Current Status of Chromoendoscopy and Narrow Band Imaging in Colonoscopy

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ABSTRACT

Colonoscopy, the preferred procedure for colon cancer screening, has well-documented limitations. To improve colonoscopy's effectiveness, augmented endoscopy techniques, such as chromoendoscopy and narrow band imaging (NBI) have been evaluated. Both techniques are inexpensive, safe, and relatively easy to perform. Chromoendoscopy has an increasingly important role in surveillance of IBD, but significant work is needed to determine the optimal staining techniques and mucosal surface pattern analysis before this technique can be incorporated into routine clinical practice. NBI is a much newer technology with far less data. Well-designed prospective randomized controlled trials have failed to identify a benefit of NBI in screening colonoscopy, in surveillance for high-risk populations or as an adjunct for therapeutic procedures.

KEYWORDS: Chromoendoscopy, narrow band imaging, colonoscopy, endoscopy

Objectives: On completion of this article, the reader should be able to discuss the techniques of chromoendoscopy and narrow band imaging in colonoscopy.

In the United States, colorectal cancer is currently the fifth leading cancer, with an estimated 146,970 new cases annually. It is the second largest cause of cancer death: Approximately 49,920 died of the disease in 2009.¹ As dedicated colonoscopists, we must focus on our ability to meticulously detect and remove colorectal neoplasia with the ultimate goal being colorectal cancer prevention.

The practice of removing neoplastic colonic lesions during colonoscopy to reduce the incidence of colorectal cancer has been justified by the results of the National Polyp Study Workgroup cohort study, which showed that colonoscopy with removal of identified polyps reduced the incidence of colorectal cancer 76 to 90%.²

Currently, white light colonoscopy (colonoscopy), albeit imperfect, is the preferred colorectal cancer screen-

ing test.³ It is the best screening test to both detect and remove colonic neoplasms. However, substantial miss rates for adenoma and cancers have been reported with colonoscopy. The colonoscopy-miss rate for adenomas is not completely understood, but has been well documented by several studies showing a significant discordance in adenoma detection rate (ADR) during screening colonoscopy among practicing colonoscopists.

ADENOMA DETECTION RATE

Published ADRs during colonoscopy have ranged from 7% to 44%, whereas the mean number of adenomas detected per subject screen has ranged from 0.09 to 1.05.⁴⁻⁸ To study more closely the missed adenoma rate of colonoscopy, same-day tandem (back-to-back) colonoscopies have shown an overall adenoma-miss

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rate as high as 24%. Miss rates for adenomas ≤ 5 mm was 27%; adenomas 6–9 mm, 13%, adenomas ≥ 10 mm, 6%; and advanced adenomas, 11%.^{9–11} In individuals with Lynch syndrome (hereditary nonpolyposis colorectal cancer), miss rates as high as 55% have been reported.¹² Colonoscopy-miss rates for colorectal cancer has been reported at $\sim 4\%$.¹³ Answers to the question of how meticulous a colonoscopist must be to prevent colorectal cancer are unknown, but evolving.

Computed Tomographic Colonography

In 2008, the American College of Radiology Imaging Network published one of the largest prospective, multicenter, head-to-head comparisons of computed tomographic colonography (CTC or virtual colonoscopy) to white light colonoscopy for adenoma detection in 2,531 asymptomatic adults ≥ 50 years. CTC's sensitivity for adenomas or cancers ≥ 10 mm was 90%, but the sensitivity for adenomas or cancers < 5 mm was only 65%.¹⁴ These results were not as promising as Pickhardt's groundbreaking study reporting a 93.8% sensitivity of CTC for polyps ≥ 10 mm, which no subsequent multicenter study has ever achieved.¹⁵ In May 2009, the Centers for Medicare and Medicaid Services concluded "the evidence is inadequate to conclude that CT colonography is an appropriate colorectal cancer screening test. . . CT colonography for colorectal cancer screening remains noncovered." However, the American College of Gastroenterology added, for the first time, CTC every 5 years as an alternate cancer detection test in their updated 2009 colorectal cancer screening guideline, removing double-contrast barium enema as an approved colorectal cancer detection test.³

QUALITY METRICS

Quality indicators for colonoscopy have focused mainly on the cecal intubation rate, adequacy of colonic cleansing, and colonoscopists' ADR as the most salient quality metrics for practicing colonoscopists.

Withdrawal Time

Several prospective studies have shown significant positive correlation between ADR and longer mean withdrawal time during colonoscopy in which no polyps are found or removed. Detection rates of adenomas and advanced adenomas (adenomas ≥ 10 mm, adenomas of any size with any villous features, and any polyp with high-grade dysplasia) were both significantly greater among endoscopists whose mean withdrawal time was ≥ 6 minutes. The advanced ADR was 2.46 times higher for colonoscopists whose average withdrawal times on a no-polyp-find colonoscopy were ≥ 6 minutes when com-

pared with colonoscopists whose average withdrawal times were < 6 minutes.¹⁶

More recent studies have shown that a minimum withdrawal time of at least 7 minutes provided significantly greater ADRs.^{17,18} The mean withdrawal time to virtually prevent colorectal cancer has not yet been defined.

Bowel Preparation

High-quality bowel preparation for colonoscopy is paramount to facilitate maximum mucosal visibility for colonoscopists. Several recently published prospective, randomized, blinded, controlled trials have compared whole-dose polyethylene glycol electrolyte (PEG-E) versus split-dose PEG-E, demonstrating that patients who received split-dose colonic preparation have a significantly better colon cleansing than those receiving whole-dose colonic preparation.^{19–22}

High-Resolution Colonoscopy

A comparative study of ADR between standard-resolution (SR) and high-resolution (HR) colonoscopy with optimized withdrawal technique of at least 6 minutes and wide-angle field of view colonoscopy versus standard field of view showed no significant difference in ADR.^{23,24}

Timing of Colonoscopy

Two studies investigating colonoscopists' fatigue on ADR have shown that time of the day that the colonoscopy is performed appears to be an independent predictor of adenoma detection, irrespective of adequate bowel preparation or completeness of the colonoscopy.^{25,26} Sanaka and colleagues' study of 3,619 asymptomatic outpatients with adequate bowel preparation and complete colonoscopy—in which 48.3% were performed in the morning and 51.7% in the afternoon—reported an ADR of 29.3% in the morning group versus 25.3% in the afternoon group ($p = 0.008$). In addition, there was a trend toward declining ADR for each subsequent hour of the day ($p = 0.01$).

Nonpolypoid Colonic Neoplasm

Flat adenomas have recently gained much attention and are a possible cause of missed adenomas or interval colorectal cancers because they may go unrecognized or may be dismissed by colonoscopists; their visualization at colonoscopy mandates an adequate bowel preparation and a meticulous examination of the colonic mucosa. The incidence of flat colonic neoplasia has been elucidated by Gorgun et al, whose evaluation of 3,115 adenomas removed during colonoscopy found 83% to

be sessile, 10% to be flat, 6% to be pedunculated, and 1% to be depressed.²⁷ This prevalence of flat and depressed adenomas was validated by a report of 1,819 adults Veterans Affairs Administration colorectal cancer screening patients.²⁸

With the known limitations of colonoscopy addressed, we will review the ability of chromoendoscopy and narrow band imaging (NBI) to enhance mucosal detection of neoplastic tissue in both screening and surveillance colonoscopy.

CHROMOENDOSCOPY

Background

Chromoendoscopy, the technique of endoscopically applying contrast dyes to improve the detection of mucosal abnormalities, first appeared in the literature in the 1970s.^{29,30} Initially, this procedure was described as an adjunct in gastric cancer screening, where it facilitated the identification of dysplastic tissue. Tada³¹ first adapted the technique for colonoscopy in 1974. Over the next 20 years, the majority of the experience with this technique appeared in Japanese publications; however, in the 1990s, as interest grew in improving colonic adenoma detection, more trials of chromoendoscopy were conducted worldwide.

Chromoendoscopy techniques have been employed for the study of several conditions, including Barrett's esophagus, esophageal cancer, gastric cancer, celiac disease, and colon cancer. Although several inexpensive staining agents have been investigated, none to

date have been approved by the U.S. Food and Drug Administration (FDA) for chromoendoscopy.

Types of Stains and Dyes

Chromoendoscopy staining agents can be broadly organized into the categories based on their mode of action (Table 1). Contrast dyes, including indigo carmine, pool in the crevices and irregularities of surface mucosa and highlight potentially abnormal tissue.

Vital dyes, such as methylene blue and crystal violet are actively absorbed by the gastrointestinal mucosa. Metaplastic or neoplastic mucosa often absorbs vital stains differently than normal mucosa, and these differences serve to highlight abnormal structures.

Finally, reactive dyes such as Congo red and phenol red respond to specific host conditions. Phenol red is pH sensitive, and when used in the stomach, it aids in the identification of *Helicobacter pylori* infection by changing color in lower acid concentrations. In chromoendoscopy of the colon, the majority of clinical trials have been conducted using two staining agents: methylene blue and indigo carmine.

Staining Techniques

A multitude of techniques have been described for the application of surface stains during chromoendoscopy. Some methods deliver the contrast dye prior to endoscopy by mixing it in the colonic lavage solution or administering it by mouth immediately after the colon preparation is completed.³² Although convenient, these

Table 1 Staining Agents for Chromoendoscopy

Stains	Mechanism of Action	Main Application
ABSORPTIVE STAINS		
Lugol's solution	Stains glycogen-containing epithelium	Esophageal squamous cell cancer Barrett's esophagus
Methylene blue	Absorbed by epithelial cells, dysplasia, and cancer stain poorly	Barrett's esophagus Gastric cancer Chronic ulcerative colitis Colonic neoplasms
Toluidine blue	Stains nuclei	Oral and esophageal squamous cell cancer
Crystal violet	Stains nuclei	Colonic neoplasms Define margins of EMR
CONTRAST STAINS		
Indigo carmine	Highlights mucosal topography	Colonic neoplasms
REACTIVE STAINS		
Phenol red	pH sensitive color change	<i>H. pylori</i> infection
Congo red	pH sensitive color change	Ectopic gastric mucosa Gastric cancer Adequacy of vagotomy <i>H. pylori</i> infection

EMR, endoscopic mucosal resection.

Table 2 Spray Catheters for Chromoendoscopy

Manufacturer	Name	Length	Use	U.S. Price (11/09)
Olympus, Inc., Melville, NY	PW-6P-1	190 cm	Reusable	\$225
	PW-5L-1	165 cm	Reusable	\$225
	PW-5V-1	240 cm	Reusable	\$225
	PW-6C-1.A	105 cm	Reusable	\$245
	PW-6C-1.B	105 cm	Reusable	\$215
Wilson-Cook Medical, Inc., Winston Salem, NC	GT-7-SPRAY	240 cm	Single use	\$81

methods suffer from inconsistent mucosal staining and are not routinely used.

The most widely accepted technique for applying surface stains employs a spray catheter inserted through the working channel of the colonoscope. This technique, while time consuming, allows for adequate surface preparation and targeted application of surface dyes. Spray catheter chromoendoscopy typically begins with cecal intubation using standard white light. Next, the colonic mucosa is prepared and stained in a segmental fashion starting with the cecum and progressing anatomically through the ascending, transverse, descending colon, sigmoid colon and rectum.

Most commonly, the mucosa is washed free of debris under white light. Some protocols call for the use of atropine or glucagon to minimize gut contractions and prevent uneven spraying. Once the mucosa is adequately prepared, a spray catheter (Table 2) is advanced ~1 to 2 cm from the surface mucosa and dye is delivered until the entire mucosal surface is covered. Excess dye is removed prior to mucosal examination. The additional time required for chromoendoscopy varies dramatically depending on the technique used and operator experience.

Successful chromoendoscopy depends not only on adequate mucosal staining, but also on observer identification of abnormal mucosa. Interpretation of stained mucosa is subject to observer variation.³³⁻³⁵ Most commonly, this is accomplished by the classification of the mucosal appearance according to a system described by Kudo et al (Fig. 1).³⁶ Organizing lesions into groups based on mucosal surface patterns, this system allows endoscopists to estimate a lesion's malignant potential based on its endoscopic appearance. Kudo and colleagues' original work used high-magnification endoscopes capable of 70× to 150× magnification to assist in surface pattern analysis; not all chromoendoscopy trials have been conducted with high-magnification endoscopy.

Several researchers have adapted the technique for use with high-resolution endoscopy: a technology that boasts enhanced surface detail from improved image resolution, but only minimal (1.5×) magnification. Both high-magnification and high-resolution endoscopy have been described as adjuncts to chromoendoscopy; however, neither is central to the technique.

Safety Concerns

The use of surface dyes during chromoendoscopy has, in some cases, generated safety concerns. Prior *in vitro* biochemical studies have established that in the presence of light methylene blue can generate single-strand breaks in DNA.³⁷⁻³⁹ Around the time the first large prospective trials using methylene blue chromoendoscopy in the colon were published, Olliver et al⁴⁰ released an *in vivo* evaluation of methylene blue chromoendoscopy for surveillance of Barrett's esophagus. Using DNA electrophoresis assays to assess levels of DNA damage, the authors evaluated tissue samples taken before and after staining. Higher levels of DNA damage appeared in the samples exposed to methylene blue and white light.

Kiesslich⁴¹ reported 20-month safety data on patients who had been subjects of chromoendoscopy. The subjects all had long-standing ulcerative colitis and had been enrolled in a prior chromoendoscopy investigation using methylene blue. At follow-up colonoscopy, significantly fewer lesions were found in the chromoendoscopy group when compared with controls. Citing these findings, he endorsed the use of methylene blue

Figure 1 Pit pattern classification. (Reprinted from Miyamoto, Muto, Hamamoto, et al. Diagnosis of colorectal tumorous lesions by magnifying endoscopy. *Gastrointest Endosc* 2006;44:9, with permission from Elsevier.)

and concluded that prior observations regarding DNA damage were unlikely to have biologic consequences. In another endorsement, Dinis-Ribeiro and colleagues reported 3-year safety data on patients under methylene blue chromoendoscopy surveillance for chronic atrophic gastritis.⁴² Here again, the authors noted a lower incidence of neoplasia in the study population when compared with surveillance studies using white light.

As an alternative to methylene blue, indigo carmine is generally regarded as a safe dye because it is not absorbed by the colonic mucosa. In a direct comparison of the toxicity of these two dyes, Davies⁴³ published an *in vitro* study using adenocarcinoma cell cultures that were exposed to white light for 2 minutes in the presence of either 0.1% indigo carmine or 0.1% methylene blue. Assays were performed on each group to quantify the DNA strand breaks. No significant increase in DNA damage was detected in the indigo carmine group when compared with the control group. The methylene blue group, on the other hand, had a significant increase in DNA damage. Drawing on these findings, Davies suggested that, assuming equivalent efficacy of the chromoendoscopic dyes, indigo carmine should be preferentially considered. To date, however, no long-term data exist that capture adverse clinical outcomes, and some groups continue to use methylene blue chromoendoscopy.

Adenoma Detection in Chromoendoscopy

Several trials have evaluated the ability of chromoendoscopy to increase detection of adenomas during screening colonoscopy. Kiesslich et al⁴⁴ performed one of the first large prospective trials of this technique. The study included 100 patients and implemented selective mucosal staining. Abnormal mucosa seen on white light exam was further stained with 0.4% indigo carmine dye and characterized according to the Kudo classification system. In the subset of patients where no lesions were identified, the entire sigmoid colon was stained with 0.4% indigo carmine and reexamined. Using this technique the authors found 178 additional lesions in the sigmoid colon. This study failed to control for withdrawal time, which may have explained the increased detection with indigo carmine.

As larger and more carefully controlled studies have been published, some of the early promise of chromoendoscopy has faded. Booker et al⁴⁵ conducted one of the first large randomized controlled trials of pan-colonic chromoendoscopy versus standard colonoscopy. This study included 259 patients and reported a statistically significant increase in detection rate for diminutive adenomas (89 vs. 36), as well as number of patients with ≥ 3 adenomas (15 vs. 3), in the chromoendoscopy group. Despite these findings, there was no significant overall increase in the detection of adenomas. In addition, this

study failed to control for withdrawal time. Withdrawal times in the chromoendoscopy group were significantly longer than the control group (9 minutes, 5 seconds vs. 4 minutes, 52 seconds). Thus, the increased detection reported in the chromoendoscopy group may have been a result of a longer examination time and not from the contrast staining.

Hurlstone⁴⁶ designed a second large randomized trial of pan-chromoendoscopy that controlled for scope withdrawal time and mucosal lavage volume. This study included 260 patients and compared pan-chromoendoscopy using 0.4% indigo carmine dye to a control group of targeted chromoendoscopy. Hurlstone reported a higher number of adenomas in the pan-chromoendoscopy group (112 vs. 57). The reported flat lesions (54 vs. 82), right-sided lesions (31 vs. 79), and patients with ≥ 3 adenomas (4 vs. 13) were significantly higher in the pan-chromoendoscopy group.

Unfortunately, Hurlstone's findings were not replicated in a third randomized controlled trial investigating chromoendoscopy conducted by Le Rhun et al.⁴⁷ This large prospective trial included 203 patients and compared adenoma detection of SR video colonoscopy against HR pan-colonic chromoendoscopy using indigo carmine 0.4%. The authors found that HR colonoscopy detected more polyps than SR colonoscopy. They also noted that the HR group found a higher number of flat adenomas < 5 mm. Unlike Booker's or Hurlstone's studies, this trial did not find a higher number of patients with ≥ 3 adenomas in the HR group. In fact, the total number of adenomas detected was not statistically different between the HR and SR groups.

Chromoendoscopy in High-Risk Populations

Although the weight of evidence appears to not support the use of chromoendoscopy for adenoma detection in routine screening colonoscopy, several trials have investigated the benefit of chromoendoscopy in enhancing detection of dysplasia in high-risk populations.

In 2003, Matsumoto et al⁴⁸ published the results of a chromoendoscopy surveillance program for patients with ulcerative colitis. The trial lasted 7 years; it followed 57 patients who had been diagnosed with pan-colitis at least 5 years earlier, and included 117 pancolonoscopic chromoendoscopies using indigo carmine 0.2%. A higher diagnostic accuracy for dysplasia in biopsies targeted by chromoendoscopy versus random biopsies from standard colonoscopy was found (sensitivity of 38.1% vs. 85.7%, respectively).

In a similar study, Kiesslich et al⁴⁹ performed a randomized controlled trial of chromoendoscopy to evaluate the early detection of intraepithelial neoplasia and colitis-associated colon carcinomas in patients with ulcerative colitis. In this study, 263 patients were randomized to receive either white light colonoscopy

with random biopsies or pancolonoscopic chromoendoscopy with targeted biopsies using 0.1% methylene blue. The trial found a stronger correlation between the endoscopic assessment of colonic inflammation and histopathologic findings in the chromoendoscopy group. Further, statistically higher numbers of intraepithelial neoplasias were detected in the chromoendoscopy group (32 vs. 10; $p = 0.003$). Chromoendoscopy allowed for the differentiation between nonneoplastic and neoplastic lesions with a sensitivity and specificity of 93%.

Rutter et al⁵⁰ investigated pancolonoscopic surveillance chromoendoscopy in patients with long-standing ulcerative colitis. The study featured 100 patients examined using a back-to-back design, beginning with white light colonoscopy using random mucosal biopsies followed by pancolonoscopic chromoendoscopy using mucosal biopsies targeted by 0.1% indigo carmine staining. The authors failed to show a significant difference in detection of dysplasia between the two groups (7 vs. 2), but noted a strong trend toward significance ($p = 0.06$). Further, they found that biopsies targeted by dye spraying yielded significantly more dysplastic lesions than random biopsies did (5 vs. 0; $p = 0.02$).

Marion et al⁵¹ subsequently published a prospective trial comparing chromoendoscopy with methylene blue 0.01% to white light colonoscopy in 115 patients with inflammatory bowel disease (IBD). The authors detected significantly more dysplasia in the chromoendoscopy group (17 vs. 9; $p = 0.001$).

Although the majority of studies of chromoendoscopy in high-risk populations have examined patients with long-standing IBD, other high-risk groups have been evaluated. Hurlstone et al⁵² conducted a prospective study of 25 patients who fulfilled the modified Amsterdam criteria for hereditary nonpolyposis colon cancer (HNPCC). This study assessed the efficacy of high-magnification chromoendoscopy in the detection of neoplastic lesions in HNPCC. During their study, the authors employed a phased withdrawal protocol whereby the endoscope was withdrawn in segments. The colon was examined first with white light, then with targeted chromoendoscopy, and finally with complete segmental staining. Pancolonoscopic chromoendoscopy using 0.5% indigo carmine as a contrast dye yielded significantly more adenomas than conventional colonoscopy: 35 versus 17 ($p = 0.001$). Additionally, significantly more flat adenomas were identified with chromoendoscopy: 4 versus 35 ($p = 0.004$).

The role for chromoendoscopy in surveillance colonoscopy for patients with IBD remains unclear. The Consensus Conference of Colorectal Cancer Screening and Surveillance in IBD recommendations only obliquely reference chromoendoscopy.⁵³ This report endorsed the incorporation of chromoendoscopy into surveillance colonoscopy given its ability to increase detection of dysplastic lesions.

Chromoendoscopy for Familial Adenomatous Polyposis

Finally, Matsumoto⁵⁴ et al published a study comparing chromoendoscopy to NBI, white light colonoscopy, and autofluorescence in patients with familial adenomatous polyposis (FAP). Autofluorescence is a developing technology that detects differences in light-emitted tissues when observed under blue light. This very small, prospective study of 13 patients with known FAP showed that chromoendoscopy detected the greatest number of adenomas when compared with the other techniques. In addition, researchers noted that chromoendoscopy detected significantly more left-sided lesions ($p < 0.05$).

Chromoendoscopy to Predict Histology

The gold standard for the diagnosis of colorectal polyps is mucosal resection and histologic evaluation. However, as experience with chromoendoscopy and mucosal pit pattern analysis grew, some researchers set out to determine whether chromoendoscopy could provide an accurate prediction of the underlying histology of suspected lesions. Tung and colleagues⁵⁵ conducted a trial of chromoendoscopy in 141 patients that compared endoscopic prediction of lesions to biopsy results; they found that the endoscopic prediction had a sensitivity and specificity of 93.8% and 64.6%, respectively, for neoplastic lesions. Not long after this study, Eisen et al⁵⁶ published a multicenter study including 299 patients and 520 polyps, targeting suspected lesions during standard colonoscopy with indigo carmine 0.8% as a contrast, predicting the histology endoscopically, and finally obtaining mucosal biopsies. The endoscopic prediction of adenomatous polyps using chromoendoscopy had a sensitivity and specificity of 82%, but an accuracy of only 68%. In a single-examiner, large, prospective trial including 1,850 patients, Hurlstone et al⁵⁷ performed a similar evaluation of the ability of chromoendoscopy to predict a lesions' final pathology; the sensitivity and specificity of chromoendoscopy were 98% and 92%, respectively.

Although not yet a suitable replacement for tissue biopsy, endoscopic prediction of histology using chromoendoscopy may yet prove to be an important tool in therapeutic endoscopy.

Chromoendoscopy for Evaluation of Mucosal Resection Margins

Hurlstone et al⁵⁸ have described a technique using chromoendoscopy to assess adequacy endoscopic mucosal resection. In a large study of 602 patients, the authors reported a sensitivity of chromoendoscopy for predicting remnant tissue in the lateral and deep margins after mucosal resection of 79% and 80%, respectively.

This technique may prove useful in the prediction of remnant tissue after endoscopic mucosal resection.

Narrow Band and Multiband Imaging

NBI is a technology designed to increase contrast on endoscopic examination without the time-consuming application of a surface dye. Olympus (Tokyo, Japan) has trademarked NBI technology: two main variations exist. In the United States, the system incorporates filters to limit the endoscopic light source to two wavelengths: 415 nm and 540 nm. A second system commercially available in Europe and Japan incorporates three discrete wavelengths: 415 nm, 445 nm, and 500 nm. The differences in these systems are largely related to differences in the image processors used in these geographic regions. Sometimes referred to as optical chromoendoscopy, NBI improves mucosal detail in two ways. First, it increases the relative contribution of surface structures to the final endoscopic image, as the shorter wavelength light does not penetrate deeply into the mucosa. Second, it highlights vascular structures by incorporating the specific wavelength that corresponds to the peak absorption spectrum for hemoglobin: 415 nm.⁵⁹ Fuji Corporation (Saitama, Japan) has developed a multiband imaging technology to compete with NBI. Multiband imaging relies on a digital imaging processing technique that augments images taken during white light endoscopy, generating a virtual image that accentuates the contributions of specific wavelengths of light. To date, no published trials exist that compare the efficacy of NBI and multiband imaging.⁶⁰

Narrow Band Increased Detection

Although the great majority of research in NBI has focused on Barrett's esophagus, several trials have studied the use of NBI in the colon. Three randomized controlled prospective clinical trials have examined the effect of pancolonoscopic NBI on ADRs during screening colonoscopy. The first, conducted by Inoue et al, included 243 patients and reported a significantly higher number of adenomas detected, as well as a higher number of diminutive (<5 mm) adenomas detected in the patients examined with pancolonoscopic NBI versus white light endoscopy.⁶¹ The results of this study fueled speculation that perhaps NBI colonography would provide a simpler, dyeless alternative to chromoendoscopy. Critics of the study noted that the number of NBI examinations was not distributed equally among endoscopists, raising the concern that endoscopy technique rather than NBI augmentation could explain the higher detection rates. A second trial by Adler et al included 401 patients and failed to show a higher detection rate.⁶² In the early phases of Adler's trial, preliminary data indicated a higher ADR with NBI. Over the course of the study,

however, the ADR in the NBI group remained constant whereas the detection rate in the white light group improved. In the end, the difference in adenoma detection was not statistically significant between the two groups. The researchers further speculated that the increasing trend in white light detection rates may have been the result of a training effect that performing NBI colonography has on endoscopists. A third randomized controlled trial by Rex et al⁶³ failed to show a significant difference in sensitivity between NBI and white light endoscopy. This trial included more than 434 patients and controlled for interobserver variations by using only one endoscopist. The authors found no difference between the NBI or white light examination groups in either the prevalence of adenomas or the total number of adenomas detected.

NBI Adenoma Detection in High-Risk Populations

Only one randomized controlled trial has evaluated adenoma detection using NBI colonoscopy in patients with IBD. Dekker et al⁶⁴ conducted a prospective randomized crossover study comparing the ADR of white light colonoscopy to NBI colonoscopy in 42 patients with long-standing ulcerative colitis. The examinations were conducted at least 3 weeks apart. During the procedures, targeted biopsies were taken of suspicious tissue. In addition, random four-quadrant biopsies were taken during the conventional endoscopy. This trial found no significant difference in adenoma detection between the two examinations. The authors did qualify their results by noting that the NBI system used in the study was a prototype system and suffered from low light intensity.

NBI for Improved Prediction of Underlying Histology

Interest in perfecting optical biopsy technology has generated several trials aimed at determining the accuracy of NBI colonoscopy in predicting the histology of observed lesions.⁶⁵⁻⁷⁰ Several systems have been described, categorizing both mucosal pit patterns and vascular features of surface mucosa during narrow band endoscopy. However, no single system has been adopted in NBI colonoscopy the way that Kudo's pit pattern classification system has been in chromoendoscopy. In 2009, Van de Broek et al⁷¹ published a review of narrow-band colonoscopy studies. Using a random-effects pooled data analysis, they concluded that the overall sensitivity and specificity of NBI colonoscopy in correctly predicting neoplasia were 92% and 86%, respectively. In a separate analysis of trials of NBI in patients with long-standing ulcerative colitis, Van de Broek and colleagues concluded that the sensitivities and

specificities were not as good, ranging from 75 to 80% and 81 to 84.2%, respectively.^{72,73}

CONCLUSION

Colonoscopy continues to be the preferred procedure for colon cancer screening and has robust data to support its use in cancer surveillance. Despite this, several large, well-defined trials have identified its limitations. Significant strides have been made in developing ways to improve colonoscopy's effectiveness. Augmented endoscopy techniques, including chromoendoscopy and NBI, represent two of the best studied new techniques designed to improve the effectiveness of colonoscopy.

Both techniques are inexpensive, safe, and relatively easy to perform. According to the 2005 recommendations of the Consensus Conference of Colorectal Cancer Screening and Surveillance in IBD, chromoendoscopy should take an increasingly important role in surveillance of IBD. However, before this technique can be incorporated into routine clinical practice, work is needed to build consensus on optimal staining techniques and mucosal surface pattern analysis.

Several large, randomized controlled trials suggest that chromoendoscopy does not confer advantages to screening colonoscopy. The data are mixed with respect to surveillance examinations in high-risk populations; yet, several studies involving patients with IBD suggest that this technique could significantly improve disease surveillance. Chromoendoscopy may also hold promise as an adjunct in therapeutic endoscopy, though the experience of using chromoendoscopy to assess the adequacy of complete tissue resection is very limited.

NBI, by comparison, is a much newer technology, and available data evaluating NBI are far less extensive. Despite this, several clinical trials have examined a broad range of potential uses. Well-designed prospective randomized controlled trials have failed to identify a benefit of NBI in screening colonoscopy. Though fewer studies have examined NBI use in surveillance for high-risk populations or as an adjunct for therapeutic procedures, the available data do not demonstrate an advantage of this technique over standard colonoscopy.

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