



Real-World Experience of AI-Assisted Endocytoscopy Using EndoBRAIN—An Observational Study from a Tertiary Care Center

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J Digest Endosc 2023;14:3–7.

Abstract

Background and Aims Precise optical diagnosis of colorectal polyps could improve the cost-effectiveness of colonoscopy and reduce polypectomy-related complications. We conducted this study to estimate the diagnostic performance of visual inspection alone (WLI + NBI) and of EndoBRAIN (endocytoscopy-computer-aided diagnosis [ECAD]) in identifying a lesion as neoplastic or nonneoplastic using EC in real-world scenario.

Methods In this observational, prospective, pilot study, a total of 55 polyps were studied in the patients aged more than or equal to 18 years. EndoBRAIN is an artificial intelligence (AI)-based system that analyzes cell nuclei, crypt structure, and vessel pattern in differentiating neoplastic and nonneoplastic lesion in real-time. Endoscopist assessed polyps using white light imaging (WLI), narrow band imaging (NBI) initially followed by assessment using EC with NBI and EC with methylene blue staining. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of endoscopist and EndoBRAIN in identifying the neoplastic from nonneoplastic polyp was compared using histopathology as gold-standard.

Results A total of 55 polyps were studied, in which most of them were diminutive (36/55) and located in rectum (21/55). The image acquisition rate was 78% (43/55) and histopathology of the majority was identified to be hyperplastic (20/43) and low-grade adenoma (16/43). EndoBRAIN identified colonic polyps with 100% sensitivity, 81.82% specificity (95% confidence interval [CI], 59.7–94.8%), 90.7% accuracy (95% CI, 77.86–97.41%), 84% positive predictive value (95% CI, 68.4–92.72%), and 100% negative predictive value. The sensitivity and negative predictive value were significantly greater than visual inspection of endoscopist. The diagnostic accuracy seems to be superior; however, it did not reach statistical significance. Specificity and positive predictive value were similar in both groups.

Conclusion Optical diagnosis using EC and EC-CAD has a potential role in predicting the histopathological diagnosis. The diagnostic performance of CAD seems to be better than endoscopist using EC for predicting neoplastic lesions.

Keywords

- ▶ EndoBRAIN
- ▶ endocytoscopy
- ▶ polyp

Introduction

Colorectal cancer (CRC) is a formidable health problem worldwide. In India, the annual incidence rates (AARs) for colon cancer and rectal cancer in men are 4.4 and 4.1 per 1,00,000, respectively. The AAR for colon cancer in women is 3.9 per 100000.¹

Artificial intelligence (AI) known as computer vision in computer-aided diagnosis (CAD) and detection (CADE) helps in identifying health-related conditions based on medical imaging. Convolutional neural network (CNN) is a type of deep machine learning algorithm that uses convolutions of the input image to extract the most relevant information that helps to classify the image into different entities. Based on the accumulated data features, a deep CNN can diagnose newly acquired clinical images prospectively.^{2,3}

Precise optical diagnosis of colorectal polyps could improve the cost-effectiveness of colonoscopy and reduce polypectomy-related complications. It is difficult for community-based nonexperts to obtain sufficient diagnostic performance. CAD has potential for better accuracy and lower interobserver variability. Nonexpert endoscopists may more easily achieve accuracy levels sufficient to meet the preservation and incorporation of valuable endoscopic innovations (PIVI) threshold.⁴ The EndoBRAIN technology has a potential in this regard with studies showing improved adenoma detection rate (ADR) and diagnostic accuracy reaching the PIVI thresholds.

Removing precancerous polyps from the bowel during a colonoscopy is the cornerstone of CRC screening and prevents polyps developing into bowel cancer. Many polyps never grow into cancer and it can be difficult for the clinicians performing the procedure (endoscopists) to tell which ones are precancerous. This means many polyps are removed unnecessarily, with a considerable waste of resources. The EndoBRAIN system uses optical diagnostic technologies like endocytoscopy (EC) and narrow band imaging (NBI). EC enables in vivo observation of cells and nuclei at 520x ultramagnification using methylene blue staining, and combined with NBI, can observe microvessels in detail.⁵⁻⁸ EndoBRAIN may prove to be cost-effective by reducing biopsies and histopathology examinations. Usage of these technologies, especially in a high-volume center, may help us improve patient care, at the same time with cost-effectiveness.⁹

Methods

This was a prospective, observational study conducted to estimate the accuracy of visual inspection alone and of EndoBRAIN (EC-CAD) in identifying a lesion as neoplastic or nonneoplastic using EC. The study population included individuals 18 years or older who were scheduled for screening, surveillance, diagnostic, or therapeutic colonoscopy. Patients with inflammatory bowel disease, polyposis syndrome (e.g., familial adenomatous polyposis, serrated polyposis), history of chemotherapy or radiation therapy for colorectal lesions, and inability to undergo polypectomy (e.g., intake of anti-coagulants, comorbidities, or patient refusal) were excluded

from the study. Subjects who were scheduled for colonoscopy and found to have a polyp on white light endoscopy were included. Patients underwent colonoscopy with Olympus colonoscope (CF-HQ290, Olympus, Tokyo, Japan) equipped with EndoBRAIN technology and performed using EVIS LUCERA ELITE CV-290 processor (Olympus, Tokyo, Japan). Experienced endoscopist who performed more than 5,000 colonoscopies have performed the procedure. Endoscopic diagnosis of polyp was done under white light imaging and NBI using Japan NBI expert team classification. EC-NBI and/or EC-stain images were acquired from the polyps. The acquired images were assessed by endoscopist in real-time and was asked to give a diagnosis (nonneoplastic/neoplastic) who was blinded to the EndoBRAIN diagnosis and histopathological diagnosis. The EndoBRAIN diagnosis of the polyp on EC NBI (nonneoplastic/neoplastic) and/or EC stain (nonneoplastic/neoplastic) images was documented by the assistant. Resected polyps were sent for histopathological assessment who were blinded to the endoscopic diagnosis. Pathological assessment of polyps was performed by senior pathologist with experience in the gastrointestinal histopathology. The number of polyps from which good quality EC images could be acquired is calculated (image acquisition rate). The sensitivity, specificity, accuracy, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio, and negative likelihood ratio in identifying a neoplastic lesion are calculated. Polyps from which EC images could not be acquired were excluded from this analysis.

Statistical Analysis

Baseline characteristics of the polyps were described using descriptive statistics. Categorical data are described using percentages and frequencies and compared using Fisher's exact test or chi-squared test. The normality of continuous data was assessed by Kolmogorov-Smirnov test and represented as mean (standard deviation) or median (interquartile range). Comparison of the continuous data was done by independent Student's *t*-test for parametric data and Mann-Whitney U-test for nonparametric data. Statistical analysis was performed at 5% level of significance and *p* less than 0.05 was considered as statistically significant.

Results

This is a pilot study conducted from January 2021 to June 2021. Institute review board and ethical board clearance was obtained prior to initiating the study (AHF/AIGH-IRB:02/46/2021). Study was conducted in accordance with ethical principles for human subjects as stated in the declaration of Helsinki. Informed consent was obtained from all the participants. Baseline characteristics showing number of polyps, image acquisition rate, and histopathological details were elucidated in ►Table 1. A total of 55 polyps were studied. Most of the polyps were diminutive and most of them were located in rectum. Good quality EC images using either EC-NBI or EC-stain mode were acquired from 43 out of 55 polyps (78.2%). However, the image acquisition rate was

lower in diminutive polyps at 66.7% (24 out of 36 polyps). Histopathological examination of the polyps from which EC images were acquired showed 22 (51%) nonneoplastic and 21 (49%) neoplastic polyps. EndoBRAIN (EC-CAD) detects a polyp as neoplastic or nonneoplastic using EC in real-time (► **Supplementary Video S1**). Nonneoplastic polyp on EC showed narrow serrated lumina and dense pattern of small roundish nodules (► **Fig. 1**). Neoplastic polyp showed slit like smooth lumina and regular pattern of fusiform or roundish nuclei (► **Fig. 2**). The sensitivity, specificity, PPV, NPV, and accuracy of endoscopist in identifying a neoplastic polyp based on EC were 90.48% (95% confidence interval [CI], 69.2–98.8), 81.81% (95% CI, 59.7–94.8), 82.61% (95% CI, 65.95–92.1), 90% (95% CI, 70.36–97.15), and 86% (95% CI, 72.07–94.70), respectively, with a positive likelihood ratio of 4.98 and negative likelihood ratio of 0.12. The sensitivity, specificity, PPV, NPV, and accuracy of EndoBRAIN in identifying a neoplastic polyp based on EC were 100%, 81.82% (95% CI, 59.7–94.8%), 84%(95% CI, 68.4–92.72%), 100%, and 90.7% (95% CI, 77.86–97.41%), respectively, with a positive likelihood ratio of 5.5 and negative likelihood ratio of 0. The sensitivity and NPV of EndoBRAIN were significantly better than that of endoscopist ($p < 0.05$). Though diagnostic accuracy is more with EndoBRAIN, it did not reach statistical significance ($p = 0.5$). Specificity and PPV were similar in both groups (► **Table 2**).

Discussion

In the past decade, development in AI and its applications in the medical field were exponential. Being third-leading malignancy, technical, operator, and human dependent limitations are missing out on a significant proportion of polyps during colonoscopy in CRC patients. These errors ultimately

Table 1 Baseline characteristics

Total no of polyps	55
Size	
Diminutive polyps	36 (65.4%)
Polyps of size 5 mm–1cm	10 (18.1%)
Polyps of size > 1 cm	9 (16.3%)
Location	
Rectum	21 (38.1%)
Left colon	15 (27.2%)
Right colon	19 (34.5%)
Image acquisition rate	43/55 (78.2%)
Image acquisition rate from diminutive polyps	24/36 (66.7%)
Histopathology of polyps from which endocytoscopy images acquired (n = 43)	
Hyperplastic	20
Inflammatory	2
Low-grade adenoma	16
High-grade adenoma	5

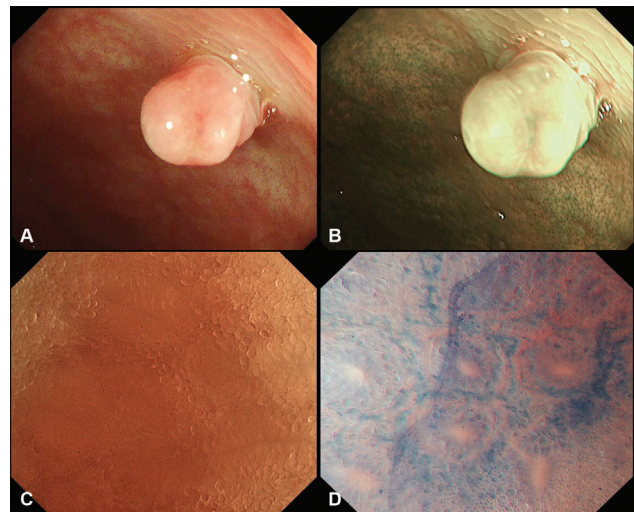


Fig. 1 Nonneoplastic polyp. (A) White light imaging showing sessile polyp of size 5 mm (Paris 1s). (B) Narrow band imaging (NBI) showing sessile polyp with invisible vascular pattern with regular dots (Japan NBI expert team type 1). (C and D) Endocytoscopy with NBI and stain showing narrow serrated lumina and dense pattern of small roundish nodules (EC1b).

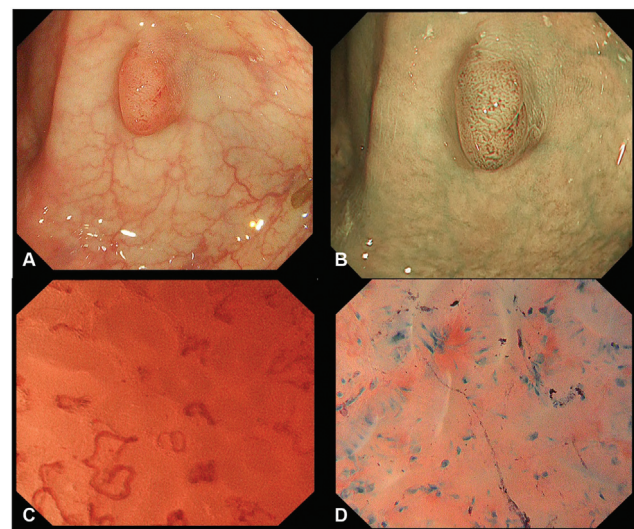


Fig. 2 Neoplastic polyp. (A) White light imaging showing sessile polyp of size 5 mm (Paris 1s). (B) Narrow band imaging (NBI) showing sessile polyp with regular vessel distribution and caliber with regular surface (Japan NBI expert team type 2A). (C and D) Endocytoscopy with NBI and stain showing slit-like smooth lumens with uniform fusiform or roundish nuclei (EC2).

affect the patients and their overall CRC management. It was also reported that with each 1% increase in ADR, an equivalent 3% decrease in the subsequent risk of cancer was reported.^{10,11} In view of this, the highest level of accuracy is highly essential and much needed to deal with such unmet problems with minimal errors that can be feasible only with AI. AI has its own advantages in diagnosing the polyp characteristics easily, early, accurately, and economically than the existing conventional ex-vivo microscopic analysis methods.¹² Considering the facts, the AI powered CADe and diagnosis (CADx) systems were developed to improve the

Table 2 Comparison of evaluation of endocytoscopy between endoscopist and EndoBRAIN ($n = 43$)

	Endoscopist (confidence interval)	EndoBRAIN (EC-CAD) (confidence interval)	<i>p</i> -Value
Sensitivity	90.48% (69.2–98.8)	100%	0.03
Specificity	81.81% (59.7–94.8)	81.82% (59.7–94.8)	0.9
Positive predictive value	82.61% (65.95–92.1)	84% (68.4–92.72)	0.86
Negative predictive value	90% (70.36–97.15)	100%	0.03
Accuracy	86% (72.07–94.70)	90.7% (77.86–97.41)	0.5

Abbreviation: EC-CAD, endocytoscopy-computer-aided diagnosis.

nonhistological polyp evaluation with better accuracy and reduced intra- and interobserver variability.¹³

To overcome the limitations with the existing CADx systems, Kudo et al¹⁴ and Mori et al¹⁵ have collaborated, designed, and developed an advanced novel AI technology-based CADE (EndoBRAIN-EYE) and CADx tool—EndoBRAIN to help the surgeons in real-time (in-vivo) to differentiate the nonneoplastic lesions from neoplastic and help in avoiding unnecessary resection.¹⁶ To the best of our knowledge, this is the first of its kind study in India to use EndoBRAIN (an AI software tool) to differentiate neoplastic versus nonneoplastic polyp in real-time during a colonoscopy.

The first step during the procedure is identification and differentiation of cancerous lesions from noncancerous lesions in vivo using high-quality images acquired and analyzed in real time. The image acquisition rate in our study (78.2%) was highly efficient and it was in line with a large multicenter study conducted by Mori et al (83.6%).¹⁷ This parameter is important in the context that unless a high-quality EC image is acquired, EndoBRAIN does not give us an output. The image acquisition was difficult in diminutive polyps at high magnification because minimal movement at the time of freezing the image can lead to false results. Images were also difficult to obtain polyps located in traditionally difficult locations like hepatic and splenic flexure. Better bowel preparation, higher procedure volumes, and strategies such as examining the polyp at 12'0 clock position are few ways to improve the image acquisition in our experience.

Study by Mori et al is one of the most significant and the first benchmark study ever conducted using EndoBRAIN to clarify the value of an AI-assisted colonoscopy system in identifying cancerous lesions under the strictly controlled environment.¹⁷ Another important parameter to be considered as a benchmark for optical diagnosis in adoption of AI systems as a clinical decision support device for diminutive polyp management is PIVI thresholds. Higher the accuracy of optical polyp diagnosis, higher will be the PIVI acceptance. Based on the PIVI threshold, anyone of the paradigm will be opted in the end clinically—“resect and discard” or “leave in situ.” In the present study, the accuracy rate of EndoBRAIN was 90.7%, exceeding the initiative threshold of more than 90% for the “resect and discard” strategy as proposed by the American Society for Gastrointestinal Endoscopy.⁴ Diagnostic accuracy reports of our study (90.7%) were observed to be similar to the reports obtained from Misawa et al⁶ (87.8%) and Shin et al.¹⁴ In our

study, an improvement in accuracy of EndoBRAIN (90.7%) over endoscopist (86.05%) was also observed to be same as Jin et al where the use of CADx has improved the overall accuracy of optical polyp diagnosis from 82.5 to 88.5% ($p < 0.05$).¹⁸ With advancement of technology like this, many nonexpert endoscopists around the world can now easily achieve accuracy levels sufficient to meet the PIVI threshold.

Another major parameter to consider is NPV, where the NPV results (100%) from our study were observed to be better than multiple studies from the literature allowing diminutive hyperplastic polyps to be left in situ without a pathological diagnosis. In studies conducted by Mori et al¹⁷ and Shin et al,¹⁴ the NPV in both the stain mode and NBI mode was observed to be only more than or equal to 93%.

Whereas with the other parameters concerned such as EndoBRAIN sensitivity, specificity, and PPV values were also reported and they were observed to be better than values from endoscopists. Reports from our study were almost similar with the results published by the team who developed the EndoBRAIN itself. However, the sensitivity, specificity, PPV values of our study and EndoBRAIN team were reported to be 100, 81.82, 84 and 96.9, 100, 100%, respectively.¹⁵ Reports from Shin et al also showed almost similar results as our study in both stained EC and EC-NBI.¹⁴ Overall, results from our study suggest that the sensitivity and NPV are statistically significant and better in EndoBRAIN than that of endoscopists group suggesting the efficiency of the EndoBRAIN and its unlikely nature to miss a neoplastic polyp. In addition, EndoBRAIN is a good alternate to conventional methods in terms of cost-effectiveness, time-saving, and the trauma involved throughout the process. In future, these AI-based diagnostic systems like EndoBRAIN can be a game changer in reducing the unnecessary surgeries/resections because of their high accuracy, NPV, and specificity. In future, these AI systems also have a high potential to transform clinical endoscopic practice positively forever over the existing conventional procedures.

There are some limitations to our study. First, sample size is very small; hence, it is difficult to generalize the findings to community. Second, sessile serrated adenoma (SSA) that appears similar to hyperplastic polyps on digital chromoendoscopy was not studied in our study. As such the incidence of SSA is low and predominant distal location of polyps in our study may be the reason for not having SSA. Further polyp surveillance studies with EndoBRAIN involving SSA are

required to conclude on “do not resect” strategy. Third, objective assessment of additional time required to perform procedure and cost-effective analysis was not performed.

Conclusion

Optical diagnosis using EC and EC-CAD has a potential role in predicting the histopathological diagnosis. The diagnostic performance of CAD seems to be better than endoscopist using EC for predicting neoplastic lesions. Large-scale data analysis in Indian population is needed prior to community practice.

Supplementary Video S1

Title slide: Real-world experience of artificial intelligence-assisted endocytoscopy using EndoBRAIN—An observational study from a tertiary care center. Nonneoplastic polyp showing white-light imaging, narrow band imaging (NBI), endocytoscopy with NBI and methylene staining. Neoplastic polyp showing white-light imaging, NBI, endocytoscopy with NBI, and methylene staining. Online content including video sequences viewable at: <https://www.thieme-connect.com/products/ejournals/html/10.1055/s-0042-1758535>.

Conflict of Interest

None declared.

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