

# The location-based resect and discard strategy for diminutive colorectal polyps: a prospective clinical study

## Authors

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## ABSTRACT

**Background** Clinical implementation of the resect-and-discard strategy has been difficult because optical diagnosis is highly operator dependent. This prospective study aimed to evaluate a resect-and-discard strategy that is not operator dependent.

**Methods** The study evaluated a resect-and-discard strategy that uses the anatomical polyp location to classify colonic polyps into non-neoplastic or low risk neoplastic. All rectosigmoid diminutive polyps were considered hyperplastic and all polyps located proximally to the sigmoid colon were considered neoplastic. Surveillance interval assignments based on these a priori assumptions were compared with those based on actual pathology results and on optical diagnosis. The primary outcome was  $\geq 90\%$  agreement with pathology in surveillance interval assignment.

**Results** 1117 patients undergoing complete colonoscopy were included and 482 (43.1%) had at least one diminutive polyp. Surveillance interval agreement between the location-based strategy and pathological findings using the 2020 US Multi-Society Task Force guideline was 97.0% (95% confidence interval [CI] 0.96–0.98), surpassing the  $\geq 90\%$  benchmark. Optical diagnoses using the NICE and Sano classifications reached 89.1% and 90.01% agreement, respectively ( $P < 0.001$ ), and were inferior to the location-based strategy. The location-based resect-and-discard strategy allowed a 69.7% (95%CI 0.67–0.72) reduction in pathology examinations compared with 55.3% (95%CI 0.52–0.58; NICE and Sano) and 41.9% (95%CI 0.39–0.45; WASP) with optical diagnosis.

**Conclusion** The location-based resect-and-discard strategy achieved very high surveillance interval agreement with pathology-based surveillance interval assignment, surpassing the  $\geq 90\%$  benchmark and outperforming optical diagnosis in surveillance interval agreement and the number of pathology examinations avoided.

## Introduction

Optical polyp diagnosis based on image-enhanced endoscopy (IEE) allows for classification of diminutive polyps into neoplastic and non-neoplastic [1]. As the majority of colorectal polyps found during colonoscopies are diminutive ( $\leq 5$  mm) and have a low risk for harboring advanced histology [2, 3], replacing histopathology evaluation with optical diagnosis has been deemed a cost-effective and safe alternative [3–5]. This potential for cost-savings has led groups such as the American Society for Gastrointestinal Endoscopy (ASGE), the British Society of Gastroenterology (BSG), and the European Society of Gastrointestinal Endoscopy (ESGE) to issue guidelines to support and guide the practical implementation of the “resect-and-discard” strategy [6–9].

The ASGE Technology Committee, in its Preservation and Incorporation of Valuable endoscopic Innovations (PIVI) statement, recommended the implementation of the resect-and-discard strategy if it reaches  $\geq 90\%$  agreement with histopathology in determining post-polypectomy surveillance intervals [6]. However, the ASGE position paper emphasized that optical diagnosis should be performed by adequately trained, monitored, and audited endoscopists to increase the accuracy of optical diagnosis and the proportion of high confidence histology predictions [6, 10, 11]. The ESGE considers training in optical diagnosis as an important prerequisite for the implementation of IEE and recommends the use of validated classification systems to support the use of optical diagnosis with advanced endoscopic imaging, along with sufficient photodocumentation [9, 12].

Although the concept of resect-and-discard presents a great potential to improve colonoscopy practice, its widespread clinical implementation has not been achieved. A recent survey revealed that endoscopists have failed to adopt the use of the resect-and-discard strategy in clinical practice because of concerns about making the wrong diagnosis and subsequently an erroneous surveillance interval assignment, with its potential medicolegal repercussions [13].

To circumvent the problems associated with optical diagnosis, we developed a simplified and operator-independent resect-and-discard strategy. This location-based resect-and-discard (LBRD) strategy does not rely on optical diagnosis and does not require any special operator skills to be acquired or audited. Our group has recently published a retrospective study evaluating this concept [14]. The aim of the current prospective study was to determine how the LBRD strategy would perform in a prospective cohort when tested against optical diagnosis.

## Methods

### Study setting and population

The study population consisted of 1187 patients who presented at Montréal University Hospital Center (CHUM) between May 2017 and December 2018 for elective colonoscopy. **Fig. 1 s** (see online-only Supplementary material) shows the flowchart of study participant selection. Patients between 45 and 80

years of age undergoing screening, surveillance, or diagnostic colonoscopies were eligible to be included in the study. Patients with known inflammatory bowel disease, active colitis, coagulopathy, familial polyposis syndrome, poor general health (American Society of Anesthesiologists class  $>3$ ), undergoing emergency colonoscopies (procedures in the emergency or intensive care unit or patients with active upper or lower gastrointestinal bleeding), missing or non-definitive information on demographic or colonoscopy characteristics, and age out of the predefined study range were excluded ( $n=70$ ). Of the 1117 patients included in the study, 635 were found to have only larger polyps ( $>5$  mm) or a normal colonoscopy. A total of 921 diminutive polyps were detected and 482 patients (43.1%) had at least one diminutive polyp.

The study was approved by the Research Ethics Board of CHUM (CERCHUM; Research Ethics Committee number, CER 16.367). Informed consent for study participation was obtained from each patient before colonoscopy.

### Study procedure

All patients were prepared for colonoscopy using a standard bowel cleansing preparation. A research assistant documented standard colonoscopy quality metrics such as cecal intubation, bowel preparation score (Boston Bowel Preparation Scale), and withdrawal time during the procedure. The size, location, and morphological characteristics (using the Paris endoscopic classification [15]) of each detected polyp were documented. All detected polyps were removed and sent for histopathology evaluation as per the institutional standard of care.

### Histopathological assessment

The histopathological assessment was performed by board-certified pathologists at CHUM, according to current practices and institutional standards for all polyps. Polyps were categorized as neoplastic or non-neoplastic. Neoplastic polyps were defined as all adenomatous polyps, including cancerous, and all sessile serrated adenomas/polyps (SSA/Ps) [16]. Advanced adenomas were defined as all diminutive polyps with a villous component or exhibiting high grade dysplasia in the absence of invasive colorectal cancer (CRC) [4].

### Location-based resect-and-discard strategy

The LBRD strategy was applied in the following manner: all diminutive polyps anatomically located in the rectosigmoid colon were a priori considered to be non-neoplastic (hyperplastic polyps), while all diminutive polyps located in the proximal colon (from cecum to descending colon) were considered neoplastic (low risk adenomatous polyps). This model therefore uses the anatomical location of a diminutive polyp as the sole criterion for predicting histology (neoplastic vs. non-neoplastic) and does not depend on optical diagnosis criteria.

### Optical diagnosis and classification systems

Ten experienced endoscopists performed the colonoscopies. All endoscopists underwent formal training in narrow-band imaging (NBI) optical diagnosis of colorectal polyps before including their first study patient. All detected diminutive

polyps underwent IEE using i-Scan OE (Pentax Medical, Tokyo, Japan) and were classified according to their surface and vascular patterns using three different optical diagnosis classification systems. NBI magnification was available to be used at the endoscopists' discretion.

During optical diagnosis, each endoscopist made a real-time prediction of each polyp histology according to the NBI International Colorectal Endoscopic (NICE) [17], Workgroup serrated polypS and Polyposis (WASP) [18], and Sano [19–21] classification systems [22]. A research assistant documented the polyp characteristics, pathology predictions, and the endoscopists' level of confidence (low or high) in their histology prediction during the procedure. Patients with missing documentation on optical diagnosis for diminutive polyps or on histopathology reports (i.e. polyp resected but not retrieved [2.3%]) were excluded from the analyses.

### Surveillance interval assignment

Each patient was assigned a surveillance interval based on: (a) the LBRD strategy; and (b–d) real-time optical diagnosis using the (b) NICE classification, (c) Sano classification, and (d) WASP classification. For calculation of the surveillance intervals with all of the strategies, all concomitant adenomas >5 mm, poor bowel preparation, and positive family history of CRC were considered in the final decision.

After histopathological assessment of the polyps, surveillance intervals were assigned based on histopathological outcomes in order to obtain a reference standard. Both the 2012 and 2020 US Multi-Society Task Force (USMSTF) guidelines were used for calculation of the pathology-based surveillance intervals to address the impact of changes in the new guideline on actual practice [4, 23].

Surveillance interval assignments according to the LBRD strategy and optical diagnosis strategies were then compared with the pathology-based assignments. If the guideline suggested a time period for the surveillance interval, the longer end of the interval was used (e.g. 10 years for a surveillance interval of 5–10 years) for comparison and determination of the agreement between pathology and the LBRD/optical diagnosis strategies.

### Study outcomes

The primary outcome of the study was the surveillance interval agreement of the LBRD strategy when compared with the pathology-based reference standard for the complete cohort of patients and for a subcohort of patients with adequate bowel preparation [6]. The surveillance intervals for optical diagnosis using i-Scan and the different validated classification systems (NICE, Sano, and WASP) were also compared with the pathology-based intervals.

Secondary outcomes were: the diagnostic properties of the LBRD strategy and optical diagnoses, including accuracy, sensitivity, specificity, positive predictive value (PPV), and, particularly, negative predictive value (NPV), to determine whether the ASGE PIVI benchmark of  $\geq 90\%$  NPV for the diagnosis of neoplastic diminutive rectosigmoid polyps could be reached [6].

Additional secondary outcomes were the calculation of the proportion of patients who could have received an immediate notification of surveillance interval and the proportion of histopathology examinations that could have been avoided using the different strategies.

### Sample size calculation

The sample size calculation for our primary outcome was based on the surveillance interval agreement of the LBRD strategy compared with the pathology-based surveillance interval recommendations. We assumed that the LBRD strategy could achieve a 92.5% agreement with pathology-based recommendations. For the lower margin of the 95% confidence interval (CI) to be above 90% (quality benchmark proposed by the ASGE), we needed to enroll at least 480 patients in whom at least one diminutive polyp was found. Considering a prevalence of 45% neoplastic and non-neoplastic diminutive polyps in our study cohort and a potential rate of about 5% of pathology specimens that could not be retrieved from the colon, we therefore needed to screen at least 1091 patients.

### Statistical analyses

The study reports diagnostic accuracy following the STAndards for the Reporting of Diagnostic accuracy studies (STARD) guidelines [24]. Descriptive statistics are presented as numbers and frequencies for categorical variables, and mean (standard deviation [SD]) or median (range) for continuous variables with normal and non-normal distribution, respectively, as necessary.

The surveillance interval agreement between the LBRD strategy, optical diagnosis, and histopathology results are presented as proportions with 95% CIs. Agreements among the different strategies were compared using McNemar's test with a two-tailed significance level of  $P < 0.05$ . The proportions of correct and incorrect (shorter or longer) surveillance intervals compared with the reference standard are also presented.

The diagnostic properties of optical diagnosis and the LBRD strategy were calculated, including sensitivity, specificity, PPV, NPV, and accuracy. Based on the prior definition of the 2020 USMSTF guideline, we categorized diminutive polyps into hyperplastic and adenomas.

The proportion of patients who could have received immediate surveillance interval recommendations according to the different strategies were calculated as follows: (a) reference value – the total number of patients without polyp identification during colonoscopy (normal colonoscopy) divided by the total number of patients; (b) LBRD strategy – the sum of the number of patients without any polyps plus the patients with only diminutive polyps divided by the total number of patients; (c) optical diagnosis using each classification – the sum of the number of all patients without any polyps plus the patients with only diminutive polyps optically diagnosed with high confidence divided by the total number of patients.

The proportion of pathology examinations needed was calculated as follows: (a) reference value – the number of polyps sent for histopathology evaluation divided by the total number of polyps; (b) LBRD strategy – the number of non-diminutive

polyps divided by the total number of polyps; (c) optical diagnosis using each classification – the number of diminutive polyps optically diagnosed with low confidence divided by the total number of polyps. All measurements were presented with 95% CIs.

SPSS version 26.0 (IBM Corp., Armonk, New York, USA) and MedCalc version 19.4 (MedCalc Software bv, Ostend, Belgium; <https://www.medcalc.org>) were used for these analyses.

## Results

### Patient, procedures, and polyp characteristics

A total of 1117 patients (median age 63.3 [range 45.0–80.9] years; 52.3% men) were prospectively enrolled into the study.

► **Table 1** presents details on the demographic and clinical characteristics of the study patients. The majority of colonoscopies were performed for the indications of screening (30.7%) and adenoma surveillance (20.4%).

The polyp and adenoma detection rates were 58.0% and 38.5%, respectively. Of the 921 diminutive polyps detected, 906 (98.4%) were removed and 885 (96.1%) were retrieved. A total of 393 polyps (42.7%) were located in the rectosigmoid. Advanced histopathology was detected in 14 diminutive polyps (1.5%). All polyps reported as “intramucosal cancer” in the histopathology report were considered high grade dysplasia to avoid confusion with CRC invading the submucosal layer [25]. No high grade dysplasia or cancer was detected among the patients with at least one diminutive polyp.

### Surveillance interval agreement

In the whole cohort of patients with valid surveillance interval calculations, the agreement between the location-based and pathology-based determination of surveillance interval was 97% (95%CI 0.96–0.98) when using the 2020 USMSTF guidelines and 93.6% (95%CI 0.92–0.95) when using the 2012 USMSTF guidelines (significant difference between agreements according to the 2020 and 2012 guidelines; McNemar’s test,  $P < 0.001$ ). Moreover, the surveillance interval agreement of the LBRD strategy and pathology using the 2020 guideline in patients with adequate bowel preparation was 96.6% (95%CI 0.95–0.98). The detailed agreement values are shown in ► **Fig. 1**.

Overall, use of the different classification systems for optical diagnosis did not affect the surveillance interval agreement. The agreements between the surveillance intervals determined by optical diagnosis using the NICE classification and pathology using the 2020 and 2012 USMSTF guidelines were 89.1% (95%CI 0.87–0.91) and 90.1% (95%CI 0.88–0.92), respectively. Optical diagnosis using the Sano classification reached the ASGE PIVI benchmark using both the 2012 and 2020 USMSTF guidelines. However, optical diagnosis using the WASP classification did not reach the recommended benchmark using either USMSTF guideline (87.9% and 86.8%). Moreover, none of the optical classification systems could reach the recommended benchmark of 90% agreement with pathology-based surveillance interval assignment in the cohort of patients with adequate bowel preparation (NICE classification system 88%

► **Table 1** Demographic and clinical characteristics of the 1117 study patients and characteristics of the 921 detected diminutive (1–5 mm) polyps.

Demographic characteristics	
Age, median (range), years	63.3 (45.0–80.9)
Sex, male, n (%)	584 (52.3)
ASA class <sup>1</sup> , n (%)	
▪ 1	494 (44.2)
▪ 2	539 (48.3)
▪ 3	83 (7.4)
Anticoagulant use, n (%)	245 (21.9)
Family history of CRC in first-degree relatives <sup>1</sup> , n (%)	319 (28.6)
Colonoscopy characteristics <sup>1</sup>	
Colonoscopy indication, n (%)	
▪ Screening	343 (30.7)
▪ FIT positive	38 (3.4)
▪ Adenoma surveillance	228 (20.4)
▪ CRC surveillance	39 (3.5)
▪ Anemia/bleeding	200 (17.9)
▪ Diarrhea	45 (4.0)
▪ Other <sup>2</sup>	223 (20.0)
Cecal intubation during colonoscopy <sup>3</sup> , n (%)	1051 (94.1)
Total Boston Bowel Preparation Scale $\geq 6$ <sup>4</sup> , n (%)	983 (88.0)
Patients with no polyp, n (%)	469 (42.0)
Patients with $\geq 1$ diminutive polyp, n (%)	482 (43.2)
Patients with only diminutive polyps, n (%)	388 (34.7)
Polyp characteristics	
Number of diminutive polyps, n/N (%)	921/1322 (69.7)
Anatomical location, n (%)	
▪ Cecum	71 (7.7)
▪ Ascending colon	159 (17.3)
▪ Hepatic flexure	24 (2.6)
▪ Transverse colon	141 (15.3)
▪ Splenic flexure	12 (1.3)
▪ Descending colon	121 (13.1)
▪ Sigmoid	220 (23.9)
▪ Rectum	173 (18.8)
Polyp size, mean (SD), mm	3.1 (1.3)
Histopathology result <sup>5</sup> , n (%)	
▪ Hyperplastic polyp	293 (31.8)

► **Table 1** (Continuation)

Demographic characteristics	
▪ Tubular adenoma	401 (43.5)
▪ Tubulovillous adenoma	12 (1.3)
▪ Villous adenoma	2 (0.2)
▪ Traditional serrated adenoma	3 (0.3)
▪ Sessile serrated adenoma/polyp	27 (2.9)
▪ Other benign lesions	149 (16.2)
▪ Hyperplastic or mucosal protrusion	361 (39.2)
▪ Neoplastic adenoma	445 (48.3)
▪ Adenoma with advanced histology <sup>6</sup>	14 (1.5)
Adenoma with serrated histology <sup>7</sup>	30 (3.2)
Location-based neoplastic polyps	528 (57.3)
Location-based non-neoplastic polyps	393 (42.7)
Hyperplastic diminutive polyps in proximal colon <sup>5</sup>	78 (8.5)
Hyperplastic diminutive polyps in rectosigmoid colon <sup>5</sup>	215 (23.3)

ASA, American Society of Anesthesiologists; CRC, colorectal cancer; FIT, fecal immunochemical test.

<sup>1</sup> Missing data in 1 patient (0.1%).

<sup>2</sup> Other indications included: surveillance owing to family history of CRC; pre- and post-graft or organ donation; change in bowel habits, such as constipation; post-polypectomy surveillance; screening for inflammatory diseases; to rule out diverticulitis; abdominal pain; celiac disease follow-up.

<sup>3</sup> Missing data in 2 patients (0.2%).

<sup>4</sup> Missing data in 8 patients (0.7%).

<sup>5</sup> Missing data for 34 polyps (3.7%).

<sup>6</sup> Including tubulovillous adenoma and villous adenoma (no polyp with high grade dysplasia was found).

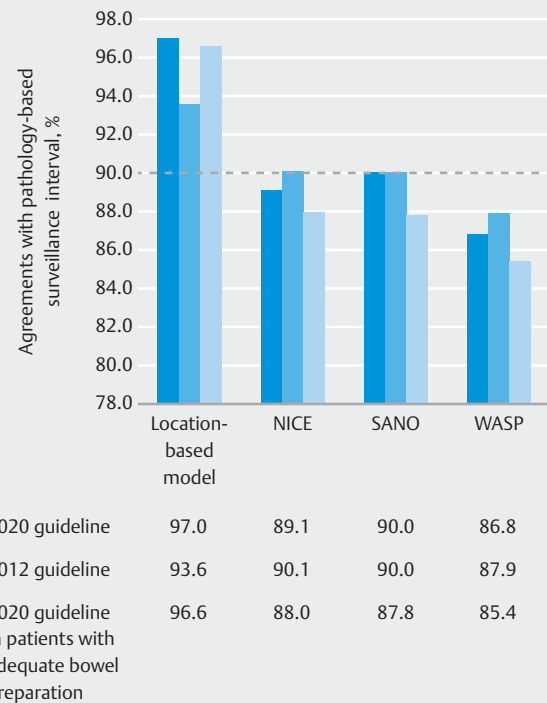
<sup>7</sup> Including sessile serrated adenoma, traditional serrated adenoma.

[95%CI 0.86–0.90]; Sano classification system 87.8% [95%CI 0.85–0.90]; WASP classification system 85.4% [95%CI 0.83–0.88]).

Surveillance interval agreement between the LBRD strategy and pathology using the 2020 guideline was significantly greater than the agreement between pathology and optical diagnosis using the NICE, Sano, and WASP classifications (McNemar's test,  $P < 0.001$  for all comparisons).

### Accuracy of surveillance interval assignment

► **Fig. 2** shows the proportion of patients with at least one diminutive polyp who were assigned correct surveillance intervals. Use of the LBRD strategy resulted in more correct surveillance intervals compared with the implementation of optical diagnosis using any of the classification systems. Using the LBRD strategy according to the 2020 USMSTF guideline, only 16 patients were assigned a longer surveillance interval, which was significantly lower than the number of patients assigned a longer surveillance interval by optical diagnosis using the WASP (52 patients), Sano (51 patients), and NICE (54 patients) classifications (number of patients calculated out of the whole co-



► **Fig. 1** Agreement of surveillance intervals between pathology outcomes and the location-based resect-and-discard strategy and optical diagnosis in all patients with valid colonoscopies and in a subcohort of patients with adequate bowel preparation. The dashed black line represents the 90% benchmark recommended by the ASGE PIVI statement.

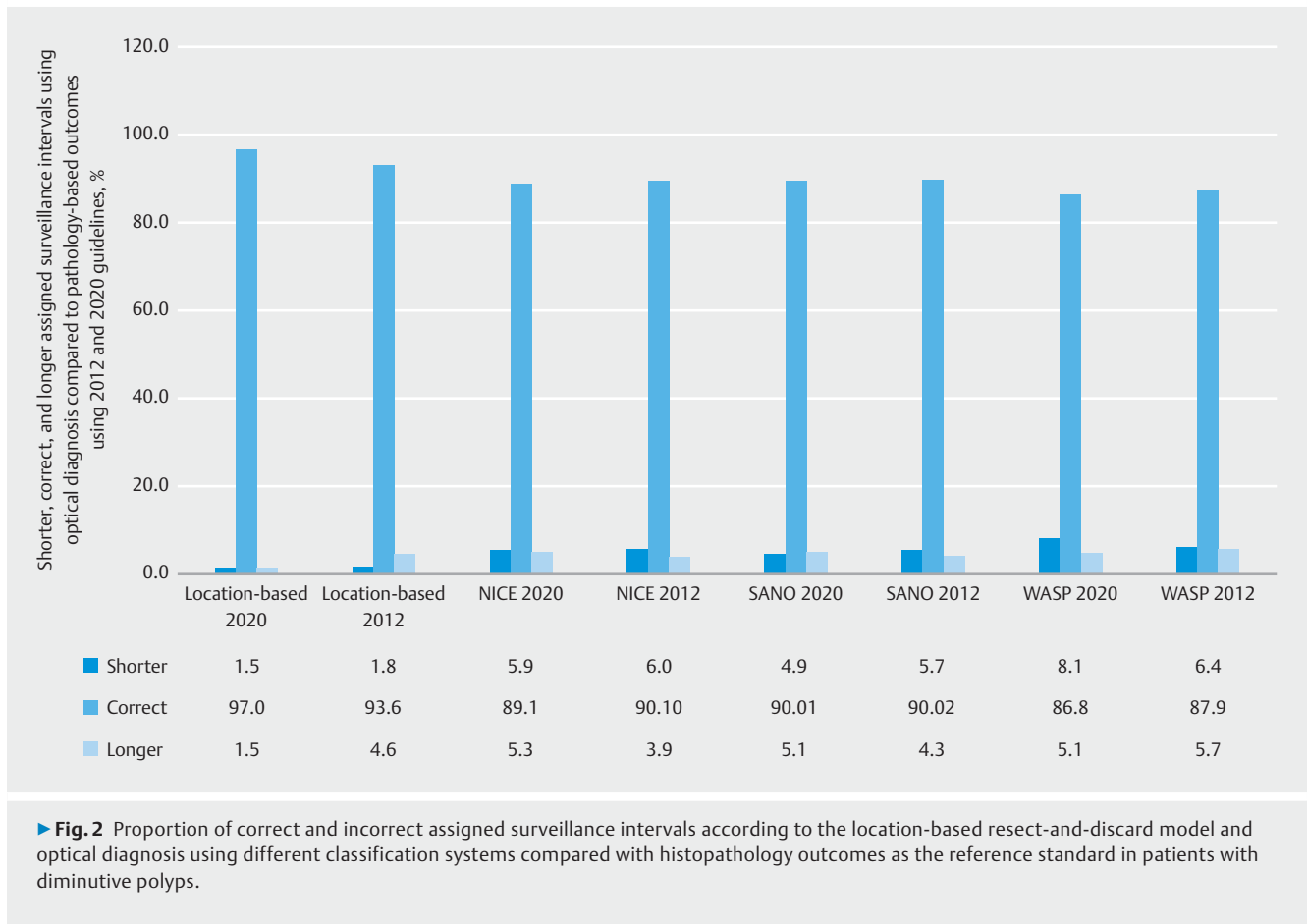
hort of patients with available pathology and optical diagnosis results).

The individual surveillance interval assignments by each method are presented in **Table 1 s**. The results of the surveillance interval agreements in the subcohort of patients with adequate bowel preparation and only diminutive polyps are presented in **Table 2 s**.

### Diagnostic properties of the location-based resect-and-discard and optical diagnosis strategies

► **Table 2** presents the accuracy of the pathology prediction when using the LBRD strategy and optical diagnosis using i-Scan.

Overall, the LBRD strategy could not surpass the ASGE PIVI benchmark of NPV  $\geq 90\%$  in distinguishing hyperplastic from neoplastic rectosigmoid polyps when including either all diminutive polyps throughout the colon or only rectosigmoid diminutive polyps. Furthermore, regardless of the classification system used for predicting polyp histology, optical diagnosis also did not reach the PIVI benchmark for distinguishing hyperplastic from neoplastic polyps.



### Location-based resect-and-discard strategy and optical diagnosis benefits

The LBRD strategy would be able provide a significantly higher proportion of patients with an immediate surveillance interval recommendation (76.7% [95%CI 0.74–0.79]) compared with optical diagnosis using the NICE and Sano classifications (67.4% [95%CI 0.65–0.70]; McNemar's test,  $P < 0.001$ ) (► **Fig. 3**).

The total reduction in histopathology examinations following the LBRD strategy was 69.7% (95%CI 0.67–0.72), which was significantly higher than the reduction following optical diagnosis using the NICE and Sano classifications (both 55.3%; McNemar's test,  $P < 0.001$ ). The reduction in histopathology examinations for optical diagnosis using the WASP classification was lower than for the NICE and Sano classification systems (McNemar's test,  $P < 0.001$ ) (► **Fig. 3**).

In a subgroup analysis of patients with at least one diminutive polyp ( $n = 482$ ), 208 patients (43.2%) would have received an incorrect diagnosis using the LBRD strategy (► **Table 3**). However, only 25 patients (5.2%) would have received an incorrect post-polypectomy surveillance interval recommendation. Among the remaining 183 patients, the majority were given the correct surveillance interval based on the presence of no more than two adenomas or hyperplastic polyps  $\leq 10$  mm in size.

### Discussion

In this prospective clinical study, the operator-independent LBRD strategy performed well and above the 90% PIVI quality benchmark required for its clinical implementation for recommending surveillance interval as a replacement for pathology-based recommendations. No cancers were missed in our cohort of patients with diminutive polyps. The risk of delayed surveillance intervals was low, implying safety for the clinical implementation of this approach. The significantly greater surveillance interval agreement of the LBRD strategy with pathology using the 2020 guideline compared with the 2012 guideline explains the improved results compared with our previously published retrospective study [14]. The LBRD strategy would allow a greater number of patients to receive surveillance interval recommendations on the same day as their colonoscopy procedure, and fewer polyps would require histopathology evaluation compared with optical diagnosis and standard colonoscopy practice.

The findings offer a scheme for facilitating and overcoming the challenges of broad implementation of a resect-and-discard strategy in routine clinical practice. The LBRD strategy uses the anatomical location as the only criterion to predict polyp histology, making the surveillance interval assignment independent of an endoscopist's skill. The approach also eliminates the need for any advanced imaging technologies, and

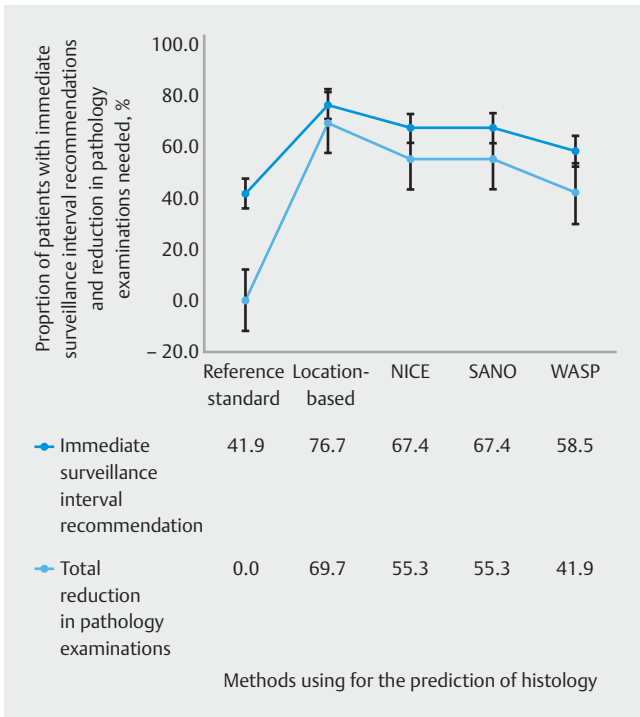
► **Table 2** Diagnostic properties of the location-based resect-and-discard strategy and optical diagnosis in patients with diminutive polyps (n=921).

	Location-based strategy <sup>1</sup>	NICE (i-Scan1)	NICE (i-Scan2)	Sano <sup>2</sup> (i-Scan2)	Sano (i-Scan3)	WASP (i-Scan2)	WASP (i-Scan3)
High confidence level, n (%)	–	732 (79.5) <sup>3</sup>	725 (78.7) <sup>4</sup>	–	–	554 (60.2)	550 (59.7)
Hyperplastic polyp, n (%)	–	483 (52.4)	492 (53.4)	481 (52.2)	487 (52.9)	367 (39.8)	383 (41.6)
Adenoma, n (%)	–	368 (40.0)	363 (39.4)	350 (38.0)	348 (37.8)	404 (43.9)	390 (42.3)
Serrated/sessile serrated adenoma/ polyp, n (%)	–	59 (6.4)	57 (6.2)	81 (8.9) <sup>e</sup>	76 (8.2)	141 (15.3)	139 (15.1)
Missing data, n (%)	–	11 (1.2)	9 (1.0)	9 (1.0)	10 (1.1)	9 (1.0)	9 (1.0)
Hyperplastic polyps (pathology-based) in the proximal colon diagnosed with high confidence, n/N (%)	–	55/78 (70.5)	57/78 (73.1)	–	–	33/78 (42.3)	49/78 (62.8)
Diagnostic properties for all polyps <sup>5</sup> , % (95%CI)							
▪ Sensitivity	77.5 (73.4–81.3)	67.7 (63.1–72.1)	67.0 (62.4–71.4)	67.9 (63.4–72.3)	66.9 (62.4–71.3)	77.6 (73.5–81.4)	81.6 (77.5–85.1)
▪ Specificity	73.4 (67.9–78.3)	80.8 (75.7–85.1)	81.8 (76.9–86.1)	80.1 (75.1–84.6)	80.5 (75.5–84.8)	61.6 (55.8–67.2)	68.2 (62.8–73.4)
▪ PPV	81.6 (78.4–84.3)	84.3 (80.8–87.2)	84.9 (81.3–87.8)	83.8 (80.3–86.8)	83.8 (80.3–86.9)	75.4 (72.5–78.2)	77.5 (74.5–80.3)
▪ NPV	68.2 (64.1–72.1)	62.2 (58.7–65.5)	62.1 (58.6–65.4)	62.2 (58.7–65.6)	61.7 (58.2–65.0)	64.5 (59.9–68.9)	73.4 (69.0–77.3)
▪ Accuracy	75.9 (72.6–78.9)	72.9 (69.5–76.1)	72.9 (69.6–76.1)	72.8 (69.4–76.0)	72.3 (68.9–75.6)	71.3 (67.9–74.5)	75.9 (72.63–78.9)
Diagnostic properties for rectosigmoid polyps <sup>6</sup> , % (95%CI)							
▪ Sensitivity	70.0 (60.0–78.8)	69.0 (58.9–77.9)	59.0 (48.7–68.7)	58.6 (48.2–68.4)	58.6 (48.2–68.4)	59.0 (48.7–68.7)	NA
▪ Specificity	67.3 (60.6–73.5)	67.8 (61.0–74.0)	88.3 (83.2–92.3)	88.3 (83.2–92.3)	89.2 (84.3–93.0)	89.7 (84.8–93.4)	100.0 (98.3–100.0)
▪ PPV	50.0 (44.2–55.7)	50.0 (44.2–55.8)	70.2 (61.2–77.9)	69.9 (60.8–77.6)	71.6 (62.4–79.3)	72.8 (63.6–80.4)	NA
▪ NPV	82.8 (77.8–86.8)	82.4 (77.5–86.4)	82.2 (78.4–85.4)	82.2 (78.4–85.4)	82.3 (78.6–85.5)	82.3 (78.6–85.5)	68.2 (68.2–68.3)
▪ Accuracy	68.1 (62.7–73.3)	68.1 (62.7–73.3)	79.0 (74.0–83.3)	78.9 (74.0–83.3)	79.5 (74.6–83.9)	79.9 (75.0–84.2)	68.2 (62.8–73.4)
CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value.							
<sup>1</sup> For differentiating neoplastic from non-neoplastic rectosigmoid polyps.							
<sup>2</sup> Hyperplastic polyp (HP – MS I), sessile serrated adenomas/polyp (SSA/P–IIo), low grade adenoma/tubular adenoma (TA–II), high grade adenoma/tubulovillous adenoma/superficial cancer (TVA–IIla), and invasive cancer (IIlb); no confidence level was reported for the MS classification.							
<sup>3</sup> Missing data in 10 patients (1.1%).							
<sup>4</sup> Missing data in 12 patients (1.3%).							
<sup>5</sup> For differentiating adenoma from hyperplastic polyps, including valid histopathology outcomes for all polyps.							
<sup>6</sup> For differentiating adenoma from hyperplastic polyps, including valid histopathology outcomes in rectosigmoid polyps.							

consequently increases the usefulness of conventional colonoscopy, particularly in community-based practice settings that have limited access to optical and state-of-the-art equipment, or related training opportunities.

Implementation of the LBRD strategy would also eliminate the need for the endoscopist to assign a confidence level to their histology prediction when using optical diagnosis [26].

Our results are aligned with those of previous publications [22, 27, 28]. As shown in previous studies [29], the accuracy of optical diagnosis can be improved following appropriate training before study initiation. However, several previous studies showed that optical diagnosis cannot reach the recommended quality benchmarks of 90% diagnostic accuracy suggested by the AGSE PIVI [6], especially when applied in community practice [22, 30].



► **Fig. 3** Proportion of patients who received an immediate surveillance interval and total reduction in pathology examinations following a location-based resect-and-discard method or optical diagnosis.

► **Table 3** Effect of incorrect diagnosis based on location-based resect-and-discard strategy on assignment of surveillance interval among the 482 patients with at least one diminutive polyp.

<b>≥ 1 incorrect optical diagnosis based on location-based resect-and-discard strategy, n (%)</b>	<b>208 (43.2)</b>
▪ Incorrect diagnosis did affect surveillance interval*	25 (5.2)
▪ Incorrect diagnosis did not affect surveillance interval	183 (38.0)
Basis of surveillance interval recommendation, n (%) (n = 183)	
▪ Family history of colorectal cancer	36 (19.7)
▪ Inadequate bowel preparation	31 (16.9)
▪ ≥ 2 diminutive adenomas or ≥ 10 hyperplastic polyps ≤ 10 mm or normal mucosal variations	90 (49.2)
▪ ≥ 3 diminutive adenomas	5 (2.7)
▪ Larger adenomas	21 (11.5)
* Among patients in whom an incorrect diagnosis would have affected their next surveillance interval, 16 patients (64.0%) would have been assigned a shorter interval and 9 (36.0%) a longer surveillance interval.	

Furthermore, although the prediction of polyp histology using optical diagnosis techniques relies on validated classification systems, the optimal scale when using the i-Scan system remains unknown. Indeed, previous studies found that optical diagnosis could achieve the quality benchmarks when using

the NICE [31] and SIMPLE classifications [29], but the WASP classification performed poorly in combination with i-Scan [32]. We found that the surveillance interval agreements between optical diagnosis using the NICE and Sano classifications and the pathology-based method could reach the recommended ASGE PIVI benchmark and were not significantly affected by the choice of NICE or Sano classification. In contradistinction, optical diagnosis did not achieve the required threshold when the WASP classification was used by endoscopists (► **Fig. 1**).

In the subcohort of patients with adequate bowel preparation, none of the optical classification systems could reach the recommended benchmark. Further studies should investigate the recently proposed SIMPLE classification system.

Optical diagnosis has not gained widespread acceptance, especially in North America, owing to concerns about making a wrong diagnosis, the potentially resulting medicolegal issues, and assigning incorrect surveillance intervals to patients [13]. Society endorsement of a truly operator-independent resect-and-discard strategy would likely address many of these issues. Such a strategy could be the proposed LBRD strategy, the adoption of artificial intelligence (AI)-assisted optical diagnosis, or a combination of both.

AI is a very promising method that has improved the detection rate and accuracy of optical diagnosis of diminutive adenomatous polyps [33, 34]. Nevertheless, this method still depends on the endoscopist's skill to present a clear and stable endoscopic image that centers on the polyp image in an optical chromoendoscopy mode. Although AI-assisted endoscopy could achieve better accuracy than optical diagnosis for predicting the polyp histology [33, 34], our current study suggests that a dedicated polyp recognition technology may not be needed as a simple LBRD strategy could confidently allocate surveillance interval in clinical practice, with a lower number of incorrect assignments made by endoscopists due to non-adherence to guidelines or low confidence optical diagnosis [35]. The strategy can also be used in endoscopy settings that have no opportunity to update their endoscopy units with state-of-the-art AI-assisted systems, and to supplement the diagnostic decisions for any low confidence diagnoses that occur with any other approach.

This study has several limitations. First, there was not a specific and validated training program for optical diagnosis in i-Scan settings. Therefore, the endoscopists participated in an interactive training program that was previously validated based on the NBI and NICE classification using still endoscopic images [36]. The endoscopists were also trained for the Sano and WASP classification systems using additional images that included the relevant polyp features' criteria used in those systems. Second, the SIMPLE classification was validated in 2018 based on both i-Scan and NBI after the initiation of this study [29, 37]. Therefore, we optically evaluated and documented polyp features based on the available validated classification systems. Third, although the LBRD strategy showed promising results in the allocation of post-polypectomy surveillance intervals, the low NPV of both the LBRD strategy and optical diagnosis to diagnose neoplastic diminutive rectosigmoid polyps indi-



cates that these approaches are not yet ready for routine clinical implementation.

Fourth, since the endoscopists used several optical polyp classifications, they could not be blind to their previous optical histological prediction. To best mitigate this problem, they were asked to perform the optical diagnosis using first WASP, second NICE, and finally the Sano classification system. A research assistant was present to show a laminated version of each classification system's diagnostic criteria upon the endoscopists' request to avoid any bias. Fifth, the number of performed optical diagnoses and the level of expertise were not similar among all the endoscopists. Therefore, it was difficult to evaluate the effect of each endoscopist's performance on the final results of this study.

In conclusion, our study demonstrated very high (97%) post-polypectomy surveillance interval agreement between the LBRD strategy and the reference standard (pathology using the 2020 USMSTF guideline). Moreover, the location-based strategy outperformed optical diagnosis. Clinical implementation of the LBRD strategy is likely safe and feasible, but would require endorsement from endoscopy societies and further monitoring of its performance under routine clinical conditions in diverse settings, such as community-based practices. The LBRD strategy could however mitigate the complexities of optical diagnosis by being independent of operator experience and having no requirement for specialized equipment.

## Clinical trial

Trial Registration: ClinicalTrials.gov | Registration number (trial ID): NCT04032912 | Type of study: Prospective

## Competing interests

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