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Review Article

Current Practice and Emerging Endoscopic Technology in the Diagnosis of Colorectal Cancer: A Narrative Review of Enhanced Imaging and Optical Biopsy

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Abstract

Gastrointestinal endoscopy has undergone significant transformation since its first introduction in the early 20th century. Despite advances in modern endoscopy, its precision in detecting and removing colorectal cancer (CRC) varies; colorectal polyps or cancer are still missed in 2.1-5.9% of cases. Additionally, post-colonoscopy CRC occurs in 30% of patients who have undergone incomplete polyp resection. When biopsies are taken, only 11.4% are found to be malignant, rendering 88.6% of tissue removal unnecessary. To address these shortcomings, modern endoscopy is evolving. Current endoscopic modalities include wide-field and microscopic-field endoscopy. Wide-field view endoscopy remains the most frequently used type and includes the current standard of practice—white light endoscopy—as well as other modalities such as virtual and dye-based chromoendoscopy, ultrathin endoscopy, and capsule endoscopy. Microscopic field endoscopy encompasses several new emerging modalities that can provide microscopic resolution capable of diagnosing lesions *in vivo* (optical biopsy), thus reducing the number of unnecessary biopsies. However, the emerging technology comes with a learning curve and requires time for endoscopists to master and achieve interobserver agreement. Consequently, there is a growing opportunity to develop machine learning technology to assist with the learning process. We review current modalities available for the diagnosis of CRC, including the current standard of practice, new enhanced imaging modalities, and optical biopsy.

Introduction

Gastrointestinal (GI) endoscopy was first introduced in the 1920s. The initial endoscopes were rigid and were replaced by semiflexible endoscopes in 1932.[1] Early endoscopy provided little diagnostic information with only partial visualization of the colon and caused significant discomfort to the patient.[2] Endoscopy underwent a major transformation with the development of fiberoptics in the 1950s, which used aligned pliable glass fibers within endoscopes, allowing for real-time image transmission.[2,3] This new technology was first used in 1957 by Hirchowitz to visualize the GI tract.[3] Decades later, endoscopy has firmly established its role in screening and surveillance of GI pathology, particularly colorectal cancer (CRC). As CRC continues to be the second leading cause of cancer-related deaths in the United States, endoscopic screening remains a widely accepted diagnostic tool.[4] Despite advances in modern endoscopy, the quality of the procedure continues to vary depending on the endoscopy modality used and the skill level of the operator.[5] As a result, about 5% of colorectal polyps or cancers are still missed during colonoscopy.[4] Of the polyps that are resected, around 30% are incompletely resected, leading to post-colonoscopy CRC.[6] Malignancy is found in only 11.4% of targeted biopsies in patients undergoing colonoscopy. This means that many biopsies are taken from healthy tissue unnecessarily, increasing the risk of intraprocedural and postprocedural complications.[7] We review and discuss current endoscopic modalities available and how they compare in their ability to detect CRC, with the intention of increasing the capture of CRC *in vivo* and decreasing unnecessary biopsies (Table 1).[7–35]

Viewpoints

Endoscopic modalities can be categorized into wide-field and

Keywords: Colonoscopy; Colorectal cancer; Endoscopic modalities; Endoscopic mucosal resection; Artificial intelligence; Colonic polyps.

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Table 1. Comparison of endoscopic imaging modalities and diagnosis of colorectal cancer

Endoscopy modality	Mechanism	Advantages	Limitations	Sensitivity for CRC detection	Specificity for CRC detection
WLE	White light from LED or xenon lamp[10]	Requires little training; HD, UHD, CF, and DF modes are available[8]	Poor sensitivity for lesion detection[8]	68%[10]	85%[11,12]
Virtual chromoendoscopy (NBI)	Optical filtering, spectral variations, and their interaction with mucosa[9]	Easily accessible to operators/ compatible with most HD endoscopes; Provides contrast without the use of dye	Lack of classification criteria; Poor understanding of learning curves of trainees and interobserver reliability; NBI has low illumination capacity; No agreement on its superiority over HD-WLE in CRC detection[9,12–15]	81.8–99.2%[18]	85.2–99.6%[18]
Dye-based chromoendoscopy	Utilizes exogenous dyes (Lugol's iodine, methylene blue, indigo carmine)[9]	A more available and more inexpensive version of CE[9]	Relies on how uniformly the dye is applied and the clinician's skills; Lack of interpretation criteria[11]	92%[11,12]	82%[11,12]
Ultrathin endoscopy	Smaller diameter compared to traditional endoscope; Light source similar to WLE[23]	Little or no sedation; Higher rate of patient acceptance; Fewer complications; Faster recovery time[16]	Poor maneuverability; Decreased resolution; Limited biopsy ability[16]	N/A	N/A
Capsule	Small imaging sensor, light source, imaging optics, and a power supply;[9] Data collected transmitted wirelessly via electric-field propagation[17]	Well tolerated by patients; Increases diagnostic yield of colorectal polyps and cancer in patients who had incomplete optical colonoscopy;[19] Can be used as an alternative to primary colonoscopy and FIT[20]	Lack of active locomotion[11]	79–96%[20]	66–97%[20]
CLE	Scanning laser producing fluorescence images of the mucosal layer with micron-level resolution[9]	CLE provides a resolution of 1–3.5 µm with imaging depths up to 70 µm and FOV of 200–300 µm[9]	Expensive; Small FOV can cause sampling error[9]	83%[21]	90%[21]
Endocytoscopy	Reflectance imaging, similar to WLE, but with optical magnification 500-fold to 1000-fold;[9] Contrast (methylene blue or crystal violet) can be used to enhance the visualization of nuclear and glandular structures[22]	Resolution is 1.7–4.2 µm, FOV of 120–700 µm; compatible with VCE[7]	Expensive; Lack of classification systems;[24] Imaging depth is limited to surface only	85.0%[26]	90.7%[26]
OCT	Low-coherence light source gathers reflectance information from different tissues and translates it into cellular morphology; No contrast used[9]	OCT resolution is around 10 µm, depth 1–2.5 mm (deepest from the microscopic endoscopic modalities), large FOV with pullback (large-area scanning);[7] Allows for visualization of multiple layers and assessing disease progression under the mucosal surface	Expensive[25]	87.5%[28]	75%[28]
HRME	Uses fluorescence for contrast along with proflavine[9]	Resolution of 4.4 µm with FOV of 790 µm; Low cost[27]	Interobserver variability and does not have diagnostic criteria in place to guide operators[26]	70%[26]	94%[26]
CADe	Uses machine learning and AI algorithms to visualize and detect adenomas[29–31]	Aids operator in polyp detection[29–31]	Some studies suggest that CADe may not improve ADR clinically[34,35]	71–99%[30,31]	63–99%[30,31]
CADx	Uses machine learning and AI algorithms to diagnose adenomatous versus benign polyps[29–31]	Aids operators in diagnosis of polyps[29–33]	Primarily improves accuracy among non-experts[30]	82–98%[30,31]	70–97%[30,31]

ADR, adenoma detection rate; AI, artificial intelligence; CADe, computer-aided detection; CADx, computer-aided diagnosis; CE, chromoendoscopy; CF, close focus; CLE, confocal laser endomicroscopy; CRC, colorectal cancer; DF, dual focus; FIT, fecal immunochemical test; FOV, field of view; HD, high definition; HRME, high-resolution microendoscopy; LED, light-emitting diode; NBI, narrow band imaging; OCT, optical coherence tomography; UHD, ultra high definition; VCE, video capsule endoscopy; WLE, white light endoscopy.

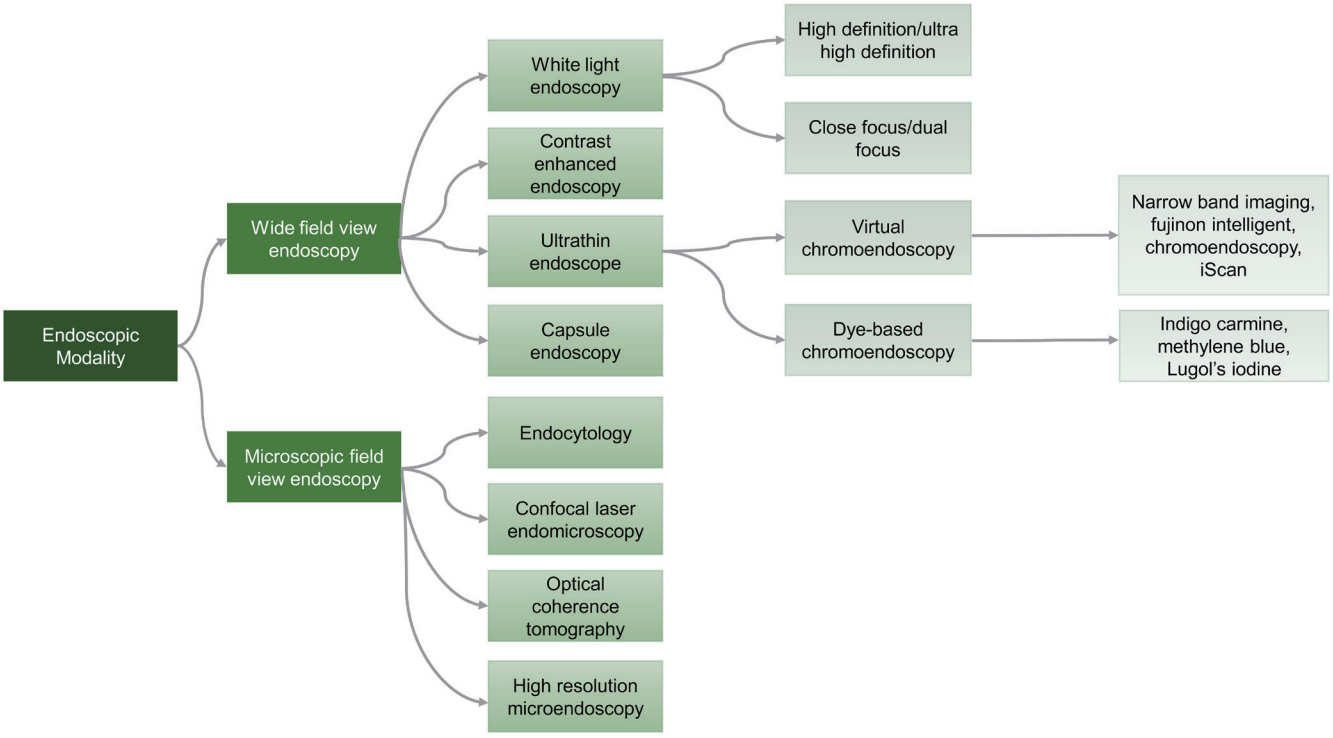

Fig. 1. Categorization of endoscopic modalities utilized in the diagnosis of colorectal cancer (CRC).[8,9]

microscopic field endoscopy (Fig. 1).[8] Wide-field endoscopy encompasses white light endoscopy (WLE), contrast enhanced endoscopy, ultrathin endoscopy, and capsule endoscopy. WLE can be further classified into high definition (HD), ultra-high definition (hereinafter referred to as UHD), close focus, and dual focus endoscopy. Contrast enhanced endoscopy includes virtual chromoendoscopy and dye-based chromoendoscopy. Virtual chromoendoscopy comprises two main techniques: pre-processing (narrow band imaging (NBI)) and post-processing (I-scan, Fujinon intelligent chromoendoscopy (FICE)). Dye-based chromoendoscopy uses physical dyes, such as indigo carmine, methylene blue, and Lugol's iodine, to enhance imaging. Microscopic view endoscopy includes confocal laser endomicroscopy, endocytoscopy, optical coherence tomography (OCT), and high-resolution microendoscopy.[8,9]

Wide field view endoscopy

Wide-field view endoscopy remains the most frequently used type of endoscopy.[9] This includes WLE, virtual chromoendoscopy, dye-based chromoendoscopy, ultrathin endoscopy, and capsule endoscopy. We will discuss these modalities in the following section.

White light endoscopy

WLE was one of the first endoscopic modalities available and remains the current standard of practice for screening and diagnosing GI pathology, particularly for CRC.[7] WLE uses a white light source, such as light-emitting diodes or a xenon lamp, to visualize mucosa, allowing for realistic images of the mucosal structures.[8] Recent advances in WLE have introduced 1080p HD, 4K/8K UHD, close focus, and dual focus modes, which significantly enhance WLE's ability to visualize mucosal lesions. Close focus and dual focus modes function by adjusting the structure of lens located at the end of the endoscope. Specifically, close focus enhances visualization of the mucosal surface and its capillaries by allowing closer proximity of the endoscope, which cannot be achieved by magnification alone. Dual focus mode is similar to close focus but further allows endoscopists to alter the depth of field.[9]

One advantage of WLE is that it usually requires minimal training. However, one limitation of this technique is its low sensitivity for CRC detection.[10] Studies have reported a sensitivity of 68% and specificity of 85% for HD-WLE in detecting colorectal adenomas.[11,12,36] Efforts to improve HD-WLE's diagnostic yield are ongoing, with recent advances including wider field of view (FOV) endoscopes that allow for panoramic visualization (245–330 degrees).[37] Preliminary studies revealed that the new wider FOV HD-WLE endoscopes increased colonic polyp detection rates. Another innovation in HD-WLE is the third eye retroscope, an optical technology that runs through the scope, allowing for retroflexion while in forward view. This provides a continuous retrograde view throughout the procedure.[38] Reports have shown that the third eye retroscope has improved the adenoma detection rate.[39]

Contrast-enhanced endoscopy

Virtual chromoendoscopy

One major difference between WLE and virtual chromoendoscopy is that WLE uses the complete visible light spectrum as its light source. In contrast, virtual chromoendoscopy utilizes an optical filter to assess selected light frequencies and their interaction with mucosal structures. The spectral variations interact with tissues, enhancing some of the mucosal structures better than white light alone, thereby increasing diagnostic yield. This technology is easily accessible to operators during endoscopic procedures, and most HD-WLE endoscopes are compatible with virtual chromoendoscopy, allowing for rapid alternation between modes. Virtual

chromoendoscopy modes include NBI, FICE, and iScan. NBI utilizes blue (415 nm) and green (540 nm) light to enhance mucosal structures and capillary networks.[9] These wavelengths correspond to the peak absorption of hemoglobin, making structures high in hemoglobin appear darker. NBI further enhances the borders between different tissue types, facilitating neoplasia detection.[8] NBI can be used in real-time during the procedure and is considered a pre-processing modality. FICE and iScan, on the other hand, are applied post-process to enhance mucosal structures.

FICE: FICE is a post-processing modality of chromoendoscopy. Unlike pre-processing modalities that filter the light source, post-processing modalities break down images by wavelength and then reconstruct them with enhanced contrast.[40] A recent meta-analysis concluded that FICE had better predictive outcomes for detecting subjects with polyps compared to other modalities, including HDSL colonoscopy. However, some studies have shown no difference in detection rates of colonic polyps.[41]

iScanThis modality of chromoendoscopy is also post-procedural. iScan generates enhanced imaging without filtering the light source, using computer-based surface enhancement, contrast enhancement, and tone enhancement modes.[13] Although iScan has been promoted as useful in high-risk patient populations, its accuracy has been debated. Some studies showed insignificant superiority of iScan compared to other modalities, while another study concluded that HD imaging with iScan significantly increased the detection of colonic mucosal lesions for diminutive and small colorectal polyps.[9]

NBI: NBI is a pre-processing modality that allows for enhanced contrast without dyes by filtering the light source for specific wavelengths.[10] As discussed previously, NBI uses light frequencies that enhance visualization of the vasculature, making it a valuable tool for detecting angiogenesis, which plays a critical role in cancer pathogenesis and the conversion of preneoplastic lesions to neoplasms.[8] This allows for real-time lesion differentiation; however, it relies on the provider's ability to interpret findings. The need to standardize findings obtained by NBI prompted the development of the international endoscopic classification of CRC with NBI (hereinafter referred to as NICE classification).[14]

The NICE classification categorizes lesions into three major groups based on color compared to background mucosa, vascular pattern, and surface. Type 1 lesions, most likely representing hyperplasia (can be monitored), are the same or lighter in color, with no to some isolated "lacy" vessels, and a surface pattern of "dark or white spots of uniform size" or no pattern. Type 2 lesions, likely adenomatous (require polypectomy), are brown compared to the background, with brown vessels around white structures and a surface pattern that is oval, tubular, or branched. Type 3 lesions, likely invasive carcinomas (require endoscopic removal), are brown or dark brown, with irregular, discontinuous vessel patterns and an amorphous or inconsistent surface pattern.[14]

A meta-analysis by Atkinson *et al*. demonstrated that NBI had a greater detection rate for colorectal adenoma compared to WLE.[15] However, another study failed to replicate these results in a community-based setting.[16] Some studies indicated that NBI did not significantly improve the adenoma detection rate (ADR) of colonic adenomas or polyps compared to other modalities.[39] Additionally, studies reported that NBI showed no additional benefit over HD-WLE in CRC screening.[42] The sensitivity and specificity of NBI in detecting CRC have been reported to range from 81.8–99.2% and 85.2–99.6%, respectively.[43] Another meta-analysis comparing a newer generation of NBI against HD-WLE and first-generation WLE found that the newer generation of NBI significantly increased colonic ADR.[17]

While virtual chromoendoscopy, especially NBI, is a promising endoscopic modality, it faces several limitations. These include a lack of universal classification criteria for modalities other than NBI (FICE and iScan), poor understanding of trainee learning curves, and interobserver reliability.[9] Additionally, NBI has lower illumination capacity, leading to dimmer imaging compared to other modalities, which becomes significant when investigating colonic segments with deeper haustra, such as the cecum.[9]

Dye-based chromoendoscopy

While virtual chromoendoscopy utilizes a computer-based selection of light frequencies to enhance visualization, dye-based chromoendoscopy uses exogenous dyes to enhance mucosal structures that may be otherwise challenging to visualize on WLE. The variety of dyes includes absorptive stains such as Lugol's iodine and methylene blue and contrast stains such as indigo carmine.[9] Dye-based chromoendoscopy is frequently used in combination with HD-WLE and is a more accessible and less expensive version of CE. Limitations of dye-based chromoendoscopy include operator-dependent application of dye and lack of standardized interpretation criteria, which can be challenging to establish given the multiple dye options and differences in their application.[11,12] Recent reports on dye-based chromoendoscopy found sensitivity and specificity for detecting CRC or colonic polyps to be 92% and 82%, respectively.[12,13] In clinical practice today, dye-based chromoendoscopy is primarily utilized for endoscopic surveillance of dysplasia in patients with inflammatory bowel disease.[18] It is less often used for routine CRC surveillance due to the wait time required for the dye to dry and the difficulty in appreciating certain lesion shapes with dye application variability.[18] New explorations in dye-based chromoendoscopy have utilized oral methylene blue preparation for endoscopy, which has been associated with higher rates of adenoma detection.[19]

Ultrathin endoscopy

Ultrathin endoscopy is another modality that can be considered for CRC screening. It has a significantly smaller diameter of 6 mm compared to the 13 mm of a traditional endoscope. As a result, it allows for the procedure to be performed with little or no sedation. It is easier for patients to tolerate, with less reported overall and maximum pain, and has a higher cecal intubation rate compared with standard colonoscopes.[20] The downside to ultrathin endoscopy is poor flexibility, decreased resolution, and lack of biopsy capabilities.[21] Ultrathin endoscopy has been primarily used for upper GI lesions, such as Barrett's esophagus, with 98% sensitivity and 100% specificity.[37] To date, there is no sensitivity and specificity data for CRC detection using this modality, but promising results have been reported on improved cecal intubation rates when using ultrathin endoscopy compared to traditional endoscopy.[20] A study by Hamada *et al*. reported that smaller caliber colonoscopes, like ultrathin endoscopes, were associated with lower rates of colonoscopy-associated pain compared to traditional endoscopes.[22] Given the limited literature available on the diagnostic value of ultrathin endoscopy in CRC screening, more research is needed to further investigate its sensitivity and specificity for CRC detection.

Capsule endoscopy

Capsule endoscopy is a unique modality that uses a "pill" form instead of a traditional endoscope to visualize the GI tract. It comprises a small imaging sensor, light source, imaging optics, and a power supply.[9] Data collected can be transmitted wirelessly via electric-field propagation.[44] Its small size typically makes it well

tolerated by patients. Capsule endoscopy has been successfully used in the detection of upper GI pathology, particularly for small bowel lesions.[9] Despite its growing clinical application, capsule endoscopy has been underwhelming compared to traditional endoscopy, with a sensitivity and specificity of 78% and 73%, respectively, and remains a second-line modality.[23] Studies have identified several barriers to the use of capsule endoscopy, especially in the United States.[24] However, there is growing interest in its application in other parts of the GI tract. A review study by Agrawal *et al*. indicated that capsule endoscopy can be utilized for imaging the upper and lower GI tracts.[45] Vuik *et al*. proposed that capsule endoscopy can be used as an alternative to the primary colonoscopy and the fecal immunochemical test.[45] They performed a meta-analysis and found that colonic polyp detection rates ranged from 24–74% and CRC detection rates were 93%. They also found that the sensitivity and specificity for colonic polyps greater than 6 mm ranged from 79–96% and 66–97%, respectively. They concluded that capsule endoscopy was superior to computed tomographic colonography and had comparable accuracy to traditional colonoscopy, making it a potential alternative for CRC screening with HD-WLE.[46] One limitation of capsule endoscopy is the lack of active locomotion, which affects the quality of imaging and its ability to visualize haustra or other luminal cavities.[9]

Microscopic field view endoscopy

Wide-field endoscopy modalities are fundamental tools in GI endoscopy. While they are effective at identifying lesions concerning malignancy, they require a biopsy and pathology analysis to establish a diagnosis. This can lead to overuse of biopsies, delayed diagnoses, patient dissatisfaction, and increased healthcare costs. Fortunately, emerging endoscopic modalities provide microscopic resolution capable of diagnosing lesions *in vivo,* reducing the number of unnecessary biopsies. Examples of these microscopic field view modalities include confocal laser endomicroscopy, endocytoscopy, OCT, high-resolution microendoscopy, and second harmonic generation endoscopy. We will discuss these modalities in the following section.

Confocal laser endomicroscopy

This modality can generate histologic findings similar in quality to standard pathology by producing fluorescence images with micron-level resolution. It works by exposing stained tissues to a laser. Confocal laser endomicroscopy uses fluorescein for contrast, enhancing mucosal crypts and vascular structures. It provides a resolution of 1–3.5 µm, an imaging depth of up to 70 µm, and an FOV of 200–300 µm. However, confocal laser endomicroscopy is very expensive, which is a significant limiting factor. Additionally, the small FOV can cause sampling errors.[9] So far, this modality has mostly been evaluated in larger academic centers, so its learning curve and practicality are yet to be established. Recent reviews found that confocal laser endomicroscopy had a sensitivity and specificity for neoplasia of 96% and 92%, respectively.[47]

Endocytoscopy

Endocytoscopy utilizes reflectance imaging, similar to WLE, but allows for optical magnification of 500-fold (endoscope-based) to as much as 1000-fold (probe-based).[9] Contrast agents such as methylene blue or crystal violet can be used to enhance the visualization of nuclear and glandular structures.[48] Endocytoscopy provides a resolution of 1.7–4.2 µm and an FOV of 120–700 µm. It is compatible with video capsule endoscopy but is limited to visualizing only the mucosal surface.[9] Multiple studies established that the diagnostic accuracy of endocytoscopy in detecting colorectal lesions ranged from 86.4% to 96.8%.[16,49] Kudo *et al*. further investigated the diagnostic value of endocytoscopy in a retrospective study and found that its sensitivity and specificity for detecting colorectal cancer were 85% and 90.7%, respectively.[49] Some limitations of endocytoscopy include high cost, a lack of standardized classification systems, poor understanding of the trainees' learning curves, and interobserver reliability.[14]

Optical coherence tomography

This modality utilizes a low-coherence light source and works by obtaining reflectance from different tissue structures. This information is ultimately converted to diagnostic data on cellular morphology. OCT does not require contrast agents. It has a resolution of around 10 µm, a depth of 1–2.5 mm (the deepest among microscopic endoscopy modalities), and a large FOV with pullback (large-area scanning).[9] As this technology allows for the visualization of deep mucosal tissues, it enables the assessment of disease beneath the visible mucosal surface. OCT has mostly been used for upper GI lesions, specifically for Barrett's esophagus-related dysplasia, with over 80% diagnostic accuracy reported.[25] There have also been promising results with the use of OCT in CRC screening.[26] Recent advances in circumferential and forward-viewing OCT imaging have improved the visualization of colorectal polyps.[50] Ding *et al*. investigated the diagnostic capabilities of OCT for the early detection of colorectal dysplasia and cancer and found a sensitivity of 87.5% and a specificity of 75%. Given the high sensitivity and ability to analyze pathology in real-time, the authors concluded that OCT could become a valuable diagnostic modality.[27] Another study found that the addition of pattern recognition to OCT significantly improved sensitivity and specificity to 100% and 99.7%, respectively, for CRC diagnosis.[51] The limitations associated with OCT include high cost and poor availability outside large clinical centers. Additionally, it cannot be used after dye is applied, as it interferes with reflectance.[9]

High-resolution microendoscopy

This modality is a low-cost alternative to the microscopic field view modalities discussed earlier.[28] Like confocal laser endomicroscopy, it uses fluorescence for contrast, along with proflavine. The modality can visualize cellular structures at the mucosal surface with a resolution of 4.4 µm and an FOV of 790 µm.[9] As a new modality, high-resolution microendoscopy introduces interobserver variability and currently lacks diagnostic criteria to guide operators. In recent reviews, researchers proposed consensus high-resolution microendoscopy image criteria and used these to analyze endoscopist performance. They found that high-resolution microendoscopy has a sensitivity of 70% and a specificity of 94% for detecting CRC. They concluded that this low-cost microendoscopic modality could be used as an alternative to confocal laser endomicroscopy in low-resource settings. Another study found that endoscopists with no prior high-resolution microendoscopy experience had greater than 90% accuracy in identifying malignant colorectal polyps when addressing the learning curve for users. A combination of HD-WLE for polyp identification and high-resolution microendoscopy for optical biopsy has the potential to help eliminate unnecessary biopsies.[37]

New and future developments in endoscopic diagnosis of CRC

As more endoscopic techniques become available, developing classification criteria for each becomes increasingly important. However, new technology comes with a learning curve, and it

takes time for endoscopists to master these techniques and achieve interobserver agreement. Consequently, there is a growing opportunity to develop and utilize machine learning technology, artificial intelligence (AI) algorithms, and robotic-assisted colonoscopy to assist endoscopists with this learning curve. This will be discussed in the following section.

AI

AI is a rapidly advancing field in optical biopsy, with AI and machine learning technologies emerging as powerful tools in colonoscopy through real-time assistance in colon polyp detection and diagnosis.[52,53] Breakthroughs in deep-learning algorithms using convolutional neural networks have drastically expanded the capabilities of AI computer vision for endoscopy.[29,54] The most significant computerized visualization capabilities in colonoscopy include computer-aided detection (CADe) and computer-aided diagnosis (CADx).[9] CADe aids the operator in polyp detection, while CADx helps predict polyp histology without requiring tissue biopsy.[53] The potential for CADe and CADx algorithms to help endoscopists perform optical biopsy and diagnosis with higher confidence is a promising new direction for clinical endoscopy.[30]

Previous studies have demonstrated that real-time use of AI CADe tools during colonoscopy improves ADR and other performance metrics. A prospective study of 1,057 patients reported an ADR in HD-WLE colonoscopy with the use of an AI-based algorithm of 29.1%, compared to 20.3% for standard colonoscopy alone.[31] Several retrospective studies also showed that CADx can differentiate between adenomatous and benign colonic polyps in real time with 94% accuracy.[55,56] A recent meta-analysis of 10 randomized controlled trials with 6,629 patients found that both ADR (relative risk [RR], 1.43; $p < 0.001$) and polyp detection rate (RR, 1.44; $p < 0.001$) were significantly greater with AI-aided colonoscopy compared with routine colonoscopy. The adenomas detected per colonoscopy (APC) and polyps detected per colonoscopy were also significantly higher in the AI-aided group compared with the routine colonoscopy group.[32]

In contrast to the positive earlier research on the use of CADe, more recent studies have demonstrated that CADe may not necessarily improve adenoma detection clinically. In a retrospective single-center study, CADe did not improve ADR or APC compared to controls.[33] A large, retrospective observational study reported a lower ADR in the CADe group compared to a pre-CADe retrospective control (30.3% vs. 35.2%; $p = 0.001$), as well as a lower polyp detection rate and lower APC.[57]

With the emergence of AI tools in endoscopy, important questions have surfaced regarding the safe and effective introduction of AI technology into clinical endoscopic practice. In response to the predicted resect-and-discard or diagnose-and-leave practices accompanying the optical diagnosis of colorectal polyps, the American Society for Gastrointestinal Endoscopy created the 2011 initiative "Preservation and Incorporation of Valuable Endoscopic Innovations." This initiative identified optical characterization of colorectal polyps <5 mm in size as a key area for new endoscopic technologies and outlined specific requirements for safely adopting diagnose-and-leave and resect-and-discard strategies for suspected hyperplastic polyps and colorectal polyps <5 mm in size.[53]

As AI continues to revolutionize colonoscopy, particularly in enhancing lesion detection and diagnosis, comprehensive education and training in the use of AI technologies will become paramount.[51,52] Further research to better understand the strengths and limitations of AI in colonoscopy is necessary, as the future of colonoscopy heads towards further integration between AI technology and individual physician ability.

Robotic colonoscopy

Robotic colonoscopy is another emerging technology that shows promise in improving the endoscopic detection of CRC. The earliest systems developed in the 1990s had inch-worm locomotion capabilities, while newer systems developed over the past two decades possess self-steering and self-propulsion technology for autonomous navigation of the colonic lumen.[34] The drive to develop robotic colonoscopy technologies arose from several needs, including increasing precision and dexterity in the procedure, avoiding looping, increasing the field of view, decreasing the pain experienced by patients, improving ergonomics, and reducing endoscopist fatigue, and flattening the steep operator learning curve associated with learning conventional endoscopy techniques.[34,35]

While these potential benefits could improve the endoscopic detection of CRC through the improvement of the colonoscopy procedure, robotic colonoscopy is not without considerable limitations. These involve high costs due to the challenge of miniaturizing the technology, limited clinical validation, and barriers to adoption in clinical practice.[34,35,58] As with any new technology, training endoscopists in its use requires time, resources, and overcoming barriers associated with changing clinical practice norms. The limited adoption of existing systems approved by the U.S. Food and Drug Administration (FDA) speaks volumes about the barriers facing robotic colonoscopy. Of the FDA-approved robotic colonoscopy technologies, only the Endotics System remains commercially available. It received the CE mark in 2017 and FDA 510(k) approval in 2020.[58] This system utilizes an electro-pneumatic self-advancing locomotion RC system and consists of a disposable colonoscope that advances in the colon using two mucosal clampers, located proximally and distally on the probe, and is controlled remotely by a handheld control unit.[58] It is the only robotic colonoscopy system currently available in clinical practice and is marketed in Europe, the UK, and Australia. Several early studies reported reduced intraprocedural pain with the Endotics system, as well as a lower risk of perforation, ease of learning how to use the system, and comparable ADR to conventional endoscopy.[59,60,61] Limitations include longer procedural time and a lower cecal intubation rate.[59,60] More recent studies and further clinical validation of the Endotics system are lacking, aside from one case reporting a painless screening colonoscopy using the robotic system on a patient who previously refused to undergo conventional screening colonoscopy due to pain.[62] Several other robotic colonoscopy systems gained FDA approval but are no longer on the market. These include NeoGuide, Invendoscope, Colonosight, and Aer-O-Scope.[57,58] More post-marketing studies need to be performed to promote greater confidence in robotic colonoscopy systems and their adoption into clinical practice.

Robotic colonoscopy is an emerging technology in the detection of CRC and offers the potential for improved precision and reliability. This potential could be seen in the future as an alternative to a conventional screening colonoscopy, given the development of robotic systems with autonomous locomotion capabilities, or as an augmentation of traditional colonoscopes with robotic devices that improve dexterity and expand intraprocedural capabilities. Integration with continuously improving AI and machine learning algorithms could further bridge the gap to widespread clinical adoption. While robotic colonoscopy is a promising area for improving CRC detection, challenges remain, primarily related to cost, clinical implementation among endoscopists, and limited studies demonstrating clinical validation.

Conclusions

New endoscopic modalities show great promise in improving CRC detection, but they come with limitations such as steep learning curves, a lack of standardized classification criteria, interobserver agreement issues, and often higher costs. More research is needed to investigate these modalities' potential to reduce mortality from CRC. Some of the limitations of emerging endoscopic modalities have provided opportunities for the development of machine learning technology and AI tools to minimize the steep learning curve and the need for standardization. More research is needed to better understand the strengths and limitations of AI and robotic capabilities in the endoscopic diagnosis of CRC and to establish best practices for AI integration in clinical endoscopy.

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Author contributions

Drafting of the manuscript (AT, DG, GM), figures and tables (AT), and critical revision of the manuscript for important intellectual content (MT). All authors have made significant contributions to this study and have approved the final manuscript.

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