Editorial

Computer-aided diagnosis to differentiate colorectal polyps: are we nearing primetime?

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Colorectal cancer screening has proven to be an effective preventative health measure (1). This is, in part, achieved by the identification and removal of neoplastic adenomatous polyps. However, within the rectum and sigmoid colon, non-neoplastic hyperplastic polyps are also common. Removing all polyps has historically been an acceptable strategy. However, this carries the potential of adverse events associated with unnecessary polypectomy and the potential of increased costs (2). Endoscopists have attempted to mitigate this commonly encountered dilemma by trying to predict a polyp's histology based on its appearance, termed "optical biopsy" (3). This is performed by carefully inspecting the polyp's surface, and can be assisted by enhanced imaging modalities such as narrow-band imaging (NBI) (4). Optical biopsy is further facilitated in that diminutive (≤5 mm) adenomatous polyps rarely harbour cancer or advanced histology (5). Therefore, if endoscopists were able to reliably decipher between diminutive neoplastic and non-neoplastic polyps, the former could be resected without pathology evaluation and the latter could be left in situ. These two strategies are commonly referred to as the "resect and discard" and "diagnose and leave" strategies, and carry the potential for significant cost-savings (2,6). Accordingly, the American Society for Gastrointestinal Endoscopy (ASGE) has suggested performance thresholds presented in the Preservation and Incorporation of Valuable Endoscopic Innovations (PIVI) guidelines (6). For the "resect and discard" strategy (PIVI-1), it is recommended that optical biopsy and polypectomy of diminutive adenomas without pathology evaluation, in conjunction with polypectomy and pathology evaluation of polyps ≥5 mm, should provide a ≥90% concordance with the recommended surveillance colonoscopy interval. This is in relation to the recommended surveillance colonoscopy interval if all polyps underwent pathology evaluation. Concordantly, for the "diagnose and leave" strategy (PIVI-2), it is recommended that optical biopsy should achieve a negative predictive value (NPV) ≥90% for adenomatous histology within the rectum and sigmoid colon. Unfortunately, a robust optical biopsy method for all endoscopists across varying levels of experience remains elusive (7).

Fortunately, the rapidly evolving field of artificial intelligence has allowed the possibility of computer-aided diagnosis (CAD) to differentiate adenomatous and hyperplastic polyps (8,9). With the above in mind, we read with great interest the recent publication by Mori *et al.* (10) which prospectively assessed, in real time, a machine learning CAD platform using endocytoscopy to differentiate neoplastic and non-neoplastic polyps. Endocytoscopy is an optical biopsy method with ×520 ultra-magnification, allowing for microvascular and cellular evaluation. This was facilitated by either NBI (NBI-CAD) or by staining the colorectal epithelium with methylene blue (stained-CAD) prior to assessment. Endoscopists were recommended to take ≥10 endocytoscopic images with NBI followed by methylene blue enhancement. CAD subsequently predicted pathology, with a 0.4 second delay, accompanied by a probability estimate between 0–100%. A final diagnosis was based on the majority of analyzed images. The primary outcome was the NPV of Stained-CAD for diminutive

rectosigmoid adenomas. Pathology evaluation was used as the gold standard. This was further stratified into best- and worst-case scenarios whereby polyps lacking either CAD or pathology were treated as true-positive/true-negative and false-positive/false negative outcomes, respectively. A total of 466 diminutive polyps (287 neoplastic, 175 non-neoplastic, 4 missing specimens) were assessed in 325 participants who underwent colonoscopy. Twenty-three endoscopists participated in the study. On average, 13 and 20 endocytoscopic images per polyp were collected for NBI-CAD and stained-CAD respectively. The median times to obtain the first CAD output for NBI-CAD and stained-CAD were 19 seconds and 73 seconds respectively. The NPV for diminutive rectosigmoid adenomas, in the worst-case scenario, was 95.2% (NBI-CAD) and 93.7% (stained-CAD). This improved to 96.5% (NBI-CAD) and 96.4% (stained-CAD) in the best-case scenario. However, the lower confidence estimate in the worst-case scenario for stained-CAD was 88.3%, which does not exceed the PIVI-2 performance threshold. A notable outcome was that each polyp's endoscopic images and pathology report were reviewed by 2 expert endoscopists. Eight polyps initially diagnosed as non-neoplastic underwent repeat pathology assessment, in a blinded fashion. Of these 8 cases, 4 of them were reclassified as neoplastic.

The study by Mori *et al.* is a pivotal step towards the incorporation of CAD into clinical practice. It is the first prospective real-time evaluation of CAD showcasing that it can meet the PIVI-2 performance threshold for differentiating colorectal polyps. The National Institute for Health and Care Excellence (NICE) recently recommended optical biopsy, instead of pathology evaluation, to differentiate adenomatous and hyperplastic polyps (11). However, stipulations included: (I) endoscopists need to be trained and accredited in optical biopsy; (II) the use of high-definition colonoscopes; and (III) high-confidence in optical biopsy assessment. Unfortunately, a systematic review and meta-analysis by the ASGE Technology Committee showed that, outside the academic environment and outside of expert endoscopists, optical biopsy does not reach the PIVI-1 and PIVI-2 performance thresholds (7). This highlights the potential impact of CAD as it can remove operator expertise as a factor for differentiating colorectal polyps.

Mori *et al.* should be commended for their landmark study. However, there are some potential limitations of their CAD platform. Most notably is the selection of endocytoscopy to perform optical biopsy, which currently has limited availability worldwide. Moreover, it will be important to clarify whether expertise significantly impacts endocytoscopy image acquisition. Within the study, 29.3% of NBI images and 36.1% of methylene-blue stained images were not analyzable. If expertise does play a role, this could to a degree mitigate the benefits of incorporating CAD, in comparison to alternative optical biopsy methods.

Arguably the most exciting aspect of artificial intelligence is that we are in its infancy, specifically in regards to its performance capabilities. A key advancement has been the development of deep learning (12) allowing the field to move away from human feature extraction and the associated limitations of human perception. CAD platforms will continue to evolve and learn, something that was utilized by Mori *et al.* as their CAD platform was updated 5 times during the study to allow for further training. However, the reliance on machine learning which this platform uses will intrinsically limit its potential in comparison to other platforms which incorporate deep learning.

Lastly, a limitation of this study was that the PIVI-1 "resect and discard" outcome was not assessed. However, the authors did provide CAD performance estimates for polyps identified above the sigmoid colon. Sensitivity, specificity, positive predictive value (PPV) and NPV ranged (worst- to best-case scenario estimates) from 92.4–92.9%, 65.6–68.8%, 93.9–94.5%, and 60.0–62.9%, for NBI-CAD, and 91.3–92.9%, 75.0–80.6%, 95.4–96.6%, and 60.0–65.8%, for Stained-CAD, respectively. The authors did suggest that a potential limitation of their platform may be its performance for differentiating more proximal polyps, which would affect PIVI-1 outcomes. It is our belief that to maximally reap the benefits of optical biopsy, both "resect and discard' as well as "diagnose and leave" need to be implemented.

Moving forward, pivotal steps towards incorporating CAD into clinical practice include: (I) continuing CAD technology development; (II) performing clinical trials; (III) obtaining regulatory approval; and (IV) establishing governmental incentivization for its incorporation (13). In addition, we need to bring CAD solutions to more standard, commonly-used endoscopy equipment. Our own group has addressed this issue with a strong proof-of-concept deep learning CAD platform showing excellent real-time performance for determining polyp histology using standard high-definition colonoscopes (9). While this platform's performance needs to be replicated in prospective clinical trials, we strongly believe that future efforts should be directed towards developing CAD technology which targets

widely available endoscopic equipment. Our goal should be to help all endoscopists.

The potential for artificial intelligence does not apply only to CAD platforms for differentiating colorectal polyps. CAD platforms for detecting colorectal polyps could have a significant impact on health outcomes, as we know improving adenoma detection correlates with a lowered risk of interval colorectal cancer and colorectal cancer-associated mortality (14). Moreover, developing CAD platforms for identifying cancer within polyps as well as assessing depth of tumor invasion have the potential to play a pivotal role in redefining current approaches for the removal of colorectal polyps (15). Lastly, a novel application could be to optimize quality assurance during pathology evaluation. By providing CAD results to pathologists, this could identify discordant evaluations thus prompting a secondary pathology evaluation, ideally by a pathologist with expertise in gastrointestinal pathology.

In summary, Mori *et al*. have taken a critical step towards integrating CAD into clinical practice with their prospective study using endocytoscopy. Demonstrating the ability to perform artificial intelligence-driven optical biopsy of colorectal polyps using standard colonoscopes in widespread clinical practice will be the next eagerly awaited step, something we believe will be shown in the very near future.

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References

1. Mandel JS, Church TR, Bond JH, et al. The effect of fecal occult-blood screening on the incidence of colorectal cancer. N Engl J Med 2000;343:1603-7.
2. Kessler WR, Imperiale TF, Klein RW, et al. A quantitative assessment of the risks and cost savings of forgoing histologic examination of diminutive polyps. Endoscopy 2011;43:683-91.
3. Lieberman D, Brill J, Canto M, et al. Management of Diminutive Colon Polyps Based on Endoluminal Imaging. Clin Gastroenterol Hepatol 2015;13:1860-6.
4. Hewett DG, Kaltenbach T, Sano Y, et al. Validation of a simple classification system for endoscopic diagnosis of small colorectal polyps using narrow-band imaging. Gastroenterology 2012;143:599-607.
5. Ponugoti PL, Cummings OW, Rex DK. Risk of cancer in small and diminutive colorectal polyps. Dig Liver Dis 2017;49:34-7.
6. Rex DK, Kahi C, O'Brien M, et al. The American Society for Gastrointestinal Endoscopy PIVI (Preservation and Incorporation of Valuable Endoscopic Innovations) on real-time endoscopic assessment of the histology of diminutive colorectal polyps. Gastrointest Endosc 2011;73:419-22.
7. Abu Dayyeh BK, Thosani N, Konda V, et al. ASGE Technology Committee systematic review and meta-analysis assessing the ASGE PIVI thresholds for adopting real-time endoscopic assessment of the histology of diminutive colorectal polyps. Gastrointest Endosc 2015;81:502-16.
8. Byrne MF, Shahidi N, Rex DK. Will computer-aided detection and diagnosis revolutionize colonoscopy?

Gastroenterology 2017;153:1460-4.
9. Byrne MF, Chapados N, Soudan F, et al. Real-time differentiation of adenomatous and hyperplastic diminutive colorectal polyps during analysis of unaltered videos of standard colonoscopy using a deep learning model. Gut 2017. [Epub ahead of print].
10. Mori Y, Kudo SE, Misawa M, et al. Real-time use of artificial intelligence in identification of diminutive polyps during colonoscopy: A prospective study. Ann Intern Med 2018;169:357-66.
11. National Institute for Health and Care Excellence. Virtual chromoendoscopy to assess colorectal polyps during colonoscopy. May 2017. Available online: www.nice.org.uk/guidance/dg28. Accessed on 17 October 2018.
12. Shin HC, Roth HR, Gao M, et al. Deep convolutional neural networks for computer-aided detection: CNN architectures, dataset characteristics and transfer learning. IEEE Trans Med Imaging 2016;35:1285-98.
13. Mori Y, Kudo SE, Berzin TM, et al. Computer-aided diagnosis for colonoscopy. Endoscopy 2017;49:813-9.
14. Corley DA, Jensen CD, Marks AR, et al. Adenoma detection rate and risk of colorectal cancer and death. N Engl J Med 2014;370:1298-306.
15. Ferlitsch M, Moss A, Hassan C, et al. Colorectal polypectomy and endoscopic mucosal resection (EMR): European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. Endoscopy 2017;49:270-97.

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