

New aspects of modern endoscopy

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Received: April 30, 2014 Revised: May 26, 2014

Accepted: June 27, 2014

Published online: August 16, 2014

Key words: Modern endoscopy; High definition endoscopy; Virtual chromoendoscopy; Autofluorescence; Endomicroscopy; Molecular imaging

Core tip: Today a competition has started between the existing endoscopic methods to be the most efficient in detecting the premalignant condition in the gastrointestinal tract. This review illustrates the current status of the available techniques in endoscopy with a focus on screening colonoscopy.

Rey JW, Kiesslich R, Hoffman A. New aspects of modern endoscopy. *World J Gastrointest Endosc* 2014; 6(8): 334-344 Available from: URL: <http://www.wjgnet.com/1948-5190/full/v6/i8/334.htm> DOI: <http://dx.doi.org/10.4253/wjge.v6.i8.334>

Abstract

The prognosis for patients with malignancies of the gastrointestinal-tract is strictly dependent on early detection of premalignant and malignant lesions. However, small, flat or depressed neoplastic lesions remain difficult to detect with these technologies thereby limiting their value for polyp and cancer screening. At the same time computer and chip technologies have undergone major technological changes which have greatly improved endoscopic diagnostic investigation. New imaging modalities and techniques are very notable aspects of modern endoscopy. Chromoendoscopy or filter-aided colonoscopy (virtual chromoendoscopy) with high definition endoscopes is able to enhance the detection and characterization of lesions. Finally, confocal laser endomicroscopy provides histological confirmation of the presence of neoplastic changes. The developing techniques around colonoscopy such as the retro-viewing colonoscope, the balloon-colonoscopy or the 330-degrees-viewing colonoscope try to enhance the efficacy by reducing the adenoma miss rate in right-sided, non-polypoid lesions. Colon capsule endoscopy is limited to identifying cancer and not necessarily small adenomas. Preliminary attempts have been made to introduce this technique in clinical routine.

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INTRODUCTION

Rapid advancements in computer and chip technology and the resulting technical options in imaging and image processing have influenced modern endoscopy today as never before in the past. A large number of technical innovations have been introduced in diagnostic endoscopy in the last few years, with the aim of improving the detection and characterization of pathological changes in the gastrointestinal tract. High-resolution image display in endoscopes of the newest generation is supported by virtual chromoendoscopy, a type of staining of mucous membranes at the press of a button. Classical chromoendoscopy is also significant for specific indications. Recent microscopic procedures such as endomicroscopy and endocytoscopy are able to not only predict pathological changes on the basis of their surface or vascular pattern, but also directly visualize the cellular architecture of the mucosa. The better the quality and clarity of images, the better the patient can be cared for. Thus, the main purpose of endoscopy can be achieved, which is early and timely detection of malignant changes. Modern endoscopy systems provide major technical innovations for

each of the three important consecutive diagnostic steps. All of these innovations can be utilized for optimized diagnostic investigation: (1) Detection-identification of changes (circumscribed *vs* diffuse); (2) Characterization of circumscribed lesions (prediction about the benign or malignant nature of the lesion); and (3) Confirmation by means of cell analysis (conventional or *in vivo* histology).

HIGH DEFINITION ENDOSCOPY

High definition became a catchword after the introduction of high definition television (HDTV) in television and entertainment technology. It produced high-resolution images that were practically incomparable with, and unobtainable by, the previously used transmission technology (PAL) in endoscopy. Further development of chip technology (CCD chip), by which more than one million pixels per image can be analyzed today, led to the achievement of much greater resolution in so-called high-resolution endoscopy than in video endoscopy of the first generation^[1]. The most recent color chips, although miniaturized, currently permit greater pixel density and a resolution of more than one million pixels per video image, which can now be visualized by the new television standard of HDTV with as many as 1080 video lines per image^[1]. This has greatly enhanced image quality compared to standard resolution (SR) with 576 lines. Thus, currently available high-resolution endoscopy systems (high definition or HD) achieve a resolution of 1400 x 1080 pixels. Combined with conventional or virtual chromoendoscopy, preliminary clinical data indicate that the technical advancement of HD endoscopy is a decisive element of better diagnostic investigation of early forms of cancer, and is thus able to exert an immediate impact on the prognosis of the disease for patients^[2]. In a large retrospective study Buchner was able to show, in 2430 patients, a significant rise in the detection rate of adenomas (HD 28.8% *vs* SR 24.3%, $P = 0.012$) by HD endoscopy.

These data were confirmed in a prospective study from Mainz, in which a significant rise in the detection rate of adenomas - especially flat adenomas - was noted in 200 patients who underwent preventive examination^[3,4]. In a recently published meta-analysis, the authors report a diagnostic gain of 3.8% by the use of the HD technique, but also mention the heterogeneity of previously obtained study data^[5-9] (Table 1).

CHROMOENDOSCOPY

The color dyes or pigments used in chromoendoscopy either react with intracellular structures of mucosa (*absorption*) or remain on the mucosal surface (*contrast stain*) (Table 2). The most commonly used staining materials in the upper gastrointestinal tract are Lugol's solution (changes in squamous epithelium) and acetic acid (changes in the columnar epithelium). In the lower gastrointestinal tract one usually employs indigo carmine or methylene blue^[10,11]. The somewhat greater expenditure of time

and the large number of available staining materials, as well as uncertainty about the quantity and concentration of staining materials have prevented chromoendoscopy from being established in the Western world. However, our knowledge of the morphology of early cancers in the upper and lower gastrointestinal tract has been enhanced very markedly by the use of chromoendoscopy, and has sensitized clinicians to the necessity of early detection, particularly that of flat lesions^[12-17]. A number of prospective studies, especially those from Asia, have clearly demonstrated the superiority of chromoendoscopy compared to pure white light endoscopy^[12-17]. A recent American multicenter study confirmed that the prevalence of flat neoplasias in screening colonoscopies by chromoendoscopy is 10% - which is three-fold higher than the rates reported thus far^[18]. Conclusion: Targeted spraying of color in the presence of mucosal and vascular changes of irregular flatness is recommended in order to unmask flat adenomas and early carcinomas. Chromoendoscopy facilitates the detection of colorectal neoplasias, and can also be used to characterize the identified lesions. Kudo's pit pattern classification standardizes surface analysis. In a meta-analysis of 22 studies, a sensitivity of 94% and a specificity of 82% was established for the differentiation of neoplastic and non-neoplastic lesions for the pit pattern classification^[13]. Chromoendoscopy is especially valuable for monitoring patients with ulcerative colitis. Here one should not use targeted staining but pan-chromoendoscopy. This type of chromoendoscopy permits detection of more numerous colitis-associated neoplasias as well as identify more patients with neoplasias^[19-25]. A recent meta-analysis mentions 14.3 as the "number needed to treat". In other words, by performing 14 colonoscopies with pan-chromoendoscopy one is able to diagnose one additional patient with intraepithelial neoplasias. Chromoendoscopy is currently experiencing a renaissance because the combination of high-resolution endoscopy and intravital staining provides an especially detailed view of the surface structure of mucosa.

VIRTUAL CHROMOENDOSCOPY

Owing to the previously described modern processor technology of high-resolution endoscopy systems and the possibility to add color by pressing a button and activating a color filter, virtual coloring is currently receiving special attention in endoscopy. The procedure of so-called virtual chromoendoscopy modulates, by the press of a button and with no loss of time, the spectrum of visible light so that the mucous membranes can be visualized in various "missing colors"^[1]. The effect of such color accents is that individual components of the mucosa, such as the surface pattern or vascular structures of the mucous membranes can be depicted more clearly^[2]. The different color spectrums are produced either by modulating the incoming light with filters (NBI technique), or by software-based processing (so-called post-processing) of the reflected light (FICE, *i*-scan technique

Table 1 High definition *vs* standard colonoscopy for the detection of colorectal adenomas

Ref.	Study design, study objective	Wide angle	No. of pts.	Adenoma detection rate	P value	Absolute increase	Relative increase
East <i>et al</i> ^[30]	Cohort	No	130	65	0.20	11%	18%
Pellisé <i>et al</i> ^[77]	Randomized	Yes	620	26	0.85	1%	4%
Burke <i>et al</i> ^[78]	Cohort	Yes	852	23	0.36		13%
Tribonias <i>et al</i> ^[79]	Randomized	Yes	390	54	0.16	8%	16%
Buchner <i>et al</i> ^[3]	Cohort	Yes	2430	27	0.01	4.2%	17%
Hoffman <i>et al</i> ^[4]	Randomized	No	220	38	0.001	25%	192%

Table 2 Vital stains in endoscopy

Stain	What is stained	Current use
Vital stains		
Methylene blue	Small/large intestinal cells	Chronic ulcerative colitis Gastric intestinal metaplasia and early cancer gastric cancer Colon polyps/neoplasms
Lugol's iodine	Normal glycogen containing squamous cells	Oesophageal squamous cell cancer and dysplasia
Cresyl violet	Small and large intestine crypts Oesophagus and gastric mucosa	Colonic polyps/neoplasms Barrett's esophagus Early gastric cancers
Contrast stains		
Indigo carmine	Cells are not stained, appearances caused by contrast pooling	Chronic ulcerative colitis Gastric intestinal metaplasia and early cancer gastric cancer Colon polyps/neoplasms
Acetic acid	Reversible interaction between the acetic acid and the cell structures	Barrett's esophagus

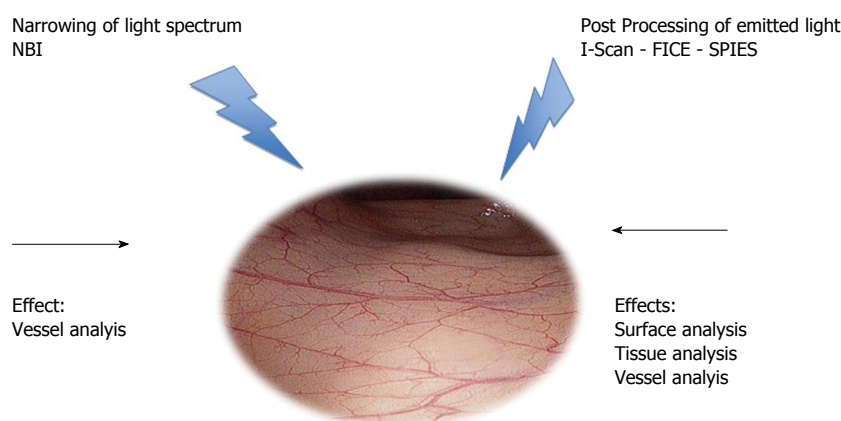


Figure 1 Digital chromoendoscopy. Digital chromoendoscopy can be achieved by simply pressing a button on the endoscope. NBI focuses on vessel architecture by narrowing the light spectrum which is emitted to the mucosa. Fujinon Intelligent Color Enhancement System, *i*-scan and STORZ Professional Image Enhancement System are technologies, which use the reflected light for post-processing light filtering which is used to obtain different effects (like surface, tissue and vessel enhancement). (mod. advanced imaging in endoscopy 2009).

or SPIES)^[1,2] (Figure 1). Thus, modern filter technology is replacing, to an increasing extent, the more time-consuming procedure of chromoendoscopy. An increasing body of data indicates that the efficacy of virtual chromoendoscopy is equivalent to that of intravital staining (with the exception of ulcerative colitis) in the upper and the lower gastrointestinal tract.

NBI

NBI (Olympus, Japan) is the oldest established method of virtual chromoendoscopy. While conventional white light video endoscopy utilizes the entire visible spectrum

of light (400 to 700 nm) to produce an image from the complementary colors red, green and blue, narrow-band imaging (NBI, Olympus, Japan) is based on an integrated filter system that narrows the spectrum of complementary colors and thus accentuates the blue light spectrum. In contrast to red light, the light waves of the blue and green spectrum do not penetrate the deeper layers of tissue. Instead, they are absorbed by blood vessels at the level of the mucous membranes and thus provide clear contrast enhancement of the architecture of mucosal vessels^[26]. Contrary to expectations, however, the first large multicenter studies showed no significant improvement in detection rates of colorectal neoplasias on com-

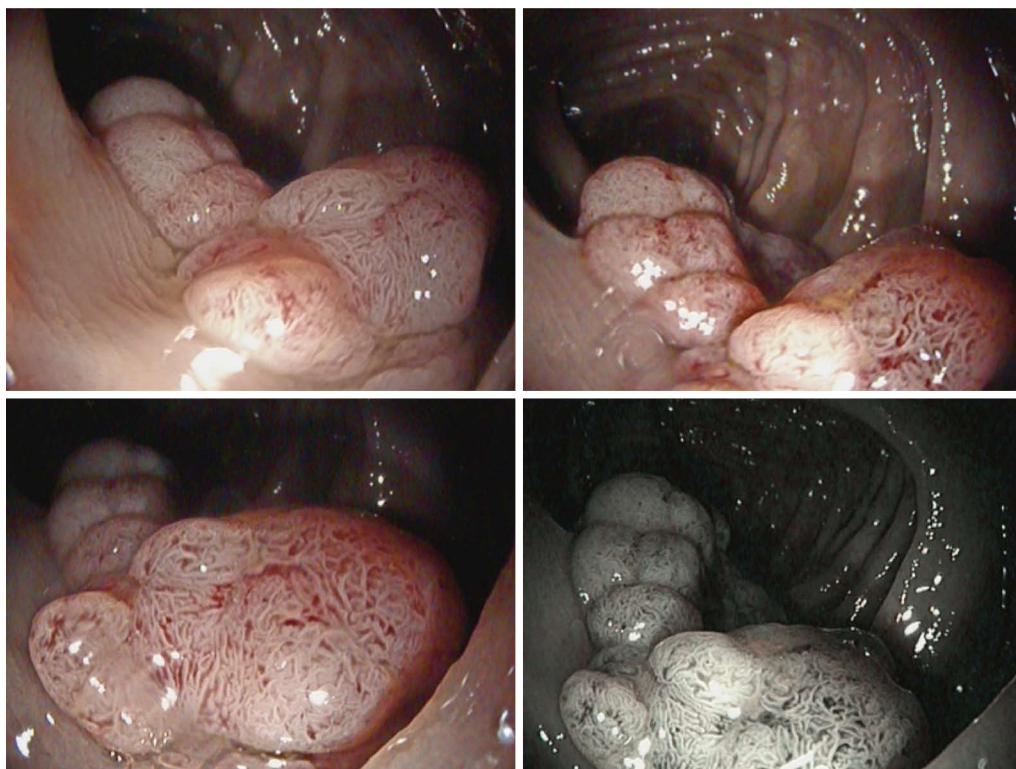


Figure 2 Virtual chromoendoscopy using STORZ Professional Image Enhancement System of colorectal lesions.

parison of high-resolution colonoscopy with and without NBI^[27-29].

East *et al*^[30] attributed the low detection rates to the poor illumination of the endoscopic image under NBI compared to conventional endoscopy. In a further recent prospective investigation, the authors attribute their high detection rate of adenomas (WL 58.3% and NBI 57.3%) to the excellent resolution of high-definition endoscopy and not to NBI but showed, in contrast to other studies, NBI to be superior in the detection of flat adenomas (21.4% *vs* 9.3%, $P = 0.019$)^[31]. Analogous to chromoendoscopy, after expiry of the corresponding learning curve NBI may be utilized with great benefit for prediction of the malignant or benign nature of lesions by way of neoplastic and non-neoplastic lesions. In the upper gastrointestinal tract, the combination of high-resolution endoscopy and NBI imaging permits better diagnostic investigation of Barrett's esophagus. According to a new classification provided by Singh *et al*^[32], mucosal forms may be graded into four types on the basis of their vascular and epithelial structures. Thus, epithelium of the cardia, Barrett's epithelium, and Barrett-associated neoplasia can be distinguished from each other with a high degree of predictive accuracy (positive predictive value: 100%, 88% and 81%). Similar data were reported in several studies performed by Jacques Bergmann's group in Amsterdam^[33-36]. However, analogous to the colon, a decisive improvement in the diagnostic investigation of neoplasias in Barrett's esophagus appears to be achieved mainly by high-resolution endoscopy^[37].

ISCAN, FICE AND SPIES

The filters *i*-scan (Pentax, Europe), SPIES (Karl Storz, Europe) and FICE (Fujinon, Europe) are based on processor-integrated software applications that alter the wavelength ranges of reflected light and thus, in contrast to NBI technology, offer a number of filter options^[2]. In addition to depicting vessels, portions of tissue and surface structures can be visualized in a selective and accentuated manner. *I*-scan technology is based on an integrated software tool that enhances the surface with the aid of the function of "surface enhancement" and, by additionally switching on specific color filters, permits virtual chromoendoscopy to be performed. Initial published studies have confirmed the efficacy of this procedure. Thus, reflux lesions in the upper gastrointestinal tract (UGI) could be diagnosed more accurately by the use of surface enhancement^[38]. In the lower gastrointestinal tract (LGI) it was found that the *i*-scan function is equivalent to chromoendoscopy for the diagnosis of neoplastic lesions in respect of detection rates and characterization. A recently published study showed a significant enhancement of detection rates, particularly those of flat adenomas, by the use of surface enhancement (SE mode) in combination with high-resolution endoscopy^[4,39]. FICE (Fujinon Intelligent Color Enhancement System) and SPIES (STORZ Professional Image Enhancement System) are other types of computer-assisted virtual chromoendoscopy (Figure 2). In both prospective studies on FICE, the authors Chung and Pohl achieved excel-

lent characterization of lesions with the aid of FICE, although a significant advantage in terms of detection rates of adenomas was not registered in either study^[40,41].

Colon capsule endoscopy

A variety of media campaigns and other initiatives have surprisingly led to only a small impact to promote screening colonoscopy^[42]. The reasons for the limited take-up of CRC screening, especially of colonoscopy, are diverse. Apart from general doubts and fears, factors such as perception of colonoscopy as painful and unpleasant may have contributed to the lack of uptake.

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^[43,44]. PillCam colon-capsule provides a screening solution, which is minimally invasive, safe, does not require sedation. It is well accepted by patients, although still requiring thorough bowel cleaning and is mainly recommended to people who have so far denied CRC screening programs^[44].

It is an easy to perform examination with an excellent negative predictive value for application in screening purposes under routine conditions. However, diagnostic accuracy for relevant size polyps (*i.e.*, sensitivity) is low. First studies have been shown to be about 65%-75% accurate for adenoma detection in the large bowel when compared with colonoscopy^[45-49]. But 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 colon capsule as the primary choice. Thus, the colon capsule has to be paid by the patient, which also hindered broad acceptance.

AUTOFLUORESCENCE AND SPECTROSCOPY

Autofluorescence endoscopy is another advancement in endoscopy, which is playing an increasingly significant role in the early detection of dysplasias. The principle of fluorescence diagnosis is based on the fact that light of a specific wavelength (approximately 400-500 nm) is not merely absorbed and reflected in tissue, but also causes fluorescence produced by auto fluorophores or exogenously introduces fluorophores [*e.g.*, 5-aminolevulinic acid (5-ALA)]^[50,51]. A variety of pathological processes such as inflammation, ischemia, and adysplasia demonstrate different fluorescence behavior compared to normal tissue. Therefore, this technology is also known as red flag technology. However, a disadvantage of the method is the fact that autofluorescence is not specific for neoplasia and is therefore associated with a high rate of false positive diagnoses. To enhance the specificity of this method, it is usually combined with HD endoscopy and NBI for characterization of the detected lesions; this is known as endoscopic trimodal imaging^[52-54]. In initial

studies on the upper and lower gastrointestinal tract, autofluorescence was tested successfully in patients with Barrett's esophagus and ulcerative colitis^[55]. We will have to wait and see whether the results of further studies will help to establish this promising method.

Field carcinogenesis is another highly interesting development. We know that certain factors even predispose mucous membranes outside the actual neoplasia for the development of neoplasia. This fact is utilized in field carcinogenesis. By measuring suitably filtered elastic light dispersion, gradients in blood supply and oxygen depletion, culminating in lesions, could be measured in the colon. In the future rapid probe investigation in the rectum might enable the investigator to predict lesions at a greater distance^[56].

Endomicroscopy

Endomicroscopy is the first endoscopic procedure that, in addition to the analysis of surface structure, permits microscopic analysis of cellular structures of the mucous membranes *in vivo*^[57,58]. The major difference compared to all other techniques is that the benign or malignant nature of a lesion cannot be predicted, but can be determined immediately *in vivo* by microscopic investigation. Confocal laser endoscopy (endomicroscopy) is based on argon laser with a wavelength of 488 nm (blue laser light), so that as many as 1012×1012 pixels per endomicroscopic image can be analyzed and evaluated after application of a fluorescent dye (usually fluorescein) by the use of a miniaturized scanner in the endoscope, or by the use of a forward deployed probe. While the first publications established the application and feasibility of this approach in patients, a number of studies have been performed since 2004 on the upper and lower gastrointestinal tract. All of these show that- assisted by simple classification systems- the endoscopist is able to perform microscopic tissue diagnosis on site^[57-60] (Figure 3). Thus, confocal endomicroscopy is currently a well established method and is frequently used in conjunction with chromoendoscopy to first detect suspicious lesions and then analyze them exactly by endomicroscopy. This does not by any means replace pathological investigation. Rather, it permits very reliable prediction of relevant findings by endomicroscopy during the investigation itself so that classical biopsies of the mucous membranes can be minimized and only targeted biopsy specimens (so-called smart biopsies) can be taken^[22]. In a large randomized study in patients with ulcerative colitis of long duration we were able to show that the number of biopsies could be reduced by a factor of ten while the diagnosis of colitis-associated dysplasias was increased fourfold. Investigations on Barrett's esophagus confirmed the role of endomicroscopy in immediate resection after *in vivo* diagnosis of a neoplasia; the evaluation of resection margins was also tested successfully^[61,62]. Furthermore, endomicroscopy offers the option of visualizing physiological as well as pathophysiological processes in human beings during endoscopy. The most striking example of this approach is the identification of cellular desquama-

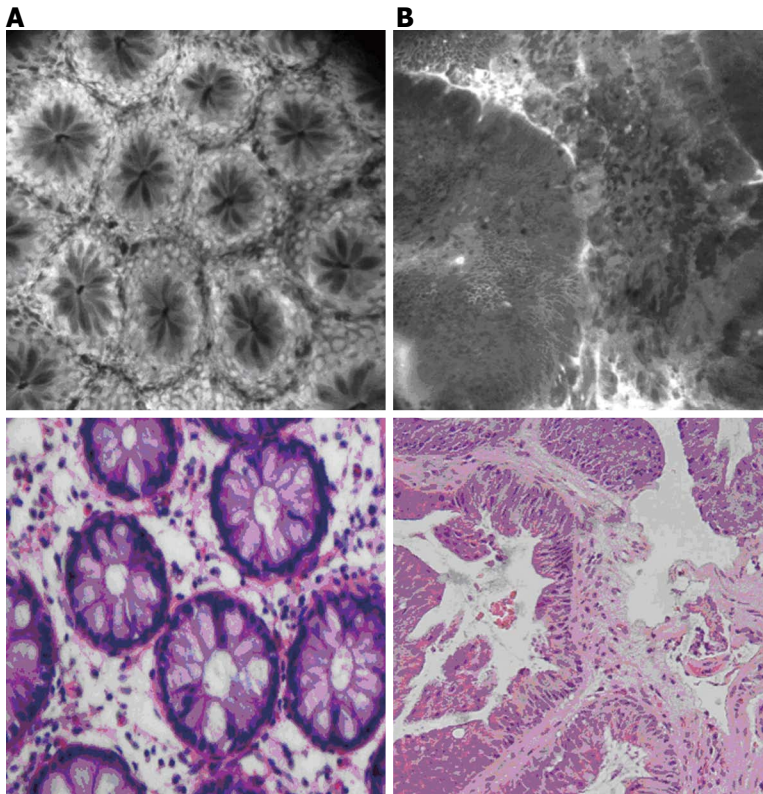


Figure 3 Confocal Endomicroscopy in normal colonic epithelium (A) and of a colonic dysplasia (B).

tion in the bowel, which is initially a manifestation of physiological regeneration. However, in patients with Crohn's disease and ulcerative colitis there was an increase in cell desquamation with the effect of subsequent closure of the gaps thus created^[63]. The development of endomicroscopy is a prerequisite for molecular imaging because, as an *in vivo* procedure it offers the option of low-artifact observation of cellular processes in metabolism, which could markedly enhance our understanding of pathophysiology^[64,65]. Thus, even the interaction of antibodies or peptides with the corresponding receptors can be observed live, which may be of fundamental significance in planning treatment with biologic agents^[66,67]. It is still not possible to use molecular imaging in clinical routine, but preliminary human studies as well as animal experiments have demonstrated the new optic possibilities it offers in endoscopy.

MOLECULAR IMAGING

Molecular imaging is one of the major bears of hope in the field of cancer research and early detection because it renders pathological changes visible at the cellular level^[66]. The optic form of molecular imaging, which provides colored views of suspicious areas on the endoscopy image, can already be used *in vivo* for various types of tumors^[66-70]. By the use of molecular probes usually applied exogenously, one can visualize specific surface molecules or metabolic processes that occur selectively in the target tissue. Thus, colorectal carcinomas could be stained in targeted fashion at the molecular level by marking antibodies to epitopes like the epidermal growth factor

receptor (EGFR) or the vascular endothelial growth factor (VEGF); this was achieved in mouse models as well as in human tissue^[66,69,70]. The advantage of antibodies is their highly specific binding to their target structure, which causes marked contrast between (stained) diseased and (non-stained) healthy tissue. Besides, in disease the biological function of the target structure is usually well established and partly even a component of current therapy protocols, such those for cetuximab or panitumumab (against EGFR) or bevacizumab (against VEGF). Molecular imaging requires special endoscopes that either permit the detection of lesions on the overview image or microscopic characterization of molecular processes during endoscopy. As a result, the use of molecular imaging for endoscopy has not been established in large patient populations, but is very likely to fundamentally influence future clinical algorithms and has already brought about a significant advancement in clinical and basic research by enhancing our comprehension of gastrointestinal diseases.

TECHNOLOGIES ON THE HORIZON

An apparently leading cause of missed polyps during colonoscopy is attributed to polyps that are located behind haustral folds in the colon, and are therefore hidden from the 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^[71]. A 6185 patient study by Westwood reported a miss-rate of 12.2% in the cap-assisted colonoscopy

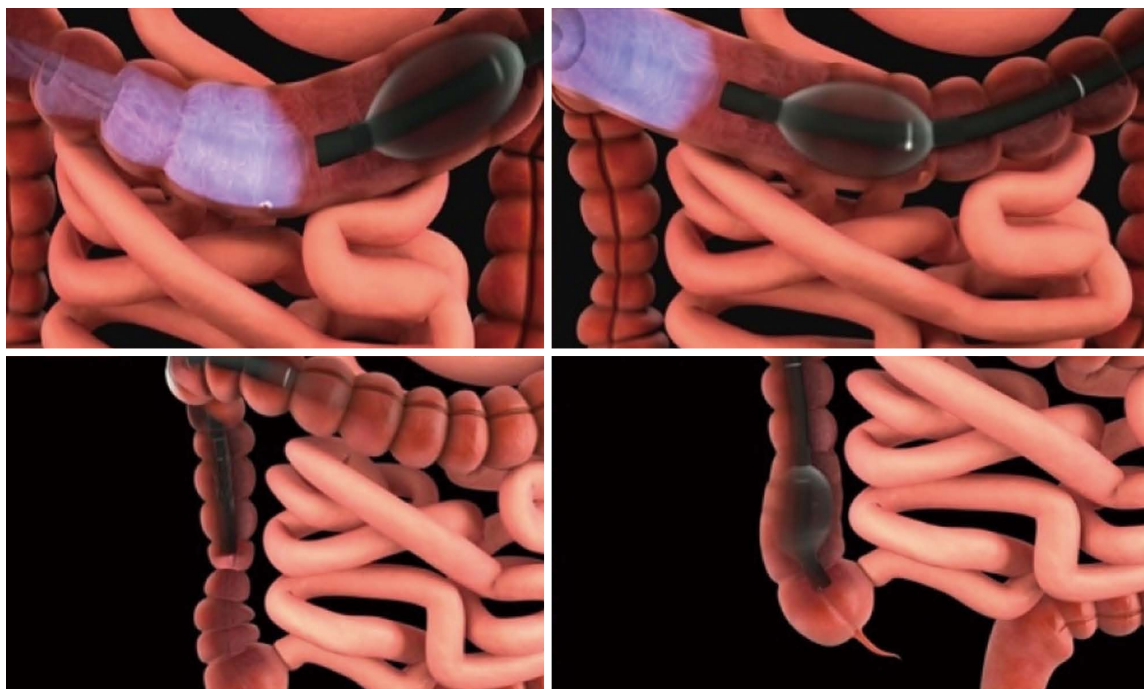


Figure 4 GEye balloon colonoscopy with inflated balloon at the distal tip of the colonoscope the balloon is inflated to straight intestinal folds in the colon.

group *vs* 28.6% miss rate in the standard colonoscopy group, implying a positive effect of cap employment on polyp detection rate^[71]. In contrast, another study performed by Tee in 400 subjects, reported that there was no significant polyp detection rate difference detection standard colonoscopy and cap-assisted colonoscopy (31.3% *vs* 32.8%, respectively)^[72]. Recently, a retro-viewing device (Third Eye Retroscope, Avantis Medical, Sunnyvale, CA) was introduced for use during colonoscopy with standard endoscopes and was analyzed in a single randomized controlled trial (same-day tandem examinations)^[73]. This technique is aimed to allow inspection of the proximal surface of haustral folds, which is 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. Using the retrograde-viewing device was associated with an increase in the total number of adenomas detected of 23% 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 detecting 10% more adenomas compared to standard colonoscopy^[74]. But 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 SC compared with colonoscopy using 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 is a balloon-colonoscopy (NaviAid™ G-EYE, Smart Medical Systems, Israel), comprising a standard colonoscope having a re-processable, permanently integrated balloon at its distal tip. The balloon pressure is controlled through a unique inflation system providing pre-determined, user-selectable, anchoring and intermediate (low) pressure levels (Figure 4). First results from a prospective multicenter back to back study included 126 patients. The G-Eye balloon-colonoscopy detected 23 additional polyps, that means a promising 115% additional adenoma detection rate. Balloon-colonoscopy's additional detection rate ratio, calculated as the ratio between balloon-colonoscopy 2nd pass additional detection and balloon colonoscopy 1st pass miss-rate, is 25.5 (115/4.51)^[75]. The results from this first multicenter study are very promising and further confirming studies are ongoing. Another reason for a high adenoma miss rate is discussed due to inadequate visualization of the proximal aspect of colonic folds and flexures. Full spectrum endoscopy (FUSE, EndoChoice, Alpharetta, GA, United States) utilizes unique imaging technology, which allows the endoscopist to view 330 degrees while maintaining identical standard colonoscope technical features (Figure 5). The results for this new technique were a 32.9% incremental polyp detection rate (per patient analysis) and a 39/49 (79.6%) incremental polyp detection rate (per polyp analysis) using this new FUSE colonoscope. Furthermore on subsequent FUSE colonoscopy, there were an additional 15/88 (17.1%) subjects who had at least one adenoma detected, yielding an additional 21 adenomas. This is a incremental 17.1% adenoma detection rate (per patient analysis) and a 21/28 (75.0%) incremental adenoma detection rate (per adenoma analysis) using FUSE colonoscopy^[76]. But as with all new technology they are

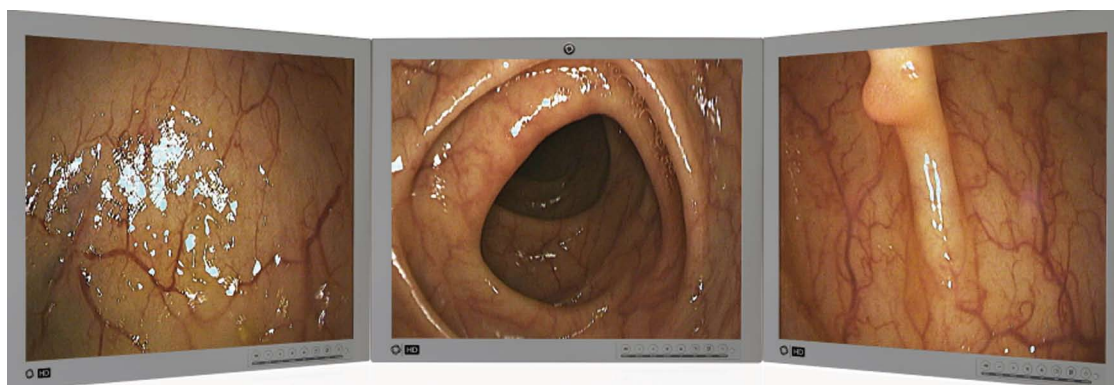


Figure 5 Full spectrum endoscopy colonoscopy utilizes unique imaging technology, which allows the endoscopist to view 330 degrees while maintaining identical standard colonoscope technical features. Property of full spectrum endoscopy, EndoChoice, Alpharetta, GA, United States.

often accompanied by initial enthusiasm, but have to be proved in a more clinical setting and practice.

CONCLUSION

New techniques of diagnostic endoscopy are being developed with rapid speed. To achieve early identification of precancerous lesions and then initiate targeted and definitive endoscopic therapy immediately, the modern endoscopist must keep abreast with new technologies. In addition to more frequent detection of neoplasias, the latter should also be characterized in greater detail on site in order to better estimate the extent of any required endoscopic intervention. In this endeavor the endoscopist is supported by common filter technologies. So-called virtual chromoendoscopy is in the process of replacing classical chromoendoscopy because it is equally effective but requires less time. Endomicroscopy signifies a crucial advancement of gastrointestinal endoscopy in the last few decades. Endomicroscopy permits, for the first time, *in vivo* investigation of mucous membranes at the cellular level. In addition to the fact that simultaneous histological investigation can be performed along with endoscopy, some diseases can now be diagnosed reliably for the first time, and physiological as well as pathophysiological processes can be observed. This development has caused molecular imaging to gain center stage in endoscopy. Apart from the fact that it has simplified better detection of suspicious lesions, oncological therapy approaches can be planned and understood better. Although gastrointestinal endoscopy has become much more complex now, the optic details provided by the new technologies will contribute significantly to improving the efficiency of the diagnosis and treatment of gastrointestinal endoscopy.

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P- Reviewer: Bugaj AM, Koulaouzidis A **S- Editor:** Ji FF

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