

Artificial intelligence for characterization of colorectal polyps: Prospective multicenter study



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ABSTRACT

Background and study aims Optical diagnosis poses challenges to implementation of "resect and discard" strategies. This study aimed to assess the feasibility and performance of a new commercially available system for colorectal polyps.

Patients and methods Nine expert endoscopists in three centers performed colonoscopies using artificial intelligence-equipped colonoscopes (CADEYE, Fujifilm). Histology and predictions were compared, with hyperplastic polyps and sessile serrated lesions grouped for analysis.

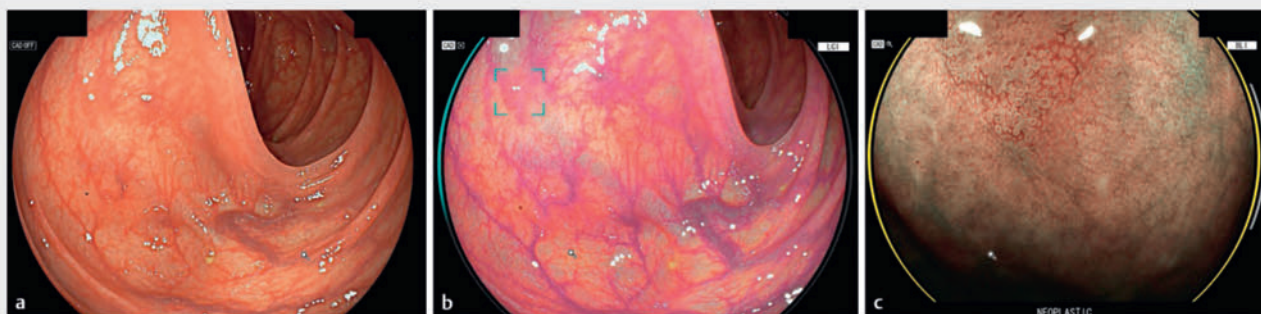
Results Overall, 253 polyps in 119 patients were documented (n = 152 adenomas, n = 78 hyperplastic polyps, n = 23 sessile serrated lesions). CADEYE detected polyps before endoscopists in 81 of 253 cases (32%). The mean polyp size was 5.5 mm (SD 0.6 mm). Polyp morphology was Paris Ip (4%), Is (28%), Ila (60%), and I Ib (8%). CADEYE achieved a sensitivity of 80%, specificity of 83%, positive predictive value (PPV) of 96%, and negative predictive value (NPV) of 72%. Expert endoscopists had a sensitivity of 88%, specificity of 83%, PPV of 96%, and NPV of 72%. Diagnostic accuracy was similar between CADEYE (81%) and endoscopists (86%). However, sensitivity was greater with endoscopists as compared with CADEYE ($P < 0.05$). CADEYE classified sessile serrated lesions as hyperplasia in 22 of 23 cases, and endoscopists correctly classified 16 of 23 cases.

Conclusions The CADEYE system shows promise for detecting and characterizing colorectal polyps. Larger studies are needed, however, to confirm these findings.

Introduction

In the United States, colorectal cancer (CRC) is the third most frequently diagnosed cancer and the third most common cause of cancer-related death among both men and women [1]. Colo-

noscopy and screening programs have shown to be effective tools for detecting colorectal polyps and removing precancerous lesions such as adenomas, thus preventing progression to CRC [2]. The Japanese Society for Cancer of the Colon and Rectum (JSCCR) recommends endoscopic management for cTis



► **Fig. 1** Example of a 3-mm polyp missed during the first pass by the endoscopist (**a** CADEYE mode off) but detected by artificial intelligence during the second pass (**b** CADEYE mode on) and **c** correctly characterized as "neoplastic".

and early invasive cT1 CRC, while invasive cT1 and higher stages should be managed surgically [3]. Invasive characteristics can be assessed endoscopically using fullness, erosion, fold convergence, deformity, and rigidity, as well as using contrast x-ray, chromoendoscopy, image-enhanced endoscopy, and endoscopic ultrasound findings [4].

Accurate initial assessment of colorectal polyp histopathology, a procedure known as "optical diagnosis," is of paramount importance because a significant proportion of small polyps, such as hyperplastic polyps, do not develop into cancer and need no further management. Therefore, being able to reliably distinguish between adenomatous and non-adenomatous polyps would enhance the cost-effectiveness and efficiency of screening and surveillance procedures [5, 6, 7].

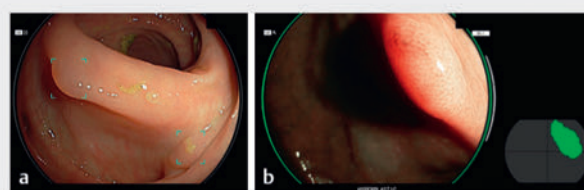
In recent years, image-enhanced endoscopy techniques, such as blue light imaging (BLI), narrow-band imaging (NBI), and i-Scan have been developed, enabling clear visualization of microvascular architectures and surface structures of colorectal polyps [8, 9, 10]. Systematic classifications based on NBI findings have been established, such as the NBI International Colorectal Endoscopic Classification and BLI Adenoma Serrated International Classification (BASIC) [11, 12].

Despite these advances, optical diagnosis poses challenges to the implementation of "resect and discard" strategies and artificial intelligence (AI) holds promise in revitalizing optical diagnosis savings [13]. In light of these challenges and potential benefits, our study aimed to assess the feasibility and performance of an AI-based computer-aided diagnostic (CAD) system named CADEYE, which is the first commercially available system to detect and characterize colorectal lesions [14].

Patients and methods

CADEYE description

CADEYE is an AI system developed by Fujifilm (Tokyo, Japan) for detecting colorectal polyps during endoscopic procedures. It is integrated into an external device called the EX-1, connected to a standard video processor and monitor. Activating CADEYE is done by pressing a button on the endoscope's handle. CADEYE utilizes an interface with colored boxes which highlight polyps and emits a sound signal when a suspicious polyp is detected. A



► **Fig. 2** Example of two small polyps in the right colon **a** detected by artificial intelligence and **b** correctly characterized as "hyperplastic" polyps. A visual map of the polyp characterized is displayed on the right inside the image to guide the endoscopist.

visual assist circle lights up in the direction of the detected polyp. The EX-1 has a built-in video recording function for storing endoscopic videos [15].

Setting and study design

Colonoscopies were conducted between June 19, 2020 and April 29, 2021 by nine expert endoscopists (i.e., with experience >10 years in optical diagnosis) across three academic centers using zoom colonoscopes (Eluxeo EC760Z, Fujifilm, Japan). The zoom function could be used at the discretion of the endoscopist. The AI system was activated in detection mode specifically in the cecum. Detection of a lesion by CADEYE was defined by hearing a sound signal (combined with a square delimiting the lesion on the screen). If this sound was heard before the endoscopist announced the lesion to the nurse, it would be considered as "CADEYE detection before the endoscopist." Once a lesion was detected, the endoscopist deactivated the AI and employed BLI to predict the histology according to the CONECCCT Classification [16]. Subsequently, the AI system was reactivated in BLI mode to classify the lesions as either neoplastic or hyperplastic (► **Fig. 1** and ► **Fig. 2**). Histopathology was assessed by pathologists at the local hospital.

This study has been conducted in accordance with the Declaration of Helsinki Ethical Guidelines for Clinical Research including, without limitation, data privacy laws and conflict of interest guidelines. All patients were informed and consented to the study at inclusion.

Data collection

The following data were collected prospectively through standardized forms filled out by the endoscopist for each included polyp: patient sex, age, indication for colonoscopy, type of intervention (biopsy or resection), size, Paris classification, polyp location, CADEYE detection before endoscopist, endoscopist histology prediction according to CONECCT Classification, CADEYE prediction (neoplastic or hyperplastic), and final histopathology report according to WHO 2019 pathology diagnostic criteria [17]. Hyperplastic polyps and sessile serrated lesions (SSLs) were combined as a single group for analysis purposes. Data were then reported in a spreadsheet.

Statistical analysis

Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for both the endoscopist and the CADEYE evaluations by comparing their performance against histopathology. To assess the precision of our estimates, we calculated 95% confidence intervals (CIs) and compared the sensitivity and specificity of the two interventions using an exact version of the McNemar test.

All statistical tests were conducted with a significance level of 0.05. We utilized Microsoft Excel to perform the data analysis.

Results

Excluded lesions

Three patients were excluded from the final analysis because of incorrect inclusion in the study (inflammatory bowel disease [IBD], lesions n = 5). CADEYE failed to produce a result in one lesion, which was a 4-mm adenoma, correctly predicted as such by the endoscopist. This lesion was subsequently excluded from the analysis. In total, six polyps were removed from the analysis.

Included lesions

In total, 253 polyps (CHU Nantes n = 125, HEGP Paris n = 86, CHU Nice n = 42) were observed in 119 patients (CHU Nantes n = 54, HEGP Paris n = 43, CHU Nice n = 22). These patients comprised 55% males, and the mean age was 65 years (range 20–81 years). Included polyps were 152 adenomas (CHU Nantes n = 88, HEGP Paris n = 60, CHU Nice n = 24), 78 hyperplastic polyps (CHU Nantes n = 45, HEGP Paris n = 19, CHU Nice n = 14), and 23 SSL (CHU Nantes n = 12, HEGP Paris n = 7, CHU Nice n = 4). The average size of the polyps was 5.3 mm (range 1–35 mm). Polyp morphology was classified as Paris Ip in 4% of cases, Is in 28%, Ila in 60%, and I Ib in 8%. Patient and lesion characteristics are detailed in ► **Table 1** and ► **Table 2**, respectively. Simplified data are represented in ► **Table 3**.

Main outcomes

CADEYE detected polyps ahead of the endoscopists in 81 of 253 cases (32%). These lesions were evaluated by histopathology as being SSL (n = 13), neoplasia (n = 50), and hyperplastic polyps (n = 18). Sensitivity was 80% (95%CI 73%–86%) for CAD EYE and 88% (95%CI 82%–93%) for the expert endoscopists (P =

► **Table 1** Indications for colonoscopy.

Indications	N (%)
Screening	19 (17)
Prior history of polyps	73 (66)
Resection	7 (6)
Symptoms	
▪ Modification of bowel habits	12 (11)
Total	111 (100)

► **Table 2** Lesion characteristics.

Polyp	N
Size in mm (mean; SD)	5.3±0.6
Paris classification	
▪ 0-Is	70
▪ 0-Ip	10
▪ 0-IIa	150
▪ 0-IIb	19
▪ 0-IIc	1
▪ 0-III	1
▪ Not reported	2
Location	
▪ Cecum + ascending	92
▪ Transverse	33
▪ Descending	34
▪ Rectosigmoid	94
Final histology	
▪ Neoplasia	152
▪ Sessile serrated lesion (SSL)	23
▪ Hyperplastic polyp	78
Simplified final histology	
▪ Neoplasia (adenocarcinomas + adenomas)	152
▪ Hyperplastic (SSL + hyperplastic polyps)	101
Total	253
SD, standard deviation.	

0.01). Specificity was 83% (95%CI 76%–90%) for CADEYE and 83% (95%CI 76%–90%) for the expert endoscopists (P = 1).

CADEYE obtained a PPV of 96% (95%CI 92%–99%) and a NPV of 72% (95%CI 64%–80%). The expert endoscopists achieved a PPV of 89% (95% CI 84% to 94%) and NPV of 82% (95%CI 74% to 89%). The diagnostic accuracy was 81% (95%CI 76%–87%) for CADEYE and 86% (95% CI 81% to 90%) for endoscopists (► **Ta-**

► **Table 3** Comparison of endoscopic assessment, CADEYE, and final histology.

	Endoscopist (n = 253)	CADEYE (n = 253)	Final histology (n = 253)
Neoplasia	150*	138*	152
Sessile serrated lesion (SSL)	31		23
Hyperplastic	72	115	78

*P < 0.05.

► **Table 4** Number of polyps classified in each category by CADEYE and by expert endoscopists compared with final histopathologic results.

		Histopathologic evaluation	
		Neoplasia (n = 152)	Hyperplasia (n = 101)
CADEYE evaluation	Neoplasia (n = 126)	121	17
	Hyperplasia (n = 111)	31	84
		Sn = 80%	Sp = 83%
		Accuracy = 81%	
		Neoplasia (n = 152)	Hyperplasia (n = 101)
Endoscopist evaluation	Neoplasia (n = 139)	133	17
	Hyperplasia (n = 98)	19	84
		Sn = 88%	Sp = 83%
		Accuracy = 86%	

Sn, sensitivity; Sp, specificity; PPV, positive predictive value; NPV, negative predictive value.

ble 4). CADEYE classified SSL as hyperplastic polyps in 22/23 cases, and endoscopists correctly classified 16/23 as SSL.

Discussion

Colonoscopy is accepted as a gold standard for CRC screening and its precursor lesions [18], and screening programs have contributed to a decrease in the incidence of CRC [19]. The term "resect and discard" describes the practice of removing small neoplastic polyps (<5 mm) during real-time diagnosis and subsequently discarding them, instead of sending them for histopathologic examination. On the other hand, "diagnose and leave" refers to the practice of leaving small non-neoplastic polyps, typically rectosigmoid hyperplastic polyps, in their original position without resection. Implementing these practices has the potential to result in substantial cost savings in colonoscopy procedures [5, 20].

First, our study is original because very few studies have established the value of CAD systems for optical prediction of histology. A recent study by Hassan et al. [21] conducted on 544 lesions showed that GI Genius Intelligent Endoscopy Module (version 3.0.0; Medtronic, Medtronic, Minnesota, United States) obtained a sensitivity of 82%, specificity of 93%, PPV of 65%, and NPV of 98% for 1- to 5-mm rectosigmoid polyps. The sensitivity and specificity obtained in our study are in line with these results and the discordance in PPV and NPV may be due to the fact that our study included larger, more complex lesions spread over all segments of the colon.

Polyp detection (CADe) for the CADEYE system has been evaluated in a recent study by Neumann et al., which showed

that it achieved 100% sensitivity in polyp detection and a negligible false-positive frame rate [14]. Its impact on the quality of endoscopies of trainee gastroenterologists has been highlighted in a study by Yamaguchi et al., where the adenoma miss rate was decreased in the CADEYE group; however, the authors noted no improvement in adenoma or polyp detection rate [22].

CADEYE for CAD has been previously assessed in a few other studies. Dos Santos et al. analyzed 110 lesions where CADEYE showed 81.8% accuracy, 76.3% sensitivity, 96.7% specificity, 98.5% PPV, and 60.4% NPV [23]. The data obtained in our study confirm these results in a larger patient sample. Another study by Li et al. analyzed 661 polyps, and CADEYE sensitivity in identifying neoplastic polyps was 61.8% and achieved an overall accuracy of 71.6%. In contrast, endoscopists achieved a higher sensitivity (70.3%, $P < 0.001$) and a higher accuracy (75.2%, $P = 0.023$) [24]. Our results also show this difference in sensitivity. In a cohort of 100 lesions analyzed by Yoshida et al., they observed no difference in optical diagnosis for the AI-assisted group versus the expert endoscopist group. CADEYE with magnified BLI obtained a sensitivity, specificity, PPV, NPV and diagnostic accuracy of 90.9%, 85.2%, 83.3%, 92.0% and 87.8%, respectively (versus 93.3%, 90.9%, 89.4%, 94.3%, 92.0% for the expert endoscopist group, respectively). However, they did observe higher diagnostic accuracy for their CADEYE group when compared with trainee endoscopists (87.8% versus 79.0%) [25].

For smaller rectosigmoid polyps, Rondonotti et al. conducted a study on 596 lesions ≤ 5 mm and achieved a high confidence diagnostic rate of 92.3%. The CADEYE-assisted NPV for

adenomatous histology met the required threshold ($\geq 90\%$) with a value of 91.0%. The accuracy was lower for nonexperts (82.3%) compared with experts (91.9%), but nonexperts showed improvement in their performance over time [26].

Our study was performed in “real-life” conditions with different indications for colonoscopy, excluding only patients with IBD or genetic polyposis. Therefore, it reflects the potential value of CADEYE in routine practice. Furthermore, in addition to characterization, it confirms that CADEYE is highly efficient for detection of colonic lesions. Indeed, 30% of lesions were detected by CADEYE before the endoscopist and no lesion was missed. We did not identify any specific characteristics associated with CADEYE misdiagnosis. The size of the polyps varied from 1 to 10 mm and Paris classification varied from 0-Is to 0-IIb, spread across the entirety of the colon.

Our study has several limitations. First, in our analysis, we grouped SSLs and hyperplastic lesions for CAD analysis because CADEYE (like all other CAD systems) cannot differentiate SSL from HP in its current version. This is likely to change in the near future. Human prediction of histology was based on CON-ECCCT Classification, with satisfying results in comparison with previous literature [16]. Second, only nine endoscopists in three centers with expertise in optical diagnosis participated in the study. In addition, we did not assess the expertise of endoscopists in interpretation of magnified images or the number of lesions for which the magnification function was used. Therefore, further studies with a larger panel of endoscopists and standardized expertise in optical diagnosis are required to determine the true additional value of CADEYE outside of tertiary-referral centers and, possibly, excluding the need for magnification imaging. Also, we did not consider the confidence level achieved by the endoscopist or CADEYE, which might have negatively impacted our results. Indeed, a previous multicenter clinical study conducted by Barua et al. evaluated 892 polyps in 518 patients. Sensitivity and specificity were 90.4%, and 85.9% for their CAD group, and high-confidence polyp diagnosis was higher in the CAD group (92.6% vs 74.2% in the standard endoscopy group) [27].

Conclusions

The CADEYE system has great clinical potential because it can be used in conjunction with normal endoscopy equipment. CADEYE has the potential to dramatically improve the quality and reduce the costs of colonoscopy, especially in community practice.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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