Michael B. Wallace, Section Editor

Optical Contrast Endoscopy: Is It Ready for Routine Use?

JONATHAN COHEN

New York University School of Medicine, New York, New York

The advent of optical contrast enhancement has generated much excitement over the past few years. There is promise of improved lesion detection, facilitated assessment of lesion margins, and therapeutic decision making based on real-time optical diagnosis. With growing numbers of endoscopists upgrading their equipment, many practitioners currently have the capability to use optical contrast in their daily clinical practice. Educational tools, such as the narrow band imaging (NBI) atlas,[1] as well as didactic lectures and dedicated workshops, have begun to disseminate wider understanding of how best to use the technology and interpret the images of normal and pathologic conditions. Some general references are useful in providing a summary of the evidence supporting the use of both dye and optical image enhanced endoscopy for various indications.[1–3]

What role will optical contrast high-resolution endoscopy play in gastroenterology practice in the coming years? An analysis of the literature provides insights as to whether optical contrast technology will be incorporated into general use, whether it will have only selective applications, and what will be needed for more widespread adoption and greater realization of its potential benefits. Much of the published investigation assessing the capabilities of this technology has been conducted using NBI (Olympus, Center Valley, PA), although data on multiband FICE technology (Fujinon, Wayne, NJ), and to a lesser extent I-scan (Pentax, Golden, CO), have been emerging.

Defining Characteristics of Dysplastic and Nondysplastic Barrett's Esophagus

Validation studies have identified the features of high grade dysplasia in Barrett's epithelium with high sensitivity and specificity (>90%) (Figures 1 and 2). Of note, these papers found optical contrast to be far less capable of detecting low-grade dysplasia.[4–7]

Targeted Biopsy in Barrett's Surveillance

An initial comparison by Kara et al[8] between NBI and indigo carmine chromoendoscopy in Barrett's esophagus showed that targeted biopsies alone using either method detected high-grade dysplasia 79% of the time compared with just 7% when random biopsies alone were analyzed. Curvers et al[9] more recently reported that blinded review of white light high-resolution versus NBI versus chromoendoscopy images showed no difference in dysplasia detection among modalities, although the high white light detection rate of 86% is difficult to top. This study also relied on highly selected still images culled by experts from a total of 9 patients for later assessment, which does not closely approximate real endoscopy conditions, in which immediate image interpretation is required. To better assess whether this new technology represents a significant enough advance in dysplasia detection to warrant adoption into routine surveillance, particular emphasis should be placed on methodologies that compare standard-resolution white light endoscopy with the high-resolution optical contrast techniques.

Recently, Wolfsen et al[10] have published an important paper that provides compelling support for the principle of targeted Barrett's surveillance. This study looked at white light esophagogastroduodenoscopy (EGD) in high-risk patients followed by NBI high-resolution endoscopy by a second endoscopist blinded to the results of the first examination. Targeted biopsies using optical contrast were shown to detect significantly more dysplasia and higher grades of dysplasia than the standard white light examinations, using only about half the mean number of biopsies to do so.

Squamous Head and Neck and Esophagus

Apart from the initial work characterizing neoplastic and non-neoplastic patterns of intraepithelial papillary capillary loops,[11] there is now convincing evidence that NBI examination leads to dramatic and significant increases in the detection of early squamous cancers in high-risk individuals. Muto et al[12] found a 15-fold increase in the oropharynx and a 2-fold increase in the esophagus during surveillance endoscopy on patients with prior cancers in those organs.

0016-5085/09/$36.00
doi:10.1053/j.gastro.2008.11.053

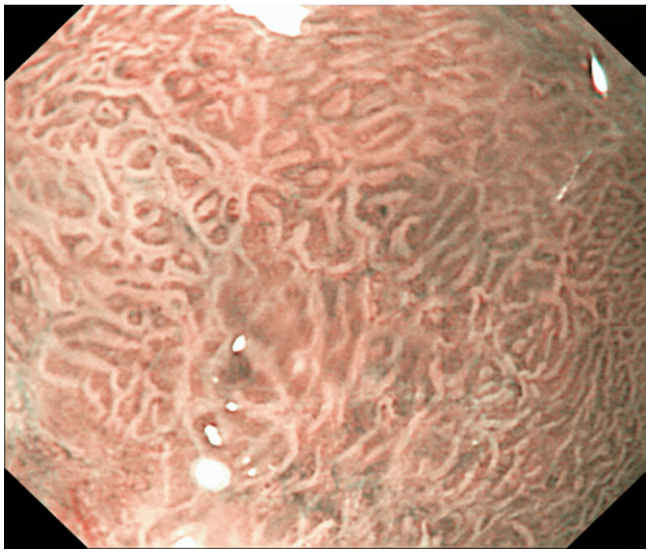

Figure 1. Magnified NBI image of Barrett's esophagus demonstrating irregular mucosal and vascular pattern, features consistent with high grade dysplasia. (Reprinted with permission from Mike Wallace, Mayo Jacksonville and Herbert C. Wolfsen, Mayo Clinic Florida.)

Gastric Cancer

Much of the literature in gastric cancer has focused on defining key features of well and poorly differentiated cancer using optical contrast and magnification.[13,14] One paper using FICE found that demarcation indicating suspicious lesions was more readily identified by students observing photos taken using contrast as opposed to those taken using white light.[15] Many visual examples of flat cancers seen well really only under contrast are published—examples are illustrated with videos in the above referenced NBI Atlas.[1] However, direct evidence that electronic imaged enhanced endoscopy improves lesion detection over standard white light endoscopy is lacking. One abstract presented at Digestive Diseases Week (DDW) 2007, showed a 96% accuracy of margin markings in 76 cases of endoscopic submucosal dissection using NBI[16] (Figure 3). The application of NBI, FICE, or I-scan to improve the rate of complete resections seems promising, but requires more supportive evidence.

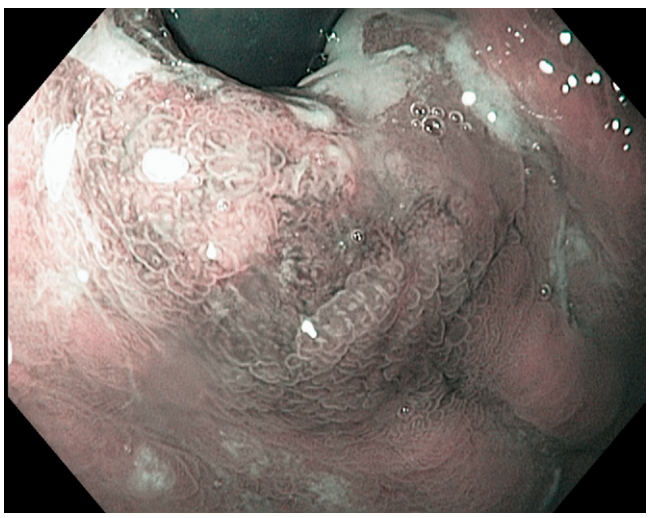

Figure 2. This retroflex image of high grade dysplasia in the cardia demonstrates an irregular mucosal topography with central depression. The NBI contrast also highlights thick and irregularly arrayed vessels. (Reprinted with permission from Mike Wallace, Mayo Jacksonville and Herbert C. Wolfsen, Mayo Clinic Florida.)

Figure 3. Optical contrast greatly enhanced the ability to discern the lateral borders of this superficial gastric cancer before endoscopic submucosal dissection.

The low-intensity light in the large cavity of the stomach using any of these methods is problematic for use of this modality in initial screening, and white light imaging usually must be performed first for detection of suspicious areas for closer, contrast-enhanced examination.

Colon Polyp Characterization

A number of studies have shown that endoscopists can correctly diagnose a polyp as being an adenoma >90% of the time.[17,18] Sano et al[18] reported this at DDW 2006 using the Lucera black and white chip colonoscope and the Kansas group published similar accuracy using the Excera color CCD scopes[19] (Figure 4). Pohl et al[20] have reported the similarly high accuracy using the FICE equipment. An abstract presented at DDW 2008 using I-scan in 54 patients showed that all neoplastic lesions present could be correctly identified by analyzing the vascularity or pattern architecture on I-scan images.[21] To date, no one has published data about characteristic features and optical diagnosis of serrated polyps. One key question is how long it takes general practicing endoscopists to achieve such highly accurate real-time classification. One abstract from 2008 described significant improvement of 4 endoscopists in correct polyp characterization to a level of 87% accuracy with experience in 300 combined cases over 1 year.[22] Although this small

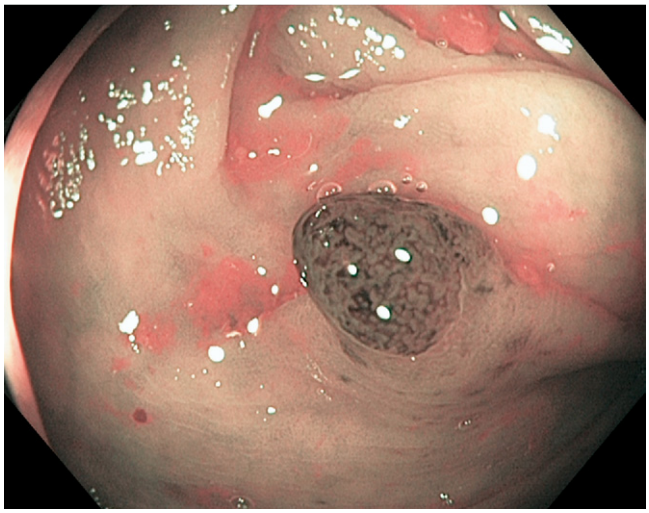

Figure 4. Small polyp seen with NBI without magnification shows sharp contrast in color between the polyp and the surrounding tissue as well as the thick brown irregular mesh capillary pattern that indicate the diagnosis of tubular adenoma with high specificity. (Reprinted with permission from Blackwell-Wiley.)

series suggests a rather rapid acquisition of skill, the learning curve needs to be better defined for those with the equipment to feel confident enough to use it routinely and make biopsy decisions based on their interpretations.

Colon Adenoma Detection

Adenoma detection remains an area of controversy. Some studies have shown increased polyp detection or decreased miss rates using optical contrast,[23–25] and others have shown similar frequency of adenomas using white versus blue light.[26–30] One study observed a steady improvement in white light adenoma detection with increasing experience using NBI, suggesting a learning effect.[30] Studies differ as to whether they are randomized trials or tandem trials looking at miss rates, whether the white light arm is high-resolution or standard-resolution white light, and whether the patients studied are normal risk screening cases or individuals at high risk for neoplastic lesions. Consistently, the new technology yields adenoma detection as high as double what even top investigators have achieved in prior trials using traditional colonoscopes. Endoscopists experienced with optical contrast generally attest to improved ability to assess the margins of sessile and flat polyps, although no investigation has yet been conducted to confirm that contrast upsizes lesions or leads to reduced incomplete polypectomy rates. Of course, for any of these improvements in diagnostic and therapeutic efficacy to alter routine clinical practice, real-world effectiveness will need to be demonstrated during subsequent evaluation in the community setting.

Inflammatory Bowel Disease

There is very little literature as to what flat dysplasia looks like under optical contrast. Matsumoto et al[31] reported a significant association of certain mucosal features seen on NBI with the presence of flat dysplasia. Prospective validation studies, similar to the studies conducted in Barrett's, are still needed to confirm that these particular abnormalities accurately predict the finding of dysplasia. Before this occurs, it will be hard for pilot trials of targeted surveillance to achieve optimal results. Once the optical contrast characteristics of inflammatory bowel disease dysplasia are well defined, then controlled investigation comparing the use of NBI or multiband imaging targeted biopsies with standard, white light, random biopsy surveillance will be possible and greatly anticipated.

Conclusions

The literature supports the routine use of high-resolution optical contrast endoscopy today for surveillance in Barrett's esophagus and for any EGD performed in patients considered at high risk for squamous cancers of the oropharynx or esophagus. Emerging data and expert opinion support the use of optical contrast high-resolution scopes in therapeutic procedures such as ablation of Barrett's and endoscopic mucosal resection or ESD in which margin assessment is critical.

In the colon, it remains to be seen whether the high yields of adenoma detection seen using high-resolution endoscopy justifies its use during routine examinations. This question is relevant regardless of whether or not the optical contrast confers additional benefit or just provides a learning effect to improve an operator's white light detection. Will the >60% adenoma detection rate reported by Rex et al[26] lead to a reduction in the interval cancer incidence of patients under surveillance in long-term follow-up? That will be the true measure of whether enhanced detection especially of small lesions and whether more complete polyp resection will have a meaningful clinical impact.

In the meantime, the undisputed advance is the enhanced optical diagnosis with >90% accuracy using NBI or FICE colonoscopes. By looking at pit and vessel patterns using this new technology, routine colonoscopy could easily be made more efficient and less costly. Considerable time and cost might be saved by adopting the practice of not removing small, clearly hyperplastic polyps in the left colon or by following a remove and discard policy once enough information has been obtained optically to determine the recommended timing of the next interval examination.

In inflammatory bowel disease surveillance, chromoendoscopy targeted biopsy has been shown to enhance the yield of detecting dysplasia.[32] There are currently insufficient data that optical contrast with NBI or FICE has similar efficacy with greater ease of use. This remains an important area of needed investigation. Additionally, as "Red Flag" technologies are developed to provide a reliably sensitive and rapid screen for such a large territory as the colon, optical contrast will need evaluation as a

potential confirmatory tool to reduce the false positives and facilitate target biopsies in the colon in this 2-step manner.

References

1. Cohen J, ed. Advanced digestive endoscopy: comprehensive atlas of high resolution endoscopy and narrowband imaging. Boston: Blackwell Publishing; 2007.
2. Song LMWK, Adler DG, Conway JD, et al; ASGE Technology Committee. Narrow band imaging and multiband imaging. Gastrointest Endosc 2008;67:581–589.
3. American Gastroenterological Association, AGA Institute. Technology assessment on image-enhanced endoscopy. Gastroenterology 2008;134:327–340.
4. Kara MA, Ennahachi M, Fockens P, et al. Detection and classification of the mucosal and vascular patterns (mucosal morphology) in Barrett's esophagus by using narrow band imaging. Gastrointest Endosc 2006;64:155–166.
5. Sharma P, Bansal A, Mathur S, et al. The utility of a novel narrow band imaging endoscopy system in patients with Barrett's esophagus. Gastrointest Endosc 2006;64:167–175.
6. Pohl J, May A, Rabenstein T, et al. Computed virtual chromoendoscopy (CVC): a new tool for enhancing tissue surface structures. Endoscopy 2007;39:80–83.
7. Hoffman A, Basting N, Goetz M, et al. High definition endoscopy (HD+) with I-scan and Lugol's Solution for the detection of inflammation and neoplasia in patients with GERD. Gastrointest Endosc 2008;67:AB98.
8. Kara MA, Peters FP, Rosmolen WD, et al. High resolution endoscopy plus chromoendoscopy or narrow-band imaging in Barrett's esophagus: a prospective randomized crossover study. Endoscopy 2005;37:929–936.
9. Curvers W, Baak L, Kiesslich R, et al. Chromoendoscopy and narrow-band imaging compared with high-resolution magnification endoscopy in Barrett's esophagus. Gastroenterology 2008;134:670–679.
10. Wolfsen HC, Crook JE, Krishna M, et al. Prospective, controlled tandem endoscopy study of narrow band imaging for dysplasia detection in Barrett's esophagus. Gastroenterology 2008;135:24–31.
11. Inoue H, Honda T, Nagai K, et al. Ultra-high magnification endoscopic observation of carcinoma in situ of the esophagus. Dig Endosc 1997;9:16–18.
12. Muto M, Saito Y, Ohmori T, et al. Multicenter randomized controlled study on the detection and diagnosis of superficial squamous cell carcinoma by back-to-back endoscopic examination of narrowband imaging and white light observation. Gastrointest Endosc 2007;65:AB110.
13. Yao K, Oishi T, Matsui T, et al. Novel magnified endoscopic findings of microvascular architecture in intramucosal gastric cancer. Gastrointest Endosc 2002;56:279–284.
14. Nakayoshi T, Tajiri H, Matsuda K, et al. Magnifying endoscopy combined with narrow band imaging system for early gastric cancer: correlation of vascular pattern with histopathology. Endoscopy 2004;36:1080–1084.
15. Osawa H, Yoshizawa M, Yamamoto H, et al. Optimal band imaging system can facilitate detection of changes in depressed-type early gastric cancer. Gastrointest Endosc 2008;67:226–234.
16. Oyama T, Tomori A, Hotta K. Efficacy of NBI system for the diagnosis of the lateral extension of superficial gastric cancer. Gastrointest Endosc 2007;65:AB162.
17. Machida H, Sano Y, Hamamoto Y, et al. Narrow-band imaging for differential diagnosis of colorectal mucosal lesions: a pilot study. Endoscopy 2004;36:1094–1098.
18. Sano Y, Horimatsu T, Fu KI, et al. Magnified observation of microvascular architecture using narrow band imaging (NBI) for the differential diagnosis between non-neoplastic and neoplastic colorectal lesion: a prospective study. Gastrointest Endosc 2006;63:AB102.
19. Rastogi A, Bansal A, Wani S, et al. Narrow-band imaging colonoscopy—a pilot feasibility study for the detection of polyps and correlation of surface patterns with polyp histologic diagnosis. Gastrointest Endosc 2008;67:280–286.
20. Pohl J, Nguyen-Tat M, Pech O, et al. Computed virtual chromoendoscopy for classification of small colorectal lesions: a prospective comparative study. Am J Gastroenterol 2008;103:562–569.
21. Hoffman A, Kagel C, Goetz M, et al. High definition colonoscopy (HD+) with I-scan function allows to recognize and characterize flat neoplastic changes as precisely as chromoendoscopy. Gastrointest Endosc 2008;67:AB125.
22. Rogart JN, Jain D, Siddiqui US, et al. Narrow band imaging without high magnification to differentiate polyps during real-time colonoscopy: improvement with experience. Gastrointest Endosc 2008;67:AB101.
23. East JE, Suzuki N, Stavrinidis M, et al. Narrow band imaging for colonoscopic surveillance in hereditary nonpolyposis colorectal cancer. Gut 2008;57:65–70.
24. East JE, Suzuki N, Stavrinidis M, et al. Narrow band imaging (NBI) improves adenoma detection in patients at high risk for adenomas: a randomised trial. Gastrointest Endosc 2007;65:AB95.
25. Gross S, Buchner AM, Cangemi JR, et al. A prospective randomized back-to-back trial comparing narrow band imaging to conventional colonoscopy for adenoma detection. Gastroenterology 2008;134:A-47.
26. Rex DK, Helbig CC. High yields of small and flat adenomas with high-definition colonoscopes using either white light or narrow band imaging. Gastroenterology 2007;133:42–47.
27. Cohen J. Adenoma detection using high definition endoscopy—does narrow band imaging increase the yield? Evidence-Based Gastroenterology 2007;8(4):79–80.
28. Kaltenbach TR, Friedland S, Soetikno RM. A new benchmark in the colorectal neoplasm miss rate during colonoscopy: results of a randomized controlled trial of wide angle view (170°) colonoscopy comparing narrow band imaging and white light. Gastrointest Endosc 2007;65:AB127.
29. Pohl J, Lotterer E, Sackmann MF, et al. A prospective Funinon intelligent colour enhancement (FICE) system versus standard indigocarmine chromoscopy: what is the impact of novel optical imaging? Gastrointest Endosc 2008;67:AB101.
30. Adler A, Pohl H, Papanikolaou IS, et al. A prospective randomized study on narrow-band imaging versus conventional colonoscopy for adenoma detection: does NBI induce a learning effect? Gut 2008;57:59–64.
31. Matsumoto T, Kudo T, Jo Y, et al. Magnifying colonoscopy with narrow band imaging system for the diagnosis of dysplasia in ulcerative colitis: a pilot study. Gastrointest Endosc 2007;66:957–965.
32. Marion JF, Waye JD, Present DH, et al. Chromoendoscopy-targeted biopsies are superior to standard colonoscopic surveillance for detecting dysplasia in inflammatory bowel disease patients: a prospective endoscopic trial. Am J Gastroenterol 2008;103:2342–2349.

Address requests for reprints to: Jonathan Cohen, MD, New York University School of Medicine, 232 East 30th Street, New York, New York 10021; e-mail: cohen.jonathan@att.net.

The author discloses the following: Dr Cohen is on a speakers bureau for Olympus Corp, USA, and serves as a consultant with Ethicon Endosurgery.