Advanced endoscopic imaging to improve adenoma detection

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Abstract
Advanced endoscopic imaging is revolutionizing our way on how to diagnose and treat colorectal lesions. Within recent years a variety of modern endoscopic imaging techniques was introduced to improve adenoma detection rates. These include high-definition imaging, dye-less chromoendoscopy techniques and novel, highly flexible endoscopes, some of them equipped with balloons or multiple lenses in order to improve adenoma detection rates. In this review we will focus on the newest developments in the field of colonoscopic imaging to improve adenoma detection rates. Described techniques include high-definition imaging, optical chromoendoscopy techniques, virtual chromoendoscopy techniques, the Third Eye Retroscope and other retroviewing devices, the G-EYE endoscope and the Full Spectrum Endoscopy-system.

Key words: Advanced endoscopic imaging; G-Eye; Full Spectrum Endoscopy-system; Chromoendoscopy; I-scan; Narrow band imaging; Fujinon Intelligent Color Enhancement; 3rd Eye; Polyps; Colorectal cancer

INTRODUCTION
Colorectal cancer is the second most common cause for cancer related death in developed countries. The age-adjusted incidence of colorectal cancer is estimated 61.2 cases and 44.8 cases per 100000...
Multiple studies have addressed the specific issue of colorectal cancer incidence and colorectal-cancer mortality among participants in the Nurses’ Health Study and the Health Professionals Follow-up Study[2]. Overall, more than 88000 participants were followed over a period of 22 years. Within this time, 1815 incident colorectal cancers and 474 deaths from colorectal cancer were documented. Multivariate hazard ratios for colorectal cancer were 0.57 after polypectomy, 0.60 after negative sigmoidoscopy, and 0.44 after negative colonoscopy. In addition, negative colonoscopy was associated with a reduced incidence of proximal colon cancer. Moreover, a reduced mortality from proximal colon cancer was observed after screening colonoscopy but not after sigmoidoscopy. Accordingly, this long-term study confirmed the efficacy of screening colonoscopy to reduce colorectal cancer.

Very recently, Corley and coworkers evaluated the association between the adenoma detection rate and patients’ risk of subsequent colorectal cancer (i.e., interval cancer) and death[3]. Over 314000 colonoscopies performed by 136 endoscopists were included. The adenoma detection rates ranged from 7.4% to 52.5%. During the follow-up period, 712 interval cancers were diagnosed. The adenoma detection rate was inversely associated with the risks of interval colorectal cancer, advanced-stage interval cancer, and fatal interval cancer. Importantly, each 1% increase in the adenoma detection rate was associated with a 3% decrease in the risk of colorectal cancer.

Therefore, the above mentioned studies highlighted the importance of a precise colonoscopic examination to reduce colorectal cancer incidence. Within recent years, various new endoscopic imaging techniques have been introduced to assist endoscopists in performing accurate endoscopic examinations. In this review we will focus on the newest developments in the field of colonoscopic imaging including high-definition imaging, optical chromoendoscopy techniques, virtual chromoendoscopy techniques, the Third Eye Retroscope and other retroviewing devices, the G-EYE endoscope and the Full Spectrum Endoscopy (FUSE)-system.

**ADVANCED ENDOSCOPIC IMAGING TECHNIQUES**

*High-definition imaging*

Multiple studies have addressed the specific issue whether high-definition white-light imaging is superior to standard white-light endoscopy for diagnosis of colorectal adenomas. Results of those studies are sometimes conflicting. In addition, interpretation is often difficult as new endoscopes are not only equipped with newer chip technology allowing high-definition imaging, but also with wide-field optics and closer focus modes. Therefore, it is not possible to determine which of these individual factors led to altered adenoma detection. One recent meta-analysis compared the diagnostic yield of colonic polyps between high-definition colonoscopy and standard video endoscopy[4]. Five studies involving 4422 patients were included. The incremental yield of high definition colonoscopy for the detection of any polyp was 3.8% with a number needed to treat of 26. For the detection of adenomatous polyps the incremental yield was 3.5% with a number needed to treat of 28. There were no significant differences between high-definition and standard video endoscopy in the detection of high-risk adenomas. Nonetheless, the pooled weighted mean difference in small adenoma detection was significantly higher with high-definition colonoscopy. In a retrospective study including 2430 consecutive patients the adenoma detection rate was significantly higher among patients who underwent high-definition white-light endoscopy compared with standard white-light colonoscopies[5]. These data are in contrast to one recent trial including 426 individuals who underwent high-definition white-light endoscopy and 426 individuals who underwent conventional colonoscopy[6]. In this study, high-definition endoscopy did not increase the detection of individuals with polyps, adenomas, or high-risk adenoma features. High-definition did also not increase the detection of individuals with clinically insignificant colonic lesions.

Importantly, one recent study aimed to investigate whether detection rates of individual endoscopists increase within 1 year before and 1 year after the switch from standard to high-definition endoscopy[7]. In this study, the adenoma detection rates of endoscopists with a low detection rate (< 20%) increased significantly after switch from standard to high-definition endoscopy (P = 0.0076) while this effect was not measurable for high-adenoma detectors (≥ 20%).

**Optical chromoendoscopy**

Optical chromoendoscopy uses optical filters within the light source of the endoscope to narrow the bandwidth of the light. The normal bandwidth consists of a red-green-blue image. The narrow band imaging (NBI; Olympus, Tokyo, Japan) narrows the red light. The resulting green-blue image improves imaging of the mucosal vascular and surface pattern morphology[8].

To date, four meta-analyses evaluated the impact of NBI for colon polyp detection as compared to white-light endoscopy. None of these could find convincing evidence that NBI is significantly better than white-light endoscopy.
light endoscopy for detection of colorectal polyps\textsuperscript{[9-12]}. The most recent meta-analysis included 7 studies with a total of 2936 patients\textsuperscript{[12]}. No statistically significant difference in the overall polyp or adenoma detection rate with the use of NBI or white-light endoscopy was detected. In addition, when the number of adenomas and polyps per patient was analyzed, no significant difference was found between NBI and white-light endoscopy.

One main disadvantage of the NBI system is the relatively dark image according to its principle of light filtering. While NBI has proven its efficacy for characterization of lesions in multiple studies its value for detection of lesions seems to be limited as the darker NBI image does mostly not allow a detailed view of the colonic structures.

Very recently, a new NBI system was launched (Olympus, Tokyo, Japan), now allowing an up to 4-times brighter image (Figure 1). The new system was already evaluated in a trial by Leung \textit{et al}\textsuperscript{[13]} which included 360 patients. Patients were randomized to undergo either NBI or high-definition white-light endoscopy. In this well designed study, both the adenoma and polyp detection rates were significantly higher in the NBI group as compared with the high-definition white-light endoscopy. In this well designed study, both the adenoma and polyp detection rates were significantly higher in the NBI group as compared with the high-definition white-light endoscopy. No significant differences were observed in the adenoma miss rates between the two groups. Therefore, these early results suggest that the new NBI system is superior to conventional white-light endoscopy. The final results of multicenter studies addressing this issue are therefore highly anticipated.

Virtual chromoendoscopy
Virtual chromoendoscopy techniques rely on the principle of digital postprocessing and include Fujinon Intelligent Color Enhancement (FICE, Fujifilm, Tokyo, Japan), i-scan (Pentax, Tokyo, Japan) and the recently introduced SPIES system (Storz, Tuttingen, Germany) (Figure 2). The technical details of the systems have been reviewed in detail elsewhere\textsuperscript{[14,15]}.

Similar to optical chromoendoscopy, results on the efficacy of virtual chromoendoscopy for improved adenoma detection are contrary with studies reporting on improved adenoma detection rates and others not. One early study by Arthur Hoffman included 220 patients which were randomized in a 1:1 ratio to undergo high-definition white-light endoscopy or i-scan\textsuperscript{[16]}. Colonoscopy performed with i-scan detected significantly more patients with colorectal neoplasia (38\%) as compared to standard white-light endoscopy (13\%). These data were confirmed in a retrospective study by Testoni \textit{et al}\textsuperscript{[17]} reporting significantly more detected lesions with i-scan as compared to standard white-light endoscopy. Contrary, Hong \textit{et al}\textsuperscript{[18]} performed a prospective, randomized trial using a back-to-back colonoscopy design. Overall, 389 patients were randomized. The adenoma detection rates during the first withdrawal of high-definition white-light endoscopy and i-scan and the adenoma miss rates of each group were not statistically different between

\begin{figure}
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\includegraphics[width=\textwidth]{Figure1}
\caption{Colonic polyp imaged with high-definition white-light (A), narrow band imaging (B), Fujinon Intelligent Color Enhancement (C) and i-scan (D). Data on detection rates are inconsistent. Nevertheless, dye-less chromoendoscopy techniques allow for a detailed and adequate examination of the mucosal pit pattern and the mucosal vascular pattern morphology to predict polyp histology in real time.}
\end{figure}
The device consists of a fiber optic which is introduced through the working channel of a standard colonoscope until it extends beyond its other end. Afterwards, the Third Eye Retroscope turns around and the colonoscope consists of three imagers integrated into the distal tip of the endoscope and at the lateral sides thereby enabling a 330° angle of view of the colon. Images are displayed on three contiguous monitors. Very recently, Ian Gralnek et al.26 presented the results of a large international multicenter study comparing standard forward viewing endoscopy with the FUSE system. Patients underwent same-day, back-to-back tandem colonoscopy with a standard forward-viewing colonoscope and the full-spectrum colonoscope after a 1:1 randomization. Overall, 185 patients were included and randomly assigned to both groups. By per-lesion analysis, the adenoma miss rate was significantly lower in patients receiving FUSE than in those in the standard forward-viewing group (7% vs 41%). Therefore, the FUSE platform represents a new and promising technology to improve the efficacy of colorectal cancer screening and surveillance.

Figure 2. RetroView devices allow for a 210 degree bending of the distal tip and are equipped with virtual chromoendoscopy techniques and large working channels to allow adequate characterization of colonic lesions and subsequent endoscopic therapy (Image with kind permission from Fujifilm).

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Retroscope technology
In 2007, the Third Eye Retroscope (Avantis Medical Systems, Sunnyvale, United States) was introduced21. The device consists of a fiber optic which is introduced through the working channel of a standard colonoscope until it extends beyond its other end. Afterwards, the Third Eye Retroscope turns around 180 degrees. The endoscopist has now two images on one monitor. One image is showing the standard colonoscopic view and one image is providing the retrograde view. Main advantage of the system is that it allows to visualize lesions located proximal (i.e., behind) the colonic folds. Various studies have evaluated the Third Eye Retroscope. One multicenter study included eight different centers and a total of 249 patients22. 257 polyps were identified with the colonoscope alone while the Third Eye Retroscope detected significantly more additional polyps and adenomas. For lesions 6mm or larger and 10 mm or larger, the additional detection rates with the Third Eye Retroscope for adenomas was 25% and 33%, respectively. Every polyp that was detected with the Third Eye Retroscope was subsequently located with the colonoscope and removed. Another, open-labeled, prospective, multicenter study at nine sites evaluated the impact of the Third Eye Retroscope on adenoma detection rates during colonoscopy23. Overall, a 16% increase in the adenoma detection rate by using the Third Eye Retroscope was detected. For lesions 6mm or larger and 10 mm or larger, the overall additional detection rates with the Third Eye Retroscope for all adenomas were 24% and 19%, respectively. Meanwhile, the data have also been confirmed by other investigators demonstrating an improved adenoma detection rate with the Third Eye Retroscope by visualizing areas located proximal (i.e., behind) colonic folds24,25.

However, despite its efficacy, one potential limitation of the Third Eye Retroscope might be that the working channel is blocked. Accordingly, in order to perform endoscopic therapy of detected lesions, one have to withdraw the device first before advancing additional equipment necessary for polyp removal. In the attempt to offer a hybrid of a therapeutic scope which also allows relatively easy visualization of areas located behind the colonic folds, new "RetroView" devices were recently introduced. These devices (3490TFi, Pentax, Tokyo, Japan and 580RD, Fujifilm, Tokyo, Japan) are slim colonoscopes allowing retroflexion of the distal tip at 210 degrees (Figure 3) In addition, the endoscopes are equipped with latest virtual chromoendoscopy techniques (i.e., i-scan; FICE) and working channels of 3.2mm thereby allowing characterization, demarcation and endoscopic therapy at once. Currently, no scientific evidence regarding the new retroviewing devices is available but multiple groups are already evaluating the potential beneficial effect of the technology.

The FUSE system
FUSE (EndoChoice, GA, United States) was recently introduced as a new platform (Figure 3). The FUSE-colonoscope consists of three imagers integrated into the distal tip of the endoscope and at the lateral sides thereby enabling a 330° angle of view of the colon. Images are displayed on three contiguous monitors. Very recently, Ian Gralnek et al.26 presented the results of a large international multicenter study comparing standard forward viewing endoscopy with the FUSE system. Patients underwent same-day, back-to-back tandem colonoscopy with a standard forward-viewing colonoscope and the full-spectrum colonoscope after a 1:1 randomization. Overall, 185 patients were included and randomly assigned to both groups. By per-lesion analysis, the adenoma miss rate was significantly lower in patients receiving FUSE than in those in the standard forward-viewing group (7% vs 41%). Therefore, the FUSE platform represents a new and promising technology to improve the efficacy of colorectal cancer screening and surveillance.
Very recently, the G-EYE endoscope (Smart Medical, Ra’anana Israel) was launched. The G-EYE relies on a standard endoscope in which a permanently integrated balloon was incorporated at its distal bending section (Figure 4). The balloon is inflated in the cecum and the endoscope is withdrawn with the balloon inflated until the rectum is reached. The inflated balloon stabilizes the endoscope during the withdrawal phase and interventions and provides additional folds straightening in order to improve adenoma detection rates. Early data provided by Kiesslich and coworkers suggest that the adenoma detection rate with the G-EYE endoscope could be increased by at least 48% (personal communication). Final results of the ongoing multicenter studies are expected by the end of the year.

CONCLUSION

In the attempt to improve adenoma detection rates various advanced endoscopic imaging techniques have been introduced within the past 5 years. Scientific evidence is still missing for some of the new technologies. It is still not fully known whether pure high-definition white-light endoscopy improves adenoma detection rates. Therefore, prospective, randomized, multicenter studies addressing this issue are highly warranted. While there was no beneficial effect of the first NBI system, recent evidence suggests that the new NBI system is superior to conventional white-light endoscopy and could improve adenoma detection rates. Again, results of multicenter studies addressing this issue are highly anticipated. Study results on the potential of virtual chromoendoscopy techniques using digital postprocessing for improved adenoma detection in the colorectum are still inconsistent. Multiple, large and multicenter studies are currently addressing this issue and the results of those studies are anticipated latest within the next two years. New endoscope platforms now allow for a more detailed view of the luminal gastrointestinal tract. Early data demonstrate the impressive potential of those new platforms to improve early diagnosis of colorectal lesions without detriment to procedure time or procedure complications. Therefore, new endoscopic imaging techniques will assist the endoscopists to improve adenoma detection rates for better diagnosis and early therapy of colorectal lesions.

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