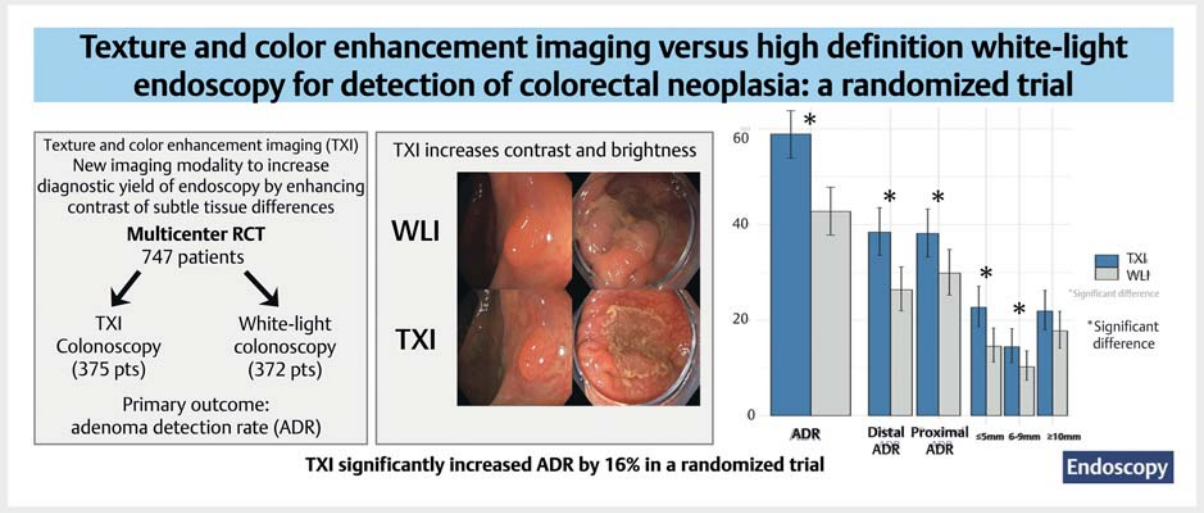
Texture and color enhancement imaging versus high definition white-light endoscopy for detection of colorectal neoplasia: a randomized trial

GRAPHICAL ABSTRACT



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ABSTRACT

Background Texture and color enhancement imaging (TXI) was recently proposed as a substitute for standard high definition white-light imaging (WLI) to increase lesion detection during colonoscopy. This international, multicenter randomized trial assessed the efficacy of TXI in detection of colorectal neoplasia.

Methods Consecutive patients aged ≥40 years undergoing screening, surveillance, or diagnostic colonoscopies at five centers (Italy, Germany, Japan) between September 2021 and May 2022 were enrolled. Patients were randomly assigned (1:1) to TXI or WLI. Primary outcome was adenoma detection rate (ADR). Secondary outcomes were adenomas per colonoscopy (APC) and withdrawal time. Relative risks (RRs) adjusted for age, sex, and colonoscopy indication were calculated.

Results We enrolled 747 patients (mean age 62.3 [SD 9.5] years, 50.2% male). ADR was significantly higher with TXI (221/375, 58.9%) vs. WLI (159/372, 42.7%; adjusted RR 1.38 [95%CI 1.20–1.59]). This was significant for ≤5 mm (RR 1.42 [1.16–1.73]) and 6–9 mm (RR 1.36 [1.01–1.83]) adenomas. A higher proportion of polypoid (151/375 [40.3%] vs. 104/372 [28.0%]; RR 1.43 [1.17–1.75]) and non-polypoid (136/375 [36.3%] vs. 102/372 [27.4%]; RR 1.30 [1.05–1.61]) adenomas, and proximal (143/375 [38.1%] vs. 111/372 [29.8%]; RR 1.28 [1.05–1.57]) and distal (144/375 [38.4%] vs. 98/372 [26.3%]; RR 1.46 [1.18–1.80]) lesions were found with TXI. APC was higher with TXI (1.36 [SD 1.79] vs. 0.89 [SD 1.35]; incident rate ratio 1.53 [1.25–1.88]).

Conclusions TXI increased ADR and APC among patients undergoing colonoscopy for various indications. TXI increased detection of polyps <10 mm, both in the proximal and distal colon, and may help to improve colonoscopy quality indicators.

Introduction

Colonoscopy is the cornerstone of colorectal cancer (CRC) screening programs, reducing CRC incidence and mortality through detection and removal of precancerous lesions [1, 2]. The adenoma detection rate (ADR), defined as the proportion of colonoscopies in which an adenoma is found by a single endoscopist, has been inversely correlated to post-colonoscopy CRC risk [3, 4]. However, a recent meta-analysis from tandem colonoscopy trials showed a 25% miss rate for colorectal neoplasia [5]. Post-colonoscopy CRCs account for 3.4%–9% of all cases of CRCs, and most of them derive from missed lesions [6, 7].

In order to maximize colonoscopy effectiveness, many technological devices have been proposed to improve ADR by increasing the visualization of the colonic surface [8, 9] or enhancing visibility of subtle lesions [10, 11]. Many clinical studies have reported an improvement in the detection rate of colonoscopy using image enhancing endoscopy systems, such as narrow-band imaging (NBI), blue-laser imaging, and linked color imaging, among others [11, 12]. However, the enthusiasm arising from preliminary results using these new technologies – mainly from prospective series or small trials carried out with a tandem design – has seldom been replicated in larger randomized controlled trials [11, 13]. In addition, a recent meta-analysis [14] based on data from individual patients included in randomized trials showed an increase in ADR when using NBI, but this positive effect was limited to patients with optimal bowel preparation, and a longer withdrawal time was shown in the NBI arms.

Texture and color enhancement imaging (TXI; Olympus, Tokyo, Japan) is a newly developed image-enhancing endoscopy technology that aims to improve the detection of lesions and other mucosal abnormalities using filter-modified white-light imaging (WLI) that enhances color, structure, and brightness [15]. The incoming image is split, texture and brightness are separately enhanced, and then images are merged together, before being sent back to the operator's screen (▶ **Fig. 1**). Although this technology has been claimed to increase the detection rate of colorectal polyps [15], no data are available evaluating the performance of endoscopists using TXI technology.

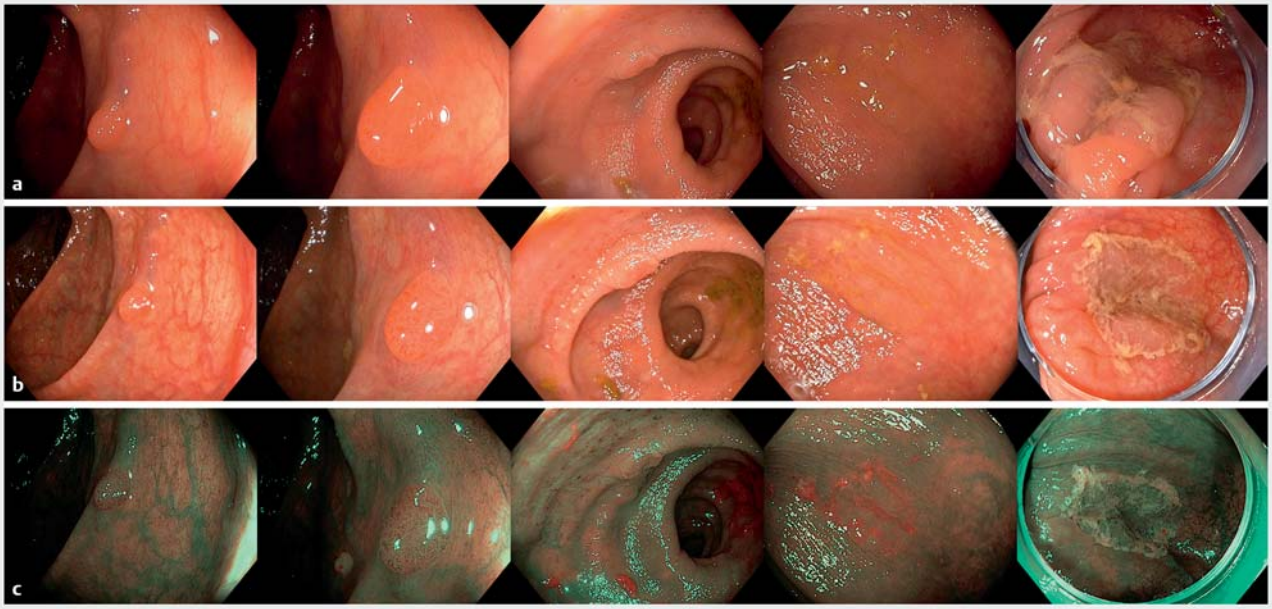
The aim of this trial was to evaluate the impact of TXI compared with standard high definition WLI endoscopy in terms of adenoma detection.

Methods

This international, parallel, randomized, multicenter trial ("TRACK" study) was performed at five endoscopy centers (two in Italy [Ospedale dei Castelli and Fondazione Policlinico Gemelli, Rome], two in Germany [Universitatsklinikum Augsburg and University Hospital Ulm], and one in Japan [Chiba University Hospital]) participating in population CRC screening programs, and was approved by all local institutional review boards (coordinating center number: 0171576/2021). The study was reported according to the CONSORT guidelines [16] for randomized controlled trials (see the online-only Supplementary material for the CONSORT checklist). This was an investigator-initiated, no-profit study, and no funding was received or solicited. The study was performed according to the Declaration of Helsinki and followed the principles of Good Clinical Practice. All authors had access to the study data and reviewed and approved the final manuscript.

Study population

The target population included individuals aged >40 years who were undergoing colonoscopy for primary CRC screening or post-polypectomy surveillance, as well as for work-up following a positive fecal immunochemical test (FIT) result (cutoff 20 µg



▶ **Fig. 1** Comparison of images. Displayed images of the same polyp (columns). Row **a** White-light imaging. Row **b** Texture and color enhancement imaging. Row **c** Narrow-band imaging.

Hb/g feces) or for symptoms/signs. Patients were excluded if they had a history of CRC, inflammatory bowel disease, or previous colonic resection, received antithrombotic therapy precluding polyp resection, or did not provide informed written consent.

Randomization

Before colonoscopy, eligible patients were randomized in a 1:1 ratio by the endoscopist to receive colonoscopy with TXI (TXI group) or high definition WLI endoscopy during insertion and withdrawal phases of the procedure. Randomization was based on a list of random numbers generated for each center by the coordinating center. Operating endoscopists were not involved in the randomization sequence or handling. Randomization was stratified by sex, age, personal history of adenomas, and indication for colonoscopy.

Colonoscopy procedures

All procedures were performed by experienced endoscopists (>2000 screening colonoscopies) at participating centers. All procedures were performed with high definition Olympus 190, 290, 1100, or 1500 series scopes with or without magnification, with a CV-1500 Video Processor System Center (Evis Exera X1; Olympus, Tokyo, Japan), incorporating the TXI technology. Magnification was used only for polyp characterization at the endoscopist's discretion.

Bowel preparation was evaluated and graded by the endoscopist performing the examination, using the Boston Bowel Preparation Scale (BBPS) [17]. Individuals with 0 or 1 in any one of the three segments were excluded from the primary analysis. The endoscopist and facility staff were allowed to adopt their standard procedures for patient management and monitoring, including use of conscious sedation. Cecal intubation was assessed by the endoscopist by the identification of the ileocecal valve and the appendix orifice via photo documentation. Intubation time and inspection time during withdrawal were measured using a stopwatch, pausing for therapeutic interventions and washing. Endoscopists were required to comply with a minimum of 6 minutes for inspection (i.e. clean withdrawal time). All polyps were classified by their location, size, and morphology according to the Paris classification [18]. Proximal location was defined as proximal to the splenic flexure. All polyps were removed (biopsy for nonresectable lesions), irrespective of size, color, or subjective interpretation, with the exception of diminutive hyperplastic-appearing polyps located in the rectum that were judged by the endoscopist to be not clinically significant.

Histopathology

All resected or biopsy specimens were fixed in 10% buffered formalin solution in separate jars. Specimens were processed and stained for histopathology using standard methods and evaluated by expert pathologists (one at each center), who were blinded to the assigned examination mode. All lesions were classified according to the Vienna classification [19].

Definitions

Patients with polyps detected were categorized as "high risk", if they had at least one polyp that met the most recent European Society of Gastrointestinal Endoscopy (ESGE) guideline [20] criteria for surveillance colonoscopy at 3 years (i.e. patients with complete removal of at least one adenoma ≥10 mm or with high grade dysplasia ["advanced adenoma"], or at least five adenomas, or any serrated polyp ≥10 mm or with dyspla-

sia), or "low risk" (return to screening or surveillance colonoscopy after 10 years) when the above-mentioned parameters were not found (i.e. patients with complete removal of 1–4 adenomas <10 mm with low grade dysplasia, irrespective of villous components, or any serrated polyp <10 mm without dysplasia). Patients with CRC were included in the high risk group. Withdrawal time was defined as the time from identification of the cecum landmark to scope removal from the patient. Clean withdrawal time was the actual time spent inspecting the mucosa (withdrawal time minus time spent washing, suctioning, or performing operative procedures).

Outcome measures

The primary outcome measure was ADR, defined as the proportion of patients with at least one adenoma (per-patient analysis). Secondary outcomes were as follows: advanced ADR, defined as the proportion of patients with at least one advanced adenoma on per-patient analysis; adenoma per colonoscopy (APC), defined as the number of total adenomas in each group divided by the total number of colonoscopies (per-polyp analysis); total polyps (i.e. polyps, adenomas, advanced adenomas, and sessile serrated lesions [SSLs]) per patient, defined as the total number of detected lesions in each group divided by the total number of patients (per-polyp analysis); the number of proximal and flat adenomas, defined as the total number of detected lesions in each group divided by the total number of patients (per-polyp analysis); non-neoplastic polyp resection rate; withdrawal time.

Statistical analysis

Based on the observed mean prevalence of adenomas (34%) among patients undergoing colonoscopies at our centers within the past 12 months, a sample size of 372 individuals per arm could allow for an 80% power ($\alpha = 0.05$; two-sided test) to show a 10% absolute increase (from 34% to 44%) in the adenoma detection rate in the TXI arm (primary end point). Calculating a 5% drop-out rate, the projected enrollment was of 744 patients [21].

The primary outcome analysis was the comparison of ADR between the two study arms. The analysis was based on study patients with available data after randomization in the intention-to-treat analysis (i.e. patients who were randomized and underwent colonoscopy). A per-protocol analysis including only patients who had successful cecal intubation and adequate bowel preparation (defined as BBPS score ≥6 and all segmental BBPS score ≥2) was also performed.

Categorical variables were described by frequency counts and percentages. Quantitative variables were described by means and SDs. Chi-squared and *t* tests were used to compare categorical and continuous variables between the two groups, respectively.

Multivariable estimations of prevalence ratios were obtained using log-binomial regression; adjustments were made for age, sex, colonoscopy indication, and BBPS score. Differences in detection rates between the study arms were expressed as relative risk (RR) with 95%CIs. We also estimated the prevalence of adenomas by colonic location (distal, including the descending sigmoid colon, and rectum) vs. proximal colon (including cecum, ascending, and transverse colon), and by morphology (Paris classification: polypoid vs. nonpolypoid lesions).

The overall APC was calculated, as well as APC stratified according to polyp morphology, size, and colon location. Using Poisson regression, we calculated incidence rate ratios to assess the relationship between study arm, age, sex, and colonoscopy indication.

All regression models were fitted with a random intercept for the effects of clusters (i.e. the study centers). Study variables (i.e. study arm, age, sex, colonoscopy indication, and BBPS score) were included in the models as fixed effects (i.e. not varying by cluster).

A *P* value of <0.05 was considered statistically significant. All statistical analyses were performed using R software version 3.5.1 (2018–07–02; R Foundation for Statistical Computing, Vienna, Austria).

Results

Study population

A total of 766 patients were considered eligible for the study between September 2021 and May 2022. After the exclusion of 19 patients (▶ **Fig. 2**), the study cohort included 747 randomized patients (mean age 62.3 [SD 9.5] years; 50.2% male). Of these, 375 were allocated to the TXI group, and 372 to the WLI group. No difference in clinical indications was found between the two groups (▶ **Table 1**), with primary CRC screening or post-polypectomy surveillance in 39.8% (297/747), work-up following FIT-positive result in 44.6% (333/747), and gastrointestinal symptoms in 15.7% (117/747). No difference between TXI and WLI groups was observed in terms of adequate cleansing (BBPS ≥2 in all colonic segments; 363/375 [96.8%] vs. 351/372 [94.4%]) and cecal intubation rate (366/375 [97.6%] vs. 365/372 [98.1%]). Mean clean withdrawal times were 7.7 minutes and 8.0 minutes in the TXI and WLI groups, respectively ($P = 0.02$). The mean number of polyps of any histology per colonoscopy was higher in the TXI group than the WLI group (1.5 vs. 1.1).

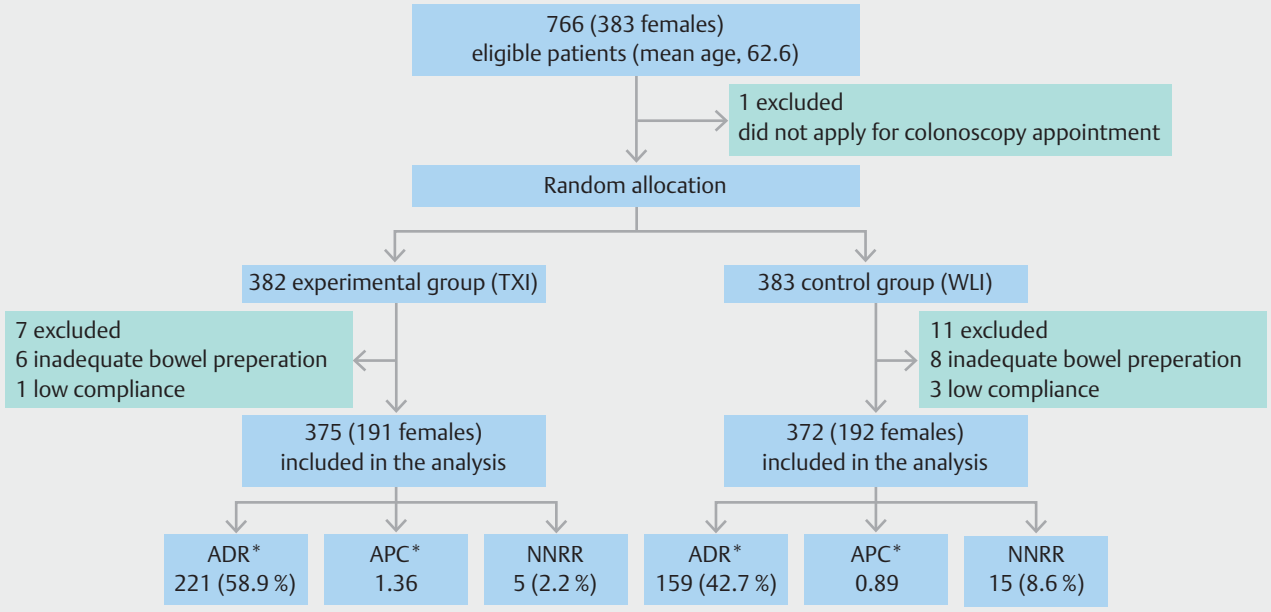
Per-patient analysis

ADR (primary outcome)

In the intention-to-treat analysis, ADR was 58.9% (221/375) in the TXI group and 42.7% (159/372) in the WLI group (RR 1.38; 95%CI 1.20–1.59). In the intention-to-treat analysis, superiority of TXI over WLI in ADR was met at a two-sided significance level of 0.05 ($P < 0.001$).

The association between ADR and study group remained significant after adjusting for sex, patient age, colonoscopy indication, study center, and BBPS score in a random effect model (RR 1.35; 95%CI 1.17–1.56) (**Table 1 s**). The per-protocol analysis produced similar results to the intention-to-treat analysis (**Table 2 s**).

Complete characteristics of patients according to polyp features are shown in ▶ **Table 2** and ▶ **Fig. 3**.



▶ **Fig. 2** Study flow chart including clinical outcomes. [1]Relative Risk 1.38 (1.20–1.59). [2]Incidence risk ratio 1.53 (1.25–1.88). ADR, adenoma detection rate; APC, mean number of adenomas per colonoscopy; NNRR, non-neoplastic resection rate.

▶ **Table 1** Patients' characteristics according to study group.

Variable	TXI (n = 375)	WLI (n = 372)
Age, mean (SD), years	62.8 (9.6)	62.2 (9.3)
Sex, n (%)		
▪ Female	187 (49.9)	184 (49.5)
▪ Male	187 (49.9)	188 (50.5)
Indication for colonoscopy, n (%)		
▪ FIT +	167 (44.5)	166 (44.6)
▪ Primary CRC screening	80 (21.3)	82 (22.0)
▪ Surveillance	68 (18.1)	67 (18.0)
▪ Symptoms	60 (16.0)	57 (15.3)
Cecal intubation, n (%)	366 (97.6)	365 (98.1)
BBPS score, mean (SD)		
▪ Right colon	2.5 (0.6)	2.4 (0.6)
▪ Transverse	2.6 (0.5)	2.6 (0.5)
▪ Left colon	2.7 (0.5)	2.6 (0.5)
Adequate preparation[1], n (%)	363 (96.8)	351 (94.4)
Clean withdrawal time[2], mean (IQR), minutes	7.7 (7.0–8.0)	8.0 (7.0–9.2)

TXI, texture and color enhancement imaging; WLI, white-light imaging; FIT, fecal immunochemical test; CRC, colorectal cancer; BBPS, Boston Bowel Preparation Scale.
[1] BBPS ≥ 2 in all segments.
[2] Time spent inspecting the mucosa (withdrawal time minus time spent washing, suctioning, and therapeutic procedures).

The proportion of patients with adenomas < 10 mm was significantly higher in the TXI group than in the WLI group (37.1 % vs. 24.5 %), whereas no statistically significant differences were observed for those with adenomas ≥ 10 mm. The difference between the two groups was significant for both ≤ 5 mm and 6–9 mm adenomas (▶ **Table 2**, ▶ **Fig. 3**).

A significantly higher proportion of polypoid (40.3 % vs. 28.0 %) and nonpolypoid adenomas (36.3 % vs. 27.4 %) was found in the TXI group (▶ **Table 2**, ▶ **Fig. 3**).

The proportion of patients with proximal adenomas was higher in the TXI group (38.1 % vs. 29.8 %); similarly, the proportion of patients with distal adenomas was higher in the TXI group (38.4 % vs. 26.3 %) (▶ **Table 2**, ▶ **Fig. 3**).

Regarding multiplicity, 214 patients (28.6 %) had ≥ 2 adenomas: the percentages of patients with multiple adenomas in the TXI and WLI groups were 32.5 % and 24.7 %, respectively (RR 1.32; 95 %CI 1.05–1.66).

No difference in the proportion of patients with at least one SSL was found between the two groups (12.0 % vs. 9.1 %).

Histopathological classification according to post-polypectomy surveillance recommendations

A total of 100 patients were categorized as high risk according to the ESGE guideline (repeat colonoscopy 3 years after complete removal of polyps) in the TXI group compared with 74 in the control group, corresponding to a detection of high risk patients of 26.7 % and 19.9 %, respectively (RR 1.34; 95 %CI 1.03–1.74). When looking at differences among specific high risk factors, we found that a significant increase in multiplicity (more than four adenomas) was found among patients in the TXI group, whereas rates of patients with high grade dysplasia or lesions ≥ 10 mm were similar between the two groups (**Table 3 s**).

▶ **Table 2** Per-patient analysis. Detection rate according to study group and lesion features (intention-to-treat analysis).

Per-patient analysis	TXI (n = 375) n (%)	WLI (n = 372) n (%)	RR (95 %CI)	*P* value
Histology				
▪ All adenoma/SSA or CRCs (ADR)	221 (58.9)	159 (42.7)	1.38 (1.20–1.59)	<0.001
▪ High risk polyp group	100 (26.7)	74 (19.9)	1.34 (1.03–1.74)	0.03
▪ Low risk polyp group	121 (32.3)	85 (22.8)	1.41 (1.11–1.78)	0.004
▪ SSLs	45 (12.0)	34 (9.1)	1.31 (0.86–2.01)	0.21
▪ SSLs with dysplasia	15 (4.0)	7 (1.9)	2.13 (0.91–5.49)	0.10
▪ Non-neoplastic polyps	28 (7.5)	32 (8.6)	0.87 (0.53–1.41)	0.57
Size category[1]				
▪ ≤ 5 mm	85 (22.7)	54 (14.5)	1.42 (1.16–1.73)	0.01
▪ 6–9 mm	54 (14.4)	38 (10.2)	1.36 (1.01–1.83)	0.047
▪ ≥ 10 mm	82 (21.9)	66 (17.7)	1.23 (0.92–1.65)	0.16
Morphology				
▪ Polypoid	151 (40.3)	104 (28.0)	1.43 (1.17–1.75)	<0.001
▪ Nonpolypoid[2]	136 (36.3)	102 (27.4)	1.30 (1.05–1.61)	0.02
Location				
▪ Proximal colon[3]	143 (38.1)	111 (29.8)	1.28 (1.05–1.57)	0.02
▪ Distal colon	144 (38.4)	98 (26.3)	1.46 (1.18–1.80)	<0.001

TXI, texture- and color-enhancing imaging; WLI, white-light imaging; RR, crude relative risk; SSA, sessile serrated adenoma; CRC, colorectal cancer; ADR, adenoma detection rate; SSL, sessile serrated lesion.
[1] According to the size of the largest neoplastic lesion. There was one missing value in the control group.
[2] There was one missing value in the control group. Including 35 (9.3 %) TXI and 30 (8.1 %) control group cases who had synchronous polypoid adenomas.
[3] Including 66 (17.6 %) TXI and 50 (13.4 %) control cases who had synchronous adenomas in the distal colon.

Per-polyp analysis

In the 226 and 174 patients who underwent polyp resection in the TXI and WLI groups, 541 and 369 adenomatous polyps were detected, respectively. Characteristics of the detected polyps and cancers are summarized in **Table 2 s, Table 4 s,** and **Table 5 s**.

The overall APC was 1.10 (SD 1.59), and it was significantly higher in the TXI group than in the control group (1.36 [SD 1.79] vs. 0.89 [SD 1.35]; incident rate ratio 1.53, 95 %CI 1.25–1.88) (▶ **Table 3**). The APC was also analyzed according to polyp characteristics, as detailed in ▶ **Table 3** and **Table 5 s**.

A statistically significant increase in APC between the two groups was found for polypoid and nonpolypoid lesions, as well as for both proximal and distal locations. The difference between groups in APC was significant for small/diminutive (< 10 mm) adenomas, but not for large adenomas (≥ 10 mm). The association between the APC and study group remained significant after adjusting for age, sex, indication, center, and BBPS score in a random effect model (IRR 1.48, 95 %CI 1.22–1.80) (**Table 6 s**).

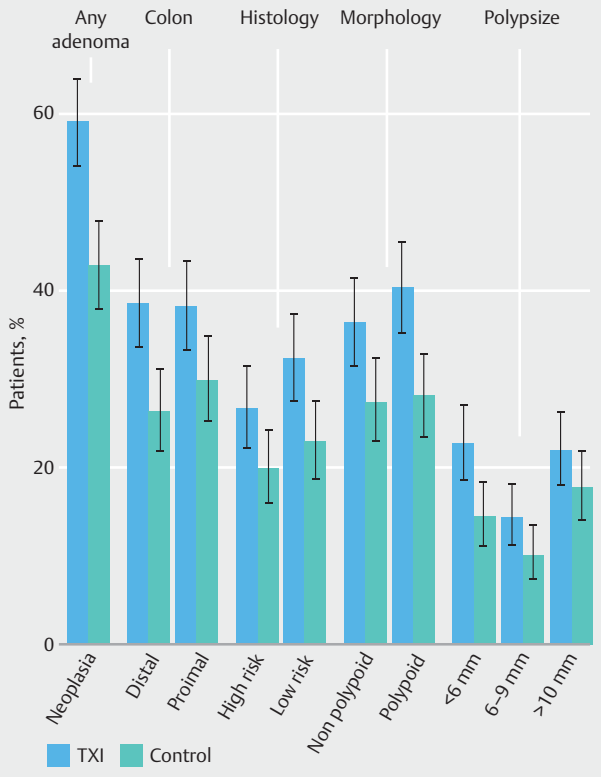
Non-neoplastic resection rate

Overall, 400 of 747 patients (53.5 %) underwent polyp resections. Of these, 20 (5.0 %) did not have histologically proven adenomas, SSLs, or CRCs. The non-neoplastic resection rates (per patient) were 5/226 (2.2 %) in the TXI group and 15/174 (8.6 %) in the WLI group (RR 0.26, 95 %CI 0.09–0.65) (▶ **Fig. 2**).

Discussion

According to our international, multicenter, randomized trial, colonoscopy using TXI showed a 38 % increase in colorectal neoplasia detection compared with WLI colonoscopy as measured by ADR, the main proxy of endoscopist proficiency. In addition, TXI showed a 34 % increase in high risk adenoma detection compared with WLI. This translates in a number-needed-to-scope with TXI imaging of 6.2 colonoscopies to find an additional patient with an adenoma, and 14.7 to find an additional patient with a high risk adenoma.

The clinical relevance of these findings is manifold. The detection and removal of colorectal neoplasia is the main objective of colonoscopy, especially among patients participating in organized CRC screening programs, who were widely represented in the study cohort. First, we found that an embedded and



▶ **Fig. 3** Per-patient adenoma detection rate (ADR) and ADR by adenoma features. TXI, texture and color enhancement imaging; WLI, white-light imaging.

▶ **Table 3** Per-polyp analysis: mean number of adenomas per colonoscopy and Poisson regression analysis by polyp characteristics among study patients.

Per polyp analysis	APC (SD)		IRR[1] (95 %CI)
	TXI	WLI	
All neoplasia	1.36 (1.79)	0.89 (1.35)	1.53 (1.25–1.88)
Morphology			
▪ Polypoid	0.77 (1.33)	0.47 (0.88)	1.66 (1.28–2.17)
▪ Nonpolypoid	0.58 (0.97)	0.42 (0.83)	1.38 (1.06–1.79)
Polyp size			
▪ <10 mm	0.94 (1.41)	0.74 (1.19)	1.28 (1.02–1.60)
▪ ≥10 mm	0.29 (0.71)	0.26 (0.69)	0.91 (0.63–1.32)
Colon location			
▪ Proximal	0.76 (1.26)	0.55 (1.05)	1.37 (1.06–1.77)
▪ Distal	0.61 (1.04)	0.34 (0.62)	1.79 (1.38–2.33)

TXI, texture and color enhancement imaging; WLI, white-light imaging; IRR, (crude) incidence risk ratio; APC, adenomas per colonoscopy.
[1] Estimates from a random-effects model controlling clustering within study center.

new advanced imaging technology, with highly impactful modifications of the light spectrum, significantly improved colonoscopy outcomes while not affecting withdrawal time or hindering the normal workflow of the examination. Indeed, although a recent meta-analysis showed that NBI used in the withdrawal phase of colonoscopy significantly increased ADR [14], this finding was limited to patients with the "best" bowel preparation (BBPS 9), whereas results were nonsignificant when patients with "adequate" preparation (BBPS ≥ 6) were included in the analysis. This was probably because NBI is affected by luminal content, which can hamper the endoscopic view and neoplasia detection, and provides benefit only in patients with perfect bowel cleansing. In addition, the use of NBI is known to result in reduced brightness compared with WLI. TXI appears to have overcome these issues, being very similar to standard WLI, and does not seem to be hindered by suboptimal bowel preparation as the appearance of luminal content is unchanged. This result is in line with the recent randomized controlled trial evaluating linked color imaging modality, which found a 19 % increase in ADR when using linked color imaging vs. high definition WLI [13]. This suggests that for polyp detection, the use of any imaging technology that increases contrast and brightness of lesions while not changing the appearance of luminal content is more practical and usable than blue light imaging technologies.

Second, the increase in ADR was consistent across different colonic locations and polyp sizes. Indeed, not unexpectedly, the most significant increase in neoplasia detection was shown in diminutive colorectal polyps, alongside an increase in small <10 mm polyps. It could be argued that this increased detection is unlikely to impact the future risk of CRC incidence and death of the single patient, although most interventions seeking ADR increase are more efficacious in the small polyp size range rather than in larger adenomas [11]. Nonetheless, this can have significant impacts on both clinical management of the single patient and in the organization of population-based screening programs. When considering the large burden of surveillance colonoscopies and the recommendations to send low risk patients back to screening in a time range of 5–10 years [20, 22], the baseline removal of a diminutive adenoma might confer an increased protection over a longer time span, reducing the need for cumbersome endoscopic surveillance. In addition, recent large cohort studies have shown that the inverse relationship between ADR and CRC outcomes is consistent also for small ADR increases in high detectors [23]. On the other hand, applying the new ESGE post-polypectomy surveillance criteria for low and high risk polyps [20], TXI showed a significantly higher proportion of patients classified as high risk and requiring endoscopic short-term surveillance compared with WLI. Although this increase seems to be explained by an increase in patients with multiplicity (>4 small adenomas), which

seem to harbor a relatively small increase in subsequent CRC risk, the recommended surveillance interval for these patients currently remains 3 years.

Third, we did not observe an increase in serrated polyp detection rate in the TXI group. This was somewhat surprising as an increase in image brightness and contrast would seem a straightforward way to increase the detection of subtle and cloudy-like lesions that are known to be difficult to spot during standard endoscopy with WLI. However, these specific characteristics seem to benefit less from this type of image enhancement than adenomas, which are reddish and have clear borders. It must be noted that in our study, the SSL detection rate was significantly higher than average SSL prevalence in previous studies [24], and that a trend toward increased detection of SSLs was found in the TXI group. This may reflect an ever-increasing awareness of SSL detection and removal, and could explain the lack of significance in the subanalysis, along with the likely underpowered sample size for this secondary outcome.

Our study has limitations. First, although the imaging processor (Evis X1) was the same across all study centers and endoscopists, we used both 1000 and 190/290 series endoscopes, all of which are compatible with high definition and TXI but with differences in image quality (high definition vs. 4K); however, this may mean that the results represent the worst-case scenario, which is likely to improve when only 4K definition scopes are used. In addition, the impact of 4K definition on lesion detection is currently unknown but could be minimal, as the difference in quality is hard to distinguish with the human eye in standard-sized monitors. Second, in contrast to previous detection studies, we decided to apply recently updated ESGE guidelines on surveillance after polyp resection to classify patients into high and low risk. Although this may reduce the opportunity for our results to be compared with previous studies using other imaging modalities, it should better reflect clinical practice and screening program policies as they are now the European standard. In addition, using current ESGE guidelines may also represent a worst-case scenario, as the criteria for high risk polyps are restricted; it could be hypothesized that the number of high risk patients and the consequent significant increase in the intervention arm would only be higher if using the previous classification. Third, it was impossible to blind the operator to the group allocation; however, this is a well-known bias of trials in colonoscopy, and a "new-technology bias", where the impact of a newly introduced technology is overinflated in the first studies evaluating it, may have been introduced. Although this cannot be excluded, randomization should have limited potential bias. In addition, TXI technology is available at no additional cost and can be used at will by the operator, limiting the negative effects that an overestimation of performance may have on any cost and time investment. Further studies might strengthen or deflate these results and are warranted. Finally, our study was largely performed in patients at higher risk of disease, as many patients underwent colonoscopy following a positive FIT result within an organized screening program, leading to an ADR in the control group that was higher than expected. This finding can actually be reassuring as ADR increase in the intervention group was nonetheless found to be significant and may increase the generalizability of our results to both post-FIT and primary colonoscopy settings. In addition, randomization guaranteed an equal representation of post-FIT colonoscopies in both groups.

In conclusion, this multicenter randomized trial showed a positive impact of TXI vs. standard high definition WLI on the detection of diminutive and small adenomas, but not large adenomas or high grade dysplasia, suggesting potential benefits of its use in everyday clinical practice.

Competing Interests

The authors declare that they have no conflict of interest.

Clinical trial

Trial Registration: ClinicalTrials.gov | Registration number (trial ID): NCT04892966 | Type of study: Prospective, Randomized, Multicentric

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