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I-Scan: Chromoendoscopy Without the Hassle?

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Background

Colonoscopy with removal and pathologic assessment of all polyps is frequently performed in patients at risk for colorectal cancer. Surveillance intervals are then determined based on quantity and size of adenomatous polyps. While colonoscopy serves as the current gold standard for colon cancer prevention and diagnosis, there is an inherent miss rate with the procedure. For example, 5% of patients diagnosed with colorectal cancer had a recent colonoscopy that failed to detect the malignancy (1). Additionally, tandem colonoscopy studies have shown an adenoma miss rate of 2.1% for adenomas > 10 mm, 13% for adenomas 5–10 mm, and 26% for adenomas of 1–5 mm (2). Several factors have been shown to contribute to miss rates including poor bowel preparation, failure to reach the lesion, flat or depressed polyps, exam performance by a non-gastroenterologists (2), overly rapid withdrawal times (3), incomplete polypectomies, or polyps hidden behind folds. Whether and to what extent technological advances in imaging can improve the detection of colonic neoplasia remains an open question.

Another drawback to colonoscopy is the cost and resources involved with full pathologic evaluation of small hyperplastic polyps, which have no malignant potential. It is likely that if small hyperplastic polyps could be left alone, the cost-effectiveness of screening and surveillance colonoscopy would improve.

In this issue of Digestive and Liver Disease, Hoffman et al performed a pilot evaluation of I-Scan (Pentax, Japan), a new endoscopic imaging system for performing screening colonoscopy. Like narrow band imaging (NBI) this is a post-processing light filter technology that is able to enhance different elements of the mucosa (SE-mode for surface analysis, v-mode for vessel characterization, or p-mode for pattern characterization). This particular instrumentation incorporates a variety of filters with increased pixels in its colour chip device (CCD) to improve the digital image. The SE-mode is designed to recognize lesions on withdrawal of the colonoscope, while v- and p- mode are proposed for characterizing the histology of lesions as hyperplastic or adenomatous.

Advantages of new endoscopy imaging techniques

To test the potential clinical utility of this new technology, Hoffman et al. evaluated the distal 30 cm of colon during 69 screening colonoscopies sequentially with high definition plus endoscopy (HD+) alone, HD+ with I-Scan, and chromoendoscopy to determine the efficacy of detection of small lesions (<5mm). Additionally, the authors evaluated the ability of the

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endoscopist to characterize a polyp as adenomatous or hyperplastic based upon the mucosal characteristics revealed in the filtered high resolution image. They found a significant increase in detection of small lesions with I-Scan compared to HD+ alone (4.7 vs. 2.48 polyps per patient ($p < 0.001$)), though not to the extent of chromoendoscopy (9.1 polyps per patient). There was no statistically significant difference in adenoma detection (5 with HD+ vs. 11 with I-scan and 11 with chromoendoscopy). Importantly, time of examination was not significantly different between HD+ alone (4 minutes) and HD+ with I-Scan (5 minutes). Chromoendoscopy did take 13 minutes. Further, they demonstrated that the endoscopist could predict an adenomatous polyp based on I-Scan mucosal characteristics with a sensitivity of 82% and a specificity of 96%.

Similar to narrow band imaging, which is somewhat more familiar to endoscopists, I-Scan is another of a series of digital imaging technologies. One of the major clinical questions is whether these modifications of white light imaging will lead to improved polyp detection and/or characterization. Chromoendoscopy is the earliest and most vigorously studied of these imaging techniques. It involves topical application of pigments or stains to highlight the colonic mucosa. Pan-chromoendoscopy has been shown to detect more adenomas than standard endoscopy (4). Additionally, it has been shown to have 93% sensitivity with 76% specificity (increased to 96% sensitivity and 94% specificity when used with magnification) in determining if a polyp is adenomatous (5). However, median withdrawal time was 17 minutes (4), making it less practical for widespread use in routine screening and surveillance.

Narrow band imaging (NBI) uses spectral characteristics of the endoscopic light to enhance mucosal patterns and capillaries without the need or time restraints of spraying dye (activated with the touch of a button on the endoscope). Preliminary studies have found that NBI does not improve polyp detection (6); however, it does have a sensitivity of 92% in correctly diagnosing adenomatous polyps. This can be improved to 96% when only high-confidence predictions are used (7).

Autofluorescence imaging (AFI) has been evaluated in a trimodal imaging system in which it was combined with NBI and high resolution endoscopy (8). AFI endoscopes use filters in the blue and ultraviolet range to allow for detection of endogenous fluorescent light emission from colonic mucosa. However, tandem colonoscopies showed no difference between polyp detection with trimodal imaging as compared to standard high-resolution endoscopy (8). AFI alone was shown to have 99% sensitivity in detecting an adenoma, though specificity was only 35% (8). Combining AFI and NBI characteristics gave 98% sensitivity with 74% specificity (8).

Room for improvement

The preliminary study by Hoffman et al. did show an improved detection of small polyps with I-scan but it is unclear whether the improved detection is related to improved resolution or a function of the filtered processed image. On the other hand, polyp characterization with I-Scan in this study compared a little less favourably than published reports of NBI, AFI, and chromoendoscopy. Again, it is not clear whether this difference is significant or whether it is related to the fact that this particular study concentrated on detecting minute polyps. For clinical management of small polyps, sensitivity is clinically important to avoid leaving potentially pre-malignant tissue intact. A low specificity poses little harm to the patient as it simply leads to the low-risk resection and pathologic evaluation of hyperplastic polyps, which is currently the standard. While I-Scan has superior specificity, in an era where guidelines recommend removal of all adenomas, the sensitivity of 82% reported with I-Scan in this study is too low for widespread replacement of pathology. Indeed, given that pathologists sometimes struggle with histological diagnosis when viewing a fixed and stained specimen under the stage of a

microscope it is unclear whether an imaging technique will ever be able to completely supplant histology.

Overall, the improved polyp detection rates of chromoendoscopy and I-Scan predominantly involved hyperplastic and small adenomatous polyps. The clinical significance of these polyps is unclear. Further, imaging techniques alone are not going to significantly decrease miss rates of cancer or advanced adenomas since the failure to detect advanced neoplasia is related to multiple factors that have nothing to do with imaging quality including endoscopist skill, polyp location, and quality of the preparation. As a result, the overall improvement in colon cancer prevention with these technologies remains unknown and may not be very significant.

The true impact of these technologies will be realized if they allow us to characterize small polyps without the need (and risks) of removal and without the cost and resources necessary for pathologic evaluation. For this goal to be attained with I-Scan, further study will be necessary to maximize diagnostic accuracy of polyp characterization. Additionally, evaluation of the learning curve for endoscopists and perhaps certification requirements may be necessary before an endoscopist is qualified to say a polyp is hyperplastic. Further, some form of incentive will be necessary to encourage widespread use of the technology. At present, biopsy of small polyps may be viewed favourably by Western endoscopists, as it increases procedural reimbursement and has minimal risk. To ask practicing gastroenterologists to assume the responsibility of polyp characterization for lower reimbursement is sure to be met with resistance. Further, studies with CT colonography question the concept that small adenomas should even be removed given their low likelihood of malignant transformation. As more data surface regarding the natural history of small adenomas, consideration of removal or endoscopic characterization of the polyps smaller than 5 millimetres may become obsolete.

In summary, the role of advanced imaging technologies outside of the research setting has not been fully defined and varies significantly from institution to institution. This preliminary evaluation shows that I-scan is promising technology to investigate further for detection of small polyps and polyp characterization without significantly altering exam time. Given the convenience it may be a reasonable alternative to chromoendoscopy. Further research in this area is critical to define the clinical application of this and other imaging advances.

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