The role of endoscopic imaging for an improved diagnosis of colorectal neoplasia
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Citation for published version (APA):
van den Broek, F. J. C. (2010). The role of endoscopic imaging for an improved diagnosis of colorectal neoplasia
CHAPTER 11
Narrow-band imaging versus high definition endoscopy for the diagnosis of neoplasia in ulcerative colitis

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Submitted
ABSTRACT

Background & aims: Controversy exists about which colonoscopic technique is most sensitive for the diagnosis of neoplasia in patients with ulcerative colitis (UC). We compared new-generation narrow-band imaging (NBI) to high-definition endoscopy (HDE) for the detection of neoplasia and evaluated NBI for the differentiation of neoplastic from non-neoplastic mucosa.

Design: Randomized cross-over trial.

Setting: Academic Medical Centre Amsterdam.

Patients: Patients with UC underwent both NBI and HDE colonoscopy in random order with at least 3 weeks between the two procedures which were performed by different endoscopists. Lesions detected during the first examination were left in-situ in order to enable detection during the second examination also.

Interventions: NBI and HDE colonoscopy.

Main outcome measures: Neoplasia detection and diagnostic accuracy of NBI for differentiating neoplastic from non-neoplastic mucosa by using the Kudo classification and vascular pattern intensity (VPI).

Results: Twenty-five patients were randomized to HDE first and 23 to NBI. Of 16 neoplastic lesions, 11 (69%) were detected by HDE and 13 (81%) by NBI (p=0.727). Of 11 patients with neoplasia, 9 (82%) were diagnosed by HDE and 8 (73%) by NBI (p=1.0). The sensitivity, specificity and accuracy of the Kudo classification were 76%, 66% and 67%. Corresponding figures for VPI were 80%, 72% and 73%.

Conclusion: NBI does not improve the detection of neoplasia in patients with UC compared to HDE. In addition, NBI proves unsatisfactory for differentiating neoplastic from non-neoplastic mucosa. Studies comparing chromoendoscopy with NBI may reveal which technique is best for the diagnosis of neoplasia in UC patients.

Trialregister.nl Identifier: ISRCTN56671833
Introduction

Chronic inflammation of the colonic mucosa in patients with ulcerative colitis (UC) can lead to intraepithelial neoplastic changes that may ultimately develop into colorectal cancer.\(^1\)\(^,\)\(^2\) Colonoscopic surveillance is recommended in these patients in order to detect intraepithelial neoplasia in an early and curable stage.\(^3\) However, UC-associated neoplasia is difficult to visualize as it mainly develops in inconspicuous mucosa resembling inflamed tissue.\(^4\)\(^,\)\(^5\) Guidelines therefore recommend taking random biopsies of apparently normal tissue in addition to targeted biopsies of suspicious lesions.\(^6\)\(^,\)\(^7\)

Several endoscopic techniques have been evaluated with respect to their possibility to improve the detection of neoplasia in UC patients, as well as with respect to their ability to differentiate between neoplastic and non-neoplastic tissue in-vivo.\(^8\) Chromoendoscopy (CE) has shown to improve the diagnosis of neoplasia in two randomized trials and in several observational studies when compared to conventional white light endoscopy.\(^9\)\(^-\)\(^13\) Kiesslich et al demonstrated a 3-4.5 fold increase in neoplasia detection by using CE. In addition, mucosal pit pattern analysis enabled differentiation between neoplasia and non-neoplastic histology with an overall accuracy of 93%. Nevertheless, implementation of CE in clinical practice has hampered since it is labour-intensive, time-consuming and requires additional expertise and experience.

Narrow band imaging (NBI) is a push-on-a-button technique that utilizes optical light filters in order to enhance mucosal details without dyes.\(^14\)\(^-\)\(^16\) In a previous study NBI failed to improve the detection of neoplasia; however, a first generation prototype NBI-system was used which rendered low quality NBI-images.\(^17\) Optical improvements and high-definition technology have been inserted in the currently commercially available NBI-system which has never been evaluated for UC surveillance.

Next to these advanced endoscopic techniques, continuous technical improvements have led to an enhanced endoscopic image during conventional white light endoscopy as well. Currently available endoscopes contain charge coupled devices with >800,000 pixels (i.e. high-definition). These endoscopes provide much clearer images than the conventional colonoscopes, which contained <400,000 pixels.

The aims of this study were to compare the new generation NBI versus high-definition endoscopy (HDE) for the detection of neoplasia in UC patients and to evaluate NBI for the real-time differentiation of neoplasia from non-neoplastic mucosa.

Methods

Patients
Patients with UC who were scheduled for colonoscopic surveillance at the Academic Medical Centre, University of Amsterdam, were invited for participation. The inclusion criteria were: disease history ≥8 years, endoscopically proven colitis proximal to the splenic flexure in the past with currently inactive disease defined by a Truelove and Witts activity index of ≤2.\(^18\) An objective diagnosis of UC was also mandatory, based on former endoscopic and histopathological findings. Exclusion criteria were: non-correctable coagulopathy, age ≤18 years, insufficient
bowl preparation for accurate mucosal inspection and inability to provide informed consent. The study was approved by our institutional review board.

**Endoscopic equipment**

Colonoscopies were performed using the Lucera system with sequential red-green-blue illumination (CV-H260, Olympus, Tokyo, Japan) incorporating HDE, NBI and optical magnification (100x). Switching between these imaging modes was done by pressing a button on the shaft of the endoscope (CF-H260, Olympus, Tokyo, Japan). High-definition monitors (1080i) were used during the procedures.

**Study design and randomization**

This was a randomized cross-over trial in which all patients underwent colonoscopy twice on different occasions, once with NBI and once with HDE in randomized order (see figure 1). A time interval of at least 3 weeks between the two procedures was chosen to allow healing of biopsy sites, so that sampling sites could not be recognized during the second examination. Apart from taking biopsies, no lesions were removed during the first examination. The two procedures were performed by different, experienced endoscopists, who were blinded for the endoscopic and histological findings of the first examination. Randomization was done by opening opaque sealed envelopes (containing notes with either ‘HDE first’ or ‘NBI first’ in a 1:1 ratio) once the cecum had been reached during the first procedure.

**Colonoscopy**

Patients were prepared with four litres of hypertonic polyethylene glycol solution (Kleanprep, Norgine Inc., Amsterdam, the Netherlands) and underwent both colonoscopies under conscious sedation with midazolam and/or fentanyl. The level of bowel preparation was scored as poor (<90% of colonic mucosa visible), good (90-99%) or excellent (100%). In case the bowel preparation was scored as poor, the patient was excluded.

The endoscope was first advanced to the cecum using the HDE mode in all patients. Lesions found during the insertion phase were neglected and left unharmed. When performing the NBI examination, the endoscope was switched to the NBI-mode once the cecum had been reached. Cecal intubation was confirmed by identification of the appendiceal orifice and ileocecal valve or by intubation of the ileum. At the start of withdrawal, 20 mg butyl scopolamine was given to reduce colonic motility and repeated at the discretion of the endoscopist.

During withdrawal from the cecum, the colon was scrutinized for the presence of dysplasia-associated lesions or masses (DALM’s), mucosal irregularities, ulcers and strictures. Detected lesions were classified according to the macroscopic classification of early gastrointestinal neoplasia. In addition, the size (mm), segment of the colon (cecum, ascending, transverse, descending, sigmoid colon and rectum) and distance from the anus (cm) of each lesion were recorded. Digital still images of all detected lesions were taken in both HDE and NBI mode for reference. If lesions were detected during HDE, the imaging mode was switched briefly to NBI in order to take these images. During NBI-inspection of each lesion, its pit pattern (type I-V) was scored according to Kudo et al as well as its vascular pattern intensity (VPI; paler, same or darker than surrounding mucosa) according to East et al. For both procedures the total procedural time (excluding time for introduction but including time for biopsies or resections) were recorded.
**Biopsy protocol**
During the first of the two examinations all detected lesions were only biopsied but otherwise left *in situ*. Hence all primarily detected lesions could be detected again during the second colonoscopy. Only during the second procedure it was allowed to perform endoscopic resection of lesions. Biopsy material and endoscopic resection specimens were sent for histopathological examination.

During the second colonoscopy four quadrant random biopsies were taken every 10cm of colon. Images were captured from all areas of which random biopsies were taken in order to visualize areas in which random biopsies later turned out to be positive.

**Matching of lesions**
Lesions that were detected during the two colonoscopies were matched between the procedures by comparing four lesion-related characteristics: size, shape, location (distance ab ano and colonic segment) and appearance on digital images. Matching of lesions was done by an independent observer who reviewed findings and images made during both colonoscopies and who was blinded for histology at the time of matching lesions. Differences up to 2mm in size and up to 10cm in distance ab ano were regarded as equal. Lesions were considered as definitely matched in case all 4 lesion-related characteristics corresponded between the procedures; otherwise lesions were considered as non-matched.

**Histopathology**
Biopsy material and endoscopic resection specimens were processed using standard procedures and evaluated by two pathologists, one of whom was a gastrointestinal expert. The pathologists were blinded for detection technique and endoscopic diagnosis. Histology was classified according to the Vienna criteria of gastrointestinal epithelial neoplasia, ranging from no intraepithelial neoplasia to invasive neoplasia.21

**Outcome measures**
The primary outcome measure was the neoplasia detection rate of NBI versus HDE. Secondary outcome measure was the sensitivity, specificity and overall accuracy of NBI for the differentiation of neoplasia and non-neoplastic mucosa (both Kudo classification and VPI). The histological diagnosis was used as reference standard to calculate accuracy measures for the differentiation between neoplastic and non-neoplastic lesions.

**Statistical analysis and sample size**
Two main analyses were carried out to compare NBI and HDE: per-lesion and per-patient analysis (i.e. each neoplastic lesion or each patient with neoplasia served as outcome measure). For these analyses we compared the detection of neoplasia by targeted biopsies only. Testing for a difference in detection was done by comparing the number of discordant lesions, i.e. the number of lesions detected by NBI but missed by HDE *versus* the number of lesions detected by HDE but missed by NBI using the McNemar test.

The accuracies of the Kudo classification and VPI were calculated by comparing their endoscopic classification with histopathology (i.e. reference standard). A pit pattern type I/II was
considered non-neoplastic, as well as a VPI-score of paler/same. The sensitivity, specificity and overall accuracy of both classifications were compared by examining the number of discordant findings using the McNemar test. The Standards for Reporting of Diagnostic Accuracy (STARD) initiative was used for reporting of the diagnostic test accuracy.22

For sample size calculation we assumed that the yield of NBI for detecting neoplasia would be as high as CE, because both techniques enhance mucosal morphology.23 Based on previous CE studies, we estimated a 3-fold increased neoplasia detection with NBI.9, 11, 12 The percentage of patients with neoplasia on HDE was assumed to be 7.5%. A power of 90% and a significance level of 5% were selected, which resulted in a sample size of 49 patients.

Results

Patient characteristics and colonoscopy findings

Between December 2006 and July 2009 a total of 53 patients signed informed consent; 2 were excluded due to poor bowel preparation, 2 patients were unwilling to undergo the second colonoscopy, and 1 had endoscopically active pancolitis despite a low disease activity index. Hence, 48 patients underwent both colonoscopies of whom 25 were randomized to HDE first and 23 to NBI first (figure 1). None of the participants experienced complications.

Patient characteristics are presented in table 1. Because of the cross-over study design each patient could serve as his or her own control, thereby preventing any bias due to differences in patient characteristics by chance (such as can occur in a study with a parallel randomized design). The median examination time for NBI procedures was 26 minutes (12-86) versus 21 minutes (10-65) for HDE (paired Wilcoxon test; p=0.075).

During NBI colonoscopies, a total number of 105 lesions were identified and sampled versus 77 during HDE (p=0.048). Of those lesions, 19 were detected during both NBI and HDE. Hence, a total of 163 lesions were found during one or both of the two procedures within 42 patients (matched lesions that were found during both procedures were counted only once). The mean lesion size was 9.9mm (median 7.0; range 1-85) and 67 (41%) were ≤5mm. Eighty-nine lesions (55%) were located proximal to the splenic flexure; and 120 (74%) were macroscopically flat.

From 7 lesions no material for histology was retrieved, 19 lesions showed normal colonic mucosa, 47 hyperplastic changes, 29 reactive epithelial changes, 1 chronic inflammation, 7 active inflammation, 17 indefinite for neoplasia, 14 sessile serrated adenoma, 21 low-grade intraepithelial neoplasia (LGIN) and 1 high-grade IN. No invasive neoplastic lesions were found.

During the first of the two colonoscopies, 44 small lesions (27%) were completely removed by the biopsy forceps (due to diminutive size) and hence could not be detected during the second colonoscopy. Most of these removed small lesions (n=33; 75%) were removed during HDE examination. Five of these lesions were LGINs (4 removed during HDE first) and 1 was a HGIN (removed during HDE first). All primarily removed lesions were excluded from the main (paired) analysis, leaving 119 lesions for the comparison of HDE vs. NBI.
Figure 1: Flow chart of randomized cross-over trial with paired data-analysis. Lesions that were detected during the first examination (with either high-definition endoscopy or narrow-band imaging) were sampled by a biopsy forceps but largely left in situ, in order to enable detection during the second examination as well.

* Diminutive lesions, e.g. <5mm, that were completely removed by the biopsy forceps could not be detected again during the second examination.
Table 1: demographics of all included patients

<table>
<thead>
<tr>
<th>Demographic</th>
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<tbody>
<tr>
<td>Mean age, yrs (SD)</td>
<td>56 (11)</td>
</tr>
<tr>
<td>Male</td>
<td>35 (73%)</td>
</tr>
<tr>
<td>Mean UC duration, yrs (SD)</td>
<td>23 (9.7)</td>
</tr>
<tr>
<td>Personal history of neoplasia</td>
<td></td>
</tr>
<tr>
<td>No previous endoscopies</td>
<td>4 (8%)</td>
</tr>
<tr>
<td>Low-grade intraepithelial neoplasia</td>
<td>7 (15%)</td>
</tr>
<tr>
<td>High-grade intraepithelial neoplasia</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Invasive neoplasia</td>
<td>0</td>
</tr>
<tr>
<td>Primary sclerosing cholangitis</td>
<td>8 (17%)</td>
</tr>
<tr>
<td>Family history of colorectal cancer</td>
<td>7 (15%)</td>
</tr>
<tr>
<td>Anti-inflammatory drug use</td>
<td>39 (81%)</td>
</tr>
<tr>
<td>Mean duration of anti-inflammatory drug use, yrs (SD)</td>
<td>17 (12)</td>
</tr>
<tr>
<td>Number of previous neoplasias (mean nr per patient)</td>
<td>18 (0.38)</td>
</tr>
</tbody>
</table>

Bowel preparation

<table>
<thead>
<tr>
<th>Examination time, median (range)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>First colonoscopy</td>
<td>19 (10-62)</td>
</tr>
<tr>
<td>Second colonoscopy</td>
<td>30 (13-86)</td>
</tr>
</tbody>
</table>

Table 2: Number of neoplastic lesions (all low-grade intraepithelial neoplasia) that were detected by either narrow-band imaging, high-definition endoscopy or both. Discordant (‘shaded’) cells demonstrate the number of neoplastic lesions that were detected by only narrow-band imaging or high-definition endoscopy. * McNemar test: p=0.727

Neoplasia detection of HDE vs. NBI

Per-lesion analysis: Of the 119 lesions, 94 (79%) were detected by NBI and 44 (37%) by HDE (p<0.001). Of the 16 neoplastic lesions (histologically all were LGIN), 11 (69%) were detected by HDE and 13 (81%) by NBI (p=0.727); eight of the neoplastic lesions were detected by both NBI and HDE (see table 2). Seven of the neoplastic lesions were considered DALMs needing surgical intervention, either due to large size or due to the presence of neoplasia in their adjacent ‘normal’ mucosa. Six out of these 7 DALMs (86%) were detected by both NBI and HDE (p=1.0).

When including neoplastic lesions that were entirely removed during the first of the two colonoscopies, the total number of neoplastic lesions detected by HDE was 16 vs. 14 by NBI (paired Wilcoxon test; p=0.564).
Per-patient analysis: A total of 11 patients with neoplasia were left for the paired per-patient analysis, 9 (82%) of whom were diagnosed by HDE vs. 8 (73%) by NBI (p=1.0). When including neoplastic lesions that were entirely removed during the first colonoscopy, a total of 14 patients were diagnosed with neoplasia, 8 (57%) of whom were detected by NBI vs. 12 (86%) by HDE (McNemar; p=0.219).

Random biopsy protocol: A total number of 1580 random biopsies were taken, corresponding to a mean number of 33 per patient (range 15-60). Three biopsies (0.19%) demonstrated LGIN. Two of those positive random biopsies were taken just adjacent (within 10cm) of DALMs that were already visualized during both NBI and HDE inspection. The third positive random biopsy was an unequivocally confirmed LGIN that was missed by both NBI and HDE, taken in an area with increased vascularisation in a tubular colonic segment (figure 2). This patient is currently scheduled for an additional surveillance colonoscopy.

Differentiation of neoplasia and non-neoplastic mucosa
In 3 out of the 156 lesions with known histology, no Kudo classification could be assessed during colonoscopy due to unclear pit pattern (inconclusive test results); in 6 lesions no VPI could be assessed. The sensitivity, specificity and accuracy of the Kudo classification for differentiating neoplastic from non-neoplastic lesions were 76% (95%-CI: 55-89), 66% (57-73) and 67% (60-74) (see table 3). Corresponding figures for VPI were 80% (58-92), 72% (63-79) and 73% (65-79). Differences in overall accuracy between the Kudo classification and VPI were statistically non-significant (p=0.211).

<table>
<thead>
<tr>
<th>NBI</th>
<th>Histopathology</th>
<th>Neoplasia</th>
<th>Non-neoplastic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kudo type III-V</td>
<td>16</td>
<td>45</td>
<td>PPV 26%</td>
</tr>
<tr>
<td>Kudo type I-II</td>
<td>5</td>
<td>87</td>
<td>NPV 95%</td>
</tr>
<tr>
<td>VPI dark</td>
<td>16</td>
<td>37</td>
<td>PPV 30%</td>
</tr>
<tr>
<td>VPI light/same</td>
<td>4</td>
<td>93</td>
<td>NPV 96%</td>
</tr>
</tbody>
</table>

Table 3: Correspondence between endoscopic real-time classification by narrow-band imaging (Kudo classification and vascular pattern intensity (VPI)) and histopathology (i.e. reference standard).
Number of inconclusive test results: n=3 for Kudo and n=6 for VPI.
PPV, positive predictive value; NPV, negative predictive value
Discussion

Recently, several endoscopic studies have suggested CE to be superior to standard colonoscopy for the detection of neoplasia during UC surveillance.9-13 The routine use of CE has however been hampered since it is time-consuming, operator-dependent, by some considered to be a messy technique and may even obscure lesions due to pools of dye. In addition, after dyespraying it is impossible to switch back to the standard endoscopic view. Narrow-band imaging mimics CE by enhancing the mucosal surface using spectral characteristics of the endoscopic light.14 Previous research in UC surveillance demonstrated that the use of a first generation prototype NBI-system did not improve the detection of neoplasia, possibly due to the lack of brightness and hence a too dark overall NBI image.17 In the present study a new generation NBI-system was used with improved brightness and high-definition technology. Again NBI did not prove to be better than HDE as it detected 13 out of 16 neoplastic lesions (81%) versus 11 out of 16 (69%) with HDE (p=0.727). In the per-patient analysis HDE detected even more patients with neoplasia than NBI (9 vs. 8 out of 11 patients with neoplasia).

Several features of NBI and HDE may explain these disappointing results. First, the new generation NBI-system still provides a darker overall image when compared to HDE. This phenomenon forces endoscopists to inspect the colonic mucosa in close proximity instead of in overview. The longer inspection time with NBI when compared to HDE (29.6 vs. 24.4 minutes; p=0.039) may be explained by this issue. Secondly, the high-definition technology during white light endoscopy may level out any difference in contrast between NBI and HDE. Previous studies comparing NBI to HDE for sporadic adenoma detection also showed comparable detection rates, whereas those detection rates were higher than in historical studies using conventional colonoscopes.24, 25 Thirdly, it must be mentioned that the NBI-system used in the present study was of the sequential illumination technology (CV-260, Olympus Inc, Tokyo, Japan), using a monochromatic charge coupled device (CCD). However, the colour CCD-chip which is used in most countries (CV-180, Olympus Inc) may lead to different results as the overall image brightness may still be different. Studies using this commercially available NBI-system should be performed as well to evaluate possible differences compared to the present study.

One may consider the limited number of included patients as a shortcoming of the present study. However, the paired nature of our study design highly increased the statistical power since each patient functioned as his or her own control. The statistical power increased even more by comparing the detection of each neoplastic lesion instead of each patient with neoplasia as outcome parameter. Our sample size therefore was sufficient to detect a difference between NBI and HDE that would be comparable to the difference that has previously been encountered for CE when compared to standard colonoscopy (3-fold increased neoplasia detection).9 A true limitation of our study was that lesions may have become smaller during the second colonoscopy, since a biopsy was already taken during the first procedure, and hence may have been more difficult to detect. To prevent any systematic impact of this factor, we randomized the order of examinations. Furthermore, diminutive (≤5mm) lesions may even have been removed by the biopsy forceps during the first procedure and hence may have been undetectable during the second examination. Therefore we chose to exclude removed lesions from the paired analysis, which reduced the statistical power of the study. Differences between NBI and HDE in detection capa-
bility of small neoplastic lesions hence may have remained unobserved. However, the clinical significance of finding diminutive neoplastic lesions is debatable.

As our study demonstrated that NBI did not improve the detection of neoplasia in UC patients, the question arises whether we should routinely use CE for UC surveillance because two previous randomized trials demonstrated that CE was associated with a 3-4.5 fold increased neoplasia detection.9, 10 However, both trials have been performed by the same research group from Mainz, Germany, including an endoscopist who was highly experienced in CE. No additional randomized trials have been performed at this moment; hence the results from Kiesslich et al should be confirmed by others. Some supporting evidence has already been provided by observational studies using either a (historical) cohort study or a back-to-back colonoscopy research design.11-13 These study designs however prevent drawing firm conclusions for clinical recommendations. In addition, conventional white-light colonoscopes were used in these previous studies as opposed to the high-definition white-light colonoscopes in our study. Since we did not compare the new-generation NBI system to conventional colonoscopy, we are currently unable to compare the results of NBI against CE in any way. Although we expected (and powered our study) to find 7.5% of patients with neoplasia by HDE, we found 9 out of 48 patients (19%) to have neoplasia with HDE. This high yield of neoplasia may be induced by our inclusion criteria but any effect of the high-definition technology cannot be ruled out. Additional randomized trials are therefore needed, preferably comparing CE to NBI with respect to neoplasia detection in UC patients.

Our secondary objective was to evaluate NBI for the real-time differentiation of neoplastic and non-neoplastic mucosa. Accurate differentiation during ongoing endoscopy would enable selective use of targeted biopsies of endoscopically suspicious areas only. Both the Kudo classification and the VPI proved unsatisfactory for this purpose, as their respective sensitivities were only 76% and 80%, and their respective specificities 66% and 72%. If only biopsies would have been taken from lesions with either a suspicious Kudo pit pattern or suspicious VPI, still 3 out of 22 neoplastic lesions (14%) would have been left in situ (results not shown), which appears unacceptable.

The main explanation for the disappointing results of NBI for differentiating neoplasia from non-neoplastic tissue is that inflammatory changes in UC patients disrupt the normal colonic pit pattern and normal vascular intensity. This makes accurate differentiation between non-neoplastic and neoplastic mucosa more difficult. Previous studies support our findings that mucosal changes due to inflammation hamper the possibility to reliably differentiate between non-neoplastic (e.g. chronically inflamed) and neoplastic tissue. Assessment of the Kudo classification by NBI has previously shown to be associated with a sensitivity and specificity of 75% and 81% as well.26 An alternative classification (honeycomb appearance, villous or tortuous pattern), introduced by Matsumoto et al, showed similar figures of 80% and 84% respectively.27

Two novel techniques have shown to be good candidates to overcome the disappointing diagnostic accuracy of NBI for differentiation purposes: autofluorescence imaging (AFI) and confocal laser endomicroscopy (CLE). Previous studies have demonstrated that the combined use of NBI together with AFI (i.e. tri-modal imaging) highly increased the diagnostic accuracy for real-time differentiation.26, 28 By using tri-modal imaging, the sensitivity and negative predictive value among UC patients could be increased to 100% in a pilot study, a promising figure that
should be confirmed in larger studies.26 Alternatively, CLE has shown promising results as well. Contrary to NBI and AFI, which are techniques that enable to predict histology, CLE in fact is in-vivo histology. Kiesslich et al showed that CLE was associated with a sensitivity and specificity of 95% and 98% in expert hands.10 Future studies should confirm these figures and focus on learning curves among endoscopists to interpret histological images. Comparison of tri-modal imaging and CLE may then be very interesting.

Due to the current lack of an accurate technique for differentiation of neoplastic from non-neoplastic mucosa, it is still possible to detect neoplastic mucosal changes in random biopsies. In our study, 3 out of 1580 random biopsies demonstrated LGIN. Two of those positive random biopsies proved clinically non-relevant as these were found in mucosa adjacent to a visible DALM. The chance of finding neoplasia within ‘normally’ appearing mucosa in close proximity of a DALM is known to be high.29 However, one LGIN in this study could not be visualized by either NBI or HDE and was only detected by random biopsies (figure 2). Therefore, the use of NBI cannot obviate the need for taking random biopsies at this moment. Since this single positive random biopsy was taken in a tubular colonic segment with augmented vascularisation, it may be postulated that random biopsies may have clinical significance in colonic segments with severe inflammatory changes (e.g. scarring, pseudo polyps, tubular colon) as suggested previously by Rutter et al.30

In summary, the present study demonstrated that NBI did not improve the detection of neoplasia in patients with longstanding UC when compared to HDE. Furthermore, the sensitivity and specificity of NBI, by using both the Kudo classification as well as the vascular pattern intensity, proved unsatisfactory for accurate real-time differentiation of neoplastic and non-neoplastic colonic mucosa. Whether the use of CE must be advocated during colonoscopic surveillance of patients with UC should be elucidated by additional head-to-head comparison studies of CE versus NBI or HDE.

>> For figure 2; see page 141
Reference List


Rex DK, Helbig CC. High yields of small and flat adenomas with high-definition colonoscopes using either white light or narrow band imaging. Gastroenterology 2007;133:42-47.


