AP&T Alimentary Pharmacology and Therapeutics

Review article: newer optical and digital chromoendoscopy techniques vs. dye-based chromoendoscopy for diagnosis and surveillance in inflammatory bowel disease

G. E. Tontini*,†, M. Vecchi†,‡, M. F. Neurath* & H. Neumann*

*Department of Medicine I, University of Erlangen-Nuremberg, Erlangen, Germany.
†Gastroenterology and Digestive Endoscopy Unit, IRCCS Policlinico San Donato, San Donato Milanese, Italy.
‡Department of Medical Science for Health, University of Milan, Milan, Italy.

Correspondence to:
Drs H. Neumann and G. E. Tontini, Department of Medicine I, University of Erlangen-Nuremberg, Ulmenweg 18, 91054 Erlangen, Germany.
E-mails: helmut.neumann@uk-erlangen.de; gianeugeniotontini@gmail.com

Publication data
Submitted 14 June 2013
First decision 16 July 2013
Resubmitted 4 September 2013
Accepted 5 September 2013
EV Pub Online 3 October 2013

This uncommissioned review article was subject to full peer-review.

SUMMARY

Background
Recent innovations in gastrointestinal endoscopy have changed our traditional approach to diagnosis and therapy in patients with inflammatory bowel diseases (IBD). While traditionally used dye-based chromoendoscopy (DBC) techniques suffer from several limitations that reduce their utility in daily routine practice, newer 'dye-less' chromoendoscopy (DLC) techniques offer a great potential to overcome most of these limitations.

Aim
To review available optical and digital chromoendoscopy techniques, by critically discussing their potential for diagnostic and surveillance colonoscopy in patients with IBD.

Methods
A literature search on the use of dye-less and dye-based chromoendoscopy in IBD patients was performed.

Results
In long-standing IBD, DBC improves detection of dysplasia (diagnostic odds ratio = 17.5, 95% CI = 1.2–247.1) as well as prediction of inflammatory disease activity and extent of disease compared with standard video-colonoscopy. Narrow band imaging (NBI) shows no improvement in dysplasia detection rates compared with white-light endoscopy and DBC ($P = 0.6$). Moreover, NBI results in a suboptimal differentiation of dysplastic from nondysplastic lesions. No data regarding digital DLC techniques (i.e. FICE, i-scan) for dysplasia detection in IBD are yet available. Both NBI and i-scan are superior to white-light endoscopy in assessing the activity and extent of colorectal IBD.

Conclusions
Although the potential benefits of newer optical and digital dye-less chromoendoscopy techniques over traditionally used DBC are substantial, only DBC can currently be recommended to improve dysplasia detection in long-standing IBD. In contrast, DLC has the potential to quantify disease activity and mucosal healing in IBD.

Aliment Pharmacol Ther 2013; **38:** 1198–1208

doi:10.1111/apt.12508

INTRODUCTION

Chronic inflammation in inflammatory bowel diseases (IBD) represents a major risk factor for the development of colitis-associated cancer (CAC).[1–3] In 2001, a large meta-analysis assessed a pooled cumulative CAC incidence of 2% at 10 years, 8% at 20 years and 18% after 30 years of disease.[2] Unlike sporadic colorectal cancer, the growing pattern of neoplastic tissue in IBD is often flat, multifocal and anaplastic.[4–7] At present, diagnosis of dysplasia is the most reliable biomarker of malignancy, being present in 70% of CAC.[8] Based on these findings, colonoscopic surveillance is strongly recommended by national and international guidelines starting 8–10 years after the onset of symptoms and every 1–2 years after that in extensive colitis.[9–12] Surveillance is aimed at early detection of nonpolypoid (formerly known as 'flat lesions') and early dysplastic lesions and includes four random biopsies every 10 cm plus targeted sampling of macroscopically suspicious lesions. However, this biopsy protocol has failed to clearly demonstrate a significant gain in mortality rates and cost-effectiveness, as significant lesions may be overlooked according to their nonpolypoid appearance.[1, 13–19] In addition, recent data have shown that most gastroenterologists do not follow the biopsy protocol, as it is a time- and cost-expensive approach.[20–25]

To improve patient outcome, dye-based chromoendoscopy (DBC) has been introduced more than one decade ago, enabling the detection of significantly more dysplastic lesions in long-standing IBD. In addition, DBC allowed for an improved diagnosis of disease severity and extent.[15, 26–34] In this context, it has been estimated that methylene blue-aided chromoendoscopy yields a 2.2-fold increase in dysplasia detection rate, particularly due to the enhanced detection of nonpolypoid lesions.[15, 34, 35] Similar results were shown with the use of indigo carmine.[30, 33] A recent meta-analysis of six randomised controlled trials demonstrated a pooled sensitivity, specificity and diagnostic odds ratio of 83.3% (95% CI = 35.9–99.6%), 91.3% (95% CI = 43.8–100%) and 17.5 (95% CI = 1.2–247.1), respectively, for dysplasia detection in long-standing ulcerative colitis (UC) by using DBC compared with standard video-colonoscopy.[36] Based on these results, DBC has already been included in most national and international guidelines to improve standard surveillance protocols in highly specialised centres.[9–12] However, DBC has some potential limitations hampering its feasibility in daily routine clinical practice.[37, 38] First, there are additional costs for dye spraying and operator training. Furthermore, it is a time-consuming procedure and the dye does not always coat the surface evenly (Figure 1). Finally, the dye does not provide a detailed evaluation of the subepithelial capillary network, which is an important feature in the diagnosis of gastrointestinal neoplasia and disease activity.[37, 39]

In the attempt to overcome most of these limitations, recent advances in endoscopic imaging have been implemented into daily routine practice (Table 1). Newer dye-less chromoendoscopy (DLC) techniques allow for a detailed examination of both the mucosal surface and the mucosal vascular pattern (MVP) morphology by just pushing a button on the handle of the endoscope, thereby enabling high-contrast imaging of the mucosal surface in real time without the use of special equipment. These newer DLC techniques are divided into: (i) optical chromoendoscopy and (ii) digital chromoendoscopy (Table 2).

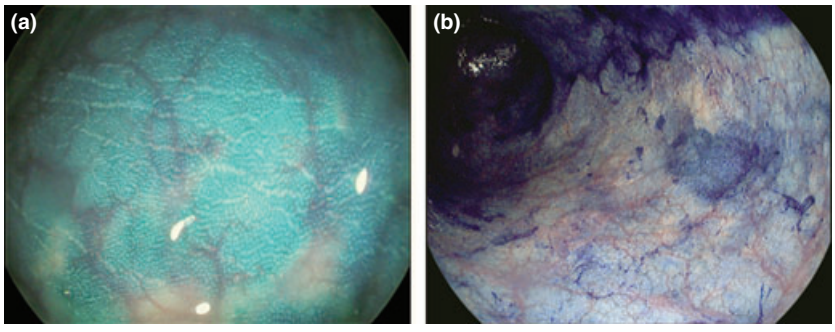

Figure 1 | Methylene blue-aided chromoendoscopy yields an improved characterisation of subtle mucosal changes (a). One disadvantage of the technique is the often inhomogeneous staining pattern, as the dye does not always coat the whole surface evenly (b).

Table 1 | Potential advantages of dye-less chromoendoscopy in comparison to dye-based chromoendoscopy

Enhancement of mucosal vascular pattern
Handiness: evenly staining just pushing a button
Time: no additional time consumption
Safety: no allergic reaction or potential DNA damage
Skill: swift learning curve

Table 2 | Summary of currently available dye-less chromoendoscopy techniques

Technology	Brand	Company	Specifications
Optical DLC	NBI	Olympus	Evis Exera II & III
	CBI	Aohua	AQ-100
Digital DLC	i-scan	Pentax	EPKi, EPKi-5000, EPKi-7000
	FICE	Fujifilm	EPX-4400

NBI, narrow band imaging; CBI, compound band imaging; FICE, Fuji intelligent colour enhancement.

In this review, we will focus and critically discuss the potential of advanced endoscopic imaging using DLC for diagnosis and surveillance in patients with IBD.

OPTICAL DLC

High-definition (HD) video endoscopes use white light from a xenon source for illumination and capture the reflected light by means of a charge-coupled device chip, which is integrated into the distal tip of an endoscope. The spectral composition of the reflected light depends on the emission spectrum of the light source and the features of the tissue (e.g. inflammatory, dysplastic). The depth of penetration into the mucosa depends on the light wavelength: it is superficial for blue band, deep for red and intermediate for green (range of penetration: 0.15–0.30 mm).[40] Haemoglobin streaming into the MVP absorbs the greatest amount of visible light, with a principal peak in the blue part of the spectrum (415 nm).

Optical chromoendoscopy is based on optical lenses integrated within the light source of the endoscope, thereby narrowing the bandwidth of spectral transmittance. The two systems currently available for optical DLC are Narrow Band Imaging (NBI; Olympus, Tokyo, Japan) and Compound Band Imaging (CBI; Aohua, Shanghai, China). By pushing a button on the handle of the endoscope, optical DLC provides higher image contrast (i.e. ratio of density or brightness between a pattern and its background) and allows visualisation of the superficial capillary networks and of subepithelial vessels.[40–44] Multiple studies have shown that optical DLC could enhance the detection of subtle irregularities and allows for characterisation of the MVP (Figure 2). Muto *et al.* have recently reviewed a detailed description of NBI.[41] No scientific data are currently available on the recently introduced CBI.

DIGITAL DLC

Digital DLC is based on digital post-processing of the endoscopic images in real time from the video processor instead of narrowing the light by the use of optical filters.[39, 45] Currently, two digital DLC techniques are available, including (i) Fujinon Intelligent Color Enhancement (FICE; Fujifilm, Tokyo, Japan) and (ii) i-scan (Pentax, Tokyo, Japan). Both techniques are enabled by pushing a button on the handle of the endoscope, thereby reconstructing virtual images in real time.

While FICE has no standardised settings, a recent international consensus recommended uniform settings

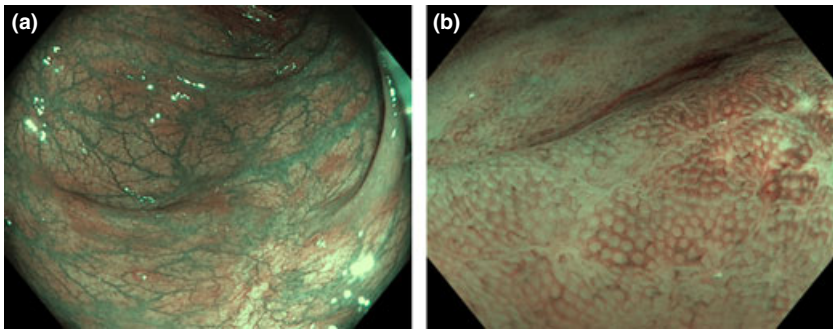

Figure 2 | High-definition endoscopy with narrow band imaging (NBI) (a) and dual-focus NBI (b) in a patient with a *Mayo ulcerative colitis endoscopic score* of 1. NBI improves visualisation of the mucosal vascular pattern. Dual-focus NBI with 80-fold optical magnification yields an accurate assessment of subtle mucosal changes.

for i-scan (Figure 3). The main advantage of this approach is that it allows better comparability between different studies. This was previously only possible for studies evaluating optical chromoendoscopy techniques. In particular, i-scan processes the reflected light using three different algorithms: surface enhancement (SE), contrast enhancement (CE) and tone enhancement (TE). SE augments luminance, edges contrast and allows a detailed evaluation of the mucosal surface and lesion borders. With CE, areas lower in luminance intensity compared with surrounding pixels are recognised and refined upon a slight suppression of red and green frequencies; as a result, relatively dark areas are stained in a slightly bluish colour, thereby enhancing the presence of vessels, to apply a more detailed topography of subtle irregularities and of the MVP. TE divides the reflected white light into three colours (red, green and blue) and performs a selective modification of each frequency followed by image reconstruction in real time. The three i-scan settings are recommended as follows: (i) i-scan 1 for detection of lesions. This algorithm uses only SE to refine imaging of subtle surface abnormalities without altering the brightness of the endoscopic picture. (ii) i-scan 2 mode was established for characterisation of lesions. The algorithm combines SE and TE, thereby enhancing minute mucosal changes and vessel structures. (iii) i-scan 3 adds CE to the endoscopic image (in addition to SE and TE) and is recommended for demarcation of lesions, as it digitally adds blue colour to darker edges within the endoscopic image.

The FICE system is similarly based on a computed spectral estimation technology that digitally processes the white-light endoscopic image in real time. Nevertheless, standardised settings are currently missing, thereby hampering the use of FICE in daily routine practice and comparison of different studies.

DLC IN IBD – DETECTION OF NEOPLASIA

Detection of colorectal dysplasia in IBD is of paramount importance, being the most reliable biomarker of CAC.[8, 46] Progression from chronic inflammation to cancer was previously supposed to strictly follow a step-by-step sequence from low-grade dysplasia, to high-grade dysplasia and cancer.[47] Recent evidence suggests a shift of this paradigm. Driven by different pathways, invasive cancer seems to have the potential to develop *de novo* and from low-grade dysplasia without the intermediate stage of high-grade dysplasia.[48] Accordingly, low-grade dysplasia is considered the definitive interventional point at which the prophylactic colectomy for CAC in chronic UC should be discussed.[49] In addition, IBD-related neoplasia may arise in nonpolypoid mucosa with normal endoscopic appearance or may arise as dysplasia-associated lesion or mass (DALM).[50] For an optimised therapy, these lesions have to be distinguished from those arising from sporadic adenomas in healthy or noncolitis mucosa (adenoma-like mass; ALM).[51] In this context, advanced endoscopic imaging using DLC has been studied to increase accuracy and effectiveness of current surveillance programmes in IBD (Table 3).

Recently, a cross-sectional pilot study including 46 patients with long-standing UC evaluated the positive predictive value of conventional white-light endoscopy and NBI for diagnosis of early colorectal neoplasia.[52]

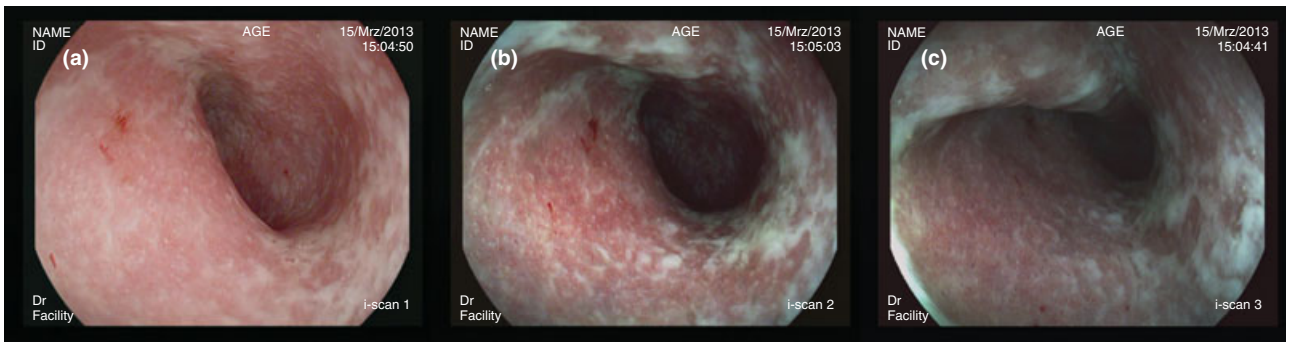

Figure 3 | High-definition endoscopy with digital chromoendoscopy using different i-scan settings. Panel a shows i-scan 1 mode, which is used for detection of lesions. This algorithm uses surface enhancement (SE) to refine imaging of subtle surface abnormalities without altering the brightness of the endoscopic picture. i-scan 2 mode (b) combines SE and tone enhancement (TE) for characterisation of lesions and enhancement of subtle mucosal changes and vascular structures. Panel c highlights i-scan 3 mode, which adds contrast enhancement and is recommended for demarcation of lesions, as it digitally adds blue colour to darker edges within the endoscopic image.

Table 3 | Summary of the main studies addressing the use of dye-less chromoendoscopy in IBD

Main studies addressing the use of DLC in IBD

Author-Journal-Year	No. of patients	Study design and setting	Endoscopic techniques	Indication	Endoscopic efficacy	Statistics	Evidence provided
Dekker, *Endoscopy*, 2007	42	Crossover trial with randomised order in UC surveillance	NBI vs. Standard WLE	Surveillance – dysplasia detection	True-positive lesions: 9 with NBI and 12 with WLE False-positive lesions: 43 with NBI and 16 with WLE Missed dysplastic lesions: three with NBI (two HGD, one not reported), four with WLE (two LGD, one HGD, one intramucosal cancer)	$P = 0.672$ $P = 0.015$	Comparable dysplasia detection rate between NBI and standard WLE. NBI leads to detection of more false-positive lesions than WLE
van den Broek, *Endoscopy*, 2011	48	Crossover trial with randomised order and matching lesion in UC surveillance	NBI + HD vs. WLE + HD	Surveillance – dysplasia detection	True-positive lesions: 13 with NBI and 11 with HD-WLE Missed dysplastic lesions (all LGD): three with NBI, five with HD-WLE	$P = 0.727$	Comparable dysplasia detection rate between NBI and HD-WLE
				Surveillance – Dysplasia differentiation	Sensitivity, specificity and overall accuracy of the Kudo classification by NBI in differentiating neoplastic from nonneoplastic lesions were 76%, 66% and 67% respectively	Not applicable	Unsatisfactory NBI accuracy differentiating neoplastic from nonneoplastic mucosa
Ignjatovic, *Am J Gastroenterol*, 2012	112	Parallel randomised trial in UC surveillance	NBI + HD vs. WLE + HD	Surveillance – Dysplasia detection	True-positive lesions: five with NBI and seven with HD-WLE False-positive lesions: 12 with NBI and 4 with HD-WLE	$P = 0.57$ $P = 0.06$	Comparable dysplasia detection rate between NBI and HD-WLE
van den Broek, *Gut*, 2008	50	Crossover trial with randomised order in UC surveillance	NBI + HD vs. AFI + HD	Surveillance – Dysplasia differentiation	Sensitivity, specificity and overall accuracy of the Kudo classification by NBI in differentiating neoplastic from nonneoplastic lesions were 75%, 81% and 80% respectively	Not applicable	Moderate NBI accuracy differentiating neoplastic from nonneoplastic mucosa
Pellise, *Gastrointest Endosc*, 2011	60	Crossover trial with randomised order in IBD surveillance	NBI + HD vs. DBC with Indigo carmine and WLE + HD	Surveillance – Dysplasia detection	True-positive lesions: 10 with NBI and 12 with DBC False-positive lesions: 126 with NBI and 196 with DBC Missed dysplastic lesions: 7/22 with NBI and 3/22 with DBC	$P = 0.644$ $P = 0.001$ $P = 0.200$	Comparable dysplasia detection rate between NBI and DBC with indigo carmine. NBI leads to detection of less false-positive lesions than DBC

Table 3 | (Continued)

Main studies addressing the use of DLC in IBD

Author-Journal-Year	No. of patients	Study design and setting	Endoscopic techniques	Indication	Endoscopic efficacy	Statistics	Evidence provided
Bisschops, *Endoscopy*, 2012	108	Parallel randomised trial in UC surveillance	NBI + HD vs. DBC with methylene blue and WLE + HD	Surveillance – Dysplasia detection	True-positive lesions: 18 with NBI (of 112 raised polyps) and 26 with DBC (of 156 raised polyps) Median withdrawal time: 20 min for NBI and 27 min for DBC	$P = 0.385$ $P = 0.003$	Comparable dysplasia detection rate between NBI and DBC with methylene blue. NBI enables faster examination than DBC
Kudo, *Endoscopy*, 2009	30	Observational trial in mild or inactive UC	NBI + HD	Diagnosis – Prediction of microscopic activity	Distorted mucosal vascular pattern with 'obscure' NBI appearance correlates with signs of microscopic inflammation, such as cell infiltration, goblet cell depletion, distorted crypts and basal plasmacytosis	All *P* values are equal to 0.0001	NBI may predict signs of active microscopic inflammation
Neumann, *Inflamm Bowel Dis*, 2013	78	Parallel randomised trial in active or inactive IBD	i-scan + HD vs. WLE + HD	Diagnosis – Prediction of microscopic activity	i-scan shows better agreement with histological results compared with HD-WLE, assessing both disease extent (92% vs. 49%) and disease activity (90% vs. 54%)	$P = 0.001$ $P = 0.066$	i-scan may predict signs of active microscopic inflammation, thereby refining the assessment of disease extent and severity

DLC, dye-less chromoendoscopy; DBC, dye-based chromoendoscopy; NBI, narrow band imaging; HD-WLE, high-definition white-light endoscopy; AFI, auto-fluorescence imaging; UC, ulcerative colitis; LGD, low-grade dysplasia; HGD, high-grade dysplasia.

Each protruding and nonpolypoid lesion was further observed by using magnifying NBI colonoscopy. By modifying the classification for 'magnifying chromoscopic findings',[53–56] the surface structure was classified into three different patterns: (i) 'honeycomb-like', (ii) 'villous' and (iii) 'tortuous'. Notably, the last surface structure was significantly related to dysplasia on histology (8% compared to 0.4% in 'honeycomb-like' and villous patterns. $P = 0.003$), meaning that the 'tortuous' pattern revealed by NBI may be a clue for the identification of colorectal neoplasia.[52] Moreover, a recent crossover trial randomised 42 patients with long-standing UC (defined as pancolitis and disease duration of at least 8 years) and compared dysplasia detection rates between standard white-light endoscopy and NBI.[57] Importantly, no statistically significant differences in the detection rates of dysplastic lesions were detected between NBI (nine lesions) and standard white-light endoscopy (12 lesions) according to a per-lesion analysis ($P = 0.672$).

A later study by the same group compared HD white-light endoscopy with HD endoscopy with NBI in 48 patients with long-standing UC, but failed to reveal any significant difference between both groups.[58] NBI detected 13 dysplastic lesions, while HD white-light endoscopy detected 11 dysplastic lesions ($P = 0.727$). Besides using a crossover design with matched lesions to increase the statistical power, potential limitations of the study have to be discussed: first, the biopsy protocol

applied during the first examination resulted in up to 44 (27%) small lesions, which were completely removed due to their diminutive size (five low-grade and one high-grade dysplasia). Second, biopsied lesions may have become predictably smaller or changed their original appearance, shrinking the power of a real comparison between two different techniques. Nevertheless, the results have recently been confirmed by a multicentre trial including 112 patients with long-standing UC.[59] According to the per-lesion analysis, the overall detection rate of neoplastic lesions was again comparable between the HD white-light and the NBI group (7 vs. 5; $P = 0.57$).

Taken together, the results of the above-mentioned studies suggest that NBI could not improve the detection rate of colorectal dysplasia in IBD. No data regarding the use of digital DLC techniques for dysplasia detection in IBD are currently available.

Previous studies using DBC had shown that pan-chromoendoscopy with either methylene blue or indigo carmine has the potential to improve detection rates of colorectal dysplasia in patients with long-standing UC.[15, 32–36, 60] To date, two studies have compared DLC with DBC to evaluate dysplasia detection rates in IBD.

The first study by Pellisé *et al.* used a crossover design with randomised order (NBI vs. indigo carmine) of 60 clinically inactive colonic IBD patients 8 years after the onset of symptoms.[61] In the per-lesion analysis, NBI showed a similar true-positive biopsy rate compared with DBC (10 vs. 12, $P = 0.644$), but an inferior false-positive biopsy rate (126 vs. 196, $P = 0.001$). Furthermore, NBI clearly scored over indigo carmine-aided chromoendoscopy in terms of a shorter withdrawal time (mean 15.7 min for NBI and 26.9 min for DBC, $P < 0.01$), according to the fewer number of 'suspicious lesions' recognised and biopsied (136 with NBI and 208 with DBC, $P = 0.001$). Nevertheless, when the rate of missed neoplastic lesions was taken into account, the per-patient analysis (6/13 with NBI and 2/13 with DBC, $P = 0.2$) and the per-lesion analysis (7/22 with NBI and 3/22 with DBC, $P = 0.2$) showed a slightly positive trend towards DBC.

The second study used a multicentre parallel randomised design and included 108 patients with long-standing UC undergoing surveillance colonoscopy.[62] The preliminary study results revealed that methylene blue-aided chromoendoscopy and NBI have a comparable detection rate of true neoplastic lesions in endoscopically detected, suspiciously elevated lesions. Eighteen of 112 raised polyps were detected with NBI and 26 of 156 raised polyps with DBC ($P = 0.385$). Furthermore, given the shorter withdrawal time of DLC (median 20 min for NBI and 27 min for DBC, $P = 0.003$) and the easier applicability, the authors suggested that NBI might have the potential to replace DBC for surveillance in IBD in the future.

Besides the detection of pre-neoplastic and neoplastic lesions in IBD, DLC was also evaluated for the characterisation of colorectal lesions in IBD (Table 3). One recent published study by van den Broek *et al.* reported that, according to the Kudo classification, accuracy of NBI for *in vivo* differentiation of neoplastic and nonneoplastic lesions in IBD was 67%.[58] Another study by the same group reported a moderate efficacy of NBI for prediction of dysplasia in IBD (sensitivity 75%, specificity 81% and accuracy 80%).[63] Taken together, these preliminary data did not support the use of NBI to predict histology in IBD. In this context, the presence of slight mucosal disease activity and tissue alterations, driven by chronic inflammation, have to be discussed to explain the relatively low impact of NBI for the characterisation of dysplastic lesions in IBD.

ASSESSMENT OF MUCOSAL HEALING, DISEASE ACTIVITY AND EXTENT

Looking beyond colorectal dysplasia detection and characterisation, DLC has also been evaluated for diagnosis of early inflammatory changes in IBD (Table 3). Emerging evidence suggests that mucosal healing is a key treatment goal that predicts sustained clinical remission and resection-free survival of IBD patients.[64] Accordingly, mucosal healing has become a pivotal prognostic parameter in the management of IBD, thus highlighting the importance of endoscopy for monitoring of disease activity. It has been recognised that increased vascular density and angiogenesis may play a crucial role in the pathogenesis of IBD and could be closely related to disease activity.[65–74] Indeed, angiogenesis and MVP could represent the proof of earlier or residual mucosal activity in spite of a deep clinical remission.[75–80]

In a pilot study based on 14 IBD patients, immunohistochemical staining with CD31 revealed a significant increase in mucosal angiogenesis in NBI 'positive areas' (increased MVP intensity) in comparison to conventional white-light endoscopy ($P < 0.05$).[75] However, based on a small sample size, the study demonstrated the potential of NBI for *in vivo* imaging of intestinal neoangiogenesis in IBD patients.[75]

Another pilot study evaluated small-bowel findings in patients with Crohn's disease by using double balloon enteroscopy with FICE. Notably, FICE could not

improve the detection or delineation of ulcers and erosions due to Crohn's disease.[81] Nevertheless, the study was designed to assess the application of FICE for different small-bowel pathologies and included only three Crohn's disease patients. Moreover, active disease with ulcers and wide erosions are commonly revealed by standard white-light endoscopy, thereby lowering space to show any technological gain related to DLC.

In contrast, evaluating less severe markers of inflammation, Kudo *et al.* analysed the MVP in asymptomatic or mildly active UC by using both HD white-light endoscopy and NBI, while histology was defined as the golden standard.[76] While HD white-light endoscopy was feasible to detect the presence of a 'distorted' vascular pattern (defined as either irregular or tortuous), NBI revealed a more intense visualisation of vessel structures, thereby enabling the distinction between 'clear' and 'obscure' MVP. Both acute and chronic signs of microscopic inflammation were remarkably correlated with the 'obscure' MVP ($P < 0.05$), while only a minority among the chronic signs of inflammation correlated with the 'distorted and clear' MVP ($P = 0.0007$). Therefore, evaluation of the MVP with NBI yielded a more precise determination of acute microscopic inflammation in patients with quiescent UC. The same group performed two additional studies, confirming the strong correlation between NBI vascular findings and histological clues of inflammation.[77, 78] Reviewing these evidences, the authors distinguished the 'distorted' MVP observed in conventional colonoscopy from two different NBI patterns: one defined as 'clear' and the other one as 'obscure'.[79] Histopathological findings such as inflammatory cell infiltration, goblet cell depletion, distorted crypts and basal plasmacytosis were significantly more often found in biopsy specimens from 'obscure' appearing areas under NBI. Accordingly, NBI has the potential to predict histological severity in mild and inactive disease stages.

These data have also been confirmed in a recent parallel randomised trial evaluating i-scan for prediction of disease severity and extent in patients with mild or inactive IBD.[80] In this study, 78 IBD patients were consecutively and randomly enrolled to receive either HD white-light endoscopy or HD endoscopy with i-scan. Average duration of the examination did not differ between two groups. Comparing the endoscopic prediction of inflammatory extent and activity with the histological results, i-scan agreement scored 92% and 90%, respectively, while HD white-light endoscopy scored for 49% and 54% respectively. These differences were partially statistically significant ($P = 0.001$ and $P = 0.066$ respectively). Therefore, i-scan has the potential to improve the assessment of mucosal disease severity and extent in patients with IBD.

CONCLUSION AND FUTURE PERSPECTIVE

In the last decade, several endoscopy units have adopted the use of optical and digital DLC techniques to improve detection and characterisation rates of neoplastic lesions and assessment of mucosal healing in patients with long-standing IBD. These newer DLC techniques are integrated into modern endoscopes and highlight the mucosal and vascular pattern morphology in real time by just pushing a button on the endoscope.

Despite an increasing, scientific and clinical, interest in these DLC techniques, most studies have failed in showing a significant benefit and improvement of DLC in comparison to traditionally used DBC.

Studies based on surveillance of long-standing IBD suggested that NBI could not improve dysplasia detection compared with white-light endoscopy.[52, 57–59] On the contrary, NBI showed an equivalent dysplasia detection rate compared with DBC with indigo carmine dye spraying.[61] Beyond that, studies on digital DLC techniques for detection of neoplastic lesions in IBD are still missing. Characterisation of colorectal lesions in IBD is of paramount importance for subsequent therapy. In this context, preliminary data have shown an insufficient accuracy of NBI for characterisation of neoplastic from nonneoplastic colorectal lesions in IBD, while no data are available on the use of digital DLC for characterisation of colorectal lesion in IBD.[58, 63] In addition, no data are available on the effectiveness of DLC techniques for *in vivo* diagnosis of DALM and ALM. The differential diagnosis of these entities is therefore still based on clinical and histological findings.[51, 82, 83]

In contrast, by using histology as the reference standard, both NBI and i-scan have recently been shown to improve diagnosis of activity and extent of the disease in patients with IBD in comparison to white-light endoscopy. Therefore, these techniques harbour the potential to predict histological severity in mild and inactive disease stages and to redefine the term of mucosal healing.[75–80]

Taken together, at present, evidence suggests that DLC does not improve dysplasia detection rates over DBC. Moreover, based on currently available data, DLC techniques are not an adequate substitute for histology in suspected IBD-associated dysplasia. Future developments should assess the use of DLC in detection of

subtle inflammatory changes and mucosal angiogenesis in IBD.

AUTHORSHIP

Guarantor of the article: Gian Eugenio Tontini, MD, PhD.
Author contributions: GET: study concept and design; acquisition of data; analysis and interpretation of data; drafting of the manuscript; critical revision of the manuscript for important intellectual content; statistical analysis; study supervision. MV: critical revision of the manuscript for important intellectual content. MFN: critical revision of the manuscript for important intellectual content. HN: study concept and design; analysis and interpretation of data; drafting of the manuscript; critical revision of the manuscript for important intellectual content; study supervision. All authors approved the final version of the manuscript.

ACKNOWLEDGEMENTS

Declaration of personal interests: Helmut Neumann has served as a speaker or consultant or advisory board member for Pentax, Mauna Kea Technologies, Spectra Science, Abbvie, Abbott, MSD, Recordati, Eisai, Siemens, Falk and Medwork. Markus Neurath has served as a speaker or consultant or advisory board member for Abbott, Essex Pharma, Giuliani, MSD and Pentax.
Declaration of funding interests: Helmut Neumann has received funding from Pentax, Olympus, Siemens, Cook Medical, DLR, DGVS and ASGE. Markus Neurath has received funding from Abbott, Essex Pharma, Giuliani, MSD and Pentax. Gian Eugenio Tontini has gained a grant from the Italian Group for the study of IBD (IG-IBD) supporting his research work at the Department of Medicine I, University of Erlangen-Nuremberg.

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