

Special REPORT

i-SCAN and the New OE Optical Enhancement Technology in the Gastrointestinal Tract

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Endoscopic imaging of the gastrointestinal (GI) tract has been routinely performed using white-light endoscopy (WLE).¹ However, this approach has been shown to miss a significant number of lesions and may be unable to detect subtle, but meaningful, signs of inflammation in inflammatory bowel disease (IBD), thereby resulting in delayed or suboptimal therapies.^{2,3} “Traditional WLE has important limitations: WLE cannot characterize the vascular pattern in detail. Furthermore, it cannot detect subtle inflammation in patients with IBD, and it can easily miss a flat lesion indicative of dysplasia,” said Marietta Iacucci, MD, PhD, clinical associate professor in the Division of Gastroenterology & Hepatology at the University of Calgary in Calgary, Alberta, Canada.

Various strategies have been developed to overcome the limitations of conventional and widely used high-definition WLE. Helmut Neumann, MD, PhD, professor of medicine and head of the Endoscopic Research

Group at the University of Erlangen-Nuremberg in Erlangen, Germany, noted that “dye-based chromoendoscopy, which involve the application of stains to the mucosal surfaces during endoscopy to highlight mucosal differences as well as to detect dysplastic and malignant changes that are not apparent in white light, are useful, but also have important drawbacks that limit their overall utility. These limitations include the use of expensive, consumable dyes, problems with inhomogeneous applications of the dye, added procedural time required to apply the dyes, a learning curve to learn how to interpret results using the dyes. Also, the dye does not always coat the area evenly; we have areas that are understained and areas that are overstained, and this is a major limitation of this approach, which has been used for more than 20 years.”

Virtual chromoendoscopy was developed as a strategy to preserve the superior imaging qualities of

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dye-based chromoendoscopy without the need to employ the dyes themselves. This approach utilizes principles of image-enhancement technology to provide digital contrast in real time during endoscopic procedures. In particular, contrast enhancement of blood vessels and mucosal surfaces allows recognition of pathological lesions that typically are not otherwise visible with conventional white-light imaging.¹ “High-definition WLE is extremely good to identify lesions in the colon, rectum, or even in the stomach, but again, we are missing contrast and subtle lesions by only using WLE,” Prof. Neumann said.

Imaging Technology: Overview of OE Optical Enhancement and i-SCAN™

One such image-enhancement technology was introduced over 8 years ago: PENTAX i-SCAN™ (PENTAX Medical), which is featured in specific video processors, such as the company’s EPK-i series, provides enhancement of per-pixel luminosity in real time, allowing clinicians to examine variations of image enhancement as the endoscopic evaluation progresses (Figure 1).^{4,5} As Prof. Neumann explained, “When compared with dye-based chromoendoscopy, use of the i-SCAN system is important in that it’s ‘at push-of-a-button’ technology. Thus, it’s not necessary to spray any substances inside of the colon—following the push of a button, the video processor itself performs the detail enhancement. The gastroenterologist or endoscopist can concentrate fully on the endoscopic image, which is most important for adequate diagnosis.”

However, since the introduction of i-SCAN, further advancements of this type of imaging technology have sought to provide images of even higher contrast so clinicians can better visualize alterations in tissues and structures. One of the latest advancements for i-SCAN incorporates image-enhanced endoscopic technology using a pre-processor, band-limited light described as OE Optical Enhancement (OE), so named because of its use of optical filters to limit certain spectral characteristics of its light

while maintaining the processing and enhancement of the digital image (Figure 2).^{1,6} Unlike i-SCAN, which uses white light alone to illuminate tissues and structures, OE technology aims to achieve higher overall transmittance by connecting the peaks of the hemoglobin absorption spectrum (415, 540, and 570 nm), thus creating a continuous wavelength spectrum.¹

“It’s extremely important to understand the different capabilities of i-SCAN and OE,” Prof. Neumann said. “Digital post-processing is i-SCAN and OE is combining digital chromoendoscopy and optical chromoendoscopy. With i-SCAN, we are highlighting the surface pattern morphology. With OE, we are highlighting the mucosal vascular pattern morphology.” Optical chromoendoscopy relies on the depth of penetration of the 7 wavelengths of color that comprise white light into the mucosa to differentiate blood vessels containing hemoglobin, which absorb certain wavelengths (peak absorption, 415 nm), from other areas of mucosa, which reflect them. Inflamed or malignant masses also absorb wavelengths that lead to a darker appearance on digital images, helping to identify them during virtual endoscopy.⁶ Prof. Neumann noted how this technology is similar to narrow band imaging (NBI): “Both are narrowing the red light, leaving more blue and green light, providing a more-intense look at the vascular pattern morphology. The main advantage of OE to me is that the image appears brighter compared to NBI, particularly in the stomach.”

Both i-SCAN and OE are designed to provide differing modes of image enhancement. i-SCAN offers 3 modes: Mode 1, Mode 2, and Mode 3, which alter both light and color attributes for image clarity.⁵ OE offers 2 modes using different filters that also alter image light and color, but does so based on the peaks of the hemoglobin absorption spectrum. For example, i-SCAN Mode 1 maintains brightness and limits color alterations while enhancing the image edges by augmenting light–dark contrast between target pixels. OE mode 1 uses the main wavelengths of light that correspond between the peaks of the hemoglobin absorption spectrum and raises baseline transmittance of this

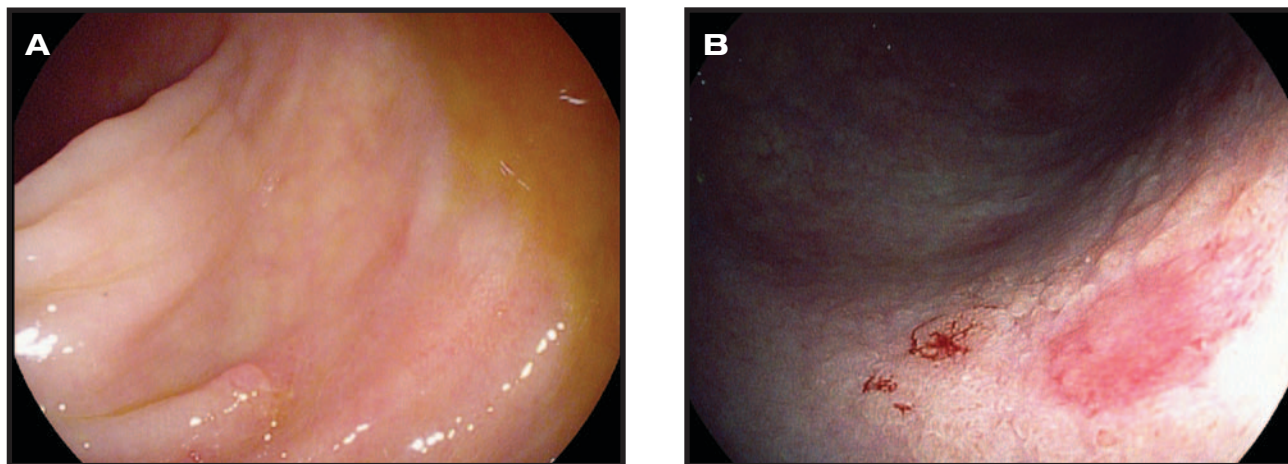


Figure 1. Standard white-light endoscopy almost missed a flat colonic lesion (A); PENTAX i-SCAN™ Mode 1 assisted in characterizing the mucosal, vascular pattern and margins of the lesion (B).

Images courtesy of Marietta Iacucci, MD, PhD.

light with additional luminescence. This feature aims to improve the visualization of microvessels (Figures 3 and 4).^{1,7}

OE mode 2 aims to match the natural tone of the image with color alterations as well as improve the image's white-light contrast (Figure 5). Overall, the use of optical filters in OE allows for improved observation of microsurface patterns on the mucosal surface (Figure 6).¹

"OE essentially is a combination of digital chromoendoscopy and optical chromoendoscopy. Thus, with this technology, we have a better visualization of both the surface pattern and the vascular pattern morphology, and this makes this technique so unique at the moment in the field of endoscopy," Prof. Neumann said. Additionally, according to an observational study of OE technology led by Carlos Robles-Medranda, MD, head of the Endoscopy Division at the Instituto Ecuatoriano de Enfermedades Digestivas of OMNI Hospital in Guayaquil, Guayas, Ecuador, "new endoscopes have been developed, which combine high-definition images with optical magnification called MagniView™. These scopes magnify the image up to 136 times at a superior quality than standard scopes without optical zoom."

Dr. Iacucci said, "Currently, with i-SCAN and OE, this is the only equipment that can provide several multimodal platforms of electronic chromoendoscopy within the same equipment. This provides flexible options to fully assess mucosal and vascular patterns."

Drs. Iacucci, Neumann, and Robles-Medranda also each noted other differences in the capability of OE technology versus i-SCAN, particularly in relation to its visualization abilities in different regions of the GI tract.

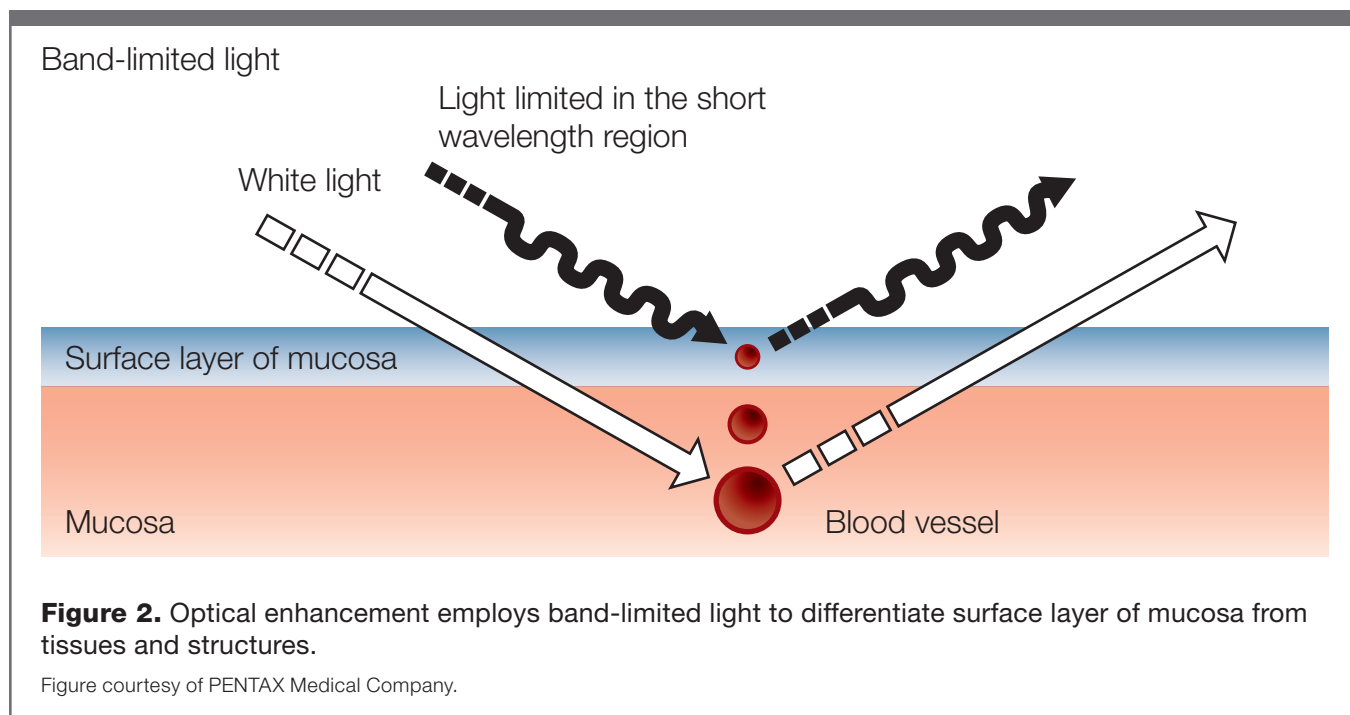
Experience in the Upper Gastrointestinal Tract

Researchers have investigated the use of i-SCAN digital image enhancement technology for endoscopic evaluation of the upper GI tract. For example, Cammarota et al performed

a prospective, single-center study of 115 patients undergoing upper endoscopy for histologic evaluation of duodenal mucosa.⁸ All patients underwent upper endoscopy using high-resolution view in association with i-SCAN technology. During endoscopy, duodenal villous patterns were evaluated and classified as normal, partial villous atrophy, or marked villous atrophy. Results were then compared with histology. Investigators reported that the i-SCAN system had 100% accuracy for the detection of marked villous atrophy patterns and had 90% accuracy for the detection of partial villous atrophy or normal villous patterns.⁸ These data also were confirmed by Poon et al who have demonstrated a significant correlation between endoscopic grade using high-definition i-SCAN in combination with water immersion (WI) technique and Marsh histologic grade ($rs=0.806$; $P<0.00001$). The authors concluded that high definition i-SCAN-WI endoscopy can reflect the histologic severity of celiac disease more accurately than conventional WLE alone especially for those with a patchy distribution of villous atrophy.⁹

Dr. Robles-Medranda commented that the use of i-SCAN with the newer OE technology may be of even greater utility in characterizing diseases of the upper GI tract (Figure 7). "This technology is very helpful for the detection of various lesions that are not always well visualized when using standard WLE," he said. "For example, in my experience, it is much more helpful in detecting lesions associated with esophagitis or gastroesophageal reflux disease (GERD) as well as with gastric lesions, including dysplastic lesions than standard WLE. With the OE technology and MagniView,³ we can even observe lesions that were not previously defined and that may be pathognomonic of nonerosive reflux disease, such as minimal esophageal lesions and intrapapillary capillary loops."

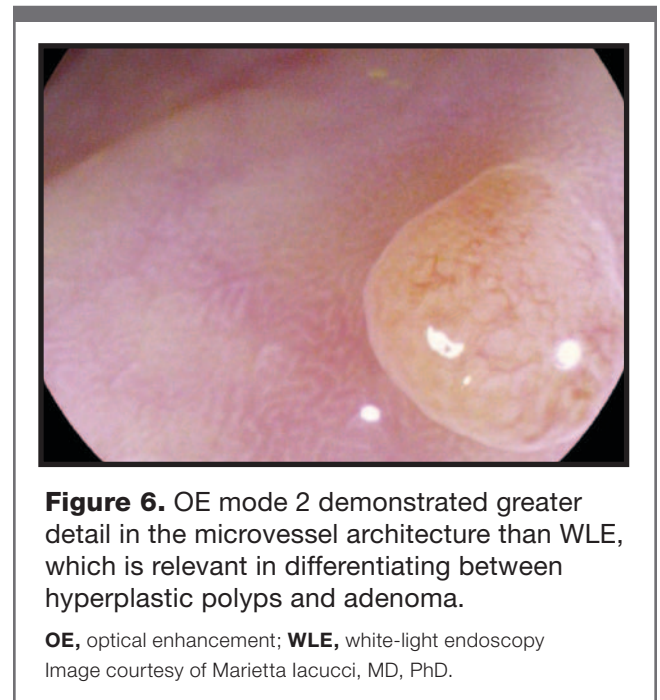
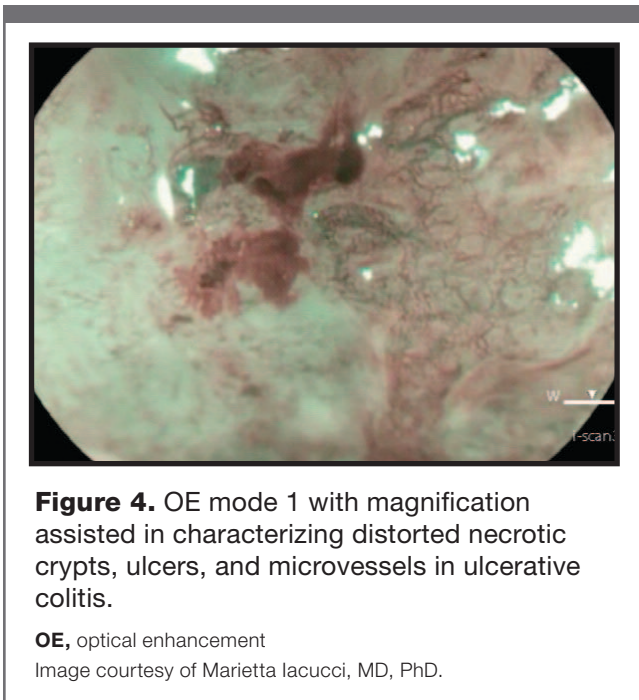
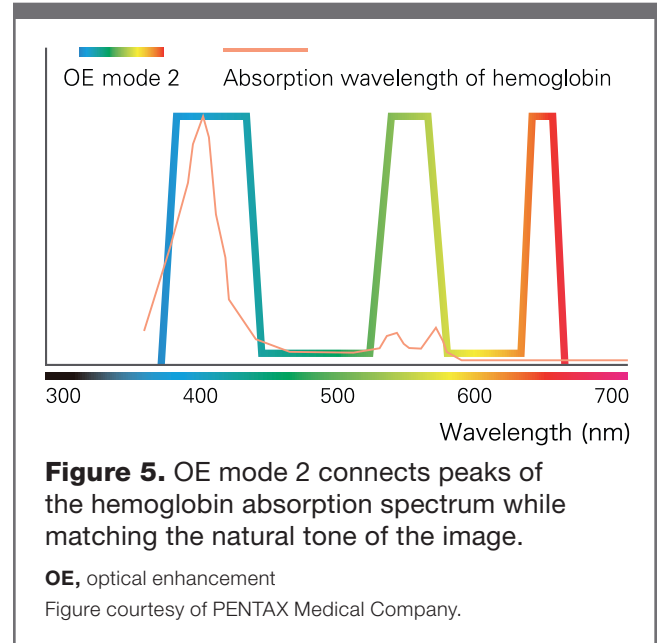
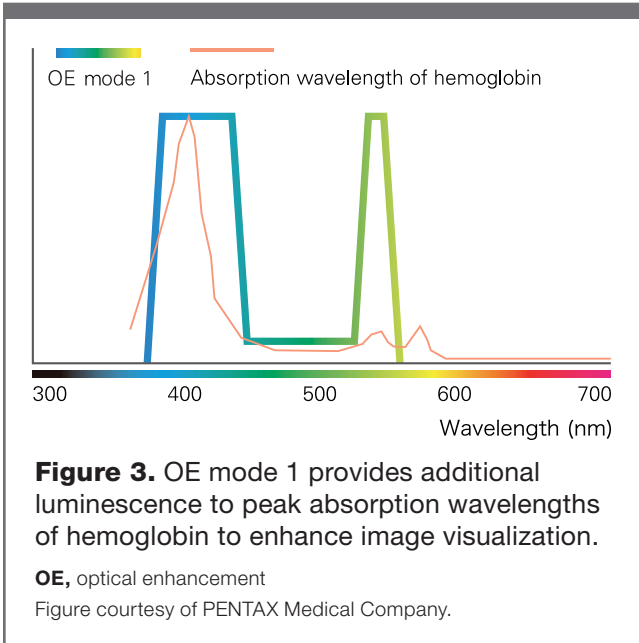
Dr. Robles-Medranda's team recently conducted a study to evaluate the diagnostic ability of i-SCAN with the OE imaging



^a The MagniView scope for the upper GI tract (gastroscope) has not been cleared for use in the United States.

technology and MagniView scopes to detect minimal esophageal lesions (MEL) and intrapapillary capillary loops (IPCLs), and to predict reflux in nonerosive reflux disease (NERD) patients.¹⁰ Endoscopic findings were compared with reference data from pH-impedance measurements and histopathologic assessment of biopsies to assess relative diagnostic utility. In the study, 57 patients were analyzed, including 36 patients with NERD and 21 control patients with nonreflux disease. IPCLs were observed in 94.4% of patients with NERD and in 38% of control patients ($P < 0.05$), and IPCLs were more commonly detected in patients whose biopsies showed signs of inflammation.¹⁰

The ability of OE plus MagniView to predict GERD was compared with pH-impedance measurement, the gold standard. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of the system for this purpose were 94.4%, 61.9%, 80.9%, 86.67%, and 82.4%, respectively. Based on these data, Dr. Robles-Medranda's team concluded that the OE system plus MagniView scope can detect MEL and predict GERD with high sensitivity and accuracy. Furthermore, the presence of MEL was strongly correlated with histologic indicators of inflammation.¹⁰ Dr. Robles-Medranda will present these data at Digestive Disease Week 2016 in an oral presentation.



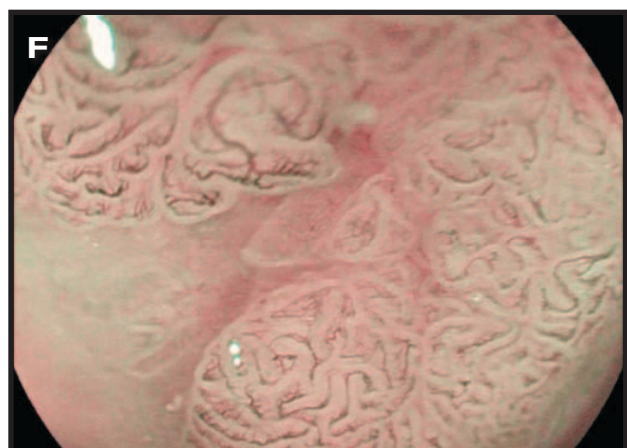
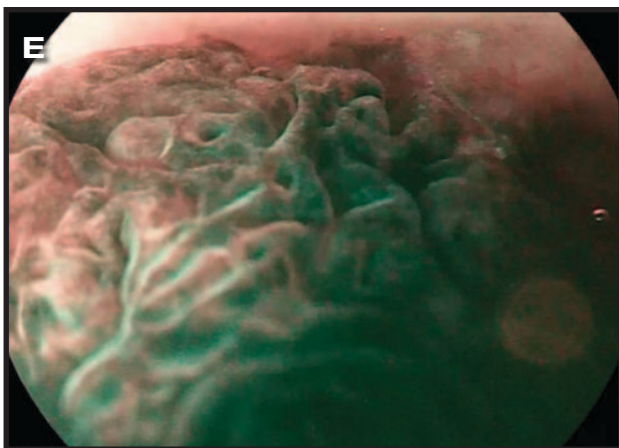
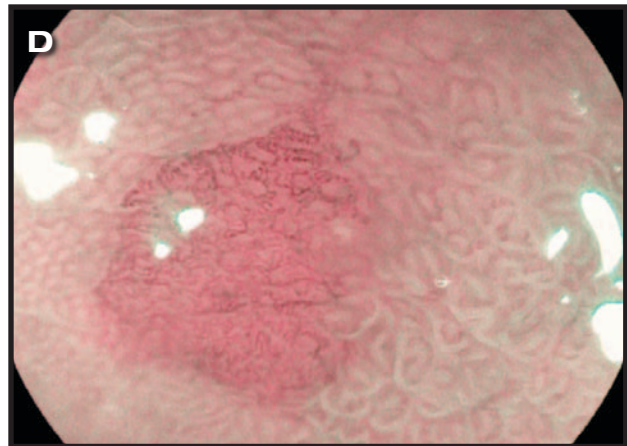
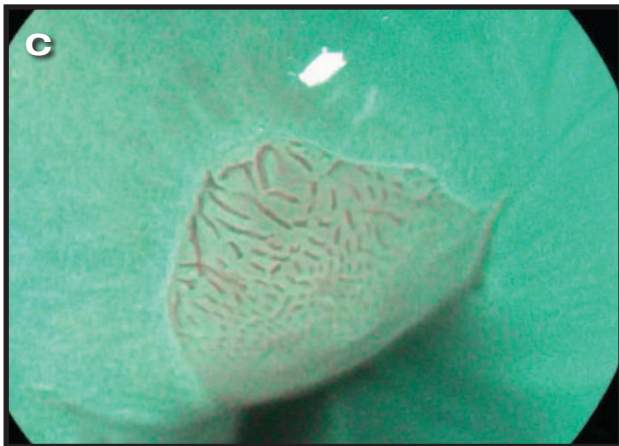
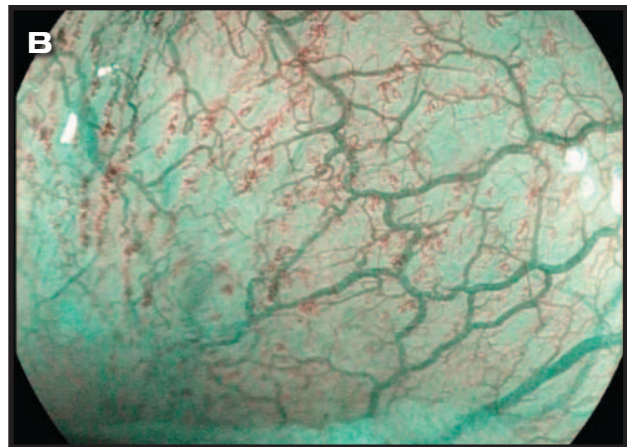
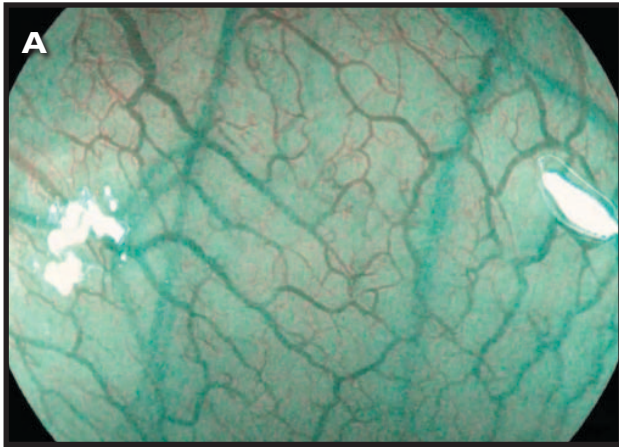


Figure 7. PENTAX Medical OE images showing endoscopic evaluations of upper GI structures: normal esophagus (A); intrapapillary capillary loops in a patient with nonerosive reflux disease (B); Barrett's esophagus (C); early gastric cancer (D); and adenomatous polyps (E and F).

GI, gastrointestinal; OE, optical enhancement
Images courtesy of Carlos Robles-Medrand, MD.

Dr. Robles-Medranda further commented, "With the i-SCAN, OE, and magnification, I can see very small details that I can't see when using standard WLE. I can recognize the microscopic aspects of the pit patterns of the mucosa; I can recognize vascular lesions; and I can predict the histologic feature of the mucosa that is under inspection."

Experience in the Lower Gastrointestinal Tract

The utility of this digital image enhancement technology also has been studied in the endoscopic evaluation of the lower GI tract (Figure 8). Dr. Iacucci noted "i-SCAN, OE imaging technology, and magnification are very important tools to help recognize and characterize lesions of the lower GI tract, even flat lesions." Indeed, in a review of patients who underwent endoscopic procedures with either WLE or i-SCAN, Hancock et al reported that i-SCAN was useful in diagnosis or therapy of right-sided serrated adenomas, flat tubular adenoma, rectal adenocarcinoma, anal squamous cell cancer, solitary rectal ulcer, and radiation proctitis.⁴

Dr. Iacucci added: "This technology has been used beyond characterizing polyps in the lower GI tract. It can also be used to assess conditions such as microscopic colitis, and to enable early diagnosis and characterization of colonic lesions in patients with inflammatory bowel disease." The latest OE with magnification can assess details in mucosal and vascular pattern, and margins and mucosa surrounding these lesions in IBD patients. This ability will aid endoscopists in planning early endoscopic therapeutic management with organ-sparing endoscopic resection, rather than colectomy.¹¹

In a case report, Iacucci and Urbanski noted that WLE characterizes microscopic colitis as having normal mucosal appearance with microscopic inflammation at histology; however, this finding may be limited in extent or patchy and, therefore, may be missed on random biopsies unless biopsies are numerous.¹² While the mucosa of a patient with microscopic colitis appeared normal with WLE, inspection with i-SCAN showed an irregularity

of the colonic mucosal pattern (ie, nodular-mosaic with a small honeycomb pit-pattern appearance). Dr. Iacucci's group concluded that the i-SCAN technology could permit macroscopic endoscopic recognition of microscopic colitis and thereby improve the diagnosis of microscopic colitis by allowing targeting of biopsies and prompting more-extensive biopsies.¹²

Dr. Iacucci also noted that this technology has tremendous potential in the diagnosis or management of patients with IBD. In a study designed to assess the comparative utility of i-SCAN versus WLE, Iacucci et al studied 78 patients with ulcerative colitis. Mayo endoscopy subscores were assigned to patients according to findings on WLE, and targeted biopsies were taken and assigned a histologic grade using the Harpaz score (0=normal or inactive chronic colitis, 1=mildly active chronic colitis, 2=moderately active chronic colitis, 3=severe chronic active colitis).¹³ Mucosal pattern on i-SCAN assessment was graded as 1=normal, 2=mosaic pattern, 3=roundish rosette, 4=tubular-gyrus, and 5=nodular roundish rosette, while the vascular pattern was graded as 1=normal, 2=dropout vessels, 3=spiral isolated vessels, 4=crowded tortuous vessels, and 5=honeycomb irregular crowded vessels.¹³

Iacucci et al reported that there was a high degree of correlation between the i-SCAN scores and histologic grading and the Mayo endoscopy subscore. The overall high-definition mucosal and vascular patterns were significantly correlated with Mayo endoscopic subscores ($r_s=0.86$; 95% CI, 0.79-0.91; $P<0.0001$). Also, mucosal and vascular patterns both were significantly correlated with New York Mount Sinai (NYMS) histologic score ($r_s=0.66$; 95% CI, 0.51-0.77 and $r_s=0.54$; 95% CI, 0.35-0.68; $P<0.0001$, respectively). The overall i-SCAN scores also were significantly correlated with NYMS histologic scores ($r_s=0.65$; 95% CI, 0.49-0.76; $P<0.0001$).¹³ Therefore, Iacucci et al also confirmed data by Neumann et al.¹⁴

More interesting was that a significant number of patients with endoscopic Mayo subscore 0 demonstrated a high proportion of abnormal vascular pattern and mucosal pattern on

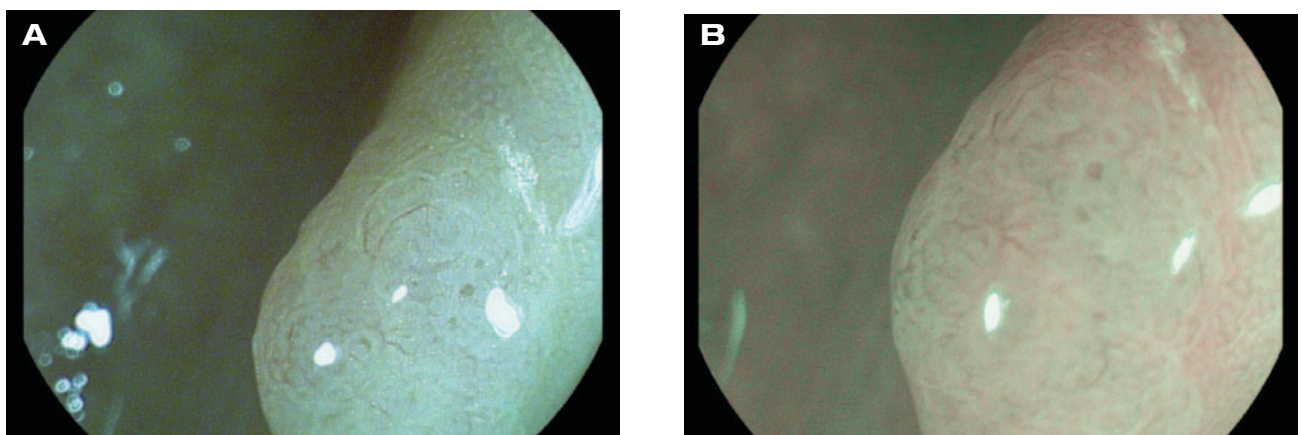


Figure 8. PENTAX i-SCAN™ Mode 2 (A) and OE mode 1 (B) with magnification to assist in characterizing the mucosal and vascular pattern of sessile serrated adenoma.

OE, optical enhancement

Images courtesy of Marietta Iacucci, MD, PhD.

i-SCAN colonoscopy. These data suggest that endoscopic assessment with i-SCAN might be a good strategy to assess for disease activity and mucosal healing in patients with ulcerative colitis, and that it is capable of detecting lesions and subtle inflammation that are not otherwise detected via conventional WLE.¹³ The new green, orange, and red tone enhancements of OE with magnification can define more accurately all of the subtle and chronic mucosal inflammatory changes in ulcerative colitis. Dr. Iacucci also will present these data at Digestive Disease Week 2016 in an oral presentation.

In another study of the use of i-SCAN technology for the detection of dysplastic lesions in patients with long-standing IBD, Iacucci et al reported that i-SCAN had a sensitivity of 100%, specificity of 83.3%, positive predictive value of 64.71%, and negative predictive value of 100%, suggesting that this digital image progressing technology could be an excellent tool to exclude the presence of dysplastic lesions in patients with IBD.¹⁵

Adding support to these data, Gasia et al have shown that in a large cohort of 454 patients with long-standing IBD, targeted biopsies identified greater proportion of subjects with neoplasia than random biopsies. Targeted collection of biopsies appears to be sufficient for detecting colonic neoplasia in patients undergoing HD colonoscopy, dye chromoendoscopy (DCE), or virtual chromoendoscopy (VCE), but not WLE. The authors could not show that DCE was superior if high-definition endoscopes and VCE were used.¹⁶

Future Outlook

After using OE technology and i-SCAN, all of the expert faculty members noted that the future outlook for this technology may include its potential to facilitate *in vivo* diagnosis. "Because this technology enables me to see signs of underlying inflammation and provides endoscopic correlates of pathology in patients that were not previously considered to have organic disease, such as those with nonerosive reflux disease, I suspect that we will be able to avoid the need for further testing, such as manometry and pH testing," Dr. Robles-Medrandá said.

Prof. Neumann added: "This future for OE, in my opinion, not only is guidance of endoscopic therapy, but also its ability to be used for *in vivo* characterization of the tissue. I think we will be using it to diagnose Barrett's esophagus, celiac disease, and type of colorectal polyps. In fact, we also know that it's extremely helpful for *in vivo* diagnosis of colorectal polyp histology to differentiate hyperplastic lesions from adenomas or cancers."

Dr. Iacucci agreed with Prof. Neumann and Dr. Robles-Medrandá: "The latest generation of OE Optical Enhancement imaging technology has the capability to redefine the whole spectrum of acute and chronic inflammatory changes in IBD as well as detect early dysplastic lesions in IBD. In the future, we will be able to tailor therapy of IBD, preserve their colon, and reduce complications and hospitalization. We may change the natural history of the disease in the future by recognizing and treating subtle inflammation and early dysplasia."

Resect and Discard

In a publication by the Preservation and Incorporation of Valuable Endoscopic Innovations initiative, the American

Society for Gastrointestinal Endoscopy (ASGE) advocated for the use of real-time endoscopic technologies that can help predict the histology of colorectal polyps.¹⁷ The organization stated that rather than submitting low-risk polyps for pathologic assessment, the polyp should be discarded and the endoscopic assessment of histology should be used to determine the implication of the polyp for the patient's next post-polypectomy surveillance interval. The principal value of the "resect and discard" paradigm is a reduction in costs otherwise incurred for pathologic assessment of these low-risk polyps.¹⁷

Dr. Iacucci noted that the capabilities of the i-SCAN technology with OE and magnification suit this ASGE initiative. "This endoscopic technology has the capabilities, in real time, to improve visualization of microvessels with sufficient amount of light to improve characterization, and to help when deciding if we need to remove a polyp, and whether we can discard it, or whether it should be submitted to pathology for precise characterization," she said. "It will help clinicians embrace the new policy of the ASGE of 'resect and discard,' and will be a great way to save resources for the community."

Ability To Guide Endoscopic Resection, Avoid Surgery

Prof. Neumann explained that the i-SCAN technology with OE could help facilitate endoscopic mucosal resection and help patients avoid surgery. "On endoscopy, we are always deciding based on this so-called mucosal pit pattern if a lesion is only superficially invasive or deeply invasive. Superficially invasive would mean that we can perform an endoscopic resection, and deep invasion would mean that we have to perform a surgical intervention with resection of the lymph nodes. The advantage of i-SCAN, and now recently introduced OE, is that both technologies are adding much more contrast to the endoscopic image. It's not white light anymore, but now it's a colored image, and therefore it is now much easier for us to detect subtle lesions and also to perform this prediction of mucosal invasion; is it, in essence, one tumor, or is it going deeper? So, can we perform endoscopic resection, or would it be better to send the patient to the surgeon for resection of the lymph nodes as well? This is the main advantage of these new technologies."

Dr. Iacucci added: "The new guidelines for the management of inflammatory bowel disease include an expanded discussion of the resectability of any identified lesions. With this new technology, we have the ability to look more closely at the margin of the lesion and to predict the histology, and to decide if we can remove the lesions entirely or not. This will change the outcomes of the patient and is very important, as it has the potential to be an organ-sparing therapy," she said. "In the past, every time we found a lesion in a patient with inflammatory bowel disease, we were concerned about the malignant potential and were more likely to refer for total colectomy. This may no longer be the case. With this new technology, we can assess the margins and make a determination of its suitability for endoscopic resection, thereby avoiding the need for colectomy in many cases."

Guiding Therapy for Inflammatory Bowel Disease

Overall, Dr. Iacucci noted that OE and i-SCAN technology will have a specific benefit for IBD patients. "This technology

will help us to better assess disease activity because one can now detect the subtle endoscopic changes that correlate with disease activity, and one can use these data to decide when to initiate treatment and help guide changes in treatment,” Dr. Iacucci said. “This will help to improve the natural history of the disease and will help to reduce complications as well as the need for hospitalization and surgery.”

Prof. Neumann echoed Dr. Iacucci’s remarks regarding the potential use of this technology to improve outcomes in patients with IBD. “What we also expect is that one can also use the technology for inflammatory bowel disease, especially to predict microscopic inflammation in inflammatory bowel disease,” he said. “And this concept and assessment of mucosal healing is very important for our patients, because mucosal healing is associated with less steroid use and less hospitalization and less surgery for the patients. I suspect that the OE technology will be very helpful for the assessment

of mucosal healing in patients with inflammatory bowel disease. In this way, it will help to guide whether medical therapy should be advanced for patients with active mucosal disease or whether medical therapy can be decreased for those who demonstrate good mucosal healing.”

Conclusion

As use of OE increases, the expert faculty notes that further study of its technology, capability, settings, and design would be warranted to provide more data on its benefits for discovering and diagnosing GI adenomas and cancers. “There have been no uniform settings established yet. Studies so far have concentrated more on OE mode 1, which emits a blue light similar to competing technology, NBI, yet there are no uniform settings,” Prof. Neumann said. “For our studies, we are using some uniform settings and combining both digital chromoendoscopy and optical chromoendoscopy to get the best results.”

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