Endoscopy plays a vital role in the diagnosis and clinical management of diseases of the gastrointestinal (GI) tract, among other organ systems. Despite advances in technology, the adenoma detection rate remains suboptimal in many cases, at least partly due to the limitations of standard endoscopic imaging modalities.\(^1\),\(^2\) “Although white light endoscopy [WLE] has come a long way, there are still limitations in detecting subtle lesions. For instance, if a lesion is flat rather than the classic pedunculated polyp, it can be missed with white light endoscopy because the borders are not quite as defined and the surface of the lesion is not quite as defined,” said Steven Naymagon, MD, Department of Gastroenterology at the Icahn School of Medicine at Mount Sinai in New York City.

“The limitations of conventional white light video endoscopy are potentially that you’re not necessarily accentuating the surface characteristics and vascular changes that are associated with the progression to cancer,” said Sharmila Anandasabapathy, MD, medical director, Mount Sinai Endoscopy Center and an associate professor of medicine at Icahn School of Medicine at Mount Sinai.

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**Faculty**

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<th>Sharmila Anandasabapathy, MD</th>
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Supported by
associate professor of medicine at the Icahn School of Medicine at Mount Sinai in New York City.

Adjunctive techniques to enhance the utility of conventional high-definition white light endoscopy (HDWLE) are available, such as dye-based and spray chromoendoscopy. These techniques apply 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. However, chromoendoscopy has important drawbacks that limit its overall utility.3 “Application of the dyes to the large areas of the mucosal surfaces can be time consuming in addition to being expensive. Sometimes, you might even run out of your supply of the dye and not have it available when you need it. Also, like any drug, some patients can have an allergic reaction to the dye,” said Carlos Robles-Medranda, MD, head of the Endoscopy Division at Instituto Ecuatoriano de Enfermedades Digestivas at OMNI Hospital in Guayas, Ecuador. The dyes are inhomogeneous, which can cause unevenly coated mucosal areas that affect clinicians’ ability to assess lesions.3 “Interpreting chromoendoscopic findings is a learned process that can lead to a lot of variability in diagnosis, so it’s inconsistent,” added Dr. Anandasabapathy.

Fortunately, several high-tech approaches have been developed to approximate similar data generated by chromoendoscopy without the use of dyes, thereby facilitating the accurate detection of malignant and premalignant lesions in general endoscopic practice. These “virtual chromoendoscopic” approaches are known as image-enhanced endoscopy and include narrow band imaging (NBI; Olympus), Fuji intelligent color enhancement (Fujinon; currently not FDA-approved), and PENTAX i-SCAN™ (PENTAX Medical) technology.3

i-SCAN™ Technology

i-SCAN is a software-based, image-enhancement technology that is classified as a digital contrast method among endoscopic imaging techniques.4,5 The technology works by conducting per-pixel modifications of white light images. Although i-SCAN is technically a post-imaging technology, all processing is done on a real-time basis with no delay, which offers efficient endoscopic observation.6 The SE mode analyzes differences in luminance intensity between target pixels and surrounding ones, enhancing the edges by augmenting light–dark contrast. Compared with normal images, SE images do not differ in brightness and show only minor color variations. This mode also offers improved observation of tiny glandular structures.5 The SE mode contains low, medium, and high enhancement levels. “Surface enhancement, in general, can help you identify the borders of lesions, meaning that it helps bring out the mucosal surface and thereby allows you to delineate exactly where the lesion is,” said Dr. Naymagon.

The CE mode uses pixel-wise luminance intensity data to identify areas that are lower in luminance intensity than surrounding pixels, followed by relative enhancement of the blue component through slight suppression of red and green components in this low luminance area.6 As a result, a blue color is added to relatively dark areas, and tiny irregularities on the mucosal surface are enhanced. The minute glandular structure can be enhanced even with flat mucosa because the change in color reflects very minute depressions at the opening of the gland duct. Image processing with CE does not result in changes to image brightness, and causes only slight bluish-white staining of depressed areas.6 Like the SE mode, the CE mode contains the same 3 enhancement levels. “Contrast enhancement can bring out the subtle irregularities around the surface and allow you to inspect it in a more detailed manner. It may also help bring out some of the blood vessels and allow you to inspect the vascular pattern in the lesions,” Dr. Naymagon added.

During conventional endoscopy, white reflective rays from the mucosa are captured at the tip of the endoscope and appear on the monitor. However, i-SCAN TE mode deconstructs each component of the red-blue-green color spectrum and independently adjusts them along a tone curve before reintroducing them into an image that enhances tiny mucosal structures with subtle color changes.6 Additionally, the tone curve can be modified to enhance individual red, green, or blue components as well as to adjust image contrast. As a result, different parameters can be used that are specifically suited to characterize individual portions of the GI tract. Three types of TE have been established: TE-e for the esophagus, TE-g for the stomach, and TE-c for the colon.5

i-SCAN™ Settings

Use of the i-SCAN modes in different combinations can enable targeted imaging functions. Thus far, 3 default combination modes have been established and approved by the FDA for use during endoscopy: i-SCAN 1, 2, and 3. Switching between HDWLE and the 3 i-SCAN settings can be performed on a real-time basis with no delay, which offers efficient endoscopic observation. These modes allow the user to visualize more mucosal and vascular details compared with white light imaging.4
i-SCAN combines a variety of parameters to produce the effect of each default mode: brightness of light (off, –5 to +5), red (off, –5 to +5), blue (off, –5 to +5), light-measuring mode (ave, peak) enhancement (off, low, medium, high), SE (off, +1 to +6), CE (off, +1 to +6), TE (off, c, g, r, e, b, d), and noise reduction (off, low, medium, high). For example, i-SCAN 1 uses a combination of SE, CE, and a fast Fourier transform analysis to sharpen surface vessels and enhance the texture of surface mucosa while maintaining an image as bright as a conventional white light image. This setting provides the user with a sharper view of the HDWLE images and enhances areas of the mucosa that are depressed or elevated; vessels retain their natural red coloration.

By comparison, i-SCAN 2 adopts a combination of CE, SE, and TE-c enhancement to sharpen surface vessels, enhance surface texture, and improve the contrast of blood vessels and mucosa. In fact, this setting results in a 147% to more than 300% improvement in contrast between blood vessels and mucosa when compared with HDWLE images. Furthermore, this setting allows increased visualization of microvascularity and the peripheral capillary network and an enhanced view of the mucosa while retaining tissue color throughout use.

Finally, the i-SCAN 3 setting mimics the same levels of CE and SE as i-SCAN 1, resulting in the sharpening of surface vessels and enhancement of surface texture. Additionally, i-SCAN 3 improves contrasts between blood vessels and mucosa through engagement of the TE-g mode. The main difference between i-SCAN 2 and 3 is one of brightness due to the different tone curves employed. Although i-SCAN 2 improves contrast in vessels, it may reduce the brightness of low-intensity regions of the image. i-SCAN 3 maintains visibility within dimly illuminated distal regions by balancing tonal alterations and image brightness to avoid excessive darkening. As a result, i-SCAN 3 generates a contrast-enhanced image while maintaining uniform brightness. As with all i-SCAN modes, vessels maintain a natural red coloration when i-SCAN 3 is engaged.

“Within the individual default i-SCAN modes, the settings on brightness and tone enhancement, surface enhancement, and contrast enhancement are all specifically up-regulated and down-regulated to help you achieve certain goals. For instance, i-SCAN 1 can help you detect lesions and that uses the surface enhancement more than anything,” said Dr. Naymagon. “i-SCAN 2 is more about characterizing lesions, and that uses both surface enhancement and tone enhancement. i-SCAN 3 is a modality that I would use to help demarcate lesions, to tell where a lesion begins and ends. That mode uses contrast enhancement, tone enhancement, and surface enhancement.” Figure 2 depicts differences in the images provided by the HDWLE and the 3 default i-SCAN modes.

**Clinical Use of i-SCAN**

As Dr. Robles-Medranda explained, “the ability of i-SCAN to enhance the images of the mucosal surface and vascularity of the lesion means that it can be used as a ‘red flag’ indicator. There are certain mucosal patterns or vascular patterns that can be detected by this technology that would help you target a lesion for biopsy. Going further, in our group’s experience, the features revealed by this image enhancement also allow you to predict histology with good degree of confidence. We have data to show that i-SCAN can detect organic disease in patients who were otherwise thought to have only functional GI disease based on characterization by standard white light endoscopy.”

Dr. Anandasabapathy echoed this sentiment about i-SCAN as a “red flag” technology: “i-SCAN is a good detection technology that may better help you identify areas of abnormality. For example, the technology is very good at accentuating what we call the mucosal pit pattern, or Kudo pit pattern, which has been shown to differentiate benign polyps from those that are adenomatous or precancerous.”
In addition to pit patterns, i-SCAN image enhancement is useful for detecting and characterizing other correlates of clinical lesions, including margin details, vascular patterns, angiogenesis, and early mucosal changes. In fact, several groups of investigators have published reviews of endoscopic findings with i-SCAN and how they correlate with specific clinical lesions. For example, Hong and colleagues performed a prospective, randomized trial that used a modified, back-to-back colonoscopy to assess the efficacy of i-SCAN application during screening colonoscopy in 389 consecutive asymptomatic, average-risk patients. Analysis demonstrated that the prediction of neoplastic and non-neoplastic colorectal lesions was more precise in the i-SCAN 2 group compared with the conventional WLE group (accuracy, 88.1% vs 75.5%; $P=0.29$; sensitivity, 86.5% vs 72.6%; $P=0.02$; specificity, 91.4% vs 80.6%; $P=0.40$).

Similarly, Bouwens and colleagues investigated the use of i-SCAN technology for the prediction of polyp histology by 11 endoscopists across 550 images (396 adenomatous, 154 non-adenomatous). Mean sensitivity, specificity, and accuracy for diagnosing adenomas were 79.3%, 85.7%, and 81.1%, respectively.

Researchers also have investigated the use of the i-SCAN system for endoscopic diagnostics and management. For example, Hancock and colleagues reviewed data from 20 consecutive patients who underwent endoscopic procedures and compared mucosal lesions with HDWLE and i-SCAN. A positive end point was defined as cases in which i-SCAN imaging highlighted mucosal abnormalities not as clearly seen with WLE and where i-SCAN data subsequently affected management. The investigators reported that for upper GI tract pathology, i-SCAN assisted in diagnosis or therapy for Barrett’s esophagus with dysplasia, esophageal adenocarcinoma, viral esophagitis, gastric mucosa-associated lymphoid tissue lymphoma, gastric antral intestinal metaplasia with dysplasia, duodenal follicular lymphoma, and a flat duodenal adenoma. For lower GI tract pathology, i-SCAN assisted in diagnosis or therapy of right-sided serrated adenomas, flat tubular adenoma, rectal adenocarcinoma, anal squamous cell cancer, solitary rectal ulcer, and radiation proctitis.

Hoffman and colleagues studied the utility of i-SCAN–enhanced endoscopy versus conventional WLE in 200 patients undergoing screening colonoscopy for the prediction of histology from biopsy or resected samples. These investigators reported that i-SCAN detected significantly more patients with colorectal neoplasia (38%) compared with standard resolution endoscopy (13%). Furthermore, significantly more neoplastic (adenomatous and cancerous) lesions and more flat adenomas could be detected using i-SCAN, and final histology could be predicted with high accuracy (98.6%).

Clinical scenarios where i-SCAN potentially has advantages over conventional white light video endoscopy include the detection and characterization of lesions of the esophagus (eg, early squamous cell cancer, gastric inlet patch, minimal change gastroesophageal reflux disease, Barrett’s esophagus, early adenocarcinoma), stomach (eg, atrophic gastritis,
gastric antral vascular ectasia, early gastric cancer), duodenum (eg, celiac disease, Whipple’s disease), and large colon/rectum (eg, polyps, inflammatory bowel disease; Figures 3 and 4), among others. An overview of i-SCAN’s ability to detect adenomatous polyps and lesions is provided in the Table.

Investigators also have reported good inter- and intraobserver agreement when using i-SCAN for the discernment of pathologic GI lesions: Pigo and colleagues found that using the i-SCAN enhancement produced strong inter- and intraobserver agreement in evaluating colorectal polyps in 78 patients undergoing colonoscopy. First, a skilled endoscopist used the high-resolution technology to predict the histology of polyps in real time with subsequent analyses performed by a pathologist. Afterward, 4 other endoscopists were asked to predict polyp histology from digital images taken with i-SCAN enhancement; 6 months later, the 4 endoscopists repeated the assessment. Overall, kappa values for inter- and intraobserver agreement were 0.462 (95% confidence interval [CI], 0.373-0.537) and 0.657 (95% CI, 0.373-0.941), respectively.

Similar results were obtained in a study performed by Masci and colleagues using 400 previously recorded images of colorectal polyps captured with different i-SCAN settings.

Figure 3. Upper gastrointestinal tract with HDWLE (top left); microvascularity intensifies using the 3 different modes of i-SCAN (top right and bottom row).

HDWLE, high-definition white light endoscopy
Images courtesy of Carlos Robles-Medranda, MD.
Eight endoscopists evaluated whether the polyps were neoplastic or non-neoplastic with a moderate interobserver Fleiss’ kappa value of 0.446 ($P<0.001$).\(^\text{11}\)

Kodashima and colleagues reviewed the utility of NBI compared with i-SCAN. They noted that images on NBI were much darker than conventional white light images, particularly in large luminal diameter regions of the GI tract. In comparison, i-SCAN images were as bright as conventional white light images, thereby enabling observation of much larger areas in a distant view compared with NBI.\(^\text{6}\) Moreover, the researchers noted that i-SCAN did not need magnifying endoscopy to observe the demarcation of the lesion.\(^\text{5}\)

"In inflammatory bowel disease, most of the dysplasia that we find is flat rather than a classic pedunculated polyp that you will see in the average-risk population. i-SCAN 1 might be a good way to survey the colon and to help your eye spot abnormalities in the mucosal surface that might tell you that a lesion is there. You may then want to switch to i-SCAN 2 and 3 to help better characterize the lesion. i-SCAN 2 might help bring out the vascular pattern; if the vascular pattern looks normal, it suggests that the lesion is benign," said Dr. Naymagon.

"On the other hand, cancerous and precancerous lesions often alter the vascular pattern of the mucosa, so that is a red flag for us. Finally, i-SCAN 3 in concert with i-SCAN 2 can be used..."
to demarcate the lesion’s borders and guide where we should begin and end our resection.”

**Practical Considerations**

Several of the faculty commented on the economics of i-SCAN image enhancement technology. For example, Dr. Robles-Medranda said, “i-SCAN is quite cost-effective when compared with other endoscopic enhancement technology. There are no recurring costs for consumable reagents, as is the case with chromoendoscopy. Also, you save a great deal of time with i-SCAN, which you can use by just pressing a button, compared with the time-consuming burden of applying large volumes of stain to the extensive mucosal surfaces of the stomach and colon.”

“If the negative predictive value of i-SCAN technology for tissue histology is borne out in prospective trials, then there could be marked cost savings: It would likely reduce the number of samples that we’re sending for histopathologic examination. For example, if i-SCAN image enhancements can predict with good confidence that a lesion is not malignant, then we could simply avoid biopsy or discard these samples. However, we need additional studies before we reach that point,” Dr. Anandasabapathy said.

Dr. Naymagon commented on the ease of i-SCAN use during endoscopy: “It is the click of a button technology that makes it very simple. Having the ability to toggle between the various different modes, high-definition white light, i-SCAN 1, 2, and 3, within seconds, is very convenient. Compared with narrow band imaging, which often can be very dark and therefore interfere with lesion detection, i-SCAN modes allow you to enhance the image while maintaining brightness. With the 3 different i-SCAN modes, you can go back from one to the other to get exactly what you need and what you are looking for.”

Dr. Robles-Medranda noted the potential for customization beyond the FDA-approved modes. “Although i-SCAN settings 1, 2, and 3 are the default modes, clinicians can change any setting individually to suit their needs. Our group already has experience establishing different settings that we feel are useful, and I think it’s likely that additional default modes will be established that use these new combinations of settings,” Dr. Robles-Medranda said. In fact, Dr. Robles-Medranda and his colleagues presented data from a prospective study on the use of new combination settings at the 2013 Digestive Disease Week meeting. The authors found that compared with the 3 default i-SCAN modes, their new combination settings were more effective for diagnosing neoplastic and non-neoplastic colonic lesions.12

### Conclusion

Recognition of pathologic lesions under conventional WLE remains suboptimal. i-SCAN is a novel image-enhancement technology that allows improved recognition of pathologic lesions throughout the GI tract. For example, it can help improve polyp characterization, adenoma detection, and visualization of architectural subtleties in the mucosal lining. The system is easy to use, quickly engages with the touch of a button, and offers rapid imaging results. It is a software-based program with free upgrades, thereby enhancing cost-effectiveness. i-SCAN addresses many aspects of diagnostic endoscopy that we are trying to achieve. It is software-driven, meaning that a computer processor enhances a white light image captured by the scope to help us find whatever it is that we are looking for. The endoscopist flips a switch on the scope and it goes from white light to i-SCAN, and you don’t need any of the other equipment that conventional chromoendoscopy requires,” said Dr. Naymagon.

### Table. Accuracy of i-SCAN for Diagnosing Adenomas

<table>
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<tr>
<th>Authors</th>
<th>Target</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>PPV, %</th>
<th>NPV, %</th>
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<td>95</td>
<td>82</td>
<td>—</td>
<td>93</td>
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NPV, negative predictive value; PPV, positive predictive value

Based on references 7-10.
References

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Disclosures: Dr. Robles-Medranda reported that he serves as a consultant for and on the speakers’ bureau of Mauna Kea Technologies and PENTAX Medical. Drs. Anandasbapathy and Naymagon reported no relevant financial conflicts of interest.

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