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## Precision in detecting colon lesions: A key to effective screening policy but will it improve overall outcomes?

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### Abstract

Colonoscopy is the gold standard for the screening and diagnosis of colorectal cancer, resulting in a decrease in the incidence and mortality of colon cancer. However, it has a 21% rate of missed polyps. Several strategies have been devised to increase polyp detection rates and improve their characterization and delimitation. These include chromoendoscopy (CE), the use of other devices such as Endo cuffs, and major advances in endoscopic equipment [high definition, magnification, narrow band imaging, i-scan, flexible spectral imaging color enhancement, texture and color enhancement imaging (TXI), *etc.*]. In the retrospective study by Hiramatsu *et al*, they compared white-light imaging with CE, TXI, and CE + TXI to determine which of these strategies allows for better definition and delimitation of polyps. They concluded that employing CE associated with TXI stands out as the most effective method to utilize. It remains to be demonstrated whether these results are extrapolatable to other types of virtual CE. Additionally, further investigation is needed in order to ascertain whether this strategy could lead to a reduction in the recurrence of excised lesions and potentially lower the occurrence of interval cancer.

**Key Words:** Colonoscopy screening; Interval colorectal cancer; Post colonoscopy colorectal cancer; chromoendoscopy; Virtual chromoendoscopy; high-definition white-light endoscopy; Texture and color enhancement imaging; Indigo carmine; Adenoma; Sessile serrated lesion

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**Core Tip:** The endoscope's texture and color enhancement imaging mode, combined with chromoendoscopy, has demonstrated improvements in the characterization of mucosal colonic lesions, providing better visualization of their borders and lesion surfaces. However, its real impact on lesion recurrence and rates of interval cancers is yet to be proven through more prospective studies.

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## INTRODUCTION

Colorectal cancer (CRC), as the authors point out, is the third most prevalent cancer in men and women, representing 10% of global cancer cases. The risk of cancer increases with age, and it is most frequently diagnosed after the age of 50[1].

The colonoscopy study is the most widely accepted method for screening and diagnosing CRC, and is considered the gold standard in the field[2]. It allows for the diagnosis and resection of many preneoplastic lesions, directly contributing to the decrease in the incidence and mortality of this disease[3]. However, the efficacy of colonoscopy is closely related to its ability to detect these preneoplastic lesions[4,5].

Colonoscopy studies showed a rate of undetected polyps of approximately 22%-26% of adenomas smaller than 5 mm, and 13% of adenomas about 5-10 mm[6]. Additionally, there is some evidence suggesting that colonoscopy is more effective in preventing left-sided CRC compared to right-sided CRC[3,7]. This discrepancy is likely associated with challenges such as inadequate cleansing of the right colon and the frequent presence of pale mucosal lesions with a flat morphology in this region.

## ENHANCING THE DETECTION OF COLONIC LESIONS: METHODS AND STRATEGIES

In the interest of improving the detectability of colonic lesions, scientific societies have developed various guidelines for clinical practices, aiming to recommend the most effective methods to achieve appropriate colon cleansing[4,8].

At the same time, they have advocated for the utilization of colonoscopy with the assistance of chromoendoscopy (CE); initially defined as a method of staining tissues using pigments and colorants[9].

These substances are applied to the mucosa using an endoscopic catheter[10] to characterize and enhance the visualization of preneoplastic lesions. The ultimate objective is to facilitate their complete excision, thereby enhancing the overall efficiency of colonoscopy[11,12].

The types of colorants can be classified based on their interaction with the colonic mucosa[10,12]. (1) Reaction colorants: Examples include Congo red stain. This colorant reacts with components of the mucosa, thereby inducing characteristic color changes; (2) Absorption colorants: Examples are methylene blue, gentian violet, or acetic acid. These colorants are absorbed by the cells into the cytoplasm or nucleus, triggering changes in coloration[13]; and (3) Contrast colorants: Indigo carmine is an example. This colorant accumulates on the mucosal surface, aiding in delineating the mucosa itself and providing visual contrast[10,12].

The application of colorants can be selective, focusing on specific lesions once they have been detected with white-light imaging (WLI). Alternatively, it can be unselective, involving the spraying of larger areas of the mucosa to improve the detectability of lesions. Nevertheless, pan-CE of the colon has not shown a significant increase in the detection rate of polyps when compared to standard colonoscopy. Nevertheless, its use is not recommended as a conventional screening method[14], but it proves highly valuable in the surveillance colonoscopy of inflammatory bowel[15]. Furthermore, this complex procedure increases the duration of the exploration and costs.

The primary advantages of employing colorants reside in the simplicity of the technique and its relatively low cost, as it does not require specific or sophisticated devices. This approach enables the differentiation between neoplastic and nonneoplastic lesions, characterizes their boundaries, and examines their surface, thereby predicting the risk of deep invasion of the mucosa[16].

Essentially, this technique enhances resection procedures, mitigates the risk of interval CRC, and assists in selecting the most appropriate treatment approach. Consequently, it reduces the likelihood of unnecessary and potentially risky resections, ultimately leading to a decrease in undesirable adverse events[10,17].

Even though CE significantly increases the positive and negative predictive values in the characterization of colonic lesions, it is still inaccurate when it comes to predicting histology. As a result, CE is not considered a substitute for histologic biopsy, especially in lesions without an apparent risk of malignization.

It is worth noting that most CE studies have been conducted by expert endoscopists with considerable experience in CE. The significance of expertise becomes evident when considering the limited utility of CE in the hands of endoscopists lacking extensive experience in this technique, highlighting the importance of skill in achieving accurate results[18].

## CLINICAL IMPLICATIONS OF SCREENING COLONOSCOPIES USING CONTRAST-ENHANCED IMAGING AND ADVANCED ENDOSCOPIC EQUIPMENT

In the past 15 years, there have been substantial advancements in endoscopic equipment, markedly improving the visualization of the colonic mucosa and enhancing the detection of mucosal lesions. Modern colonoscopes now boast high-definition capabilities with resolutions surpassing a million pixels. However, despite these technological enhancements, the utilization of high-tech colonoscopes has only yielded a modest 3.5% improvement in the rate of adenoma detection compared to conventional endoscopes[19].

Various devices have been developed to adhere to the endoscope, aiming to increase the rate of colonic lesion detection. In 2018, Williet *et al*[20] published the results of a meta-analysis involving the Endo Cuff, encompassing over 12 trials and more than 8000 patients. The study demonstrated a higher rate of adenoma detection, particularly proving relevant for endoscopists with a moderate adenoma detection rate[20,21].

Various companies have developed diverse endoscopic tools to better characterize lesions and establish a strong correlation with endoscopic histology, enabling more informed decisions and maximizing the benefits of CE.

The magnification capability enables image enlargement of up to 150 times, facilitating the analysis of characteristics of colonic polyps[22] such as those obtained using the Kudo pattern. This analysis aids in distinguishing neoplastic from non-neoplastic lesions by examining the type of crypts and mucosal surface[23].

A meta-analysis comprising over 20 studies and involving a total of 5111 colorectal lesions[24], revealed a sensitivity of 89% and a specificity of 85.7% when using magnification to differentiate between neoplastic and non-neoplastic lesions. Additionally, the Kudo's classification demonstrates good concordance in both inter and intraobserver agreement for histologic prediction among expert endoscopists[25].

Virtual CE is an innovative endoscopic imaging technology that captures a more detailed image of the mucosa surface and vessels[26]. This enhancement is achieved through the use of a short-wavelength narrow-band red/green/blue filter, that selects specific wavelengths of light (415- and 540-nm short- and medium-wavelength filters), such as narrow band imaging[27], or by employing different postprocessing systems for WLI like flexible spectral imaging color enhancement (FICE) or i-scan[23,26].

Utilizing NBI, a new international classification of colorectal lesions, known as NBI international colorectal endoscopic (NICE), has been developed. This classification relies on the assessment of color, vascularization, and the pattern of the mucosal surface of the lesions[28,29].

One of the most significant advantages of this classification is its versatility, as it can be applied both with and without magnification. It boasts a diagnostic accuracy of 89%, with an impressive sensitivity of 98%. Moreover, it demonstrates a negative predictive value of 95%, making it particularly useful for effectively ruling out adenomas in small polyps[27].

Additionally, a recently introduced Japanese classification system using NBI is known as the Japanese NBI Expert Team (JNET)[28]. This classification further refines the NICE classification by subdividing it into 4 types. Within this system, NICE 2 lesions are further categorized into 2A for low-grade adenomas and 2B for high-grade adenomas, necessitating the use of magnification. Unlike NICE, the JNET classification requires the use of magnification, consequently limiting its broader applicability[22]. Another drawback is its inapplicability to serrated polyps, mirroring the limitations observed in the NICE classification.

The workgroup serrated polyps and polyposis classification combines the findings of the NICE classification with four other characteristic features commonly associated with serrated polyps. The presence of two or more of these features is adequate for diagnosing a serrated sessile lesion[30].

Several studies have also compared high-definition colonoscopy with NBI colonoscopy, revealing no discernible differences in the rate of polyps and adenomas detection. However, the NBI classification has proven to be significant in the characterization and classification of polyps. It excels in differentiating between adenomatous and hyperplastic polyps, particularly when in the hands of expert endoscopists[26,28].

Similarly, additional studies have found comparable effectiveness between colonoscopy using I-scan mode and FICE mode[26]. While both techniques demonstrate efficacy in detecting non-neoplastic lesions, there are no significant differences observed when compared to high-definition WLI regarding the rate of adenoma detection.

Studies comparing NBI with i-scan and NBI with FICE have not revealed any significant differences in the characterization of mucosal lesions or in the detection of polyps[28].

Blue laser imaging (BLI) produces an image by combining two sources of laser light with different wavelengths. It utilizes a laser of 450 nm with fluorescence light equivalent to xenon light, and another laser of 410 nm within the blue light spectrum. The simultaneous use of both lasers enhances the information about the mucosal surface and vascular pattern[31]. This system offers four modes that can be selected on the endoscope, each with a distinct contrast, making it more suitable for the exploration of specific characteristics of the lesion.

Very recently, a new system called TXI (Texture and color enhancement imaging) has been developed to improve endoscopic visualization. It enhanced three aspects of white light—texture, brightness, and color—allowing for better definition of subtle changes in the explored tissues[32].

In the recent issue of the *World Journal of Gastrointestinal Endoscopy*, the study by Hiramatsu *et al*[33] aims to explore the variances in detectability of the borders and surface characteristics of polypoid lesions seen during a screening colonoscopy, employing various endoscopic modes including WLI, CE, TXI, and TXI + CE. This retrospective study, conducted by a board-certified fellow/trainer, is characterized by its simplicity, intelligence, and effective execution. The recorded images were subsequently assessed retrospectively by a team of senior endoscopists using a straightforward scoring system. The outcome of the author's study demonstrates that the combination of TXI and CE is the most effective method for characterizing the features of polypoid lesions, surpassing WLI and even CE alone.

## DISCUSSION

For many years, it has been widely established that initially, CE[10,15,17] or, to a lesser extent, virtual CE with NBI, BLI, or I-Scan, were promising methods for enhancing the detectability of colonic lesions[23,26,27]. However, the use of CE from the outset of the exploration resulted in increased time consumption and added expenses.

Undoubtedly, the skills of the endoscopist, the use of efficient colon cleansing techniques for a clear colon, and the duration of the procedure - especially during scope withdrawal[34] - greatly impact the detection of different lesions, particularly serrated ones in the cecum or ascending colon. These factors also reduce the likelihood of interval CRC[35].

While there is a well-established understanding that detecting a higher number of polyps during procedures correlates with a reduced rate of interval cancers[4,5], it's important to recognize that this correlation may be influenced by the ability to accurately identify and delineate challenging lesions, like sessile serrated adenomas (SSAs). The author's study is not designed to investigate this topic directly, but rather to analyze various methodologies to enhance the visualization of surface characteristics and polypoid lesion borders.

It is crucial to acknowledge that, based on our current knowledge, there is no definitive evidence establishing a direct correlation between the number of polyps detected during a screening procedure and an immediate increase in the detection of colon cancer in the same session, nor a decrease in morbidity within the studied cohort. However, it is recognized that a relationship exists between missed lesions or incomplete resected lesions and interval colon cancer[35], and it's conceivable that the number of missed lesions might be higher in procedures with a low rate of adenomas detected.

The complexity involved in surface identification and border delineation, especially for SSAs, highlights the need for the implementation of advanced screening techniques and a comprehensive approach. This is crucial to reduce the likelihood of missing these lesions or conducting incomplete resections during colonoscopy procedures[36].

It is essential to address certain limitations identified in the study. One significant drawback pertains to the subjective nature of the scoring system employed. The scale, ranging from 1 (not detectable without repeated careful observation) to 4 (easily detectable), may introduce a notable level of subjectivity. This subjectivity should be considered when evaluating the robustness of the study results.

An additional important consideration, and an ongoing limitation for future research, is whether these findings can be replicated using other imaging technologies, such as NBI, BLI, or i-scan in conjunction with CE. Demonstrating consistency across various modalities would enhance the generalizability and robustness of the results.

Additionally, an unexplored aspect of this research is whether the enhanced detectability of lesion borders contributes to achieving R0 resection and subsequently decreases the recurrence rate of the lesion.

Presently, our understanding suggests that for many polyps, particularly those exceeding 2 cm in size, the risk of interval colon cancer appears to be more closely associated with the type of resection—specifically, endoscopic submucosal dissection and *en bloc* resection—compared to piecemeal endoscopic mucosal resection[37].

This emphasizes the importance of achieving an R0 resection to minimize local recurrence. Moreover, the timing of the first surveillance, typically recommended between 3 to 6 months post-resection, is crucial for effective monitoring and early detection of any recurrence.

## CONCLUSION

We need to emphasize certain evident facts derived from this study. For instance, the combined use of TXI and CE proves to be most effective, surpassing the individual efficacy of both WLI and CE. Additionally, smaller lesions could also be more effectively detected, and the surface pattern and borders of the lesions could be better characterized and analyzed.

Reducing the rate of incomplete resection holds the potential to decrease the percentage of interval cancer. However, from my perspective, it is challenging to believe that these improvements will lead to a further decrease in morbidity and mortality rates related to colon cancer. This skepticism stems from the fact that these patients are already involved in a follow-up surveillance program, which is truly the primary factor responsible for saving lives.

In any case, considering the author's findings, the next step should be to investigate and confirm whether implementing this methodology results in a significant decrease in polyp recurrence.

In conclusion, the authors' proposed method of TXI plus CE is recommended for incorporation into our current screening colonoscopy methodology.

The improved characterization of polypoid lesions and enhanced visualization of their borders will significantly contribute to enhancing the overall quality of the procedure. This suggests a crucial follow-up study to assess the real-world impact of implementing the methodology described in the research. Confirming a substantial reduction in polyp recurrence rates would validate the practical efficacy of the proposed methodology and further establish its relevance in clinical settings. This has the potential to reduce the rate of interval colon cancer, emphasizing the importance of adopting advanced techniques to improve outcomes in colorectal screening. However, the impact on decreasing the burden of colon cancer remains to be substantiated.

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