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Competition in Colon Cancer Screening? What Is the Role of Colonoscopy?

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Keywords
Colorectal cancer · Colon cancer screening · Colonoscopy · Computed tomographic colonography · Magnetic resonance colonography

Summary
Background: Colorectal cancer (CRC) is one of the leading causes of cancer-related death in the Western world. The incidence could be reduced if this cancer were to be diagnosed at an early stage of disease. A competition has started between the existing screening methods to be the most efficient in detecting premalignant conditions. This review illustrates the current state of screening techniques for CRC. **Method:** Pubmed was searched for meta-analyses and prospective studies on screening for CRC, with an emphasis on colonography, computed tomographic colonography (CTC), magnetic resonance colonography (MRC), stool DNA testing, and colon capsule endoscopy, and critical appraisal of the research was done by the reviewers. **Results:** The imaging techniques (CTC and MRC) had similar detection rates for bigger lesions (≥10 mm) as colonoscopy. High-definition colonoscopy showed better efficiency with smaller lesions. The techniques developing around colonoscopy such as the retro-viewing colonoscope, the balloon colonoscope, or the 330-degree viewing colonoscope try to enhance efficacy by reducing the adenoma miss rate in right-sided, non-polypoid lesions. Colon capsule endoscopy and the stool detection systems are limited to identifying cancer but not necessarily adenomas. **Conclusion:** Colonoscopy is the preferred CRC screening strategy and the undisputed gold standard in terms of efficacy.

Schlüsselwörter
Kolorektalkarzinom · Darmkrebsvorsorgeuntersuchung · Koloskopie · Computertomographiekolonographie · Magnetresonanzkolonographie

Zusammenfassung:
Hintergrund: Das Kolorektalkarzinom (KRK) ist in der westlichen Welt einer der führenden Gründe für das Versterben im Rahmen von Tumorerkrankungen. Nur eine frühe und effektive Vorsorge vermag zurzeit die Inzidenz zu reduzieren. Folglich findet heute ein regelrechter Wettbewerb zwischen den verschiedenen Vorsorgemöglichkeiten statt, und jede nimmt für sich die beste Effizienz in Anspruch. In der nachfolgenden Übersicht werden die verschiedenen Möglichkeiten der kolorektalen Krebsvorsorge kritisch unter Beachtung der aktuellen Studienlage beurteilt. **Methode:** Die aktuelle Recherche wurde mittels Pubmed durchgeführt. Dabei wurden Meta-Analysen und prospektive Studien über Darmkrebsvorsorgeuntersuchung gesucht, und ein besonderer Schwerpunkt wurde folgend auf die Koloskopie, die Computertomographiekolonographie (CTK), die Magnetresonanzkolonographie (MRK), die DNA-Stuhltests und die Kolonkapselendoskopie gesetzt. **Ergebnisse:** Die schnittbildgebenden Verfahren (CTK und MRK) zeigten zum Goldstandard Koloskopie vergleichbare Detektionsraten, vor allem für Läsionen ≥10 mm. Die hochauflösende Koloskopie zeigte sich überlegen insbesondere bei kleineren, flachen Läsionen. Neue innovative Techniken wie das 'Retro-Viewing'-Koloskop, das neuartige Balloon-Koloskop oder das '330-Degree-Viewing'-Koloskop versuchen durch Reduktion der 'Miss'-Rate die Effizienz vor allem bei rechtsseitigen, flachen Polypen zu verbessern. Die DNA-Stuhltests und die Kolonkapselendoskopie zeigen verlässliche Aussagen nur bei Karzinomen. **Schlussfolgerung:** Die Koloskopie ist die bevorzugte Darmkrebsvorsorgeuntersuchung und ist bezüglich der Effizienz der unangefochtene Goldstandard.

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Introduction

Colorectal cancer (CRC) is a commonly diagnosed cancer with a high incidence in the Western world. It is the second most common cancer (447,000 in the year 2012) and one of the leading causes of cancer-related death (215,000 in the year 2012) in Europe [1–3]. Because 75% of all new cases occur in an average-risk population, prevention and early detection have become an integral part of prevention programs which have been established in many countries, including Germany where every insured person from the age of 55 years can receive a screening colonoscopy for early detection of CRC [4–6].

Since conventional carcinomas arise from the so-called 'adenoma-carcinoma sequence' within approximately 10 years, the most important prognostic factor for the survival of a patient with CRC is the stage at which the disease is diagnosed [7–11]. Detection programs should be performed exactly in this time window, and it is estimated that 95% of all patients with CRC would benefit from a curative approach if diagnosed at an early stage [12]. Furthermore, the US National Polyp Study Workgroup estimated that 76–90% of cancers could even be prevented by regular early detection [13, 14].

Based on 88,902 participants followed over a period of 22 years, colonoscopy and sigmoidoscopy were associated with a reduced incidence of cancer of the distal colorectum, and colonoscopy was also associated with a modest reduction in the incidence of proximal colon cancer; however, only colonoscopy was associated with reduced mortality from proximal colon cancer [15]. An increase in the proportion of the population undergoing screening colonoscopy and the removal of precancerous polyps is thought to account for at least part of this decrease, especially given the fact that the frequency of missed right-sided proximal lesions increased substantially only after sigmoidoscopy [15, 16]. However, more recent data has shown that parallel to the so-called conventional adenoma pathway exists a new serrated pathway to which the (sessile) serrated adenomas/polyps belong [17, 18]. Because of their characteristics of having a shallow and hard-to-detect growth pattern, being increasingly found in the right-sided colon, and having a greater potential of developing into CRC compared to traditional adenomas, these lesions are thought to be accountable for the so-called interval carcinomas [19, 20]. Based on this knowledge, screening modalities and screening intervals may have to be redefined.

Competition in Screening: 'The Race Is on'

Conventional Screening Colonoscopy

Today, it is evident that in individuals older than 50 years colonoscopy is an important screening option for detecting colorectal lesions. Highly ranked editorials have advocated colonoscopy as the preferred CRC screening strategy, which may have motivated physicians to switch from sigmoidoscopies to complete colonoscopy. In parallel, the percentage of physicians who believe that colonoscopy is very effective in reducing CRC mortality increased by 10–15% in the last 20 years [21–24]. Colonoscopy has maintained its place as the gold standard for screening and surveillance of CRC. The goal of every colonoscopy must be the detection of any premalignant condition of the colon (fig. 1). Advanced cancers and polypoid or protruded adenomas are easy to identify, and previous large-scale screening colonoscopy studies have assessed the use of colonoscopy for special-risk rather than average-risk populations. For example, in the study by Lieberman et al. [25], 13.9% of the screened population had a family history of CRC; in the study by Regula et al. [26], 13.3% of the 50–66 age group and 66.3% of the 40–49 age group had a family history of CRC. Schoenfeld et al. [27] screened only women; and other studies were not comprehensive as they limited their analysis to the 50–75 age range. Thus, concerns that the protective effect of colonoscopy is lower than previously believed have shifted attention to improving the precision of colonoscopy. Despite great advances and efforts having been made in recent years to optimize the quality of colonoscopy, updated guidelines have expanded the menu of recommended test options to include computed tomographic colonography (CTC), fecal DNA testing, magnetic resonance colonography (MRC), and capsule colonoscopy. Also, despite all its benefits, colonoscopy is still an invasive procedure which often requires sedation and full bowel preparation, and can in rare cases be associated with potentially life-threatening complications.

Computed Tomographic Colonography

Single or double contrast enema of the colon was the first radiologic technique to examine the lumen of the colon. Though this examination can identify stenosis or tumors, it has a low sensitivity for recognizing polyps. Furthermore, it demands advanced technology to achieve high-quality resolution with low exposure. CTC, also termed virtual colonoscopy, is an advanced radiological technique with significantly

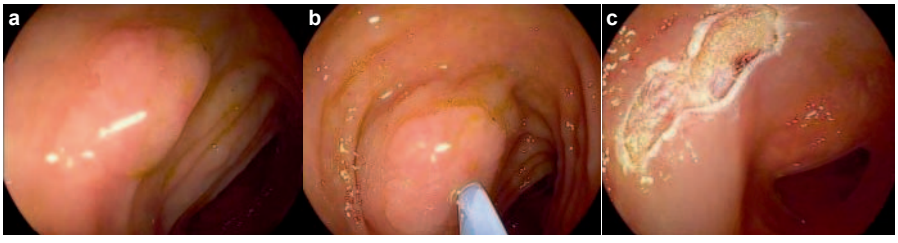

Fig. 1. a–c. Polypectomy of a flat polyp in the right-sided colon (Paris classification Ib).

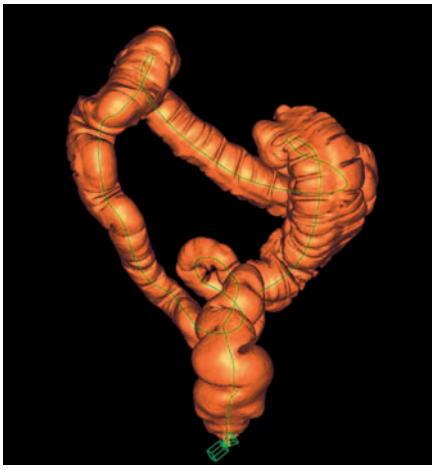

Fig. 2. Computed tomographic colonography (CTC) (property of Dr. Kukuk University Bonn, Germany).

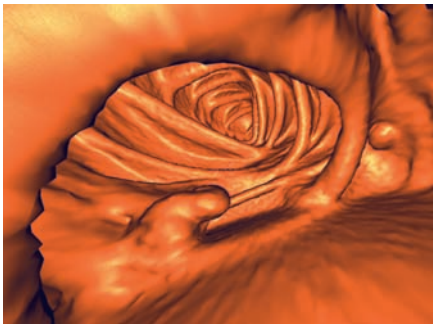

Fig. 3. Adenoma detection with computed tomographic colonography (CTC) (property of Dr. Kukuk University Bonn, Germany).

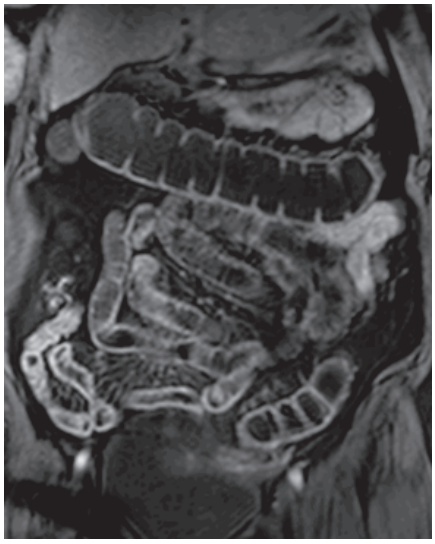

Fig. 4. Magnetic resonance colonography (MRC) (property of Dr. Kukuk University Bonn, Germany).

higher sensitivity for detecting polyps or cancers [28] (fig. 2). Modern multi-slice computed tomography with 16–64 detector rows provides resolutions of less than 0.5 mm. Cathartic bowel preparation usually based on polyethylene glycol or sodium phosphate and fecal tagging via oral contrast agents such as barium sulfate and/or iodinated contrast agents should be combined with a retrograde colon distension to achieve good image quality [29, 30]. A multitude of studies have described CTC as feasible, safe, well tolerated, and a possible screening method for CRC. A multicenter randomized trial by Atkin et al. [31] with 1,610 patients with abdominal symptoms reported a similar detection rate (11%) of CRC or polyps ≥10 mm for both CTC and colonoscopy. CTC missed 1 of 29 CRC, and colonoscopy missed none out of 55. Another recently published meta-analysis including both average- and high-risk subjects found that CTC had a sensitivity of 96% for CRC, which is comparable to colonoscopy with an estimated sensitivity of 88% for advanced neoplasia (≥10 mm) within screening populations [32, 33] (fig. 3). However, diagnostic accuracy for smaller lesions is still inferior compared to colonoscopy [34–38]. A meta-analysis of over 1,000 patients compared CTC with conventional colonoscopy, and reported high overall sensitivity and specificity for lesions ≥10 mm, but significantly lower accuracy for smaller lesions [33]. Thus, there is a substantial risk of missing advanced adenomas or cancers of <10 mm in diameter. The results of a meta-analysis by Pickhardt et al. [39] showed that 15 of the 16 missed tumors were <10 mm. Furthermore, there is an ongoing debate about which findings should trigger an immediate colonoscopy. Often, repeat CTC is recommended for polyps measuring 6–9 mm. Here, substantial criticism can be raised, because flat and depressed neoplasia might be overlooked. On the other hand, the advantages of CTC are that almost the entire surface of the colon can be visualized. The use of last-generation CTC systems can minimize the radiation dose. Further advantages of CTC are that it is less burdensome and has a very low overall complication rate (0.02%). The risk of serious adverse events is lower compared to colonoscopy which has a complication risk of 0.1–0.3% [40–43]. Whether the visualization of extracolonic structures and subsequent detection of potential pathologies is an advantage or disadvantage, is frequently debated and remains unclear since the majority of potentially important findings ultimately emerge as clinically unimportant in further tests and lead to patient anxiety and increment of health care costs for diagnostic follow-up [44, 45].

Magnetic Resonance Colonography

The radiation dose involved in CTC has led several investigators to evaluate the role of MRC. At a population level, if MRC were to be validated for screening purposes, the implications may be substantial. For MRC, the colon is filled with water combined with a paramagnetic contrast agent such as gadolinium, and the technique relies on ultra-fast, T1-weighted data acquisition collected during a single breath hold [46]. The lumen of the colon thus appears bright and the walls dark. Lesions within the wall protrude into the bright lumen, appearing as filling defects (fig. 4). The difficulty in differentiating masses from feces can be avoided by imaging the patient in prone and supine position, and more recently by using new techniques to render the lumen and feces dark while enhancing the colonic walls. This so-called fecal tagging (FT), or dark-lumen colonography, is facilitated by the oral administration of barium sulphate which renders the lumen and feces dark [47, 48]. The technique can be performed without bowel preparation,

which may even increase patient acceptance, particularly for elderly patients who are not able to tolerate full bowel preparation. However, diagnostic MRC relies heavily on good bowel distension and sufficient contrast between the bowel lumen and the colonic wall to highlight lesions, and these methodological aspects have an immediate impact on the imaging results. A number of prospective, comparative studies of MRC versus conventional colonoscopy have been reported, assessing the accuracy of MRC as a possible diagnostic tool for CRC and polyps [49, 50]. Despite the heterogeneity of the studies, the overall diagnostic accuracy of MRC was only adequate compared to colonoscopy, with a pooled sensitivity of 75% and a specificity of 96%. MRC was more useful in the detection of bigger malignant lesions, with a sensitivity of 91% and a specificity of 98% [49–55]. The potential advantages of MRC over conventional colonoscopy are that it is less invasive with less potential serious complications, requires less time for the investigation, and has been reported to have good patient acceptability. Extracolonic pathologies related to CRC such as lymph node or distant metastasis can also be evaluated during the investigation, and the MRC can hence be used for the staging process. In the future, specialized software may even enable the viewer to digitally straighten the colon in areas where folds may mask potential pathologies. However, there are also potential disadvantages of MRC, including lack of universal availability, unsuitability for biopsies, susceptibility to motion artifacts, and need for breath holding. Cost is also an important issue; one study reported MRC examination costs of approximately USD 550, and cost-effectiveness has not yet been formally investigated in clinical studies [48]. However, most of all MRC must be evaluated in terms of its potential to recognize flat and depressed neoplasias, which is challenging and only possible by meticulous inspection and classification of discrete mucosal alterations.

Colon Capsule Endoscopy

Various media campaigns and other initiatives to promote screening colonoscopy have had surprisingly little impact [56]. The reasons for the limited acceptance of CRC screening, especially of colonoscopy, are diverse. Apart from general doubts and fears, a contributing factor may be the perception of colonoscopy as being painful and unpleasant. Capsule endoscopy was introduced some years ago primarily for small bowel diagnostics, but has been extended to the colon with a modified capsule used for capsule colonoscopy [57, 58]. The PillCam® colon capsule (Given Imaging Ltd., Yoqneam, Israel) provides a screening solution which is minimally invasive, safe, and does not require sedation. It is well accepted by patients although still requiring thorough bowel cleaning, and is mainly recommended to people who have up to this point rejected CRC screening programs [58]. It is an easy-to-perform examination with an excellent negative predictive value for application in screening procedures under routine conditions. However, diagnostic accuracy for relevant-sized polyps (i.e. sensitivity) is low. First studies have shown 65–75% accuracy for adenoma detection in the large bowel when compared with colonoscopy [59–63]. However, with capsule colonoscopy, there is a fourfold increase in endoscopic screening, with men in particular finding capsule colonoscopy more acceptable. Colon capsule screening is expensive because there are no screening programs supporting it as the primary choice. Thus, the colon capsule has to be paid for by the patient, which in turn hinders broad acceptance.

Stool DNA Testing

Since 2002, the guaiac-based fecal occult blood test (gFOBT) is part of the early CRC detection program in Germany. Although the sensitivity for detecting CRC is low (13–50%) and even lower for advanced neoplasia (11–27%), several randomized controlled trials have shown that biennial gFOBT screening leads to a CRC mortality reduction of approximately 14% after 10 years of screening [64–69]. Understandably, there has been minimal impact on CRC incidence [70]. Immunological stool testing provides better sensitivities and accuracy rates, and several gastroenterology societies are now recommending this test (iFOBT) rather than gFOBT [71–73].

A new test is the so-called stool DNA test (sDNA) which offers a biologically rational approach based on tumor cell exfoliation [71]. However, along with the problems of stool collection and delivery, this examination is limited to identifying cancer and not necessarily adenomas. The study of the first-generation sDNA test by Imperiale et al. [70] using a DNA marker panel comprising 21 mutations showed a sensitivity of 52% for invasive cancers compared to 13% for FOBT and a sensitivity of 18% for advanced neoplasia. First preliminary studies have shown that by using a large pool of genetic markers the sensitivity for large adenomas was 82% and for CRC 91%, with an overall specificity of 93% [72]. A recently published, blinded, multicenter, case-control study using archived stool samples of 678 patients and a next-generation sDNA test by Ahlquist et al. [73] reported a sensitivity of 85% for patients with CRC and 54% for patients with adenomas >1 cm, with 90% specificity. Although the manufacturer recommends a 5-year screening interval, no formal evaluation of timing has been performed in clinical studies. Acceptance with caution with regard to sDNA testing has been declared by the American Cancer Society; however, the biggest limitation remains the low sensitivity for advanced adenomas, as the primary goal in cancer screening is prevention rather detection of cancer.

Interval Cancers and Adenoma Detection Miss Rate

A pooled adenoma detection miss rate of 22% (range 15–32%) in tandem colonoscopy studies and a recent large case-control study by Baxter et al. [74] have raised another question regarding the yield of screening colonoscopy in reducing mortality due to interval cancers, as screening colonoscopy was associated with significantly reduced mortality from left-sided lesions (odds ratio (OR) 0.33) but showed only minor

Table 1. High-definition colonoscopy and adenoma detection rate

Author, year [ref.]	Study design/ objective	Wide angle	Patients, n	Adenoma detection rate, %	p	Absolute increase, %	Relative increase, %
East et al., 2008	cohort	no	130	65	0.20	11	18
Pellise et al., 2008	randomized	yes	620	26	0.85	1	4
Burke et al., 2010	cohort	yes	852	23	0.36	–	13
Tribonias et al., 2009	randomized	yes	390	54	0.16	8	16
Buchner et al., 2010	cohort	yes	2,430	27	0.01	4.2	17
Hoffman et al., 2012	randomized	no	220	38	0.001	25	192

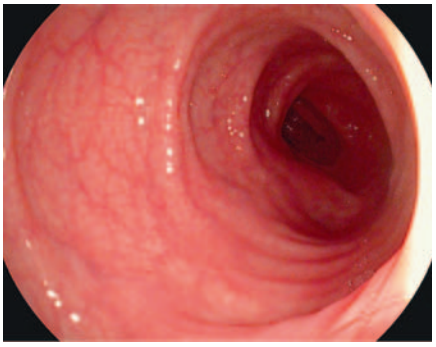

Fig. 5. High-definition colonoscopy.

advantage for right-sided lesions (OR 0.99). Thus, there is still a need to accelerate technological developments and to increase recognition of non-polypoid flat premalignant lesions, especially in the right side of the colon.

High-Definition Endoscopy

High-definition (HD) endoscopes generate more pixels than standard definition (SD) endoscopes, and recently published meta-analyses have compared the diagnostic yield of colonic polyps of HD versus SD colonoscopy [75] (fig. 5). In five studies with a total of 4,422 patients at average risk for colorectal neoplasia, HD colonoscopy allowed detection of ≥1 polyp(s) in 3.8% more patients than SD colonoscopy. For adenomatous polyps, the yield of HD colonoscopy was also significantly higher (by 3.5%). HD colonoscopy mainly improved the detection of small (≤5 mm) adenomas, but there were no differences between HD and SD colonoscopy for high-risk adenomas [75] (table 1). In a controlled trial published after this meta-analysis, the proportion of subjects in whom adenomas were detected was higher with the HD compared with the SD colonoscope (46 vs. 39%; p = 0.166), and the difference was significant for the proportion of patients with flat adenomas (10 vs. 2%; p = 0.003) and with right-sided adenomas (34 vs. 19%; p = 0.001) [76]. In a prospective and randomized trial, the combination of HD colonoscopy with some contrast enhancement (e.g. i-scan functionality) was also compared with standard video colonoscopy and showed significantly more patients with at least 1 adenoma using HD colonoscopy with contrast enhancement (38 vs. 13%); furthermore, significantly more adenomas, and in particular flat adenomas, could be identified [77]. In summary, HD colonoscopy allows detection of more adenomas in a higher proportion of patients than SD colonoscopy; the difference is mostly due to a better detection of polyps that are small (≤5 mm) and flat.

Technologies on the Horizon

An apparently leading cause of missed polyps during colonoscopy are polyps that are located behind haustral folds in the colon, and are therefore hidden from conventional, forward-viewing endoscope optics. It was demonstrated that occasional straightening of haustral folds during colonoscopy by a plastic cap mounted on the endoscope tip increases the polyp detection yield [78]. A study in 6,185 patients by Westwood et al. [78] reported a miss rate of 12.2% in the cap-assisted colonoscopy group versus a 28.6% miss rate in the standard colonoscopy group, implying a positive effect of cap employment on the polyp detection rate. In contrast, another study performed by Tee et al. [79] in 400 subjects reported that there was no significant polyp detection rate difference between standard colonoscopy and cap-assisted colonoscopy (31.3 vs. 32.8%).

Recently, a retrograde viewing device (Third Eye Retroscope; Avantis Medical, Sunnyvale, CA, USA) was introduced for use during colonoscopy with standard endoscopes, and was analyzed in a single randomized controlled trial (same-day tandem examinations) [80]. This technique is aimed at allowing inspection of the proximal surface of haustral folds not in the line of sight of the endoscope's forward-viewing optics, thereby allowing detection of polyps that are located behind such folds. Intention-to-treat and per-protocol analyses included 395 and 349 patients, respectively. Use of the retrograde viewing device was associated with a 23% increase in the total number of adenomas detected compared with standard colonoscopy (after correcting for the second-pass effect), and the relative risk of missing lesions with standard colonoscopy compared with colonoscopy using the retrograde viewing device was 2.56 for polyps (p < 0.001) and 1.92 for adenomas (p = 0.029). Previous uncontrolled studies also suggested that the retrograde viewing device may allow detection of 10% more adenomas compared to standard colonoscopy [81]. However, in the intention-to-treat analysis, the benefit in the total number of adenomas detected dropped from 23 to 14%, and the relative risk of missing lesions with standard colonoscopy compared with colonoscopy using

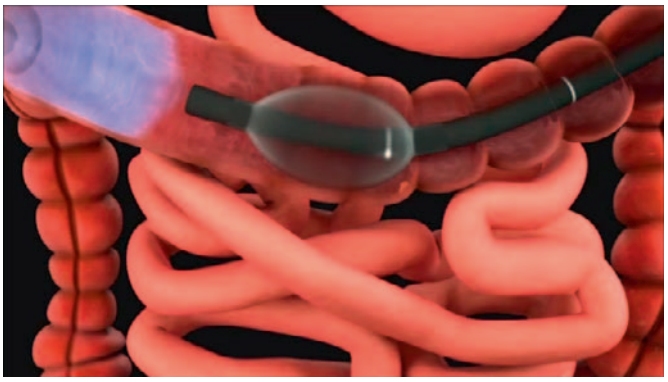

Fig. 6. G-Eye balloon colonoscopy with inflated balloon at the distal tip of the colonoscope. The balloon is inflated to straighten intestinal folds in the colon (NaviAid™ G-EYE; property of Smart Medical Systems, Ra'anana, Israel).

the retrograde viewing device became not significant for adenomas. Furthermore, the cost of this technique is still relatively high and needs the approval of more prospective studies.

The new G-Eye system (NaviAid™ G-EYE; Smart Medical Systems, Ra'anana, Israel) is a balloon colonoscope comprising a standard colonoscope with a reprocessable, permanently integrated balloon at its distal tip. The balloon pressure is controlled through a unique inflation system providing predetermined, user-selectable, anchoring and intermediate (low) pressure levels (fig. 6). First results from a prospective multicenter back-to-back study including 126 patients were as follows: The G-Eye balloon colonoscopy detected 23 additional polyps, which means a promising 115% additional adenoma detection rate. The balloon colonoscope's additional detection rate ratio, calculated as the ratio between balloon colonoscopy second-pass additional detection and balloon colonoscopy first-pass miss rate, was 25.5 (115/4.51) [82]. The results from this first multicenter study are very promising, and further studies are ongoing.

Another potential reason for high adenoma miss rates is inadequate visualization of the proximal aspect of colonic folds and flexures. Full spectrum endoscopy (Fuse™; EndoChoice, Alpharetta, GA, USA) utilizes unique imaging technology which allows the endoscopist to view 330 degrees while maintaining identical standard colonoscope technical features (fig. 7). The results for this new technique were a 32.9% increased polyp detection rate (per patient analysis) and a 39/49 (79.6%) increased polyp detection rate (per polyp analysis). Furthermore, on subsequent Fuse colonoscopy, there were an additional 15/88 (17.1%) subjects who had at least 1 adenoma detected, yielding an additional 21 adenomas. This is an increment of 17.1% in the adenoma detection rate (per patient analysis) and a 21/28 (75.0%) increased adenoma detection rate (per adenoma analysis) using Fuse colonoscopy [83]. However, as with all new technology, there often is initial enthusiasm, but advantages have to be proved in a more clinical setting and with practice.

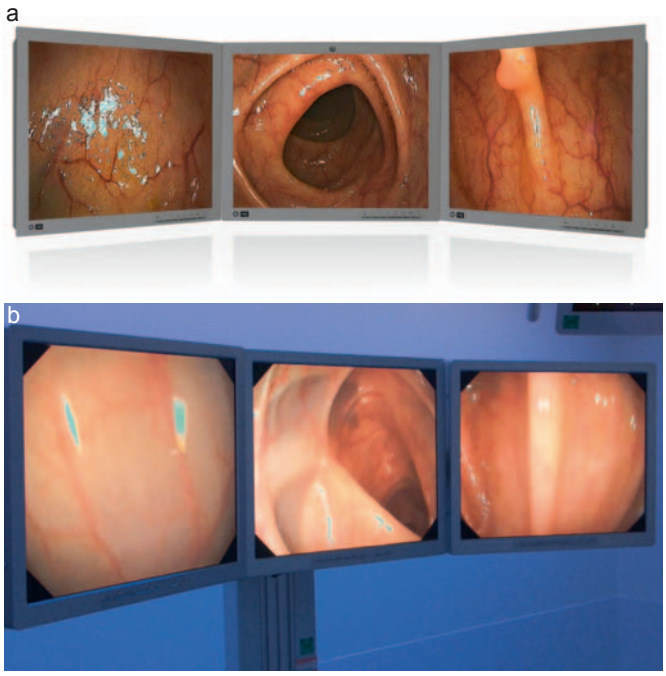

Fig. 7. a, b. Fuse colonoscopy utilizes unique imaging technology which allows the endoscopist to view 330 degrees while maintaining identical standard colonoscope technical features (property of Fuse™; EndoChoice, Alpharetta, GA, USA).

Conclusion

The optimal screening strategy for CRC in an average-risk population is dependent on the efficacy and safety of the tests, cost-effectiveness, and likelihood of patient compliance. Colonoscopy is the undisputed gold standard in terms of efficacy, having the highest sensitivity and specificity and offering the capacity to carry out therapeutic intervention during the procedure (e.g. polypectomy). Furthermore, clinical evidence amassed over several decades indicates that routine colonoscopy screening detects CRC at an earlier stage, reduces the incidence of CRC or the progression of early CRC through polypectomy, and significantly reduces cancer-related mortality. However, colonoscopy is the most invasive of the currently available screening modalities. In the ambulatory setting, the procedure-related morbidity rate of colonoscopy is 0.1–0.3%, with a 0.03% perforation rate and no mortality [74, 75]. Screening the entire population aged ≥50 years is an expensive proposition; however, the costs of missing a curable malignancy or failing to prevent cancer by not resecting a premalignant lesion (polyp) may be significantly greater. The potential advantages of CTC and MRC, including rapid image acquisition and processing, noninvasiveness, and decreased procedural risks of perforation, bleeding, and sedation complications, may serve to improve the low rates of CRC screening that are currently observed in our society. A lot of studies add to the body of literature regarding the efficacy of screening programs based on computed tomogra-

phy and magnetic resonance imaging, which are likely to become acceptable CRC screening tests on a par with colonoscopy. Issues remain, however, regarding the extension and reproducibility of these results in the true community setting. There are concerns regarding thresholds for referrals, appropriate intervals between studies, the optimal management of extracolonic findings, and radiation exposure with CTC that remain unanswered so far. Stool-based tests are categorized as tests which can primarily detect cancer early on according to the joint guideline from the American Cancer Society, the Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. Hence, considering that the primary goal is cancer prevention rather than cancer detection, they are not very suitable. Although colonoscopy remains the major gastrointestinal endoscopy procedure, it is well known that lesions are missed during routine colonoscopy and interval cancers still remain an unsolved problem. A lot of new medical devices are coming to the market to reduce the adenoma miss rate, and first studies show promising results; however, all these techniques have to be tested in further prospective studies.

Disclosure Statement

A. Hoffman, D. Teubner, and R. Kiesslich declare that no conflict of interest exists.

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