

ADVANCES IN ENDOSCOPY

Current Developments in Diagnostic and Therapeutic Endoscopy

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Novel Colonoscopic Imaging Techniques



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G&H How effective is standard white-light colonoscopy for the detection of colon cancer? Why are new techniques still needed?

RK Colonoscopy is considered to be the gold standard of colon cancer screening. In fact, colonoscopy has been shown to reduce colon cancer mortality by approximately 50%. However, colonoscopy is not as effective on the right side of the colon as it is on the left side of the colon. Flat and serrated adenomas (precancerous conditions) are more common on the right side of the colon and harbor an increased cancer risk. Multiple studies have shown that these lesions can easily be overlooked. Moreover, tandem, or back-to-back, colonoscopies have shown that at least 20% of adenomas are overlooked, which can lead to interval cancers (new or overlooked cancers that develop despite the performance of colonoscopy and recommendation of surveillance).

In addition, it has been shown that the quality of bowel preparation, experience of the endoscopist, and use of new endoscopic techniques can increase the adenoma detection rate. A recent study from Poland showed that a greater-than-20% adenoma detection rate almost eliminated the risk of interval cancers. Thus, quality markers (eg, complete colonoscopy rate, withdrawal time, adenoma detection rate, and cleanliness of the colon) have to be measured and monitored to produce high-quality colonoscopy. New colonoscopy techniques are being developed with the goal of further increasing detection rates and improving the prediction of the final histology of colorectal lesions.

G&H How does high-definition white-light colonoscopy compare with standard white-light colonoscopy for examination of the colon?

RK High-definition white-light colonoscopy is based on television technology for the consumer market that has been successfully adapted for medical applications. High definition

produces a higher resolution and displays more information on a 16:9 monitor. High-resolution charge-coupled devices currently have pixel densities of more than 1 million, which can be better visualized now on high-definition screens.

Multiple studies have investigated the value of high-definition colonoscopy. A recent meta-analysis showed that high-definition colonoscopy increases the diagnostic yield by 3.8%. It is expected that high-definition endoscopic systems will evolve as a new standard of care.

G&H How is chromoendoscopy applied in colonoscopic imaging?

RK Chromoendoscopy involves the application of dyes—most commonly methylene blue and indigo carmine—to the mucosal surface in order to highlight surface mucosal architecture. Targeted chromoendoscopy (staining of dedicated lesions) is very helpful for delineating borders and clarifying the morphology of a lesion (as polypoid, flat, or depressed). Panchromoendoscopy (staining of the entire colon) can increase the adenoma detection rate of sporadic adenomas and can lead to better identification of flat adenomas.

In addition, panchromoendoscopy has a clear indication for patients with long-standing ulcerative colitis, in whom endoscopic surveillance is recommended. In a recent meta-analysis, chromoendoscopy had a number needed to treat of 14.3 (ie, 14 people had to undergo chromoendoscopy to detect intraepithelial neoplasia in 1 additional person).

Virtual chromoendoscopy (electronic staining) can also be performed. Virtual color can be added by a push of the button. Several endoscopic manufacturers have developed their own virtual chromoendoscopy systems (eg, narrow-band imaging [NBI], Olympus; Fujinon intelligent chromoendoscopy [FICE], Fujinon; and i-scan, Pentax). Via a special filter, NBI alters light emitted to the tissue, enhancing the blue spectrum of the light, which leads to better visualization of surface ves-

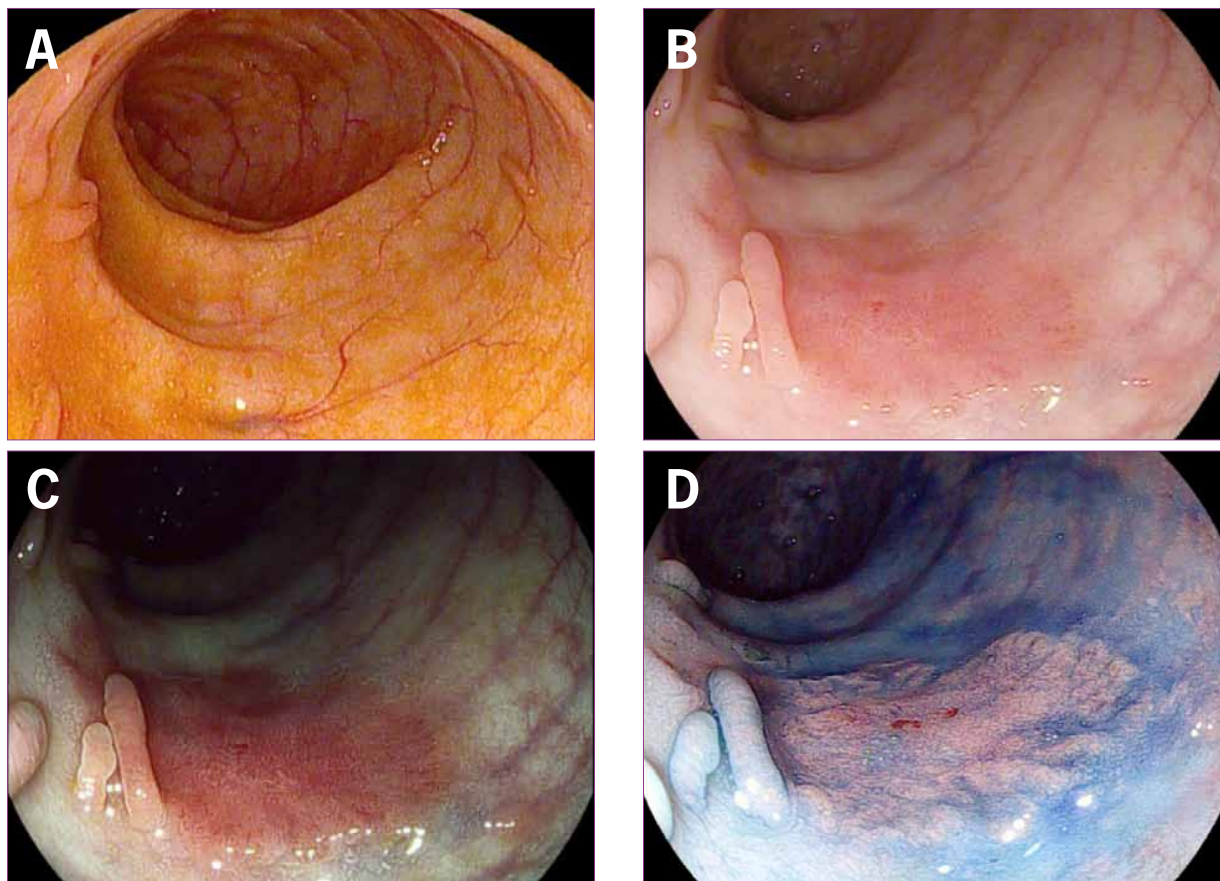


Figure 1. **A:** A standard white-light colonoscopic image of a patient with long-standing ulcerative colitis. **B:** High-definition imaging after the mucosal surface is cleaned. A flat lesion can be identified. **C:** Virtual chromoendoscopy highlights the surface architecture and borders of the lesion. **D:** Chromoendoscopy with methylene blue delineates dysplastic tissue from normal tissue.

sel architecture. FICE and i-scan also alter light emitted to the tissue but via different postprocessing filters that enhance vessel and tissue architecture.

Several studies have investigated the use of virtual chromoendoscopy for the detection of adenomas, but none of these studies have shown a benefit with this technique. Thus, no advantage is associated with continuously using virtual chromoendoscopy during withdrawal. However, based on vessel and tissue architecture, virtual chromoendoscopy can be used to better characterize lesions that have been identified. In addition, this technique is significantly better at predicting the final histology of a lesion compared with white-light endoscopy alone.

Figure 1 shows the same lesion viewed with white-light colonoscopy, high-definition colonoscopy, virtual chromoendoscopy, and chromoendoscopy with methylene blue.

G&H Are there any other novel colonoscopic imaging techniques?

RK Endomicroscopy is a technique that provides in vivo histology during endoscopy. The fundamental difference

between this technique and those previously mentioned is that histology is not predicted with endomicroscopy; instead, it can be directly visualized. Microscopic architecture of the mucosa is visualized by a magnification of 1,000 times with subcellular resolution. Individual cells, as well as cell components (eg, mucin in goblet cells), can be readily visualized, offering the ability to immediately diagnose intraepithelial neoplasia and subsequently provide a targeted endoscopic intervention (Figure 2).

Endomicroscopy requires the systemic or local application of contrast agents (fluorescein or acriflavine), which interact with a miniaturized confocal laser that is advanced as a catheter over the working channel of an endoscope or is embedded in a standard colonoscope. This technique enables the visualization of microscopic changes of the mucosa over time and provides functional imaging. For example, the mucosal barrier of the colon can be directly viewed, and mucosal healing can be measured in patients with inflammatory bowel disease. Thus, endomicroscopy has the potential to significantly alter endoscopic algorithms, reduce the number of mucosal biopsies, and improve the prediction of disease outcome via functional measurement.

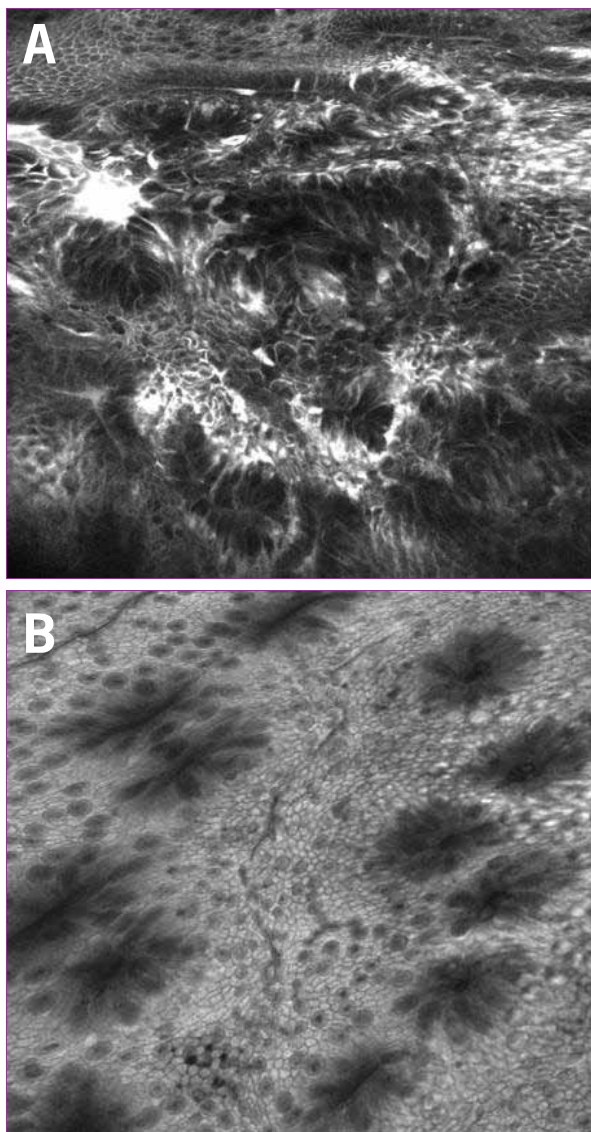


Figure 2. A: Endomicroscopy of high-grade intraepithelial neoplasia. B: Endomicroscopy of the normal colon.

Another evolving technology is molecular imaging, which provides information about the molecular signatures of colorectal neoplasia. In this technique, endomicroscopy is combined with specific contrast agents, such as antibodies or special proteins, which interact with dedicated epitopes at the cellular surface and can be visualized with a confocal microscope. Antibody-aided molecular imaging enables the characterization of receptors, such as epidermal growth factor receptor or vascular endothelial growth factor. Proteins are incorporated into malignant cells. Immediate diagnosis of a malignancy or molecular signature is possible. A future goal of this technique is to evaluate the response of chemotherapy with targeted biologic agents for the treatment of colorectal cancer.

G&H What are the limitations associated with the previously mentioned techniques?

RK High-definition colonoscopy with chromoendoscopy and virtual chromoendoscopy can be broadly used. However, the surface architecture that is made newly visible with these techniques requires additional education and training, as the patterns have to be accurately interpreted to achieve the correct diagnosis. Chromoendoscopy is increasingly being replaced by virtual chromoendoscopy. However, chromoendoscopy should still be used in patients with inflammatory bowel disease. In this patient population, conventional chromoendoscopy is superior to virtual chromoendoscopy for the diagnosis of intraepithelial neoplasia.

Endomicroscopy provides a new and unique imaging possibility for gastrointestinal endoscopy. The microscopic architecture of normal and diseased tissue has to be learned, or the findings should be discussed with a pathologist. Endomicroscopy is a time-consuming and highly examiner-dependent technique. However, endomicroscopy may provide unique diagnostic possibilities, such as functional and molecular imaging. Further studies are required for standardization of these techniques.

G&H How significant are the learning curves associated with these techniques?

RK Among the previously mentioned techniques, endomicroscopy has the longest learning curve; at least 30 supervised cases are recommended to gain proficiency. The other techniques can be rapidly learned, and interaction with the final histology report will help improve individual diagnostic skills.

G&H How safe are these techniques compared with standard colonoscopy?

RK Chromoendoscopy, particularly virtual chromoendoscopy, is very safe. Methylene blue was once thought to be genotoxic; however, new data contradict these early findings. The agents used in endomicroscopy have the potential to cause allergic reactions. However, the safety of fluorescein has been demonstrated in a large study.

G&H Has cost-effectiveness analysis been applied to these new techniques?

RK These new techniques help ensure a more accurate diagnosis of precancerous lesions of the colon. The use of techniques might help reduce costs because fewer cancers are missed. In addition, unnecessary biopsies and endoscopic interventions may be avoided. Additional studies are needed to further clarify the cost-effectiveness of these techniques.

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G&H Is use of these new colonoscopic imaging techniques becoming mainstream, or do most doctors continue to use only standard colonoscopy?

RK High-definition colonoscopy is rapidly becoming mainstream for colonoscopic imaging. Virtual chromoendoscopy systems are included as part of these high-definition endoscopic systems and are increasingly being used to characterize colorectal lesions. Efforts are being made to avoid histologic examinations because endoscopic diagnosis becomes more accurate with these new techniques (via the resect-and-discard strategy).

Endomicroscopy will be reserved for university or referral centers with a high volume of patients who have an increased cancer risk (eg, patients with ulcerative colitis).

G&H What future developments do you anticipate in this area of endoscopy?

RK Endoscopy is a dynamic field, and new developments

are continuously being made. It has been speculated that new optics will provide a nearly 360° overview of the colonic surface, which will further reduce the number of missed lesions. In addition, new fecal or serologic markers will help categorize patients into high- or low-risk groups for colorectal cancer. Then, there will be a shift from diagnostic to therapeutic colonoscopy.

Suggested Reading

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