The good lies so near – *in vivo* diagnosis of colonic polyps

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It was in 1827 when Johann Wolfgang von Goethe quoted ‘You want to roam forever? See, the good lies so near. Learn to embrace happiness, because happiness is always there.’

Endoscopic imaging has seen many revolutions within the last 10 years. Those include the development of high-definition optics using charge-coupled devices (CCDs) and complementary metal-oxide semiconductor (CMOS) sensors, virtual chromoendoscopy techniques, and wide-field optics allowing a 330-degree view of the luminal anatomy. In addition, optical biopsy techniques have been introduced that allow us to analyse structures at the cellular and subcellular layer during ongoing endoscopy and to automatically predict histology of colorectal lesions.¹

Advanced endoscopic imaging techniques aimed to identify more lesions and accurately characterize them for subsequent therapy. Remarkable, the published studies to date, evaluating the beneficial effect of high-definition endoscopy in comparison to standard white-light endoscopy, have shown inconsistent results regarding adenoma detection rates. While some studies suggest a benefit of high-definition endoscopes for adenoma detection, others do not.^{2–5} Accordingly, it is still under debate if high-definition endoscopy, even in non-academic centres, yields in higher adenoma detection rates as compared to standard white-light endoscopy. Therefore, the results of large randomized multicentre trials are highly anticipated to provide improved clarity on this issue.

Beyond adenoma detection, increasing efforts have been made to study the impact of advanced endoscopic imaging techniques for polyp characterization. This is also driven by the fact that unnecessary removal of non-adenomatous polyps’ results in enormous costs for the healthcare system related to the instruments used for polypectomy, retrieval devices, physician and nurses fees, pathology assessments, and further surveillance. In this context, the American Society for Gastrointestinal Endoscopy (ASGE) introduced a new concept on real-time endoscopic assessment of the histology of diminutive polyps.⁶ The PIVI (Preservation and Incorporation of Valuable endoscopic

Innovations) concept stated two paradigms. First, in order for colorectal polyps ≤ 5 mm in size to be resected and discarded, endoscopic technology should provide $\geq 90\%$ agreement in assignment of post-polypectomy surveillance compared to decisions based on pathological assessment of all identified polyps. Second, in order for a technology used to guide the decision to leave suspected hyperplastic polyps ≤ 5 mm in size in place, the technology should provide a negative predictive value $> 90\%$ for adenomatous polyp histology. Various studies have shown the impressive potential of newer dye-less chromoendoscopy techniques, including narrow-band imaging (NBI), Fuji intelligent chromoendoscopy (FICE), and i-scan for *in vivo* characterization of polyp histology according to the PIVI statement.^{7–9} Nevertheless, the equipment requires a significant initial financial investment which, in the current era of austerity, may act as a potential barrier to the adoption in routine clinical practice.

In this issue of *United European Gastroenterology Journal*, Longcroft-Wheaton et al.¹⁰ addressed this important issue by investigating the effectiveness of *in vivo* diagnosis of colonic polyps using indigo carmine dye-spraying with standard and high-definition endoscopes. Dye-based chromoendoscopy has traditionally been used to improve detection and characterization of lesions during luminal endoscopy. Indigo carmine acts as a contrast stain highlighting mucosal topography and is commonly used in concentrations of 0.1–0.8% after careful cleaning of the mucosa with water.¹¹ Studies have shown the impact of either pancolonoscopic or lesion-targeted spraying of indigo carmine for enhanced detection and characterization of colonic lesions.¹² Therefore, the present study carefully evaluated the impact of endoscope resolution on the

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accuracy of polyp characterization during screening colonoscopy. In total, 150 patients were included and randomized in two groups: 51 patients in the standard-definition group, in which 114 polyps were found 39 patients in the high-definition endoscopy group, in which 123 polyps were found. Only polyps 5–10 mm were included in the present study and targeted indigo dye (0.2%) administration was performed before the endoscopist rated the polyp as either neoplastic (adenoma + cancer) or non-neoplastic (hyperplastic) according to Kudo's classification before endoscopic resection.¹³ Histopathology served as the reference standard. No statistically significant differences were observed for *in vivo* characterization of colonic polyps between both groups with overall accuracies of 89% (standard-definition) and 92% (high-definition), respectively ($p=0.51$). Although negative predictive value was only 79% in the standard-definition group, as compared to 93% in the high-definition endoscopy group, this was not statistically significantly different ($P=0.17$). Surveillance intervals, based on endoscopic diagnosis were predicted correctly in 95% of patients in the standard-definition group and in 100% of patients in the high-definition endoscopy group ($p>0.4$).

The results are in line with one recent published study also comparing high-definition with standard-definition endoscopes for characterization of colonic polyps.¹⁴ Here, 293 polyps <10 mm were examined and no statistically significant differences were observed between both groups when white-light imaging was used. Nevertheless, modern high-definition endoscopes do not only utilize white-light imaging but also either optical (e.g. NBI, CBI) or digital chromoendoscopy (FICE, i-scan) techniques. Consequently, when FICE was used, high-definition endoscopy showed a sensitivity of 93% compared with 83% for standard-definition ($p=0.048$) while specificity was 81% and 82%, respectively.

Patients with insufficient bowel preparation were excluded from the current study, but it is unclear whether the quality of the preparation in the studied patients was equal. As correctly stated by the authors, one weakness of the present study is that it was designed as a single-centre study with only one experienced endoscopist evaluating all lesions. Therefore, these results may not be transferable to the general practitioners. Although all efforts have been made to blind the endoscopists regarding the scope technology, one would suspect, that is not difficult to distinguish standard-definition and high-definition imaging. Nevertheless, no statistically significant differences between both groups were found presuming that this circumstance did not bias the study to any degree. While the ASGE PIVI 2 statement is commonly used for rectosigmoid polyps ≤ 5 mm, it is worthwhile

discussing that the authors included polyps 5–10 mm in size as these are important in setting rescope intervals and most guidelines make a divide at 10 mm in terms of risk. It would be interesting to evaluate the current study settings regarding standards required for not resecting rectosigmoid polyps' ≤ 5 mm in size. At least, besides lesion characterization, detection is of paramount importance for screening colonoscopy as one can only characterize what is seen. Although high-definition imaging yielded higher polyp detection rates (3.1 polyps per patients vs. 2.2 polyps per patient) this difference was not statistically significant ($p=0.175$). Noteworthy, the study was not designed to investigate lesion detection.

Taken together, standard-definition endoscopy with indigo dye carmine spraying seems to be equal effective to high-definition endoscopy with targeted dye administration for *in vivo* diagnosis of colonic polyps. If really 'the good lies so near' should be proven in future, there should be multicentre randomized trials, even including recent developments in the field of dye-less chromoendoscopy techniques.

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