Electronic chromoendoscopy

The ASGE Technology Committee provides reviews of existing, new, or emerging endoscopic technologies that have an impact on the practice of GI endoscopy. Evidence-based methodology is used, performing a MEDLINE literature search to identify pertinent clinical studies on the topic and a MAUDE (U.S. Food and Drug Administration Center for Devices and Radiological Health) database search to identify the reported adverse events of a given technology. Both are supplemented by accessing the “related articles” feature of PubMed and by scrutinizing pertinent references cited by the identified studies. Controlled clinical trials are emphasized, but in many cases, data from randomized, controlled trials are lacking. In such cases, large case series, preliminary clinical studies, and expert opinions are used. Technical data are gathered from traditional and Web-based publications, proprietary publications, and informal communications with pertinent vendors. Technology Status Evaluation Reports are drafted by 1 or 2 members of the ASGE Technology Committee, reviewed and edited by the Committee as a whole, and approved by the Governing Board of the ASGE. When financial guidance is indicated, the most recent coding data and list prices at the time of publication are provided.

For this review, the MEDLINE database was searched through October 2013 for relevant articles by using the key words “narrow band imaging,” “NBI,” “Flexible spectral Imaging Color Enhancement,” “FICE,” “multiband imaging,” “MBI,” “i-SCAN,” “electronic chromoendoscopy,” and “virtual chromoendoscopy.” Technology Status Evaluation Reports are scientific reviews provided solely for educational and informational purposes. Technology Status Evaluation Reports are not rules and should not be construed as establishing a legal standard of care or as encouraging, advocating, requiring, or discouraging any particular treatment or payment for such treatment.

BACKGROUND

The term electronic chromoendoscopy refers to endoscopic imaging technologies that provide detailed contrast enhancement of the mucosal surface and blood vessels. These technologies offer an alternative to dye-based chromoendoscopy. Electronic chromoendoscopy technologies include narrow-band imaging (NBI) (Olympus Medical Systems Tokyo, Japan), flexible spectral imaging color enhancement (FICE) (Fujinon, Fujifilm Medical Co, Saitama, Japan), and i-SCAN (PENTAX Endoscopy, Tokyo, Japan).

Enhancement of particular mucosal features with electronic chromoendoscopy is achieved by the observation of light transmission at selected wavelengths because the interaction of particular tissue structures with light is wavelength dependent. Selective light transmittance is accomplished by optical filtering of white light in NBI, whereas FICE and i-SCAN both accomplish this through software-driven post-image processing. These 3 modalities are the topics of this review.

TECHNOLOGY UNDER REVIEW

Standard and high-definition white-light imaging

The video endoscope is equipped with a charge-coupled device (CCD) located at the tip of the endoscope. Standard-definition (SD) endoscopes contain CCD chips that offer images in a 4:3 aspect ratio, which produce signal images with resolutions of 100,000 to 400,000 pixels. High-definition (HD) CCD chips offer images in either 4:3 or 5:4 aspect ratios and produce signal images with resolutions of 850,000 to 2 million pixels.1 This signal is converted to a color image by either a red green blue (RGB) sequential system or a color CCD system by the video processor.1 An in-depth review of this technology is covered in another Technology Committee document entitled “High-Definition and High-Magnification Endoscopes.”

The light source used in endoscopy is typically a xenon arc lamp ranging from 100 to 300 W. This specialized lamp produces light by passing electricity through ionized xenon gas at high pressure. It produces a bright white light that closely mimics natural sunlight in the visible spectrum (400-700 nm). By simulating daylight, xenon lamps allow tissue examination in their natural colors during endoscopy.

Narrow-band imaging

NBI is an endoscopic optical image enhancement technology, proprietary of Olympus Medical Systems. NBI is based on the penetration properties of light, which is directly proportional to wavelength.3 Short wavelengths penetrate only superficially into the mucosa, whereas longer wavelengths are capable of penetrating more deeply...
into tissue (Fig. 1). The placement of a NBI filter directly in front of the xenon arc lamp produces 2 narrow bands of light centered at the specific wavelengths of 415 nm and 540 nm. These 2 wavelengths correspond to the primary and secondary light absorption peaks of hemoglobin, respectively.\(^4\) Capillaries in the superficial mucosa are highlighted by the 415-nm wavelength and appear brown. The longer 540-nm wavelength penetrates slightly more deeply into the mucosa and submucosa and makes the deeper veins appear blue-green (cyan).\(^3\) Because most of the NBI light is absorbed by the blood vessels in the mucosa, the resulting images emphasize the blood vessels in sharp contrast with the nonvascular structures in the mucosa (Fig. 2).

**NBI systems.** The first commercially available NBI systems were the Evis Exera II 180 system (color CCD system) and the Evis Lucera 260 spectrum series (RGB sequential system). The Evis Exera II is commercially available in the United States. These 2 systems feature white-light and narrow-band illumination integrated into a single light source. The switch between white-light endoscopy (WLE) and NBI is accomplished by the touch of a button on the endoscope or on the front panel of the light source, which results in movement of a narrow-band filter in front of the xenon arc lamp after a 1- to 2-second delay.

The next generation processors and light sources, Evis Exera III (United States and Europe) and Evis Lucera Elite (Japan) were released in 2012. An issue with the first-generation NBI systems was that the narrow-band images produced were less bright than images with white light. This was attributed to the fact that NBI uses only a narrow band of light (comprising 2 wavelengths only) while filtering out the other wavelengths of white light. The second-generation NBI systems in the Evis Exera III and Evis Lucera Elite have corrected this issue through improvements in the light source. When the endoscopist switches from white light to NBI, the brightness of the lamp light permeating from the glass fiber within the endoscope.

Tables 1 and 2 list the specifications of NBI-equipped GI endoscopes and processors that are available in the United States.

**Flexible spectral imaging color enhancement**

FICE is a proprietary digital imaging post-processing system of Fujinon.\(^5\) FICE takes white-light endoscopic images from the video processor and mathematically processes the image by emphasizing certain ranges of wavelengths. Three single-wavelength images can be selected and assigned to the red, green, and blue monitor inputs, respectively, to display a composite color-enhanced image in real time (Fig. 3).

Ten factory-determined presets are available in current FICE configured processors for a differentiated color display of the mucosa. Each preset can be button-activated from a computer keyboard. The factory-preset wavelengths can also be manually altered. There are 60 possible permutations of the available wavelengths (from 400 to 695 nm) that can be manipulated in 5-nm increments. The endoscope push-button controller can be programmed to enable switching between the conventional white-light image and up to 3 FICE presets. The switch to FICE from WLE occurs almost instantaneously. The optimal FICE preset(s) for tissue diagnosis or differentiation have not been established.

Tables 3 and 4 summarize the specifications of FICE-equipped GI endoscopes. FICE is currently not commercially available in the United States.

**i-SCAN**

i-SCAN is a software-based digital, postprocessing image enhancement technology from PENTAX Endoscopy that provides digital contrast to endoscopic images.\(^6\) Similar to FICE, i-SCAN provides enhanced images of the mucosal surface and the blood vessels through post-image processing. There are 3 i-SCAN modes: i-SCAN 1, i-SCAN 2, and i-SCAN 3. Touching a button on the endoscope can access
these modes. The switch from WLE to i-SCAN occurs almost instantaneously.

i-SCAN 1 is a surface-enhancement (SE) and contrast-enhancement (CE) mode that enhances contrast and thereby mucosal surface detail including enhanced mucosal surface texture and sharpened views of surface vessels. The image remains as bright as conventional WLE. i-SCAN 2 comprises SE, CE, and tone enhancement (TE) mode c. In addition to the enhancement of mucosal surface detail, this mode also increases the contrast between the mucosa and blood vessels, thereby improving the visibility of blood vessels. i-SCAN 3 comprises SE, CE, and TE mode g. This mode provides mucosal SE and improved visualization of blood vessels including dimly lit far-field regions (Fig. 4). i-SCAN 3 differs from i-SCAN 2 primarily in its ability to illuminate more distant regions better. Unlike NBI, red remains the predominant blood vessel color in all i-SCAN modes. Tables 5 and 6 list all commercially available i-SCAN endoscopes available in the United States.

EFFICACY STUDIES

Narrow-band imaging

The most studied of the 3 technologies is NBI. The studies reviewed used either the Evis Exera II or Evis Lucera 260 system. There are very limited data comparing these 2 systems.

Barrett’s esophagus, high-grade dysplasia, and adenocarcinoma

NBI sharpens visualization of the squamocolumnar boundary and can potentially detect Barrett’s epithelium (BE) and associated dysplasia. A prospective, controlled tandem endoscopy study conducted on 65 patients with Barrett’s esophagus indicated that HD-NBI without magnification was superior to SD-WLE in detecting dysplasia. Higher grades of dysplasia were found in 12 patients by using NBI compared with no patients by using standard-resolution WLE (18% vs 0%, \( P < .001 \)). In addition, more biopsy specimens were taken by using SD endoscopy with random biopsy strategies compared with NBI targeted biopsies (mean, 8.5 vs 4.7 biopsy specimen, \( P < .001 \)). A limitation of this study is that the authors could not determine whether the improved detection was related to the use of HD or NBI. A randomized, crossover study by Kara et al showed no difference in the detection of high-grade dysplasia (HGD) between HD-WLE and HD-NBI without magnification (sensitivity, 79% vs 86%). In this study, even though NBI identified more dysplastic lesions compared with HD-WLE, no additional patients with dysplasia were detected with NBI. A recent multicenter, randomized, crossover trial by Sharma et al compared HD-WLE with HD-NBI. Both HD-WLE and HD-NBI detected 104 of 113 patients (92%) with specialized intestinal metaplasia (SIM), but use of NBI allowed fewer biopsy specimens per patient (3.6 vs 7.6, \( P < .0001 \)). NBI also detected a higher proportion of areas with HGD (30% vs 21%, \( P = .01 \)). Taken together,
these trials suggest that both NBI and HD may individually contribute to increased detection of Barrett’s and associated dysplasia.

NBI with magnification has been investigated in an attempt to characterize HGD and SIM associated with Barrett’s esophagus based on mucosal and vascular morphology. A meta-analysis assessed the diagnostic accuracy, sensitivity, and specificity of NBI with magnification in characterizing HGD and SIM associated with Barrett’s esophagus. The meta-analysis evaluated 8 studies that included 446 patients with 2194 lesions. For diagnosing HGD, the pooled sensitivity, specificity, diagnostic odds ratio, and area under the curve were 0.96, 0.94, 342.49, and 0.99 (standard error, 0.01), respectively, in a per-lesion analysis with similar results in a per-patient analysis. For the characterization of SIM, the pooled sensitivity, specificity, diagnostic odds ratio, and area under the curve were 0.95, 0.65, 37.53, and 0.88 (standard error, 0.08) in a per-lesion analysis. A recent meta-analysis of 14 studies with a total of 843 patients evaluated the yield of esophageal dysplasia or cancer detection by using electronic chromoendoscopy compared with WLE. Electronic chromoendoscopy was found to have a paired risk difference of 0.34 (P < .001) compared with WLE.

There have been multiple studies looking at the reproducibility of NBI with magnification. Curvers et al looked at the interobserver agreement based on the mucosal and vascular morphology described previously by Kara et al. NBI did not improve interobserver agreement based on the mucosal and vascular morphology described previously by Kara et al. NBI did not improve interobserver agreement or accuracy over HD-WLE. The interobserver agreement for NBI diagnosis ranged from a κ of 0.40 to 0.56 (moderate) and did not significantly differ between expert and nonexpert endoscopists. The overall yield for correctly identifying images of early neoplasia (HGD/intramucosal carcinoma) was 81% for HD—WLE, 72% for NBI, and 83% for HD—WLE plus NBI, with no significant difference between experts and nonexperts. A simplified consensus-driven classification system was developed for easy clinical application. A total of 252 NBI images from 75 patients with Barrett’s esophagus were assessed. Interobserver agreement for mucosal and vascular patterns and dysplasia prediction was
fair: $\kappa = 0.40, 0.36, \text{ and } 0.39$ respectively, with comparable results for experts and nonexperts. Mean sensitivity and specificity of NBI surface patterns for predicting dysplasia were 47% and 72%, respectively.\textsuperscript{20}

GERD

NBI with magnification has been investigated as a diagnostic tool for GERD.\textsuperscript{22-24} Sharma et al\textsuperscript{24} evaluated 80 patients (50 GERD, 30 controls) and found GERD patients had a significantly increased number of capillaries (OR 12.6; $P < .0001$), capillary dilation (OR 20; $P < .0001$), and tortuosity of intrapapillary capillary loops (OR 6.9; $P < .0001$) compared with controls. In addition, the presence of microerosions ($P < .0001$) and increased vascularity at the squamocolumnar junction (OR 9.3; $P = .001$) was significant compared with controls. On multivariate analysis, increased number (OR 5.5) and dilation (OR 11.3) of intrapapillary capillary loops were the best predictors for diagnosing GERD.\textsuperscript{24} The intraobserver agreement in this study was modest. A further study demonstrated a significant reduction in the proportion of NBI findings of IPCL tortuosity (90% vs 4.8%, $P < .0001$), dilated intrapapillary capillary loops (86% vs 9.5%, $P < .0001$), and increased vascularity at the squamocolumnar junction (43% vs 9.5%, $P = .0082$) after proton pump inhibitor therapy.\textsuperscript{25} NBI as a diagnostic tool for GERD requires further validation with randomized, prospective studies.

Gastric neoplasia

NBI without magnification increased the diagnostic yield for detection of gastric lesions, including dysplasia and intestinal metaplasia compared with routine WLE.\textsuperscript{20} In a single-center, prospective study that included 43 patients, the sensitivity, specificity, and positive and
negative predictive values for the detection of premalignant lesions were 71%, 58%, 65%, and 65%, respectively, for NBI and 51%, 67%, 62%, and 55%, respectively, for WLE. Specificity was higher for WLE ($P < .04$), whereas sensitivity was higher for NBI ($P < .001$). Despite the findings of this study, NBI without magnification has limitations because of the large gastric lumen, which may produce darker images that make interpretation challenging.

Magnifying endoscopy with NBI has been found to be useful in diagnosing gastric neoplasia. A prospective study including 111 patients with 201 superficial gastric lesions indicated that the sensitivity and specificity of NBI with magnification (M-NBI) for lesion detection were 92.9% and 94.7%, respectively. This was significantly better than the sensitivity and specificity of HD-WLE (42.9% and 61.0%, respectively; $P < .0001$). Uedo et al found that the M-NBI finding of a light blue crest on the epithelial surface of gastric mucosa correlated with histological evidence of intestinal metaplasia. This finding had a sensitivity of 89%, a specificity of 93%, a positive predictive value of 91%, a negative predictive value of 92%, and an accuracy of 91%. Experienced endoscopists in the Asia-Pacific region recommended M-NBI over NBI alone for the detection of gastric cancer.

The vessel plus surface architecture classification system was designed by Yao et al, which incorporated M-NBI to describe the microvascular and microsurface changes in the stomach in gastric cancer. In a prospective study of 135 patients with elevated gastric lesions, by using the vessel plus surface architecture classification system, M-NBI diagnosed high-grade adenomas or early carcinomas at a higher sensitivity (82.4 vs 70.6%, $P < .0001$) and specificity (97.3 vs 54.7%, $P < .0001$) than HD-WLE. A simplified M-NBI classification system for the diagnosis of intestinal metaplasia and dysplasia of the stomach was developed. In the validation study, the finding of regular vessels with circular mucosa was associated with normal histology (83% accuracy), tubulovillous mucosa was associated with intestinal metaplasia (84% accuracy, positive likelihood ratio = 4.75), and irregular

### TABLE 3. Fujinon endoscopes with FICE capability

<table>
<thead>
<tr>
<th>Endoscopes</th>
<th>Series</th>
<th>Model no.</th>
<th>Working length, mm</th>
<th>Insertion tube, Distal end diameter, mm</th>
<th>Working channel, mm</th>
<th>Image resolution</th>
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FICE, Flexible spectral imaging color enhancement; HD, high definition.

### TABLE 4. Fujinon processors with FICE capability

<table>
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<th>Light source</th>
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<td>VP-4450HD</td>
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<tr>
<td>XL-4400</td>
<td>VP-4400HD</td>
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</table>

FICE, Flexible spectral imaging color enhancement.
vessels and mucosa were associated with dysplasia (95% accuracy, positive likelihood ratio = 44.33). The reproducibility of these patterns was high (κ = 0.62).

Ezoe et al. looked specifically at the utility of M-NBI to detect gastric small depressive lesions 10 mm or smaller. In this prospective study of 57 gastric small depressive lesions, the diagnostic accuracy was significantly higher for NBI than for HD-WLE (79% vs 44%; P = .0001), as was its sensitivity (70% vs 33%; P = .0005). The diagnostic specificity of NBI (89%) was higher than that of HD-WLE (67%), but the difference was not statistically significant. A subsequent multicenter, prospective, randomized, controlled trial of patients with small depressive lesions demonstrated M-NBI and HD-WLE accuracies of 90.4% and 64.8%; sensitivities of 60.0% and 40.0%; and specificities of 94.3% and 67.9%, respectively. The accuracy and specificity of M-NBI were greater than those of HD-WLE (P < .001); the difference in sensitivity was not significant (P = .34). NBI appears to be a useful adjunct in the diagnosis of gastric neoplasia, but cannot replace biopsy at this time.

Colon polyps

It has been suggested by some studies that NBI has the potential to improve overall detection rates of polyps, diminutive polyps, and flat lesions compared with WLE. There have been several recent meta-analyses performed comparing polyp detection rates with those of NBI and WLE. One of these was a Cochrane review performed on 8 randomized trials with 3673 participants. This review compared NBI with SD-WLE and HD-WLE together as well as SD-WLE and HD-WLE separately. There was no statistically significant difference between WLE (SD and HD) and NBI for the detection of patients with colorectal polyps (6 trials, n = 2832, relative risk [RR] 0.97), patients with colorectal adenomas (8 trials, n = 3673, RR 0.94), or patients with colorectal hyperplastic polyps (2 trials, n = 645, RR 0.87). The meta-analysis showed a significant degree of heterogeneity. The number of patients with at least 1 colorectal adenoma was not significantly different between the WLE and NBI groups irrespective of adenoma size smaller than 5 mm: RR 0.95; 6 to 9 mm: RR 1.06; 10 mm: RR 1.06. NBI compared with HD-WLE alone was not significantly different in detection rates of colorectal polyps (RR 1.10) and adenomas (RR 0.98).

The Cochrane review also compared NBI with SD-WLE. It found that polyp and adenoma detection might be superior with NBI compared with SD-WLE. NBI was superior to SD-WLE in patients with at least 1 colorectal polyp or adenoma in a fixed-effects meta-analysis (RR 0.87 and RR 0.87, respectively), but not significantly different in random-effects meta-analysis (RR 0.86). Fewer studies assessed the comparison of SD-WLE and SD-NBI; therefore, these results should be interpreted with caution.

The results of this Cochrane review were similar to those of other meta-analyses. These analyses affirm the Cochrane review, demonstrating no significant difference between HD-NBI and HD-WLE in the detection of adenomas and polyps. One of these meta-analyses additionally compared polyp miss rates between HD-NBI and HD-WLE. The miss rate analysis revealed no difference in polyp miss rate (3 studies, n = 524, OR 1.17) or adenoma miss rate (3 studies, n = 524, OR 0.65). There was 1 contradictory meta-analysis that indicated NBI superiority to SD-WLE in the detection of flat adenomas (pooled RR 1.96). This same study also indicated that the use of NBI was associated with increased colonoscope withdrawal times (pooled weighted mean difference, 0.90, P = .0006). A further study, not included in the previously described meta-analyses, also suggests higher polyp and adenoma miss rates with SD-WLE compared with NBI. In this study that included 96 patients with 177 polyps, polyp and adenoma miss rates for SD-WLE colonoscopy were 57% (60/105) and 49% (19/39); those for NBI colonoscopy were 31% (22/72) and 27% (9/33) (P = .005 and P = .036 for polyps and adenomas, respectively). Most studies evaluating adenoma detection compared single technology improvements (HD-NBI vs HD-WLE). However, current commercially available colonoscopes incorporate multiple improvements in definition and contrast. In this context, there is the potential that “newer” colonoscopes may show some improvement in adenoma detection compared with “older” colonoscopes.
Another potential role of NBI is in classifying polyps as adenomatous or hyperplastic, potentially minimizing unnecessary polyp resection or unnecessary submission of small polyps for pathology evaluation. A meta-analysis performed by Wu et al. assessed the precision of NBI as a predictor of adenomas with or without magnification. The overall sensitivity of NBI for diagnosing adenomatous polyps was 0.92, with an overall specificity of 0.83. The sensitivity and specificity were, respectively, 0.92 and 0.81 with magnification and 0.91 and 0.86 without magnification. The authors concluded that NBI with or without magnification is precise in identifying adenomas based on visualization alone. The concept of NBI serving as an optical biopsy for polyps may allow for a predict, resect, and discard strategy for diminutive polyp management.

The American Society for Gastrointestinal Endoscopy (ASGE), in an attempt to aid in the development of new paradigms for colonoscopic management of diminutive polyps, developed a Preservation and Incorporation of Valuable endoscopic Innovations (PIVI) statement for the real-time colonoscopic assessment of the histology of diminutive colorectal polyps. Several studies have evaluated the feasibility of the ASGE criteria. Repici et al. conducted a prospective, multicenter trial at academic centers for the characterization of polyps 5 mm or smaller. In this study, 204 of 226 polyps in the rectosigmoid area were characterized with high confidence. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were 83%, 95%, 88%, 92%, and 91%, respectively. Therefore, the observed negative predictive value of 92% was superior to the 90% threshold set by the ASGE for this type of lesion. The correct surveillance interval was assigned in 92% to 99% of cases, based on the American and European surveillance guidelines, respectively. Studies done in academic centers by experienced endoscopists show promise in achieving PIVI criteria. In contrast is a study by Ladabaum et al. who evaluated PIVI criteria in a community setting. In this study, the mean negative predictive value was 91% (range 86%-97%) and the correct surveillance interval was assigned in only 80% of cases.

### TABLE 5. PENTAX Endoscopes with i-SCAN capability

<table>
<thead>
<tr>
<th>Endoscopes</th>
<th>Series</th>
<th>Model no.</th>
<th>Working length, mm</th>
<th>Insertion tube, distal end diameter, mm</th>
<th>Working channel, mm</th>
<th>Image resolution</th>
<th>Endoscope cost, US$</th>
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<td>Standard</td>
<td>38,500</td>
<td></td>
</tr>
<tr>
<td></td>
<td>EC-3890LiK</td>
<td>1700</td>
<td>13.2</td>
<td>4.2</td>
<td>Standard</td>
<td>38,500</td>
<td></td>
</tr>
<tr>
<td></td>
<td>EC-3890TLi</td>
<td>1700</td>
<td>13.2</td>
<td>2.8, 3.8</td>
<td>Standard</td>
<td>38,500</td>
<td></td>
</tr>
<tr>
<td>Duodenoscopes K</td>
<td>ED-3470TH</td>
<td>1250</td>
<td>11.6</td>
<td>4.2</td>
<td>Standard</td>
<td>39,000</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ED-3670TH</td>
<td>1250</td>
<td>12.1</td>
<td>4.8</td>
<td>Standard</td>
<td>39,000</td>
<td></td>
</tr>
</tbody>
</table>

HD, High definition.

### TABLE 6. PENTAX processors with i-SCAN capability

<table>
<thead>
<tr>
<th>Light source</th>
<th>Video processor</th>
<th>Cost, US$</th>
</tr>
</thead>
<tbody>
<tr>
<td>LH-150PC</td>
<td>1190</td>
<td></td>
</tr>
<tr>
<td>EPK-i5010</td>
<td>39,000</td>
<td></td>
</tr>
</tbody>
</table>

HD, High definition.
There have been studies evaluating the learning curve after instruction on NBI-based classification of polyps.51-54 In a study by Rogart et al,54 NBI accuracy improved from 74% to 87%, with no improvement in WLE accuracy of 79% (P < .05). Ignjatovic et al52 demonstrated improved accuracy in novices, trainees, and experienced endoscopists after completing a computer-based test module comprising 30 NBI polyp images. Accuracy increased significantly (P < .001) for all 3 groups after training.

### Ulcerative colitis

There have been 2 randomized, prospective trials evaluating detection rates of dysplasia in colitis patients.55,56 A randomized, parallel-group trial including 112 patients indicated no difference between the NBI and HD-WLE groups in the proportion of patients with at least 1 area of dysplasia, with 5 patients having at least 1 dysplastic lesion in each group (OR 1.00).55 The overall dysplasia detection was 9% in each study arm.55 van den Brock et al56 showed similar results in a randomized, crossover trial. This study also evaluated the diagnostic accuracy of NBI in differentiating neoplastic from non-neoplastic mucosa. They concluded that NBI was inadequate at differentiating neoplasia with a sensitivity, specificity, and accuracy of 80%, 72%, and 73%, respectively. NBI has been investigated in the assessment of mucosal healing in ulcerative colitis (UC). Kudo et al57 performed NBI colonoscopy in patients with inactive or mildly active UC to elucidate the significance of classifying the mucosal vascular pattern (MVP) in this disease. The MVP in 157 colorectal segments of 30 patients with UC by using both WLE and NBI colonoscopy was analyzed. Acute inflammatory cell infiltrates (26% vs 0%, P = .0001), goblet cell depletion (32% vs 5%, P = .0006), and basal plasmacytosis (2% vs 21%, P = .006) were more frequently observed in segments with an obscure MVP than in those with a clear MVP.57 The authors proposed that NBI may be an adjunct in vivo tool for the assessment of the grade of inflammation in patients with quiescent UC. There have been no prospective studies evaluating the utility of NBI MVP pattern in this setting.

### FICE and i-SCAN

Because there are fewer published studies on FICE and i-SCAN than NBI, these 2 technologies are discussed together in the following.

### Esophagus

In a study including 57 patients, comparing FICE with chromoendoscopy with acetic acid in the detection of HGD in BE, FICE and chromoendoscopy both had a sensitivity of 87% for detecting neoplastic lesions. Sensitivity of directed biopsies alone for the detection of lesions in a per-patient analysis was 83% for chromoendoscopy and 92% for FICE, which was not statistically significant.58 A study by Osawa et al59 examined the ability to more clearly visualize palisade vessels and to distinguish the demarcation between BE mucosa and gastric mucosa by using FICE images and WLE. In the 40 cases evaluated, the median color contrast difference between BE and gastric mucosa of the FICE images was significantly higher than that of WLE images (P < .0001).

In a further prospective, randomized, controlled trial, 514 subjects undergoing endoscopy to evaluate for esophagitis by using the modified Los Angeles classification were randomized to i-SCAN (n = 246) or HD-WLE (n = 268) groups. The diagnostic yield of reflux esophagitis was significantly higher in the i-SCAN group compared with the HD-WLE group (30.1% vs 21.6%, P = .034). However, this study is limited because they consider the Los Angeles classification as the criterion standard and not biopsy, so the true or false positive rate in this study is unclear. Interobserver agreement by using randomly selected video clips was better in the i-SCAN group compared with the HD-WLE group (κ = 0.793 vs 0.473).60

### Gastric neoplasia

FICE and WLE were evaluated in a prospective study of 82 patients with depressed-type early gastric cancer. Greater median color differences between malignant lesions and the surrounding mucosa were present in FICE images compared with conventional images, resulting in images with better contrast (27.2 vs 18.7, P < .0001).61 A prospective study assessed the accuracy of a magnified i-SCAN in the diagnosis of gastric neoplasia. This study included 183 patients (43 patients with gastric lesions). Magnified HD-WLE had a sensitivity, specificity, positive predictive value, negative predictive value, and likelihood ratio of 87.5%, 71.4%, 41.2%, 96.2%, and 3.06, respectively. Although magnified i-SCAN with TE and SE slightly increased the diagnostic yield, there was no significant difference compared with magnified HD-WLE.62

### Polyps

In a large prospective, multicenter study, 1318 patients were randomized to undergo either FICE or HD-WLE colonoscopy. This study demonstrated no difference between the FICE and HD-WLE groups in adenoma detection rate (0.28 in both groups), total number of adenomas (184 vs 183), or detection of subgroups of adenomas. The number of hyperplastic polyps was also the same in both groups (127 vs 121; P = .67).63 The results were the same for both the screening and the diagnostic colonoscopy subgroups. Withdrawal time was similar in both groups (8.4 vs. 8.5 minutes, P = .55).63 Similar results were reported by Chung et al,64 who found no significant difference between FICE and HD-WLE in adenoma detection rate (mean, 0.64 vs 0.55 per patient; P = .65).
There was 1 prospective study that looked at polyp classification with FICE in 763 subjects who were undergoing screening colonoscopy. Pit patterns and vascular patterns were used to predict the histology of 525 polyps smaller than 10 mm by using FICE with and without magnification. The performances of the FICE analyses were calculated and compared with the histopathological results. The overall accuracy achieved by FICE with magnification in the diagnosis of adenomas (87.0%) was significantly greater than FICE without magnification (80.4%; \( P < .05 \)).

In a prospective study comparing HD i-SCAN with SD-WLE in 220 patients undergoing colonoscopy, HD i-SCAN detected significantly more patients with colorectal neoplasia (38%) compared with SD-WLE (13%, \( P < .0001 \)). However, the limitations of this study are that the i-SCAN colonoscopy was in high definition, and the adenoma detection rate was unusually low in the SD-WLE group. Hong et al evaluated adenoma detection rates as well as prediction of neoplasia. In a prospective, randomized, controlled trial, 389 average-risk individuals undergoing screening colonoscopy were evaluated by using both i-SCAN and HD-WLE. The adenoma detection rates with HD-WLE, i-SCAN 1, and i-SCAN 2 were similar (\( P = .742 \)). Also they observed no significant difference in the adenoma miss rates (\( P = .513 \)). However, the prediction of neoplastic and non-neoplastic colorectal lesions was more precise in the i-SCAN 2 group compared with the HD-WLE group (accuracy, 79.3% vs 75.5%, \( P = .029 \); sensitivity, 86.5% vs 72.6%; \( P = .020 \); and specificity, 91.4% vs 80.6%, \( P = .040 \)).

In a prospective, single-center cohort study of 209 diminutive polyps in 84 patients, there were no significant differences between HD-WLE and i-SCAN in the characterization of polyps of smaller than 10 mm (accuracy, 93.3% vs 94.7%; \( P = 1.00 \); sensitivity, 95.5% vs 97.0%; \( P = 0.50 \); specificity, 89.3% vs 90.7%; \( P = 1.00 \)). The negative predictive value for adenomatous histology of diminutive rectosigmoid polyps was 100% with both HD-WLE and i-SCAN. European and U.S. polyp surveillance intervals were predicted with 95.2% accuracy with HD-WLE and 97.2% accuracy with i-SCAN. Another study evaluated interobserver agreement with i-SCAN for classification of 150 polyps from 78 patients undergoing colonoscopy. Histology was correctly predicted with a sensitivity, specificity, and accuracy of 95%, 82%, and 92%, respectively. The inter- and intraobserver agreements for the prediction of histology were fair-good (\( \kappa \) values of 0.462 and 0.657, respectively).

**Comparative Studies**

**NBI versus i-SCAN**

In a single-center, open, prospective cohort study of 142 consecutive patients undergoing screening or surveillance colonoscopy, NBI and i-SCAN had a significantly higher sensitivity and improved accuracy compared with HD-WLE, for the prediction of adenomas (sensitivity, 88.8% for NBI vs 68.8% for HD-WLE, \( P = .002 \)). For i-SCAN, the sensitivity was 94.6% versus 74.3% for HD-WLE; \( P = .001 \). There were no significant differences between the NBI and i-SCAN (sensitivity, 88.8% vs 94.6%; specificity, 86.8% vs 86.4%; accuracy, 87.8% vs 90.7%, respectively; \( P > .05 \)). Additionally, there was good intra- and interobserver agreement between the NBI and i-SCAN (\( \kappa > 0.7 \)).

**NBI versus FICE**

Several studies have compared NBI and FICE for polyp detection, all of which have shown no difference. The largest of these studies was a prospective, randomized, controlled tandem colonoscopy trial with 1650 subjects that compared HD-WLE with NBI and FICE. In this study, neither NBI nor FICE increased the mean number of adenomas detected per patient compared with HD-WLE (HD-WLE, 0.37 vs NBI, 0.35 and FICE, 0.36; \( P = .591 \)). The percentage of missed adenomas also did not differ between the 3 groups (20.8% by HD-WLE vs 22.9% by NBI and 26.0% by FICE, \( P = .3 \)).

**Safety**

There have been no reported complications attributed to the use of NBI, FICE, or i-SCAN.

**Financial Considerations**

The costs of endoscope systems with NBI and i-SCAN capability are included in Tables 2 and 6. The Fujinon endoscopes with FICE capability are currently not commercially available in the United States. Electronic chromoendoscopy has the potential to avoid costs associated with tissue sampling; however, this is currently not the standard of care. There are no unique Current Procedural Terminology codes for NBI, FICE, or i-SCAN.

**Areas for Future Research**

Several areas pertaining to NBI, FICE, and i-SCAN deserve further study:

1. Further studies evaluating the cost-effectiveness of these technologies relative to the standard of care and whether enhanced imaging accuracy decreases the need for biopsy.
2. Ongoing development of validated teaching modules for NBI, FICE, and i-SCAN.
3. Identification of optimal FICE and i-SCAN settings on the basis of location and lesion(s) of interest.
4. The next generation of electronic chromoendoscopy technologies has just started being evaluated in clinical...
Electronic chromoendoscopy technologies provide image enhancement and may improve the diagnosis of mucosal lesions. Although strides have been made in standardization of image characterization, especially with NBI, further image-to-pathology correlation and validation are required. There is promise for the development of a resect and discard policy for diminutive adenomas by using electronic chromoendoscopy; however, before this can be adopted, further community-based studies are needed. Further validated training tools for NBI, FICE, and i-SCAN will also be required for the use of these techniques to become widespread.

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Abbreviations: ASGE, American Society for Gastrointestinal Endoscopy; BE, Barrett’s epithelium; CCD, charge-coupled device; CE, contrast enhancement; FICE, flexible spectral imaging color enhancement; HD, high-definition; HGD, high-grade dysplasia; M-NBI, narrow-band imaging with magnification; MVP, mucosal vascular pattern; NBI, narrow-band imaging; OR, odds ratio; PVI, Preservation and Incorporation of Valuable endoscopic Innovations; RGD, red green blue; RR, relative risk; SD, standard-definition; SE, surface enhancement; SIM, specialized intestinal metaplasia; TE, tone enhancement; UC, ulcerative colitis; WLE, white-light endoscopy.

REFERENCES


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