Chromocolonoscopy detects more adenomas than white light colonoscopy or narrow band imaging colonoscopy in hereditary nonpolyposis colorectal cancer screening

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Background and study aims: Individuals carrying germline mutations in one of the genes responsible for hereditary nonpolyposis colon cancer (HNPCC) have a lifetime risk of up to 80% of developing colorectal cancer. As there is evidence for a higher incidence of flat adenomatous precursors and because an accelerated adenoma–carcinoma sequence has been postulated for these patients, early detection of these lesions is essential. It was the aim of the present study to assess the detection rate of polypoid lesions by comparing chromocolonoscopy with standard white light colonoscopy and narrow-band imaging (NBI) colonoscopy.

Patients and methods: 109 patients were included (98 with a functionally relevant mutation in a mismatch repair gene, 11 fulfilling the strict Amsterdam criteria). In 47 patients, standard colonoscopy was followed by chromocolonoscopy with indigo carmine. In 62 patients, NBI was performed first followed by chromocolonoscopy.

Results: A total of 128 hyperplastic and 52 adenomatous lesions were detected. In the first series, 0.5 lesions/patient were identified by standard colonoscopy and 1.5 lesions/patient by chromocolonoscopy ($P < 0.001$). In the second series, 0.7 lesions/patient were detected by NBI colonoscopy and 1.8 lesions/patient by chromocolonoscopy ($P = 0.01$). At least one adenoma was detected in 15% of patients by both standard and NBI colonoscopy compared with 28% of patients by chromocolonoscopy.

Conclusion: According to this study, chromocolonoscopy detects significantly more hyperplastic and, in particular, adenomatous lesions than standard white light colonoscopy or NBI.

Introduction

Hereditary nonpolyposis colorectal cancer (HNPCC, Lynch syndrome) – the most frequent monogenic cancer predisposition syndrome of the gastrointestinal tract [1] – is due to germline mutations in one of at least four mismatch repair genes. In carriers of a functionally relevant mutation, the lifetime risk of colorectal cancer (CRC) is 80%. The adenoma–carcinoma sequence developed in familial adenomatous polyposis and sporadic CRC [2] is also accepted in principle for HNPCC. As polypectomy is able to interrupt the transformation of benign to malignant lesions, current endoscopic guidelines, albeit controversial, suggest that each person at risk for HNPCC should undergo total colonoscopy every 12–24 months, beginning at the age of 25 years or 5 years younger than the age at which CRC first affected a family member [3–8].

Generally, up to 30% of diminutive adenomatous and nonadenomatous lesions may be missed by conventional colonoscopy[9–13]. This fact could be of particular relevance for patients with HNPCC, as a higher frequency of flat adenomatous lesions and an accelerated adenoma-carcinoma sequence have been reported in this patient group [14–17]. Furthermore, there is evidence that hyperplastic polyps may also be precursor lesions leading to cancer [18]. Consequently, an increased interval CRC risk after apparently normal colonoscopy has been observed in patients with HNPCC [19].

Indigo carmine or methylene blue as contrast agents are able to enhance the detection of mucosal lesions in the colon (chromocolonoscopy) that are not identified by routine white light colonoscopy, partly because they facilitate visualization of the margins of the lesions [20–26]. Carriers of a mutation in a mismatch repair gene who require regular surveillance colonoscopy are particularly suited to compare the efficiency of chromocolonoscopy with conventional standard white light colonoscopy. Recent studies have reported a higher detection rate of significant neoplastic lesions in patients with HNPCC by using

pancolonic chromocolonoscopy [27,28]. In these studies, at least half of the patients had not undergone previous screening colonoscopy so that superiority of chromocolonoscopy compared with standard white light colonoscopy, at least in the respective patients, cannot be regarded as proven.

A modern alternative to standard colonoscopy and even chromocolonoscopy may be narrow band imaging (NBI) colonoscopy. This novel noninvasive optical technique enhances the visualization of surface structures and vascular patterns within the mucosal layer [29]. NBI may be applied to differentiate between neoplastic and non-neoplastic gastrointestinal lesions [30,31]. Machida et al. demonstrated that NBI is equivalent to magnifying endoscopy in distinguishing colonic neoplasm from non-neoplastic lesions [32–34]. Furthermore, NBI has been described as "electronic chromoendoscopy" [35], which might be a promising tool for the differentiation of neoplastic from non-neoplastic colorectal polyps in vivo without the necessity of using dye [36].

Our aim was to compare the efficiency of chromocolonoscopy with both standard white light and NBI colonoscopy in the detection of colorectal lesions in patients with HNPCC enrolled in a strict colonoscopic surveillance program.

Patients and methods

A total of 114 patients were included in the study, who either carried a functionally relevant mutation in a mismatch repair gene (*MSH2*, *MLH1*, or *MSH6*) or who fulfilled the strict Amsterdam criteria for HNPCC. All patients who showed up for a surveillance colonoscopy were enrolled in the study. Patients were excluded if the bowel preparation was inadequate (**Fig 1**), if they had a known colonic neoplasia or inflammation, if they were in poor general condition (more than American Society of Anesthesiologists grade III), or if they were receiving anticoagulant medication.

In 91% (99/109) of patients, at least one standard colonoscopy had been carried out prior to inclusion to our study and 60% (65/109) had undergone surgery for CRC (**Table 1**).

Table 1 Details of previous surgical procedures in study patients.

	Number of patients in the first series n = 25	Number of patients in the second series n = 40
Right hemicolectomy	11	15
Colon transversum resection	1	1
Left hemicolectomy	3	3
Sigmoid resection	1	11
Rectal resection	4	3
Subtotal colectomy	5	6
No information retrievable	0	1

Study design and endoscopic technique

Conventional white light colonoscopy was first performed in 47 patients. A further 62 patients were first examined using NBI. Immediately following this first examination, all patients underwent chromocolonoscopy. Two experienced endoscopists performed all examinations at the Department of Internal Medicine of the University of Bonn. All lesions identified during the first colonoscopy that differed from normal mucosa were localized and documented by an independent observer. During chromocolonoscopy, these lesions were retrieved whenever possible and further lesions if detected were assessed and registered. All of these lesions were biopsied or resected with a snare during chromocolonoscopy. This study design was chosen because it reduces visual limitations for chromocolonoscopy, otherwise, mucosal bleeding or alterations due to polypectomy during the first colonoscopy would have interfered with the evaluation of the respective part of the colon by chromocolonoscopy.

For colonoscopic examinations, the patients were prepared with 4 L of hypertonic polyethylene glycol solution lavage 24 hours prior to the procedure. The quality of the bowel preparation was documented as very good (100% mucosal visualization), good (> 95% mucosal visualization), fair (between 90% and 95%), or poor (< 90% mucosal visualization). Five patients with poor bowel preparation were excluded from the study.

Patients requesting sedation received intravenous midazolam (1–10 mg) or propofol (20–30 mg) prior to intubation of the colonoscope. Antispasmodic medication (butylscopolamine) was given at the discretion of the endoscopist during the procedure. Further doses of intravenous medication were given as clinically required.

Standard white light colonoscopy followed by chromocolonoscopy

A total of 47 patients underwent back-to-back colonoscopic examinations carried out by the same endoscopist. One observer attended all examinations and documented the endoscopist's findings. Standard colonoscopy was performed using the Olympus colonoscope CF240Z, followed by chromocolonoscopy with 0.08% indigo carmine. During all examinations, a colonoscope with standard resolution was used. Fecal fluid residue was aspirated on the first insertion to ensure optimal mucosal views.

Following initial cecal or neoterminal ileal intubation, inspection of the entire colonic mucosa was performed on withdrawal without the use of dye spray. All suspicious lesions were documented by describing the anatomical site, distance to the anal margin, appearance, and size as measured with a biopsy forceps.

When the tip of the colonoscope had been withdrawn to the anal margin, the colonoscope was reinserted to the cecal pole for chromocolonoscopy. On the second withdrawal, the lumen was sprayed in a segmental fashion with indigo carmine delivered via a dye spray catheter (Olympus PW-5V1). All lesions were documented as described above. Insertion and withdrawal times were documented. Withdrawal was measured as soon as examination of the cecum began and was stopped when the scope was withdrawn from the anus. It was also stopped whenever a polyp was identified until the polyp had been retrieved and removed and the examination re-started, as well as for any biopsy specimens that were taken. Thus, the measured withdrawal time reflects all time spent searching for polyps during withdrawal.

Narrow band imaging colonoscopy followed by chromocolonoscopy

The next 62 patients were examined by NBI colonoscopy with high-definition resolution (Olympus Exera II) and high-definition-ready screen, followed by chromocolonoscopy. For chromocolonoscopy, a colonoscope with standard resolution was always

used. One observer attended all examinations. Fecal fluid residue was aspirated on the first insertion to ensure optimal mucosal views.

Following initial cecal or neoterminal ileal intubation, inspection of the entire colonic mucosa was performed on withdrawal without the use of dye spray. For NBI colonoscopy, the colonoscope was switched to NBI mode on withdrawal. In order to assess suspicious lesions the endopscopist was allowed to switch back to conventional imaging. Intubation was performed in white-light mode. All suspicious lesions were documented by describing the anatomical site, distance to the anal margin, appearance, and size as measured with a biopsy forceps.

When the tip of the colonoscope had been withdrawn to the anal margin, the colonoscope was reinserted to the cecal pole ready for the chromocolonoscopy examination, as described above.

Endoscopic classification of lesions and removal technique

All lesions identified during chromocolonoscopy were removed completely by endoscopic biopsy, snare polypectomy, or endoscopic mucosal resection. In particular, subtle mucosal architectural changes, such as vascular net disruption, discrete mucosal unevenness, focal pallor or erythema, were documented. Flat lesions were defined as mucosal alteration with a flat or slightly rounded surface with a height of less than half the diameter of the lesion with no distinct stalk or pedicle [37]. The lesion diameter was estimated using a standard fully opened biopsy forceps (5 mm) with the height estimated by placing the closed forceps tip (2.1 mm) adjacent to the lesion margin. Pedunculated lesions were defined as those with a distinct pedicle, and sessile lesions as raised lesions with no distinct stalk or pedicle where the diameter did not exceed twice the height [37,38].

Histopathologic analysis

A designated expert gastrointestinal pathologist examined all specimens. Tissue was immediately fixed in 10% buffered formalin solution and subsequently stained with hematoxylin and eosin. Adenomas were classified according to modified Vienna criteria as either low-grade or high-grade intraepithelial neoplasia [39]. Invasive neoplasia was defined as neoplastic cellular proliferation extending into the submucosal layer 3 or to the muscularis propria [39].

Statistical analysis

Statistical differences were analyzed by the paired Student's *t*-test, McNemar test or the Wilcoxon signed rank test as appropriate. A two-sided *P*-value of less than 0.05 was considered statistically significant. Calculations were made using SPSS 14.0 (SPSS, Inc., Chicago, Ilinois, USA).

The main outcome parameter was the adenoma detection rate. From one trial of chromoendoscopy in HNPCC [28], 9% of all patients had at least one adenoma detected before chromoendoscopy. This also determined the case number calculation, assuming an adenoma rate of 9% and an increase to 33% with chromoendoscopy (80% power, significance level 0.05). It was calculated that 45 patients needed to be enrolled.

For the second series we expected a slightly higher adenoma detection rate of 12% with NBI and an increase to 33% with chromoendoscopy. For a power (1-β) of 80% with a significance level (α) of 5%, at least 61 patients needed to be recruited. At the start of the study 2005 there were no data available on the adenoma detection rate using NBI.

Ethics

Full ethical approval for the study was granted from the Ethics Committee of the Medical Faculty, University of Bonn (54/00). Signed informed consent was obtained from every patient prior to the procedure.

Results

From June 2005 to July 2007, 114 patients with HNPCC were included in the study. Patient progression through the study is shown in **Fig. 1**.

Five patients were excluded due to inadequate bowel preparation. Hence, a total of 109 patients were examined. Cecal intubation or intubation to the neoterminal ileum in patients with a previous right hemicolectomy was achieved in all 109 patients.

In 98 of the 109 patients, functionally relevant mutations in a mismatch repair gene (*MSH2*, *MLH1*, or *MSH6*) had been identified. The remaining 11 patients fulfilled the strict Amsterdam criteria for HNPCC (**Table 2**).

Standard white light colonoscopy followed by chromocolonoscopy

Overall, 47 patients with HNPCC were first screened with standard colonoscopy, which was then followed by chromocolonosco-

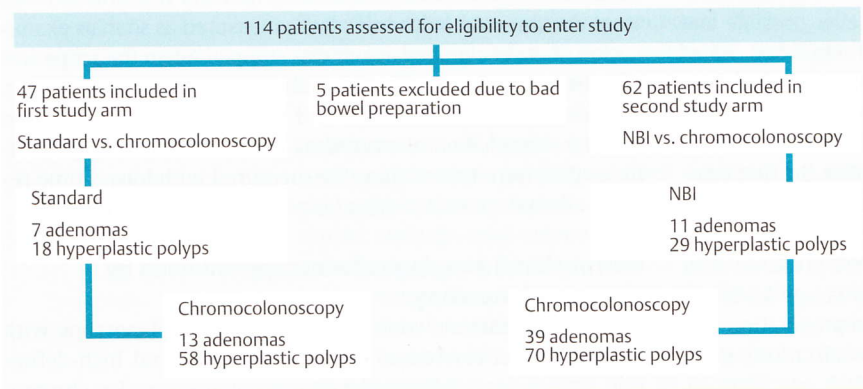

Fig. 1 Patients progression through the study. NBI, narrow band imaging.

Table 2 Summary of patients who were initially examined by either standard white light or narrow band imaging colonoscopy. Both subgroups were subsequently examined by chromocolonoscopy.

	Standard vs. chromo n = 47	NBI vs. chromo n = 62	*P*-value
Age, years	43.1 ± 10.9	46.9 ± 11.3	n. s.
Pathogenic MMR germline mutations, n	42	56	n. s.
Interval of surveillance, months	12.3 ± 7.6	12.1 ± 5.2	n. s.
Preoperated patients, n	25	40	n. s.

MMR, mismatch repair; NBI, narrow band imaging.

py. Of these 47 patients, 42 (89%) were proven carriers of a mutation in a mismatch repair gene and five patients fulfilled the Amsterdam criteria. Mean time interval since the last colonoscopy (n = 41) was 12.3 ± 7.6 months. Mean age of the patients was 43.1 ± 10.9 years.

In the first series of 47 patients, a total of 80 lesions were detected in 47 patients (1.7 lesions/patient) from the two endoscopic examinations. Nine lesions in five patients detected by standard colonoscopy could not be retrieved by chromocolonoscopy. The median size of missed lesions was 2.1 ± 2.4 mm; the median size of all lesions was 2.7 ± 3.1 mm. By standard colonoscopy, 0.5 lesions/patient were identified compared with 1.5 lesions/patient identified by chromocolonoscopy ($P < 0.001$). Overall, 58 hyperplastic lesions (1.2/patient, $P = 0.006$) and 13 adenomas with low-grade dysplasia (0.3/patient, $P = 0.032$) were detected by chromocolonoscopy, compared with 18 hyperplastic lesions (0.4/patient) and seven adenomas with low-grade dysplasia (0.1/patient) detected by standard colonoscopy alone (**Table 3**). In 18/47 patients, more hyperplastic polyps were detected by chromocolonoscopy ($P < 0.001$); no change was found in 29/47 patients. Furthermore, more adenomas were found in 5/47 patients (n. s.). No change concerning adenoma detection was noted in 42/47 patients.

Four flat adenomas were found by standard colonoscopy and eight by the subsequent chromocolonoscopy examination ($P = 0.04$). No lesion with high-grade dysplasia or carcinoma was observed. Clinical examples are shown in **Fig. 2–4**.

Intubation and extubation times are shown in **Table 4**.

Narrow band imaging colonoscopy followed by chromocolonoscopy

In the second series of the study, 62 patients were first examined by NBI colonoscopy, followed by chromocolonoscopy. Of these 62 patients, 56 (90%) were proven carriers of a mutation in a mismatch repair gene, and six patients fulfilled the Amsterdam criteria. Mean time interval since the last colonoscopy (n = 59) was 12.1 ± 5.2 months. Mean age of the patients was 46.9 ± 11.3 years.

A total of 124 lesions were detected in the 62 patients (2.0 lesions/patient); 14 lesions in 11 patients detected by NBI colonoscopy could not be retrieved by chromocolonoscopy. The median size of missed lesions was 1.8 ± 0.3 mm; the median size of all lesions was 3.8 ± 5.2 mm. By NBI colonoscopy, 0.7 lesions/patient were detected compared with 1.8 lesions/patient identified by chromocolonoscopy ($P = 0.01$). Overall, 70 hyperplastic lesions (1.1/patient, $P = 0.001$) and 38 adenomas with low-grade dysplasia (0.6/patient, $P = 0.001$) were detected by chromocolonoscopy compared with 29 hyperplastic lesions (0.5/patient) and 10 adenomas with low-grade dysplasia (0.2/patient) detected by NBI colonoscopy. In 20/62 patients, more hyperplastic polyps were detected by chromocolonoscopy ($P < 0.001$); no difference was found in 42/62 patients. Furthermore, more adenomas were detected in 18/62 patients ($P < 0.001$). The adenoma detection rate remained similar in both examinations in 44/62 patients.

Ten flat adenomas were found by NBI colonoscopy, but 31 were detected during the subsequent chromocolonoscopy examination ($P = 0.007$). One adenoma with high-grade dysplasia and one T1 carcinoma were found by both endoscopic techniques (**Table 3**).

Intubation and extubation times are shown in **Table 4**.

At least one adenoma was found in seven patients by standard colonoscopy (15%) and in nine patients by NBI (15%). When using chromocolonoscopy, at least one adenoma was detected in 31 of the patients (28%).

Distribution of adenomas in the patients who had not undergone surgery

In the subgroup of patients who had not previously undergone surgery (n = 44), 56% of the adenomas were detected in the proximal colon (**Fig. 5a** and **b**).

In the first series, 7/9 adenomas were detected in the proximal colon. In the second series, 2/7 adenomas were detected in the proximal colon.

Table 3 Detection rate of the different lesions by the three endoscopic methods.

	First series n = 47			Second series n = 62		
	Standard	Chromo	*P*-value	NBI	Chromo	*P*-value
Number of hyperplastic lesions	18*	58	0.006	29†	70	0.001
Total number of adenomas	7	13		11	39	
Morphology of adenomas						
Polypoid	3	5		1	8	
Flat	4	8	0.04	10	31	0.007
Dysplasia of adenomas						
Low grade	7	13	0.032	10	38	0.001
High grade	0	0	n. s.	1	1	n. s.
Number of patients with at least one adenoma	7	9	n. s.	9	22	0.04
Number of carcinomas	0	0	n. s.	1	1	n. s.

*Nine lesions and †14 lesions could not be retrieved by chromocolonoscopy, respectively.

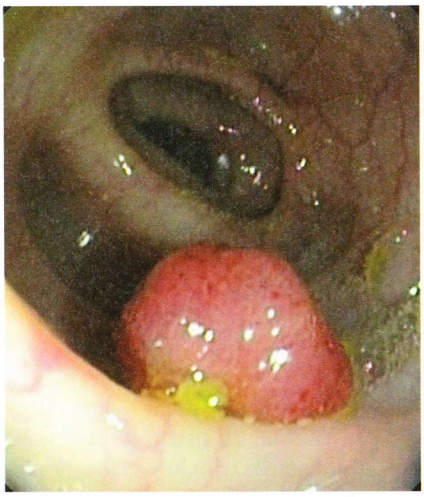

Fig. 2 Small adenoma with low-grade dysplasia detected by conventional colonoscopy.

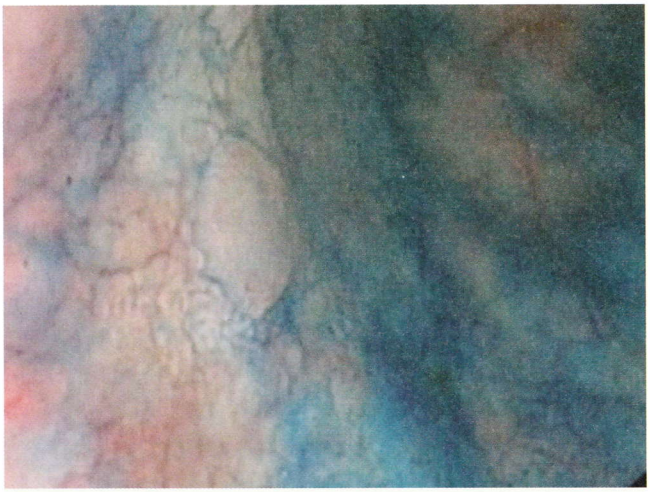

Fig. 3 Small adenoma with low-grade dysplasia detected by chromocolonoscopy.

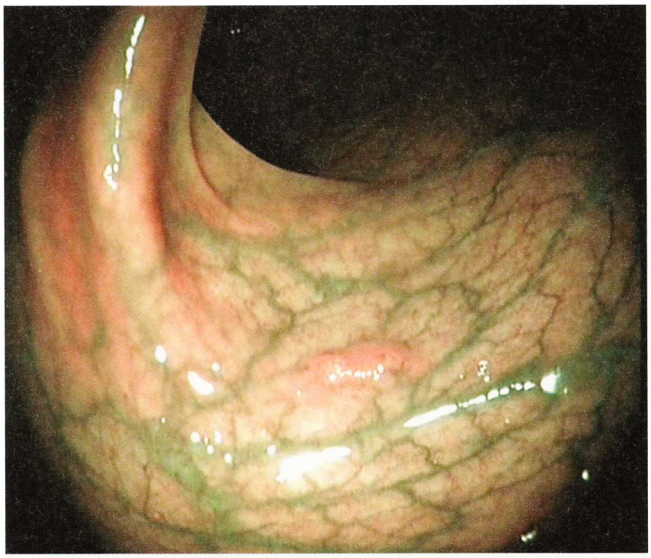

Fig. 4 Small adenoma with low-grade dysplasia detected by narrow band imaging colonoscopy.

Table 4 Intubation and extubation times in minutes.

	Standard vs. chromo n = 47	NBI vs. chromo n = 62	*P*-value
Intubation to cecum	8.4 ± 5.5	9.2 ± 4.9	n. s.
Initial standard/NBI examination to anal margin	7.6 ± 2.5	9.6 ± 4.3	n. s.
Re-intubation to cecum	8.5 ± 7.2	8.2 ± 5.7	n. s.
Second chromocolonoscopy extubation to anal margin	18.0 ± 7.5	16.7 ± 8.9	n. s.

Discussion

To our knowledge, this is the largest comparative endoscopic study in patients at high risk for CRC. The patients included in the examination were either proven carriers of a mutation in a mismatch repair gene or were identified because their family fulfilled the strict Amsterdam criteria for HNPCC. Almost all patients (92 %) had already undergone regular surveillance colonoscopy, most at intervals of 1 year. The results of this comparative study show that for the detection of small polypoid lesions in patients with a high risk of CRC, chromocolonoscopy is superior to both standard and NBI colonoscopy. Two different examination series were planned in order to define the best endoscopic technique in the surveillance of patients with HNPCC. First, chromocolonoscopy was compared with standard white light colonoscopy, which had been done previously with a smaller number of patients [27,28]. Second, the superior method from the first series was compared with the new technique of NBI.

Two previous studies have examined the efficiency of chromocolonoscopy in patients with HNPCC. Lecomte et al. studied 33 consecutive asymptomatic patients from families with HNPCC, but chromocolonoscopy was restricted to the proximal colon. Chromocolonoscopy markedly increased the detection rate of adenomas in the examined part of the colon [28]. Hurlstone et al. showed that among 25 Amsterdam II positive patients – of whom 21 were known mutation carriers – pancolonic chromocolonoscopy significantly improved the total number of adenomatous lesions detected (including flat lesions) compared with conventional colonoscopy with targeted chromoscopic techniques [27]. Unlike our study, chromocolonoscopy was the very first colonoscopy for more than half of the patients. Furthermore, longer intervals of surveillance of 2 – 3 years were reported for patients who had at least one previous endoscopic examination prior to chromocolonoscopy. Consequently, the Hurlstone study is more suited to estimate the overall adenoma prevalence among patients with HNPCC, whereas our study is more suited to assess the role of chromocolonoscopy and NBI in the surveillance setting by current guidelines.

In all, 60 % of the patients in the present study (25 of 47 patients [53 %] in the first series and 40 of 62 patients [65 %] in the second series), had previously undergone surgery for CRC (**Table 1**). In these patients, only a remaining part of the colon could be examined. This applied particularly to patients with a subtotal colectomy. Even in this highly compliant subgroup of patients with HNPCC, chromocolonoscopy was superior to standard white light colonoscopy in the detection of colorectal adenoma.

NBI colonoscopy has been regarded as a less laborious alternative to chromocolonoscopy. East et al. compared NBI with conven-

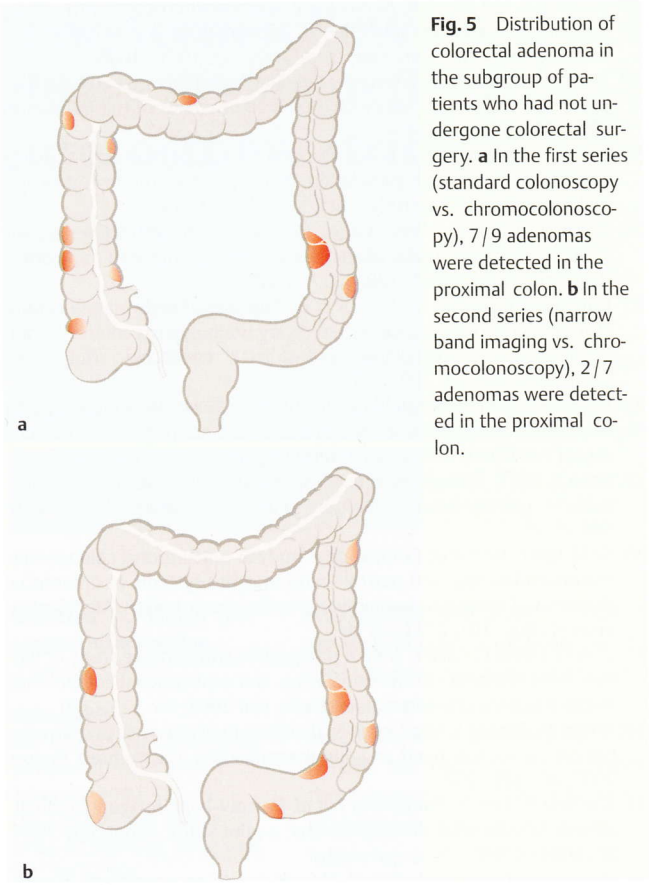

Fig. 5 Distribution of colorectal adenoma in the subgroup of patients who had not undergone colorectal surgery. **a** In the first series (standard colonoscopy vs. chromocolonoscopy), 7/9 adenomas were detected in the proximal colon. **b** In the second series (narrow band imaging vs. chromocolonoscopy), 2/7 adenomas were detected in the proximal colon.

tional colonoscopy in a cohort of patients with HNPCC, and stated that NBI in the proximal colon almost doubled the total number of adenomas detected and increased the proportion of patients with at least one adenoma [35]. By contrast, three previous studies comparing NBI colonoscopy and white light colonoscopy in patients with ulcerative colitis or standard risk failed to find different adenoma detection rates between the two methods [40–43]. Rex [42] and Adler [41] both compared NBI with white light colonoscopy in large randomized controlled trials and found no difference in the adenoma detection rate. The cohort of patients with HNPCC in the study by East et al. only contained 13% of known mutation carriers. By contrast, our cohort contained 90% mutation carriers. In our study the total number of adenomas detected does not differ much from that in the study by East. In this latter study, 54 adenomas were detected in 62 patients whereas in our group of 62 patients in the NBI series, 39 adenomas were detected. Still, one has to keep in mind that the surveillance intervals differed a lot (1 year in our cohort and 2–3 years in the study by East). Furthermore, the study design of East et al. was limited to examination of the proximal colon so that an appreciable number of adenomas or even cancer might have been missed. Goecke et al. showed that in over 20% of all patients with HNPCC, CRC occurs in the distal colon. Therefore, the distal colon must be included in all endoscopic studies involving patients with HNPCC [44]. In the present study, 44% of adenomas were found in the distal colon or rectum.

We also assessed whether NBI colonoscopy was at least as efficient as chromocolonoscopy. Again, a higher detection rate for colorectal adenomas and hyperplastic lesions was found by chromocolonoscopy. Therefore, NBI is less accurate than chromocolonoscopy with respect to detection of relevant colorectal lesions.

We did not employ high-definition scopes while performing standard white light colonoscopy or chromocolonoscopy. The NBI scope was used with high definition. The lack of high-definition scopes is probably not a limitation to this present study because Pellisé et al. [45] observed no difference in adenoma detection when comparing standard definition scopes with high-definition scopes.

As well as adenomatous lesions, we found, like others, a high proportion of hyperplastic lesions in patients with HNPCC. Although there is some evidence that hyperplastic lesions might also be precursors of CRC, the actual relevance remains to be defined [18].

There are some limitations to the present study. Whereas almost all other studies removed detected lesions immediately, we first documented their anatomical site, size, and morphologic appearance and removed them only after chromocolonoscopy. It could not be avoided, therefore, that a small proportion of potential colorectal lesions (23 lesions in 16 patients) that had been detected during the first colonoscopy could not be retrieved by chromocolonoscopy. These failures could either be definitely missed lesions, or lesions found at different insertion lengths of the colonoscope. However, all these lesions were less than 3 mm in size, except for one (6 mm) with an extremely low chance of being adenomatous. Furthermore, we cannot exclude an investigator-dependent bias, because we did not switch the endoscopist in between the two colonoscopic techniques. The fact that one knows that the same region of the colon will be investigated again might influence the result of the first investigation method.

The time to perform a pancolonic chromoendoscopy was 17.0 ± 7.5 minutes, which is comparable to the two previous chromocolonoscopy studies (14–17 minutes). Our time for the NBI examination was approximately 9.7 minutes and therefore 2 minutes longer than the examination using standard colonoscopy. This might reflect the fact, that even minor failings in bowel preparation make comprehensive and meticulous detection difficult when using NBI. Our time analysis shows that chromocolonoscopy is more time consuming than NBI or standard colonoscopy. This might also have an impact on adenoma detection. But the time-consuming element of chromocolonoscopy is mostly dye spraying. This was not excluded in our analyses.

Due to the study design the present study may overestimate the diagnostic value of chromocolonoscopy. Yet, our miss rate of adenomas was approximately 50% for standard and 70% for NBI colonoscopy. This exceeded by far the expected miss rate of about 20% for adenomas [13]. It goes without saying that intraindividual comparison of standard/NBI colonoscopy and chromocolonoscopy where either technique is applied first in a random order is not possible. The best method to evaluate two different techniques is a randomized control trial; this is not possible in a back-to-back setting if the use of dye is necessary.

In conclusion, the present data show that chromocolonoscopy improves the detection rate of significant neoplastic lesions in persons at high risk for colorectal adenomas and cancer compared with standard or NBI colonoscopy in a back-to-back setting. This remains true for patients who have already been under extensive surveillance. The higher adenoma detection rate of chromocolonoscopy should lead to a decrease of interval cancers that might occur in patients with HNPCC, despite the fact that they are undergoing regular endoscopic surveillance [19]. Thus, in the long term, chromocolonoscopy could improve disease-free and overall survival of patients with HNPCC. However, further studies are needed to address this question, preferably in a randomized control trial.

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Competing interests: None

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