add-30 s NBI (1011 cases) were matched for sex, age, and background factors with $P \leq 0.1$ using propensity score matching.

Regarding the detailed method of Add-30 s observation, the cecum and ascending colon as the right-sided colon were observed with WLI for 2 to 3 minutes as the first observation according to previous reports [17, 18] (▶ **Fig. 1**). Benign lesions < 9 mm were resected with cold snare polypectomy during the first WLI observation. Subsequently, we reinserted the colonoscope into the cecum from the hepatic flexure and the right-sided colon was observed with LCI or NBI for 30 seconds as the second observation to detect missed adenomas and SSLs. During the 30-second observation, the right-sided colon was insufflated sufficiently to observe it in a distant view. Even if the observation of the right-sided colon was incomplete during the 30-second period, the second observation was completed. When missed polyps were detected during the second observation, they were removed according to previous studies. The Add-30 s observation time was stopped during resection and then resumed after polyp resection. The 30-second period was adopted based on a previous pilot study in which we checked the observation time with LCI/NBI for the right-sided colon (the cecum and ascending colon) [17, 18]. Chromoendoscopy was not performed until Add-30 s observation was finished.

The primary outcome of this study was to compare the mean number of adenomas/SSLs per patient (MASP) between the Add-30 s LCI and NBI groups in matched cases. Secondary outcomes were the comparison of mean number of adenomas per patient (MAP), mean number of SSLs per patient (MSP), and mean number of all polyps per patient (MAPP) between the Add-30 s LCI and NBI groups. These values for the first WLI ob-



Add-30 s: additional 30 seconds, LCI: linked color imaging, NBI: narrow band imaging, WLI: white light imaging, SSL: sessile serrated lesions

▶ **Fig. 1** Study flow.

servation were also examined in the two groups. These values and the PDR, adenoma/SSL detection rate (ASDR), ADR, and increase in ASDR/ADR were compared for the first WLI observation and the first WLI observation + the second observation with Add-30 s LCI/NBI. An analysis of these values according to endoscopist experience was also performed. Lesion detection, including MASP and MAP, of four representative endoscopists who performed ≥ 50 colonoscopies with Add-30 s LCI or NBI observation were examined in each group.

To evaluate bowel preparation, we used the Aronchick bowel preparation score, which grades bowel preparation as excellent, good, fair, poor, or inadequate [20]. In the present study, excellent and good scores were defined as good bowel preparations. Endoscopic diagnosis of polyps was performed with BLI/NBI magnification according to previous reports, and all polyps diagnosed as adenomas or SSL were resected using polypectomy, endoscopic mucosal resection, or endoscopic submucosal dissection, according to size and morphology [21, 22]. Some polyps that did not require endoscopic resection, such as hyperplastic polyps or inflammatory polyps, were diagnosed with biopsy. Some lesions were not diagnosed with histopathological assessment, but with magnified BLI/NBI observation due to the retrospective nature of this study. An expert was defined as an endoscopist who was well-experienced in LCI or NBI who had performed ≥ 1,000 colonoscopies and ≥ 50 LCI or NBI withdrawals [16, 19].

Polyp size was defined as maximum diameter and was calculated in accordance with the size of the snares and biopsy forceps. Polyps were divided into polypoid and nonpolypoid morphology according to the Paris classification [23]. Histopathological diagnosis was performed according to the World Health Organization (WHO) classification. Intramucosal cancer was categorized as adenoma in this study [24]. Regarding SSL, we also followed the WHO criteria.

Most patients consumed a liquid diet and 10 mL of sodium picosulfate the day before colonoscopy and drank 1.0 L of a highly concentrated polyethylene glycol (PEG) solution with ascorbic acid (MoviPrep; EA Pharma Co., Ltd., Tokyo, Japan) and water (> 0.5 L) on the morning of the examination day, according to our previous report [25]. Other patients consumed regular PEG or magnesium citrate based on individual preference. All procedures were performed with laser and LED endoscope systems (Fujifilm Co., Tokyo, Japan) or an endoscope system with Xenon light source (EVIS Lucera Elite, Olympus Co., Tokyo, Japan), and the scopes were EC-760ZP-V, EC-L600ZP, EC-600ZP7, EC-660ZP for Fujifilm and CF-HQ290I, PCF-H290AZI for Olympus. We also used caps (D-201–14304, D-201–13404, MAJ-1990, Olympus Co., Tokyo, Japan) for almost all procedures. Use of sedative and antispastic drugs was determined by each endoscopist.

This study was approved by the Ethics Committee of Kyoto Prefectural University of Medicine (ERB-C-1704–3, approval data: June 29, 2021) as a subgroup analysis of a multicenter prospective and retrospective study organized by our department. The study was also conducted in accordance with the World Medical Association Declaration of Helsinki. An opt-out

▶ **Table 1** Clinical characteristics before and after propensity score matching.

	LCI	NBI	ASD	*P* value	LCI matched	NBI matched	ASD	*P* value
Case number	1023	1011		–	748	748		–
Age, years, mean ± SD	66.6 ± 12.2	66.6 ± 12.0		0.68	66.5 ± 12.0	67.1 ± 11.8		0.41
Sex, %, (n) (male/female), n (%)	543/480 (53.1/46.9)	573/438 (56.7/43.3)	0.072	0.10	409/339 (54.7/45.3)	405/343 (54.1/45.9)	0.012	0.84
Expert/nonexpert, n (%)	712/311 (69.6/30.4)	580/430 (57.4/42.6)	0.255	< 0.01	515/233 (68.9/31.1)	523/225 (69.9/30.1)	0.021	0.65
Insertion time, sec	441 ± 263	388 ± 247	0.207	< 0.01	413 ± 223	399 ± 238	0.066	0.17
Bowel preparation good, n, (%)	800 (78.2)	853 (84.4)	0.159	< 0.01	597 (79.8)	604 (80.7)	0.022	0.65
Antispastic drug, n (%)	676 (66.1)	615 (60.8)	0.110	0.01	500 (66.8)	517 (69.1)	0.049	0.35
Sedation, n (%)	377 (36.9)	253 (25.0)	0.259	< 0.01	227 (30.3)	231 (30.9)	0.013	0.82
1st WLI observation time for right-sided colon, sec, mean ± SD	194 ± 123	201 ± 126		0.23	196 ± 123	204 ± 131		0.22

LCI, linked color imaging; NBI, narrow band imaging; ASD, absolute standardized difference; SD, standard deviation; WLI, white light imaging; right-sided colon, cecum to transverse colon.

of the study to the patients was performed in each hospital using a website or a board in an endoscopic unit, or both.

Statistical assessment

Continuous variables, such as polyp size, were analyzed using the Mann–Whitney U-test. Categorical values were examined using the chi-square test. Propensity score matching was performed for patient and lesion characteristics ($P \leq 0.1$) between the Add-30 s LCI and NBI groups. The absolute standardized difference (ASD) value was examined to assess the validity of the matching, and a value of ≤ 0.2 was determined to be appropriate. In both Add-30 s LCI and NBI, 95% confidence intervals for MASP, MAP, MSP, MAPP, ADR, ASDR, PDR between were calculated. All statistical analyses were performed using SPSS software program (v.22.0; IBM Japan, Tokyo, Japan). $P < 0.05$ was considered to indicate statistical significance.

Results

Finally, 748 cases in the Add-30 s LCI and NBI groups were analyzed after matching (▶ **Fig. 1**, ▶ **Table 1**). In the Add-30 s LCI and NBI groups, the mean patient ages were 65.5 ± 12.0 years and 67.1 ± 11.8 years ($P = 0.41$), respectively. Rates of good bowel preparation were 79.8% and 80.7%, respectively ($P = 0.65$).

In the second observation, 148 and 147 polyps were detected in the Add-30 s LCI and NBI groups, respectively (▶ **Table 2**, ▶ **Fig. 2**). There were no significant differences in MASP (0.18 vs. 0.19, $P = 0.54$), MSP (0.03 vs. 0.04, $P = 0.88$), or MAP (0.14 vs. 0.15, $P = 0.66$) between the two groups. Regarding the first observation, there were no significant differences in the MASP and MAP between the two groups. However, there was a significant difference in the MSP between the two groups (0.06 vs. 0.09, $P = 0.03$).

The comparison between the first and first + second observations was analyzed in the Add-30 s LCI and NBI groups (▶ **Table 3**). Regarding the Add-30 s LCI group, the MASP and MAP in the first observation and the first + second observations were 0.44/0.62 ($P < 0.01$) and 0.39/0.53 ($P < 0.01$). The right-sided PDR, ASDR, and ADR in the first + second observations were also significantly higher than those in the first observation. In the Add-30 s NBI group, there were significant differences in the values between the first and first + second observations. The increase in ADR in the Add-30 s LCI and NBI groups was 7.5% and 7.2% ($P = 0.84$), respectively.

Among experts, there was a significant difference in MAP between the LCI and NBI groups (0.15 vs. 0.21, $P = 0.08$) (▶ **Table 4**). Among nonexperts, there was a significant difference in MAP between the LCI and NBI groups (0.12 vs. 0.07, $P = 0.04$). The results of each endoscopist who performed ≥ 50 colonoscopies were analyzed in the Add-30 s LCI and NBI groups (▶ **Table 5**). The increase in ADRs ranged from 3.3% to 10.9% in the Add-30 s LCI group and from 1.7 to 9.4% in the Add-30 s NBI group.

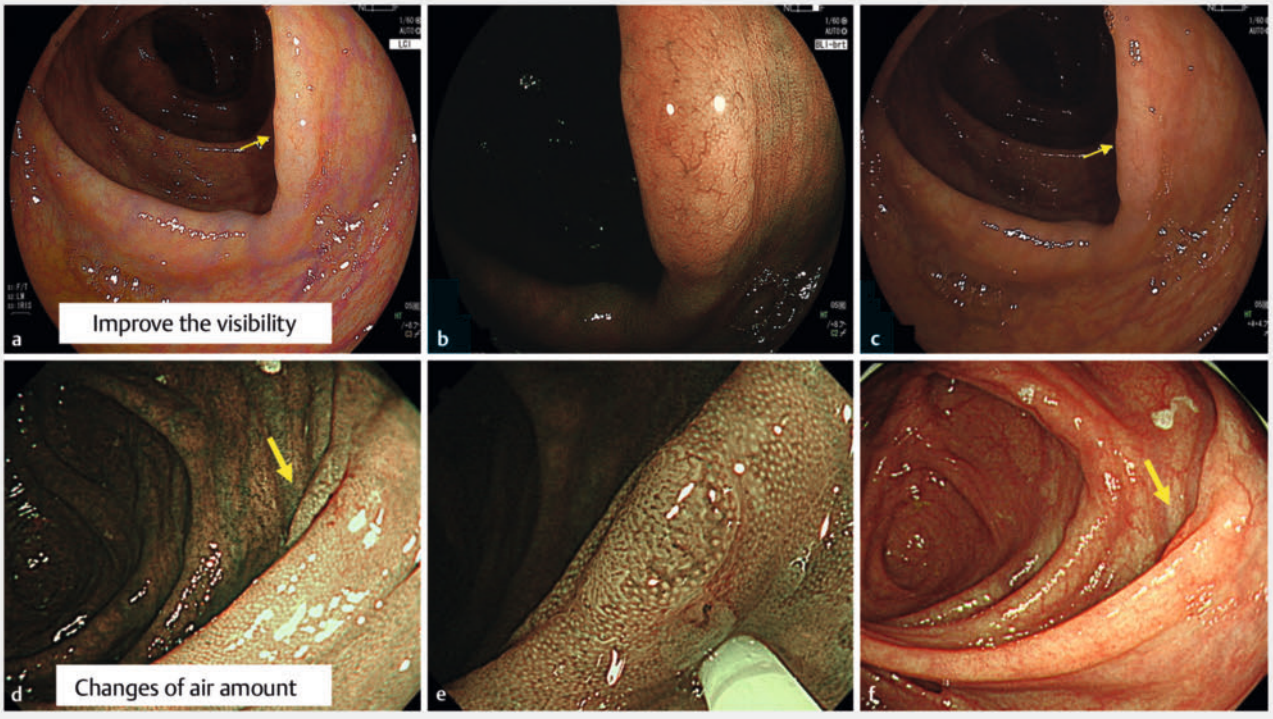
Discussion

In the current multicenter study, we examined 748 matched cases each with Add-30 s LCI or NBI observations for the right-sided colon under the same conditions for observation time, bowel preparation, and various other factors. There were no significant differences in MASP or MAP between the two groups. In addition, both Add-30 s LCI and NBI significantly increased MASP and MAP in the first + second observation more

▶ **Table 2** Lesion characteristics in Add-30 s LCI and NBI and those detected in the first WLI observation in the matched cohort.

	2nd observation LCI N = 748	2nd observation NBI N = 748	*P* value	1st WLI (LCI) N = 748	1st WLI (NBI) N = 748	*P* value
Detected polyp number, n	148	147	–	363	355	–
Polyp size, mm, mean ± SD	4.1 ± 3.0	3.9 ± 3.0	0.61	4.6 ± 3.7	4.2 ± 3.1	0.14
Polyp size, %, (n) (< 5 mm/ ≥ 5 mm)	64.6/35.4 (103/45)	73.6/26.4 (109/38)	0.38	65.8/34.2 (239/ 124)	68.7/31.3 (242/ 113)	0.50
Location, %, (n) (C/A)	23.3/76.7 (39/109)	34.3/65.7 (52/95)	0.09	30.3/69.7 (110/ 253)	28.9/71.1 (105/ 250)	0.83
Morphology, %, (n) (polypoid/nonpolypoid)	59.3/40.7 (87/61)	62.9/37.1 (91/56)	0.58	73.8/26.2 (268/ 95)	70.5/29.5 (237/ 118)	0.03
Histopathology, %, (n) (HP/ SSL/Ad)	11.5/16.9/71.6 (17/25/106)	6.7/18.0/72.4/2.8 (7/ 28/112)	0.10	9.4/11.6/79.1 (34/42/287)	7.7/70.7/3.5 (33/64/258)	0.04
MASP, [95%CI] (n)	0.18 [0.14–20.4] (131)	0.19 [16.0–21.6] (140)	0.54	0.44 [0.41–0.48] (331)	0.43 [0.40–0.47] (322)	0.76
MAP, [95%CI] (n)	0.14 [0.12–0.17] (106)	0.15 [0.13–0.18] (112)	0.66	0.39 [0.35–0.42] (289)	0.34 [0.31–0.38] (258)	0.25
MSP, [95%CI] (n)	0.03 [0.02–0.05] (25)	0.04 [0.03–0.05] (28)	0.88	0.06 [0.04–0.08] (42)	0.09 [0.07–0.11] (64)	0.03
MAPP, [95%CI] (n)	0.20 [0.17–0.23] (148)	0.20 [0.17–0.23] (147)	0.94	0.49 [0.45–0.52] (363)	0.47 [0.44–0.51] (355)	0.80

LCI, linked color imaging; NBI, narrow band imaging; WLI, white light imaging; SD, standard deviation; C, cecum; A, ascending colon; HP, hyperplastic polyp; SSL, sessile serrated lesion; Ad, adenoma; MASP, mean number of adenomas and sessile serrated lesions per patient; CI: confidence interval, MAP, mean number of adenomas per patient; MSP, mean number of sessile serrated lesions per patient; MAPP, mean number of overall polyps per patient.



▶ **Fig. 2** Two effects of additional 30-s observation with LCI and NBI. **a** Effect of improvement in visibility. A nonpolypoid lesion of 6 mm in the ascending colon could be detected during an additional 30 s (Add-30-s) observation with LCI (yellow arrow). **b** BLI magnification enabled the diagnosis of the sessile serrated lesions. **c** A recorded movie of the first WLI observation showed that the lesion had low visibility (yellow arrow). **d** The effect of changes in the amount of air. A nonpolypoid lesion measuring 6 mm in the ascending colon (yellow arrow). **e** NBI magnification enabled the diagnosis of adenoma. **f** A recorded movie of the first WLI observation showing that the lesion was behind a fold (yellow arrow).

▶ **Table 3** Lesion detection in first WLI and Add-30 s LCI/NBI observation in the matched cohort.

	Add-30 s LCI (N = 748)			Add-30 s NBI (N = 748)			P value WLI + LCI vs. WLI + NBI
	1st WLI	1st + 2nd WLI + LCI	*P* value	1st WLI	1st + 2nd WLI + NBI	*P* value	
MASP, [95%CI] (n)	0.44 [0.41–0.48] (331)	0.62 [0.58–0.65] (462)	< 0.01	0.43 [0.40–0.47] (322)	0.62 [0.58–0.65] (462)	< 0.01	0.91
MAP, [95%CI] (n)	0.39 [0.35–0.42] (289)	0.53 [0.49–0.56] (395)	< 0.01	0.34 [0.31–0.38] (258)	0.49 [0.46–0.53] (370)	< 0.01	0.23
MSP, [95%CI] (n)	0.06 [0.04–0.08] (42)	0.09 [0.07–0.11] (67)	0.02	0.09 [0.07–0.11] (64)	0.12 [0.10–0.15] (92)	0.03	0.05
MAPP, [95%CI] (n)	0.49 [0.45–0.52] (363)	0.68 [0.65–0.72] (511)	< 0.01	0.47 [0.44–0.51] (355)	0.67 [0.64–0.70] (502)	< 0.01	0.61
Right-sided ASDR, % 95%CI (n)	28.6 [25.5–32.0] (214)	38.0 [34.6–41.5] (284)	< 0.01	26.3 [23.3–29.6] (197)	35.8 [32.5–39.3] (268)	<0.01	0.39
Increase of ASDR, % [95%CI]	–	9.4 [7.5–11.7]	–	–	9.5 [7.6–11.8]	–	0.92
Right-sided ADR, % [95%CI] (n)	24.7 [21.8–28.0] (185)	32.2 [29.0–35.7] (241)	0.01	21.7 [18.9–24.8] (162)	28.9 [25.7–32.2] (216)	0.01	0.16
Increase of ADR, % [95%CI]	–	7.5 [5.7–9.6]	–	–	7.2 [5.6–9.3]	–	0.84
Right-sided PDR, % [95%CI] (n)	32.2 [29.0–35.6] (241)	42.8 [39.3–46.4] (320)	< 0.01	30.0 [26.7–33.3] (224)	40.4 [36.9–43.9] (302)	< 0.01	0.34
Increase of PDR, % [95%CI]	–	10.6 [8.5–13.0]	–	–	10.4	–	0.93

Add-30 s, additional 30 seconds; CI, confidence interval; MASP, mean number of adenomas and sessile serrated lesions per patient; MAP, mean number of adenomas per patient; MSP, mean number of sessile serrated lesions per patient; MAPP, mean number of overall polyps per patient; WLI, white light imaging; LCI, linked color imaging; NBI, narrow band imaging; ASL, adenoma + sessile serrated lesion; ASDR, adenoma and SSL detection rate; ADR, adenoma detection rate; PDR, polyp detection rate

than the first observation and resulted in an increase in right-sided ADR of 7.5% and 7.2%, respectively.

Regarding the second observation with WLI for the right-sided colon, several papers have shown efficacy in terms of an increase in ADR [26, 27]. In a recent RCT, the ADR for the right-sided colon was significantly higher in the Second Forward View (SFV) group (the first WLI + second WLI observation) than in the Standard Withdrawal Colonoscopy (SWC) group (only the first WLI observation) (27.1% vs. 21.6%; $P = 0.042$). However, median overall withdrawal time was 1.5 minutes longer in the SFV group than in the first SWC group (12.0 vs 10.5 min; $P < 0.001$) [26]. In a review of four RCTs, an additional forward observation of the right-sided colon increased the ADR by 10% [27]. However, the length of this additional observation was approximately 2 minutes and the additional 2 minutes of WLI observation performed the same way would stress patients and endoscopists. We previously reported the efficacy of Add-30 s WLI when using the EVIS LUCERA ELITE (Olympus) and laser (Fujifilm) endoscope systems, respectively [17, 18]. Increases in ADR with Add-30 s observation as the second observation were 3.9% vs. 2.3% for NBI vs. WLI and 10.2% vs. 3.8% for LCI vs. WLI. Thus, the Add-30 s WLI observation was insufficient. For these reasons, we analyzed the Add-30 s LCI and NBI observations instead of the second WLI observation for the right-sided colon in the current study, and found a substantial increase in ADR in both groups.

Add-30 s LCI and NBI were suggested to have two effects that facilitated detection of missed polyps (▶ **Fig. 2**) [17, 18]. The first suggested effect is due to improvement in visibility with LCI/NBI, which is reported to improve polyp identification [28, 29]. The second suggested effect is the change in the amount of air. By observing the right-sided colon twice, it became easier to find polyps that were hidden behind the folds by changing the amount of air.

Both LED and laser endoscope systems can be used for LCI, and both are used worldwide. A recent international RCT conducted on more than 3000 cases in 11 institutions from four countries using both laser and LED endoscope systems showed that there were significant differences in ADR and SSL detection rates in the whole colorectum between LCI and WLI (ADR: 58.7% vs. 46.7%, $P < 0.01$, SSL detection rate: 4.8% vs. 2.8%, $P < 0.01$) [30]. LCI significantly increased the ADR by 12.0% and the SSL detection rate by 2.0%. The study also showed that LCI was effective regardless of institution or country. A recent large-scale multicenter RCT using LED endoscopy showed that LCI significantly improved SSL detection [31]. Another recent RCT using LED endoscopy showed the efficacy of LCI in increasing the ADR in screening colonoscopy in comparison with

▶ **Table 4** Comparison of lesion detection according to endoscopist experience.

Endoscopist	LCI expert	NBI expert	*P* value	LCI nonexpert	NBI nonexpert	*P* value
Patient number, n	515	523		233	225	
M/F, n (%)	275/240 (53.4/46.6)	297/226 (56.8/43.2)	0.27	134/99 (51.4/47.6)	108/117 (55.6/44.4)	0.04
Age, years, mean ± SD	66.8 ± 11.8	67.7 ± 10.9	0.24	65.9 ± 12.5	65.7 ± 13.3	0.88
Insertion time, sec, mean ± SD	385 ± 205	371 ± 196	0.26	481 ± 274	461 ± 307	0.48
Antispastic drug, n (%)	359 (69.7)	407 (77.8)	0.24	141 (60.5)	110 (48.9)	0.17
Sedation, n (%)	136 (26.4)	147 (28.1)	0.53	91 (39.1)	84 (37.3)	0.70
1st WLI observation time, sec, mean ± SD	193 ± 116	199 ± 106	0.95	199 ± 106	215 ± 170	0.14
2nd MASP, [95%C] (n)	0.17 [0.14–0.21] (90)	0.22 [0.18–0.25] (113)	0.16	0.13 [9.5–18.3] (31)	0.12 [8.3–16.9] (27)	0.71
2nd MAP, [95%CI] (n)	0.15 [0.13–0.19] (80)	0.21 [0.17–0.24] (107)	0.08	0.12 [0.09–0.18] (30)	0.07 [0.04–0.11] (15)	0.04
1st + 2nd MASP, [95%CI] (n)	0.57 [0.55–0.63] (304)	0.65 [0.60–0.69] (338)	0.05	0.72 [61.6–73.5] (158)	0.55 [0.49–0.61] (124)	0.07
1st + 2nd MAP, [95%CI] (n)	0.49 [0.47–0.56] (262)	0.52 [0.48–0.56] (272)	0.56	0.61 [50.7–63.3] (133)	0.44 [37.3–50.1] (98)	0.03

LCI, linked color imaging; NBI, narrow band imaging; SD, standard deviation; WLI, white light imaging; MASP, mean number of adenomas and sessile serrated lesions per patient; CI: confidence interval; MAP, mean number of adenomas per patient.

WLI [32]. On the other hand, a a recent RCT using LED endoscopy showed that LCI was not effective for improving the ADR more than WLI in patients with Lynch syndrome [33]. Previously, our multicenter study showed the inferiority of LED and laser endoscopy with regard to polyp visibility under LCI observations performed by 12 Japanese endoscopists [28]. However, our international study from nine countries demonstrated that visibility under LCI using LED and laser endoscopes performed by endoscopists from countries outside of Japan differed from the visibility of Japanese endoscopists [34]. Regarding comparisons between LCI and NBI, a single-center RCT from China that included 136 cases in each group compared LCI (LED system, Fujifilm Co.) and NBI (EXERA 290 video system, Olympus Co.) for PDR and ADR [15]. It showed a significant difference in PDR throughout the whole colorectum between LCI and NBI (55.9 vs. 71.3%, $P = 0.008$). A significant effect on SSLs was observed between LCI and NBI (22.1% vs. 34.6%, $P = 0.02$) and comparison of the ADR revealed a marginal effect (39.7% vs. 51.3%, $P = 0.05$). However, observation times (minutes) in the NBI group were significantly longer than in the LCI group (first observation: 8.6 ± 3.1 vs. 10.0 ± 4.1, $P < 0.01$) and the time difference was 1.4 minutes. Another recent RCT comparing LCI (both LED and laser system, Fujifilm Co.) to NBI (EXERA 290 video system, Olympus Co.) showed no difference in SSL detection and ADR and there was no significant difference in withdrawal time (minutes) between LCI and NBI (7.9 vs. 7.6, $P = 0.18$) [16]. Regarding the effect of Add-30 s LCI and NBI in the current study, this observation increased the ADR by 7.5% and 7.2%, respectively, and increased the ASDR by 9.4% and 9.5%, respectively. The efficacy of Add-30 s LCI and NBI varied depending on the endoscopist. Thus, we believe Add-30 s observation is promising for preventing missed polyps and increasing the ADR regardless of LCI/NBI and endoscopist experience.

Regarding NBI, the EVIS X1 (CV-1500; Olympus Co.), an endoscope system that uses five colors of LEDs, was launched worldwide in July 2020 and it features brighter NBI and a new observational mode termed TXI [35, 36]. Our recent RCT, which included 381 cases from multiple centers, compared Add-30 s TXI with Add-30 s NBI using this new system [19]. There were significant differences in MAP (0.21/0.23, $P = 0.83$) and MASP (0.27/0.28, $P = 0.87$), and the study showed that the ADR increased by 10.2% in Add-30 s NBI. These values were higher than the values in the current study. Further prospective studies using this system are needed to compare LCI and NBI.

Our study showed that both Add-30 s LCI and NBI increased ADR with no significant difference. There were some differences between LCI and NBI regarding endoscopic experience, with LCI resulting in significantly increased MAP in nonexperts, whereas NBI resulted in increased MAP in experts. In addition, NBI makes the endoscopic view reddish and dark when residual fluid is left after poor preparation [17, 19, 28]. LCI does not have these limitations. Moreover, two modes are in a different endoscopic system (Olympus or Fujifilm). Thus, according to the skill of the endoscopist, bowel preparation, and endoscopic system, either NBI or LCI can be chosen for Add-30 s observation.

▶ **Table 5** Lesion detection of representative endoscopists in the Add-30 s LCI and NBI groups.

Endoscopist	LCI A* (expert)	LCI B* (expert)	LCI C (nonexpert)	LCI D (nonexpert)	NBI A* (expert)	NBI B* (expert)	NBI E (nonexpert)	NBI F (nonexpert)
Patient number, n	590	122	58	55	496	85	77	67
Sex, % (n) Male/female	52.3/48.7 (309/281)	53.3/46.7 (65/57)	54.2/45.8 (32/26)	61.8/38.2 (34/21)	55.6/44.4 (276/220)	68.2/31.8 (58/27)	54.5/45.5 (42/35)	50.7/49.3 (34/33)
Age, years, mean ± SD	66.8 ± 11.5	66.7 ± 13.3	69.0 ± 12.1	68.5 ± 11.0	67.2 ± 12.2	68.8 ± 11.7	63.4 ± 11.8	62.2 ± 12.9
Antispastic drug use, %, (n)	71.2 (420)	61.5 (75)	60.3 (35)	60.0 (33)	76.8 (381)	66.2 (58)	83.1 (64)	0 (0)
1st WLI observation time, sec, mean ± SD	198 ± 116	166 ± 113	186 ± 137	204 ± 149	194 ± 126	228 ± 126	243 ± 139	261 ± 128
1st WLI ASDR, %, (n)	31.3 (185)	32.8 (40)	19.0 (11)	25.5 (14)	30.4 (151)	30.5 (26)	20.8 (16)	29.9 (20)
1st WLI + 2nd LCI or NBI ASDR, %, (n)	41.2 (243)	40.2 (49)	32.8 (19)	36.4 (20)	40.3 (200)	41.2 (35)	27.3 (21)	31.3 (21)
Increase of ASDR, %	9.9	7.4	13.8	10.9	9.9	10.7	6.5	1.4
1st WLI ADR, %, (n)	25.9 (153)	28.7 (35)	17.2 (10)	25.5 (14)	25.0 (124)	28.2 (24)	15.6 (12)	26.7 (18)
1st WLI + 2nd LCI or NBI ADR, %, (n)	32.7 (193)	32.0 (39)	27.6 (16)	36.4 (20)	33.5 (166)	37.6 (32)	20.8 (16)	28.4 (19)
Increase of ADR, %	6.8	3.3	10.4	10.9	8.5	9.4	5.2	1.7

LCI, linked color imaging; NBI, narrow band imaging; SD, standard deviation; WLI, white light imaging; ASDR, adenoma SSL detection rate; ADR, adenoma detection rate. *Experts A and B in the Add-30 s LCI were similar to Experts A and B in the Add-30 s NBI group.

In the current study, the rate of detection of polyps with first WLI for right-sided colon in Add-30 s LCI and NBI groups was significantly different for MSP ($P = 0.03$). There have been no previous studies about the difference in polyp detection with WLI between Fujifilm and Olympus systems although the WLI images from the two systems are slightly different. In addition, both LED and laser were used for LCI in the current study, although the ratio could not be analyzed and it might affect this result. Further analysis should be performed to verify this.

The present study had several limitations. It was retrospective and observational. Previously reported studies included 130 and 65 cases in the NBI and LCI groups, respectively and these data were included in the current study [17, 18]. Thus, this study included 881 and 958 de-novo cases in the NBI and LCI groups, respectively. In the current study, we did not analyze the efficacy of Add-30 s WLI although previous studies showed less efficacy for WLI compared with NBI and LCI [17, 18]. We only analyzed polyps on the right-sided colon. There was a potential selection bias because the period for collecting patients differed depending on the facility. In propensity score matching, we showed that all ASD values were < 0.2 for minimizing selection bias due to matching. However, there may be a potential adjustment bias in the matching [37]. We did not use Endocuff (Arc Medical, Leeds, UK), which is a unique-shaped cap, during colonoscopy although the combination of LCI and the cap increased ADR significantly [10]. Our previous study showed that the efficacy of LCI and NBI for improving lesion visibility are different with adenomas and SSLs and it may be different from that for NBI [28, 36]. Thus, MAP and MSP were analyzed independently as secondary endpoints. Our study is not sufficient for a head-to-head comparison NBI and LCI or to determine equivalence of the two modalities because of the retrospective setting, and hypothesis-generating sample size.

Conclusions

In conclusion, our study showed that lesion detection in the right-sided colon did not differ between Add-30 s LCI and NBI overall. Add-30 s observations with both LCI and NBI significantly improved the ASDR and ADR.

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Conflict of Interest

Yoshida N and Dohi O have received a research grant from Fujifilm. Yoshida N have received payment for lectures from Fujifilm. The other author declares no conflict of interest for this article.

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