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EDITORIAL

Detection of Villous Atrophy Using Endoscopic Images for the Diagnosis of Celiac Disease

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Background

The most common cause of villous atrophy is celiac disease. The current "gold standard" in the diagnosis of celiac disease is the demonstration of villous atrophy in duodenal biopsies, which are usually obtained during a fiber-optic endoscopic foregut examination [1]. Since conventional upper tract endoscopy does not extend past the duodenum, it is not suitable to determine the length of pathological involvement of the small intestine. Moreover, since duodenal villous atrophy is often patchy [2, 3], gross mucosal features, such as scalloping of duodenal folds, reduction of duodenal folds, mosaic pattern (cobblestone appearance of the mucosal surface), and mucosal fissuring [4–7], can be used to identify involved areas. It is nevertheless possible to miss the involved areas since the gross manifestations of villous atrophy may be absent in mild disease [8, 9].

Enhancement of Endoscopic Images by i-Scan and Other Means

A number of recently developed techniques have been found useful to enhance the endoscopic images of villous atrophy, including magnification endoscopy [10], with or without chromoendoscopy [11], immersion techniques [12], and confocal endoscopy [13–16]. However, some of these methods typically require sophisticated instrumentation, special training, and expertise. One recent technology described in this issue of *Digestive Diseases and Sciences* termed i-Scan (Pentax, Tokyo, Japan), is a commercially available, software-based, virtual chromoendoscopy method [17] that can be used in real time without the need for extensive training. The technique improves tissue contrast by spectral estimation of the digitized images and therefore does not require instrumentation accessories such as optical filters within the video endoscope [18]. For image enhancement, the i-Scan technology has the following three software-derived modalities [19]:

1. Surface enhancement—recognition of feature edges is achieved based on differences in luminance intensity. Compared with normal images, surface-enhanced images have the same brightness and only slight color changes.
2. Contrast enhancement—differences in image structure are accentuated by adjusting areas of lower luminance intensity upward in the blue color component and downward in the red and green color component. This provides improved contrast of the mucosal surface as well as capillary patterns [18]. Compared with normal images, contrast-enhanced images also have the same brightness and only slight changes to color.
3. Tone enhancement—the regions of esophagus, stomach, and colon are separately enhanced by modifying the combination of color components contributing to form the color at each pixel, which is done to specifically reflect the quantitative image properties of the individual organ.

The surface and contrast enhancement modalities each consist of three levels (low, medium, and high); for the tone enhancement modality, organ type is selected (esophagus, stomach, or colon) [19]. The three modalities are arranged sequentially, so that more than one modality

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can be applied simultaneously. Switching modalities and enhancement levels is done in real time using a button on the endoscope [17, 20]. The i-Scan technology is useful to evaluate the gross anatomical structure of the small intestinal mucosal surface, including shape and contour [17]. Therefore, the aforementioned macroscopic features characteristic of villous atrophy can be better detected by i-Scan during endoscopic mucosal examination. Chromoendoscopy combined with high-definition colonoscopy and i-Scan were able to identify lesions that were missed by high-definition endoscopy alone, with i-Scan and chromoendoscopy having equal accuracy for the detection of small neoplasia [18, 21]. Therefore, i-Scan can potentially replace time-consuming chromoendoscopy [18, 21]. To date, no complications have been reported with the use of i-Scan technology [19].

A New Study Involving i-Scan Technology

In this issue of *Digestive Diseases and Sciences*, Cammarota et al. [22] report a prospective, single-center study on the diagnostic accuracy of i-Scan technology for the evaluation of the duodenal villous atrophy in patients undergoing upper endoscopy for iron deficiency anemia, diarrhea, abdominal pain, positive anti-endomysial or anti-transglutaminase antibodies, and unexplained weight loss, as compared with a "gold standard" of histologic analysis. Two expert endoscopists, blinded to each other's findings and the subject's laboratory and clinical data, evaluated the endoscopic images obtained from the population of 150 subjects. The duodenal villous patterns obtained with i-Scan were classified by the endoscopists as either marked villous atrophy, partial villous atrophy, or normal, and were compared to simultaneously obtained histology, read by blinded pathologists.

The accuracy of i-Scan for detecting marked villous atrophy patterns was 100 %, whereas the accuracy for i-Scan detection of partial villous atrophy or normal villous patterns was each 90 %. Thus, i-Scan technology was found to be useful to enhance the endoscopic images of the duodenal mucosa for predicting the presence of villous atrophy. Since i-Scan enhances the images in software without the need for dyes and without additional instrumentation, complexity and analysis time were reduced. The excellent classification results suggest that the new technology will be useful for detecting villous atrophy.

Although i-Scan has been shown to be a promising technology, there are limitations to its use. For example, when i-Scan was utilized to characterize small colonic polyps for prediction of histology, it was found that accuracy varied substantially between endoscopists [23]. This suggests that user bias may be an important factor in the efficacy of the technology. Furthermore, for cancer surveillance, it has been recommended that primary screening should be performed with conventional white light endoscopy, after which i-Scan or other digital chromoendoscopy techniques can be used to analyze suspicious lesions [24]. Therefore, i-Scan may be most useful as an adjunctive tool, not as a primary method, for evaluation of small intestinal features.

Future Directions for Endoscopic Image Enhancement

One possible technique to further determine the degree of villous atrophy is to analyze endoscopic images obtained directly or via wireless capsule using computerized image analysis, which could encompass the entire small intestine, enabling the construction of a spatial map from proximal to distal small intestine to show areas and degrees of villous atrophy [25–27]. This would be useful to determine, for example, efficacy of a gluten-free diet treatment, or to screen patients with suspected villous atrophy who have little or no evident changes that can be detected by conventional endoscopic examination. Quantitative methods can also be used to analyze biopsies [28]. Until the present time, however, the accuracy of all of these quantitative methods depends in part upon limited image resolution, the random and often oblique camera angle with respect to the small intestinal mucosal wall, and in the case of video endoscopic images, the presence of extraneous substances such as air bubbles and opaque fluids within the lumen. Therefore, improved imaging methods would be highly desirable for better quantification and for increased visualization [29].

According to Cammarota et al., i-Scan technology was less accurate in identifying mild-to-moderate villous atrophy. Further refinement of image enhancement or computerized quantification techniques should improve identification of images with lesser degrees of villous atrophy. It is only then that image enhancement techniques could possibly replace direct biopsy [30, 31] in the diagnosis of celiac disease.

In addition to studies with larger patient populations, comparison with other techniques, and use of decision analysis to determine costs associated with implementation of the more expensive systems should be performed in future studies. Further investigation using i-Scan would also be used to determine whether celiac disease and other digestive disease can be distinguished from the general population of patients undergoing upper endoscopy for unrelated indications. Moreover, the development of a numerical score associated with i-Scan technology would provide a quantitative means for comparison.

In summary, detection of villous atrophy from endoscopic images can be difficult due to the limited spatial

resolution and marginally effective enhancement techniques that are available. The authors of "Image-enhanced endoscopy with i-Scan technology for the evaluation of duodenal villous patterns," appearing in this issue of *Digestive Diseases and Sciences*, present the results of a newly developed i-Scan technique. This novel methodology is promising for improved visualization of endoscopic images when villous atrophy is present in the small intestinal mucosa. Other more quantitative methods may be useful to incorporate with the new i-Scan technology to automatically detect and localize regions of villous atrophy in celiac disease patients.

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