Image enhanced endoscopy for detection and diagnosis of colonic neoplasia – time to shift focus

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The risk of post colonoscopy colorectal cancer (CRC) due to missed colonic adenomas can potentially be mitigated. Corley et al demonstrated that adenoma detection rate (ADR) was inversely associated with the risks of interval CRC, advanced-stage interval CRC, and fatal interval CRC. Each 1.0% absolute increase in the ADR was associated with a relative 3.0% decrease in the risk of CRC.[1] ADR is a function of mucosal visibility (which depends of adequacy of bowel preparation, and irrigation and suctioning during colonoscopy), meticulous examination of the entire visible colonic mucosa (careful slow withdrawal of the endoscope, adequate air insufflation, pressing down and looking behind folds, re-examination of flexures) and the ability of the endoscopist to recognize flat subtle lesions on the exposed mucosal surface.[2] The myriad endoscopic tools available to improve adenoma detection address different aspects of the examination process during colonoscopy.[3] Distal attachments help to flatten mucosal folds and can expose adenomas hidden by folds. Full-spectrum endoscopy (FUSE) increase the extent of the endoscopic view. Indigo carmine chromoendoscopy accentuates mucosal surface contours to highlight flat lesions. Electronic image enhancement endoscopy (IEE) techniques such as narrow band imaging (NBI), blue light imaging (BLI), linked colour imaging (LCI), and i-scan optical enhancement (i-scan OE) accentuate mucosal surface details to facilitate recognition of subtle mucosal surface abnormalities to improve detection, and in the context of narrow spectrum technologies such as NBI and BLI, especially with

additional magnification, also characterization and diagnosis. Ultimately the additional benefit of such devices would depend on the prevalence and type of the specific pathology, and would need to be anchored on the foundation of appropriate cognitive training, good bowel preparation and careful meticulous examination of all mucosal surface.

In this issue of *Journal of Gastroenterology and Hepatology*, two papers address the use of IEE for colonic adenoma detection and diagnosis. Miyaguchi et al conducted a randomized controlled trail to compare LCI and white light imaging (WLI) in the context of adenoma detection. The mean adenoma number per patient, which was the primary outcome measure, was significantly higher in the LCI group than in the WLI group (1.07 vs 0.88, p = 0.04). The total number of flat and sessile-type adenomas was significantly higher in the LCI group than in the WLI group (71.1% [379/494] vs 68.0% [303/501], p = 0.03). Small polyps (≤ 5 mm) were detected at a significantly higher rate in the LCI group (63% [271/494] vs 60.8% [336/501], p = 0.04). The ADR, another secondary outcome measure, was similar between both groups. These data reflect the ability of LCI to detect flat/ sessile small lesions that may otherwise be overlooked by WLI. However, the effect size was small and incremental value over WLI somewhat limited.[4] Desai et al conducted a study to validate the BLI Adenoma Serrated International Classification (BASIC) system, developed by European experts for characterization of colorectal polyps, among 10 US-based endoscopy experts without prior experience in the use of BLI. A web-based interactive system with pre-test, learning and final test modules was utilized. The participants used the BASIC system to characterize colorectal polyps with more than 94% accuracy and a high level of interobserver agreement. However, the pre-test and post-test results were similar. In

terms of the percent agreement for each feature of BASIC domains for polyp characterization, only the surface mucus criteria had high agreement of 93.8%, with the agreement for other domains being much lower (regularity [65.6%] type of pit [40.6%], pit visibility [66.9%], pit distribution [57%]), vessel visibility [73%], and being lacy [46%] and peri-cryptal [61%]).[5]

There are intrinsic challenges and limitations in the conduct of such IEE studies. The results must also demonstrate a clinically meaningful improvement over current practice. The impact of, and interaction with, artificial intelligence (AI) in this space of adenoma detection and diagnosis, must also be considered.[2,6]

In the study by Miyaguchi et al, investigators cannot be blinded to the modality of imaging, even though it was randomly assigned. There is a risk of performance bias in that a new tool effect comes into play, with the endoscopist subconsciously trying harder with a new device. This extra effort can influence results significantly. This effect can be clearly appreciated in the context of studies evaluating the diagnostic yield of the multi-target stool DNA (MT-sDNA) test. Studies have shown that endoscopist knowledge of a positive MT-sDNA test significantly increased quality metrics such as ADR at diagnostic colonoscopy compared with blinded endoscopists, likely related to longer withdrawal time and increased attention to subtle lesions.[7] In the study by Desai et al, it is striking that the pre- and post-training test results were similar. The accuracy was already more than 94% before the start of training, even though the participants had not used BLI previously. NBI has been in use for two decades, and classification systems based on the NBI platform have been developed and the utility demonstrated. These include the NBI International Colorectal

Endoscopic (NICE), Japan NBI Expert Team (JNET),[8] and the Workgroup serrAted polypS and Polyposis (WASP) classifications.[9] It is extremely difficult to find narrow spectrum endoscopy naive observers, so there will always be contamination from previous experience for the practising endoscopist, especially experts, and hence training will not make a difference. At a fundamental level, these narrow spectrum-based technologies are similar, and the key issue is to demonstrate a significant improvement in terms of diagnostic performance of any new classification system over pre-existing systems, rather than creating a new classification system for each new technology. Data support the commonly held belief that these diagnostic classification systems should be applicable across the different narrow spectrum technologies.[10]

AI in colonoscopy has now entered clinical practice.[6] Detection of lesions is based on the WLI mode whereas prediction of histology is based on the narrow spectrum mode. Current AI performance can be further optimized; however as the AI technology improves with time, both narrow spectrum technologies and the training needed to use them may become less or even irrelevant, if the effect size for detection for AI (CADe) becomes much larger than the marginal increase with narrow spectrum technologies, as suggested by current meta-analysis [ref]. Similarly with AI expert level characterisation (CADx) can be already achieved; nevertheless AI is not “intelligent,” but is simply very high performance pattern recognition. Experience and common sense from the endoscopist will still be needed for some years to come as the datasets that are used to generate current AI algorithms are not fully generaliseable in range of lesion types, equipment, endoscopist behaviour or patient geographic location.

At the moment we still need experience and training for detection and characterisation of colonic polyps. The different IEE modalities help with visualization. But rather than replace WLI, the main role of IEE in current practice is more of an adjunct to WLI, with flexible interchange of imaging modalities, including magnification, to verify possible abnormalities, and to characterise detected lesions, when needed. The various narrow spectrum systems from different companies probably work equally well for all diagnostic classification systems. The future is not in such changed light technology solutions, as performance appears to have reached a peak, and further improvement appears marginal. A new paradigm shift is needed, and the way forward looks to be in fully integrated, AI supported detection, quality assurance and characterisation.

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