Advanced Endoscopic Imaging for Assessing Mucosal Healing and Histologic Remission in Inflammatory Bowel Diseases

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KEYWORDS

• Inflammatory bowel diseases • Chromoendoscopy • Endocytoscopy
• Confocal laser endomicroscopy • Artificial intelligence • Molecular imaging

KEY POINTS

- With the development of new biologic therapies, the assessment of endoscopic and histologic remission is of primary importance in inflammatory bowel diseases, especially in ulcerative colitis.
- A large proportion of patients with histologically active IBD are not recognized using standard-definition white light endoscopy.
- Virtual chromoendoscopy is a time-saving and widely available tool that provides a higher correlation with histologic activity than white light endoscopy.
- Confocal laser endomicroscopy and endocytoscopy allow an in-vivo cellular view of the colonic mucosa, thus providing an optimal agreement with histologic activity. These techniques are currently used in clinical practice in selected cases in referral centers. However, a more diffuse clinical application of these promising techniques is limited by costs, increase in duration of examinations and necessity of training.
- Artificial intelligence can improve reproducibility and diagnostic accuracy when assessing endoscopic and histologic activity in patients with IBD.

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INTRODUCTION

Endoscopic remission (ER) is the primary goal in the clinical management of inflammatory bowel diseases (IBD),[1] which is associated with superior disease outcomes, including risk of hospitalization and surgery.[2] Histologic remission (HR) appears to be critical, especially in ulcerative colitis (UC), with several studies showing an association with improved long-term clinical results.[3,4] However, significant discrepancy might emerge between ER and HR, especially when using white-light endoscopy (WLE), with a study showing a 24% of "false negatives" in the setting of long-standing UC in ER.[5]

In the last decade, several advancements have been made in the endoscopic field, including technological improvements in the instrumentation (endoscopes and light sources), enhanced image resolution, and the development of new image processing and interpretation techniques. Some of these techniques, such as virtual chromoendoscopy, are currently applied in clinical practice; others, such as molecular imaging, are still mainly used in research settings.

The aim of this narrative article is to describe the role, current or potential, of each endoscopic technique, from standard WLE to molecular imaging, in the assessment of mucosal healing and HR in IBD.

WHITE-LIGHT ENDOSCOPY

Definition

In standard WLE, illumination is provided from an external high-intensity source through 1 or more light-carrying fiber bundles, producing an image resolution of up to 400,000 pixels.[6] Newer generation, high-definition (HD) endoscopes can generate full HD image and video resolution of 1920 $\times$ 1080 (2.1 million) pixels with 16:9 aspect ratio. This allows the production of sharper images with fewer artifacts and better visualization of mucosal surface details.[7] This system, including an HD endoscope, processor, cabling, and monitor identifies the high-definition, white-light endoscopy (HD-WLE).

Application in Definition of Inflammatory Bowel Diseases Activity

Some studies evaluated the correlation between endoscopic activity and histologic activity by using standard WLE.

A retrospective cross-sectional study in UC patients found that 21.6% of patients in ER were histologically active but revealed a moderate correlation between the Mayo endoscopic score and the Geboes score.[8] A prospective study confirmed the previous data, revealing 23.1% of histologically active patients with UC in clinical remission who had no endoscopic signs of activity.[9] Another prospective study using standard WLE revealed good correlation coefficients between the UC Endoscopic Index of Severity and histologic indexes ($r = 0.84$, $P<.001$ for the Nancy index and $r = 0.86$, $P<.001$ for the Robarts Histologic Index).[10]

Other studies comparing endoscopic and histologic activity by using HD-WLE showed conflicting results. In one of these, Simsek and colleagues found that endoscopically inactive disease had a low sensitivity to predict HR, thus revealing a poor correlation between the endoscopic and histopathological indices.[11] Another study, analyzing 154 biopsy specimens from 82 patients with UC, showed that histologic scores exhibited a strong correlation with endoscopic subscores (Spearman's rank correlation coefficient $r = 0.774$, $P<.001$).[12]

A systematic review and meta-analysis of 12 studies found no significant differences between the pooled correlation coefficients of endoscopic and histologic scores in standard WLE ($P=.74$) and HD-WLE ($P=.65$).[13]

Limitations

The cost of purchasing new HD endoscopic equipment needs to be considered. However, HD endoscopy is already widely spread[14] and it is recommended in several other gastrointestinal (GI) fields including screening and surveillance of upper and lower precancerous lesions.

CHROMOENDOSCOPY

Chromoendoscopy comprehends a set of techniques aiming to enhance the mucosal characteristics with the use of various dyes (dye-based chromoendoscopy [DCE]) or optical and digital color programs (dye less chromoendoscopy [DLC]).[15] By using these techniques, the contrast enhancement of the mucosa results in an improved characterization of superficial patterns and the vascular network.[16]

Dye-Based Chromoendoscopy

Definition

DCE uses different dye agents which are divided into absorptive agents (the most used being methylene blue), non-absorbed dyes (including indigo carmine, **Fig. 1**), and reactive staining agents (Congo red and phenol red).[17] Reactive dyes are the least commonly used, and their diagnostic relevance is low. Non-absorbed dyes coat the colonic mucosal surface, highlighting tissue architecture because of the higher contrast of pooled dye within the small grooves between the crypts and within the colonic pits. Non-absorbed dyes allow the identification of inflamed mucosa, characterized by disruption of the pit pattern. On the other hand, absorptive dyes are absorbed by different cells by different degrees, thus highlighting different cell types. Nevertheless, they avidly stain non-inflamed rather than inflamed tissue. Because of their mechanism of action, absorptive dyes allow a stable staining pattern and a longer examination time (up to 20 minutes) if compared with non-absorbed dyes (few minutes). Both categories of staining agents are mostly applied via standard spraying or catheters.[18]

Application in definition of inflammatory bowel diseases activity

Only a few studies evaluated the utility of DCE in assessing IBD activity and extension, as its primary use is linked to the detection of dysplasia and cancer.[19]

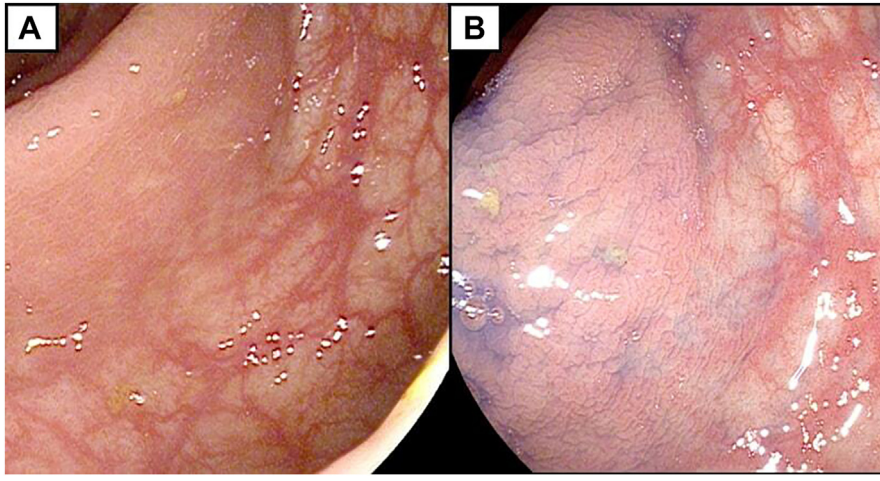

Fig. 1. Colonic mucosa before (*A*), and after (*B*), spraying with indigo carmine. (Image courtesy of Francesco Simone Conforti, MD.)

Limitations

DCE has some potential limitations hindering its feasibility in common clinical practice. First, it is a time-consuming procedure increasing colonoscopy time 2-fold to 3-fold, requiring a specific training and increasing procedural costs.[20] Second, the dye does not always coat the surface evenly, especially in condition of suboptimal large bowel preparation. On-site training of at least a week, with at least 20 procedures with DCE with an expert operator in optical diagnosis of IBD is suggested to achieve the proper competence.[21] Finally, the dye does not provide a detailed evaluation of the subepithelial capillary network, which is an important feature in the diagnosis of GI neoplasia and disease activity.[19]

Virtual Electronic Chromoendoscopy

Despite DCE, Virtual Electronic Chromoendoscopy (VEC) combines optical and digital filtering to enhance contrast without using any dye. The most commonly available systems are brand dependent and include narrowband imaging ([NBI], Olympus Medical Systems, Japan), blue light imaging (BLI) and linked color imaging ([LCI], Fujifilm, Japan), and i-Scan and i-Scan optical enhancement (OE) (i-Scan, i-Scan OE, Pentax, Japan) (see **Fig. 1**).

Narrowband imaging

NBI applies a preprocessing technique based on the optical filtering of the illumination light, reducing the spectral bandwidth to a wavelength of 415 nm for blue and 540 nm for green light, which correspond to the absorption peaks of hemoglobin.[22] By doing so, the blue and green lights are markedly absorbed by structures containing high levels of hemoglobin. Thus, the final NBI image improves the visualization of mucosal and vascular structures (**Fig. 2**).[23]

Blue light imaging and linked color imaging

BLI is a preprocessing technique which resembles NBI's hemoglobin excitation by blue light, which in this case is generated by a 4-light-emitting-diode (LED).[24] LCI is based on both pre- and post-processing techniques, which combine a short narrowband laser light with a white laser light generated by 4-LED, which enhance hemoglobin recognition by improving delineation and detection in distant areas (**Fig. 3**).

i-Scan optical enhancement

i-Scan OE combines the previously reported preprocessing short-wavelength hemoglobin OE techniques with post-processing digital algorithms that can enhance

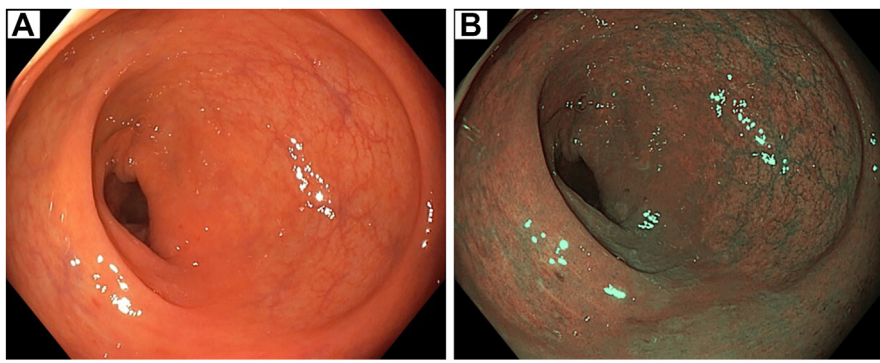

Fig. 2. Normal rectum visualized with high definition white-light endoscopy (HD-WLE) (*A*) and NBI (*B*). (Image courtesy of Felice Benedicenti, MD.)

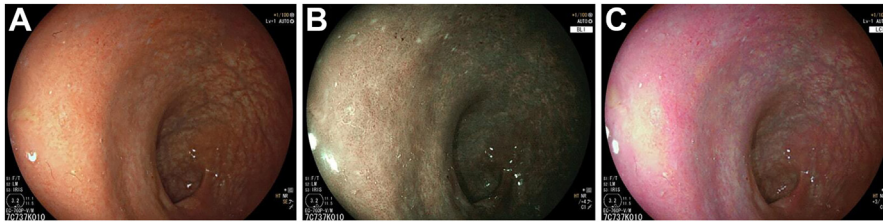

Fig. 3. Mildly active proctitis revealed at high definition-white-light endoscopy (HD-WLE) (*A*), blue light imaging (BLI) (*B*) and linked color imaging (LCI) (*C*). (Image courtesy of Francesco Segatta, MD.)

specific characteristics of WLE. The 3 existing modes, selectable by pressing a button on the handpiece of the scope, include surface enhancement (i-Scan 1) for the detection of abnormalities in the GI tract, tone enhancement (i-Scan 2) for pattern characterization, and OE (i-Scan 3) for characterization of blood vessels, glandular ducts, and mucosa.[25]

The OE function further improve visibility of the blood vessels, ducts of the glands, and surface structures by combining bandwidth-limiting light with digital image processing. The OE mode 1 highlights more blood vessels for close view characterization, while mode 2 enhances the blood vessels and the mucosa in a natural color potentially supporting panoramic viewing and screening (**Fig. 4**).

Application in definition of inflammatory bowel disease activity

Recently, VEC has been intensively studied for the assessment of disease activity in the setting of IBD. For this purpose, several scores were created, especially for patients with UC. In 2017 the Paddington International virtual Chromoendo-Scopy Score (PICaSSO) was developed and validated, including details of subtle vascular and mucosal changes reflecting acute or chronic inflammatory changes in UC patients.[26] A large prospective study by Iacucci and colleagues showed a strong correlation with 5 histologic scores to assess histologic remission, defined as a PICaSSO score less

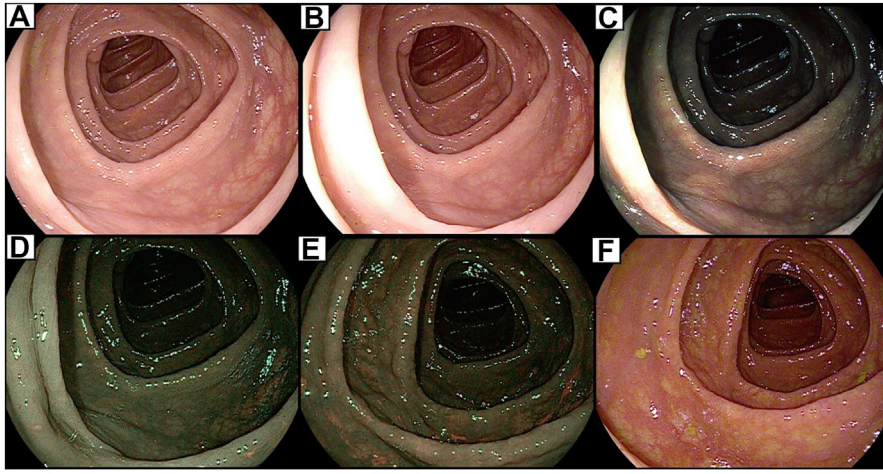

Fig. 4. Normal ascending colon at high definition-white-light endoscopy (HD-WLE) (*A*), i-Scan 1 (*B*), i-Scan 2 (*C*), i-Scan 3 (*D*), i-Scan OE 1 (*E*), i-Scan OE 2 (*F*). (Image courtesy of Francesco Simone Conforti, MD.)

than 3, with Pearson's correlation between 0.77 and 0.79.[27] Furthermore, it has also shown optimal ability as a predictor of good long-term outcomes and is currently available on all the main endoscopic platforms.[28]

Other scores are based on NBI and LCI technology. NBI combined with magnification distinguished a 3-categories score based on blood vessels morphology.[29]

As per NBI, LCI was used to create a score made of 3 categories: LCI-A (no redness), LCI-B (redness with visible vessels), and LCI-C (redness without visible vessels), which showed a strong correlation with the histopathology Matts score.[30] However, to date, PICaSSO is the only validated and reproduced score that all endoscopic platforms can use.

A meta-analysis comparing the correlations between endoscopy and histologic disease activity scores across several endoscope technologies found no significant difference among them. However, VCE was more accurate in predicting histologic remission than WLE.[13]

Although applications in the field of UC are preponderant, VEC can also be used for the evaluation of endoscopic disease activity in Crohn's Disease (CD). To overcome the limitations of the Simple Endoscopic Score for Crohn's Disease (SES-CD), a new scoring tool named the modified multiplier (MM) of the SES-CD has been developed. This score revealed to be more accurate than the original SES-CD scoring approach for predicting endoscopic remission (comparison of area under the curves on the testing cohort for MM-SES-CD vs original SES-CD: P=.0052).[31]

Limitations

It is conceivable that lesion recognition by VEC is facilitated by previous training using DCE. The issue of costs is limited because new generation endoscopic equipment is usually implemented with VEC technology. Procedural time might not significantly increase.

PROBE-BASED CONFOCAL LASER ENDOMICROSCOPY

Definition

Probe-based confocal laser endomicroscopy (pCLE) technology is an advanced endoscopic imaging technique based on a system that requires a source pinhole, a beam splitter, and an objective lens to align illumination and collection system in the same specimen plane (hence the term "confocal"). By injecting topical or intravenous fluorescent dyes with a flexible device passing through the working channel of standard endoscopes, pCLE provides a magnified, cellular level view of GI epithelia and allows for an "optical biopsy" for real-time diagnosis (**Fig. 5**).[32]

This technique has several potential applications in the IBD field. First, pCLE seems accurate in distinguish between CD and UC. In patients with CD, more discontinuous inflammation, focal cryptitis, and discontinuous crypt architectural abnormality are found. Conversely, widespread crypt distortion, decreased crypt density, and irregular surface are more frequently associated with UC.[33]

Furthermore, applications in defining disease activity have been intensively studied in the last decade.

Application in Definition of Inflammatory Bowel Disease Activity

pCLE can assess the degree of inflammation and disease activity in patients with IBD, with optimal agreement with the histologic activity. Normal intestinal mucosa is characterized by round and regular crypts. On the contrary, the CLE inflammatory characteristics in IBD include distorted and elongated crypts with irregular and wider lumens.[34]

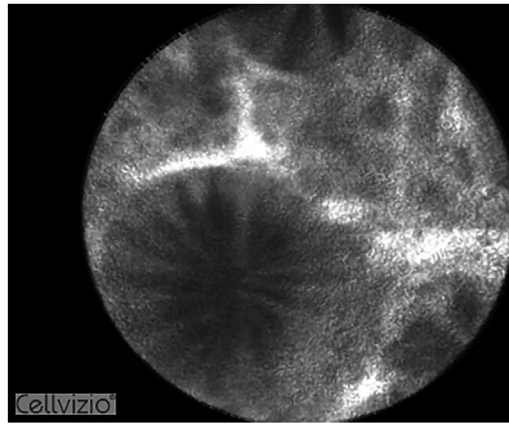

Fig. 5. Normal crypts at probe-based confocal laser endomicroscopy.

Based on these criteria, Li and colleagues showed that pCLE could predict UC histologic activity more accurately than ER as assessed by WLE. In this study on 74 UC subjects, more than half of patients with an endoscopically normal mucosa presented acute inflammation on histology. In this circumstance, microvascular alterations by CLE showed good correlation with histologic findings, while normal CLE findings predicted HR.[35]

Nevertheless, CLE seems quite reliable in defining inflammatory activity in patients with CD. Indeed, pCLE has allowed the development of a scoring system predicting histologic inflammation in non-inflamed-appearing mucosa that permitted a clear distinction between quiescent CD and healthy controls. This scoring system is based on specific pCLE parameters such as increased goblet cells and increased numbers of crypts.[36]

This optimal correspondence between inflammatory activity at pCLE and histology is confirmed also after medical therapy. In this context, a prospective study by Karstensen and colleagues showed that the improvement of endomicroscopic features after medical treatment such as crypt tortuosity, distortion of crypt openings, and decreased crypt density correlates with a decrease in histopathologic score.[37]

pCLE could also be used to forecast disease flares. In this setting, a prospective study by Buda and colleagues demonstrated that a composite outcome score combining fluorescence leakage and crypt diameter was able to predict a disease flare during a 12-month follow-up period.[38]

In another prospective, study on 49 consecutive patients with CD, CLE revealed in real-time early predictors of negative clinical outcomes during the follow-up: the presence of cryptitis at CLE was highly predictive of medical treatment escalation and transmural lesions.[39]

Recent studies investigated the role of the intestinal barrier integrity (eg, intestinal epithelial cells, tight junctions, and adherens junction) in the natural history of IBD, demonstrating a correlation between intestinal barrier dysfunction and long-term disease outcomes.[37]

In this context, pCLE can be used to study intestinal barrier permeability in vivo and in real-time, hereby enabling the characterization of functional changes invisible to any traditional pathologic study. Kiesslich and colleagues demonstrated that CLE can accurately identify the shedding of epithelial cells and any local barrier defects as plumes of fluorescein effluxing through the epithelium. In a pivotal prospective pilot

study of 47 patients with UC and 11 patients with CD in clinical remission, cell shedding and barrier loss predicted relapse within 12 months after endomicroscopic examination ($P<.001$).[40] A recent scoping review including 52 studies concluded that CLE is a useful tool in real-time assessment of histologic activity in both UC and CD.[41]

Limitations

Operator-dependency and requirement of prior training are real issues of pCLE. Overall, self-directed skills consolidation through assessment of 50 to 80 cases is recommended, after formal training, to achieve diagnostic proficiency.[32] Further concerns related with this technology are additional costs and timing and the need for fluorescein intravenous injection.

ENDOCYTOSCOPE

Definition

Endocytoscopy (EC) is a contact-type optical endoscope with an ultra-magnification endoscopy system that allows in vivo cellular observation during GI endoscopy. It requires the application of a mucolytic agent to assist the penetration of a topical contrast agent (eg, methylene blue, toluidine blue, or cresyl violet).[42] As with pCLE, EC can provide a highly accurate pathologic prediction in vivo and in real-time. Conventional magnification endoscopy needs to maintain the distance between the lens and the target lesion to obtain a focused image. In contrast, EC does not require distance to be maintained and an ultra-magnified image can be obtained by just contacting the lesion and then pulling down a magnification lever (**Fig. 6**).[43]

Application in Definition of Inflammatory Bowel Disease Activity

A score considering the shape of the crypts, distance between the crypts, and vessels, the EC system score (ECSS), was created by Bessho and colleagues In their study, the ECSS of UC intestinal mucosa, was strongly related with histologic activity.[44] Another ECSS was created by Vitali and colleagues that revealed a higher correlation with histologic activity if compared with WLE.[45]

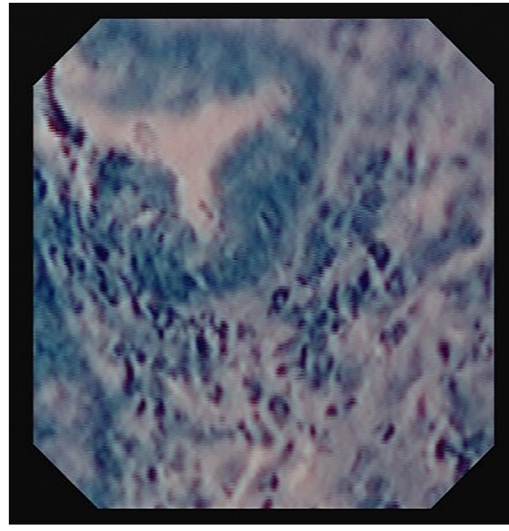

Fig. 6. Normal crypts at endocytoscopy after methylene blue spraying.

Another possible application under investigation of EC, concerns the definition of the inflammatory infiltrate. Indeed, a prospective study by Neumann and colleagues on 40 patients with IBD, EC could precisely identify the various types of inflammatory cells infiltrating the intestinal mucosa.[46]

Limitations

EC significantly increases duration of colonoscopy, as the reported duration of the EC procedure is around 45 minutes.[47] Instrumentation costs and the necessity of specific training for the endoscopists are issues to be considered.

ARTIFICIAL INTELLIGENCE

Definition

Artificial intelligence (AI) is an umbrella term that commonly refers to machines mimicking human cognitive behavior during learning and problem-solving.[48]

AI is taking an increasingly central role in the scientific world and is finding numerous applications in the medical field. In the context of GI endoscopy, AI has found application in the detection of mucosal lesions (computer-aided detection), in the characterization of mucosal lesions (computer-aided diagnosis), along with the endoscopic procedure quality assessment and copiloting (computer-aided monitoring).[49]

In this context, several studies have evaluated the utility of AI in the field of IBD endoscopy in determining disease activity.

Application in Definition of Inflammatory Bowel Disease Activity

A large study published in 2019 based on 16,514 fixed images from 3082 patients revealed an optimal performance of a deep-learning model in distinguishing moderate to severe UC from UC in endoscopic remission, compared with multiple expert reviewer (AUROC 0.97).[50] Another central neural network system trained with 26,304 colonoscopy images from 841 patients with UC showed high performances to identify Mayo score 0 and 0 to 1 (AUROCs of 0.86 and 0.98).[51] A recent systematic review underlined how AI models can assess UC endoscopic activity with high accuracy and how AI-assisted virtual chromoendoscopy could predict HR and long-term outcomes.[52]

Other studies showed that deep learning algorithms can be trained to predict endoscopic activity from full-length endoscopy videos.[53,54] A prospective study showed that AI could be useful in predicting clinical relapse in 135 patients with UC (relapse rate 28.4% vs 4.9%, $P<.001$).[55] Moreover, a deep neural network for evaluation of UC algorithm using 40,758 images of colonoscopies and 6885 biopsy results from 2012 patients with UC was able to identify HR with 92.9% accuracy (95% CI 92.1%–93.7%).[56] The future implementation of AI in IBD endoscopy seems especially useful in solving the long-standing problem of precision and reproducibility in assessing the degree of endoscopic activity. This could help in standardizing the assessment of endoscopic severity in clinical trials and in non-IBD referral centers. According to a recent systematic review and meta-analysis, experimental AI systems can assess ER in UC patients with high sensitivity, specificity and diagnostic odds ratio either working on cleared fixed images (0.91, 0.89 and 92.42, respectively) or on video (0.86, 0.91 and 70.86, respectively) collected by standard colonoscopy imaging.[57]

Recently, Iacucci and colleagues have developed 2 efficient AI models, assessing ER from VEC videos,[58] recognizing HR in digital biopsies of UC patients[59] and predicting clinical flare-up.

While all the aforementioned studies have applied AI to the field of IBD activity by mimicking and standardizing a humanized task (ie, ECSS based on predefined

descriptive criteria), AI could be also trained to identify signatures of mucosal inflammation based on computational criteria, which cannot be captured and analyzed by human eyes. The red density score described by Bossuyt and colleagues in 2020 is the first operator-independent scoring system for UC endoscopic activity.[60] This system allows a real-time quantitative analysis of inflammatory mucosal changes by measuring the hypervascularization with an HD endoscope with a white-light xenon lamp. Based on this first pilot study, the red density score significantly correlates with both endoscopic and histopathological disease activity.

Limitations

AI systems rely heavily on high-quality input data. Current algorithms are specifically fitted for a determined data set that may lack diversity in the training data. A sizable proportion of the AI models applied to the clinical setting are only internally validated. Ideally, models should be externally validated on diverse cohorts to ensure that overfitting does not become an issue,[61] but external validation enhances concerns on data security.

The cost of AI systems must be factored into the equation, but the benefit in terms of the reduction in the number of examinations patients undergo may outweigh it.[62]

Duration of examination is not concerning, as demonstrated by similar retraction time with and without AI.[63]

Operator deskilling because of the systematic adoption of AI systems in IBD endoscopy have been never demonstrated. However, it is conceivable that the constant presence of AI support will determine a faster learning curve in non-experts but also a total dependence on AI to solve more difficult tasks. That brings a substantial risk that non-expert operators could be led to misinterpretation by suboptimal AI systems facing unusual pictures (ie, training data bias).

MOLECULAR IMAGING

Conventional endoscopy relies on morphologic changes to assess the presence of pathology, thus carrying an intrinsic limitation for early diagnosis of dysplasia and cancer. Molecular endoscopic imaging (MEI) uses molecular probes or imaging agents to assess the presence of molecular markers specifically associated with cancer or disease conditions.[64] MEI also requires a new generation instrumentation including an imaging device to detect the molecular probes and their signal. Most of currently used imaging devices have a detection range restricted to 480 nm to 520 nm. Probes are usually labeled with a fluorophore, the most used being fluorescein, which carries a high image resolution with a low tissue penetration (emission range: 488–515 nm).[65] Both the probes and the fluorophore may be administered topically or systemically.

An in vivo study by Atreya and colleagues showed that the topical application of a fluorescently labeled adalimumab allowed the detection of membrane-bound TNF $(mTNF)^+$ immune cells in patients with CD. Patients with higher numbers of $mTNF^+$ cells showed a better response to adalimumab.[66] In another publication from the same study group, Rath and colleagues showed that MEI of $\alpha4\beta7$ with fluorescein isothiocyanate –labeled vedolizumab could be adopted to predict therapeutic responses and provide a rational basis for individualized therapy in CD.[67]

Despite the solid theoretic base and the promising results of preclinical studies, clinical applications of MEI in the field of IBD endoscopy are still lacking. Major issues to be addressed include the development of safe and cost-effective imaging agents and markers, and the new technical aspects that may add some time and procedural challenges to the endoscopic examination. On the other hand, the use of MEI on ex vivo

Table 1
Summary of the most relevant studies addressing endoscopic imaging for definition of mucosal healing and histologic healing – expert selection

Title	Author	Journal	Year	Study Design	Number of Patients	Main Evidence
The prognostic value of histology in UC in clinical remission with mesalazine[9]	Frieri G	Therap Adv Gastroenterol.	2017	Observational prospective	52	HR as the only factor associated with relapses. With SD-WLE, 23.1% of histologically active patients in ER.
Correlation between endoscopic and histologic activity in UC using validated indices[10]	Irani NR	J Crohns Colitis	2018	Oservational prospective	125	Good correlation coefficients of UCEIS at HD-WLE and histologic activity (Nancy index, Robarts Histologic index).
Advanced technology for assessment of endoscopic and histologic activity in UC: a systematic review and meta-analysis[13]	Nardone OM	Therap Adv Gastroenterol.	2022	Systematic review and meta-analysis	1845 (27 studies)	Similar accuracy of SD-WLE and HD-WLE in assessing histologic activity. VEC more accurate in predicting histologic remission than WLE.
An international multicenter real-life prospective study of electronic chromoendoscopy score PICaSSO in UC[27]	Iacucci M	Gastroenterology	2021	Observational prospective	307	An HD-WLE and VEC score strongly correlated with histologic activity evaluated with Robarts Histologic index, Nancy Histologic index, ECAP, Geboes, and Villanacci.
Predicting endoscopic remission in CD by theMM-SES-CD[31]	Narula N	Gut	2022	Post-hoc analysis of three clinical trials	350	Development and internal validation of a VEC score (the MM-SES-CD) to predict ER in patients with CD on active therapy.

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Table 1
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Title	Author	Journal	Year	Study Design	Number of Patients	Main Evidence
Assessment of CD activity by confocal laser endomicroscopy[36]	Neumann H	Inflamm Bowel Dis.	2012	Observational prospective	54	At CLE, increased colonic crypt tortuosity, enlarged crypt lumen, microerosions, augmented vascularization, and increased cellular infiltrates within the lamina propria were associated with histologic activity in CD.
Classification of inflammation activity in UC by confocal laser endomicroscopy[35]	Li CQ	Am J Gastroenterol.	2010	Observational prospective	73	At CLE, assessment of crypt architecture and fluorescein leakage with showed good correlations with histologic results. CLE resulted more accurate than WLE for assessing histologic activity in endoscopically normal mucosa.
Endocytoscopy for assessing histologic inflammation in UC: development and prospective validation of the ELECT (ErLangen Endocytoscopy in ColiTis) score (with videos)[45]	Vitali F	Gastrointest Endosc.	2023	Observational prospective	46	A new endocytoscopic score was validated, showing strong correlation with histopathologic scoring (Robarts Histopathology Index, Nancy Histologic Index) and was superior to WLE for grading of histologic activity.

Development and validation of a deep neural network for accurate evaluation of endoscopic images from patients with UC[56]	Takenada K	Gastroenterology	2020	Observational prospective	875	A deep neural network for evaluation of endoscopic images from patients with UC identified ER with 90.1% accuracy and HR with 92.9% accuracy.

Abbreviations: AI, artificial intelligence; CD, Crohn's disease; CLE, confocal endomicroscopy; EC, endocytoscopy; ER, endoscopic remission; HD-WLE, high-definition white-light endoscopy; HR, histologic remission; SD-WLE, standard-definition white-light endoscopy; UC, ulcerative colitis; VEC, virtual chromoendoscopy.

Table 2
Summary of the characteristics of the main endoscopic imaging techniques in the field of inflammatory bowel diseases- expert opinion

	HD-WLE	DCE	VEC	EC	pCLE	MEI	AI
Availability	+++	++	++	-	-	-	+
Activity assessment	++	-	++	+++	+++	?	+
Dysplasia detection	+	++	++	-	-	?	+
Dysplasia characterization	+	++	++	+++	+++	+	+
Current clinical application	+++	+++	+++	-	-	-	-
Prolonged examination	-	++	-	++	++	++	-
Necessity of training	-	+	+	++	++	+++	-
Additional costs	-	-	-	++	++	+++	+
Personalized medicine	-	-	-	-	-	+++	-

Abbreviations: AI, artificial intelligence; DCE, dye-based chromoendoscopy; EC, endocytoscopy; HD-WLE, high-definition white-light endoscopy; MEI, molecular endoscopic imaging; pCLE, probe-based confocal endomicroscopy; VEC, virtual chromoendoscopy.

tissue samples from endoscopic biopsies to predict response to medical therapies could reduce such safety issues. This would give a better chance of a faster path to its implementation in clinical practice in the near future.

SUMMARY

GI endoscopy has always played a pivotal role for diagnosis, staging, disease activity assessment, and surveillance in IBD patients. More recently, IBD endoscopy has been significantly enriched with dedicated knowledge, strategies, and technologies, becoming a highly qualified skill (Table 1).

In modern tertiary IBD referral centers, a dedicated IBD endoscopic team takes advantages of cutting-edge diagnostic equipment (HD system AND VEC), close interplay with clinicians, and a multidisciplinary IBD team to implement treat-to-target and personalized patient management (Table 2).

Advanced endoscopic imaging techniques for real-time optical biopsy, and pCLE and EC is nowadays a promising starting point for clinical research and an exceptional clinical resource in selected cases and academic centers with a distinguished expertise.

The next generation of AI systems is expected to standardize the disease activity assessment. It will simplify and optimize clinical research protocols and spread an improved reproducibility and diagnostic accuracy outside academic centers at relative low cost, linked to the procurement of the technology.

In a not-too-distant future, the use of MEI coupled with multi-omics AI-based computational analysis will probably guide a patient tailored therapeutic profiling and anticipate the morphologic diagnosis of colitis-associated dysplasia to the level of ultrastructural and molecular changes.

The final frontier of IBD endoscopy begins in this era.

CLINICS CARE POINTS

- HD-WLE should be preferred over standard-definition WLE for the assessment of endoscopic activity in IBD

- Virtual chromoendoscopy should be preferred over white light endoscopy for the direct assessment of endoscopic activity and the indirect assessment of histologic activity in IBD, especially in UC
- For the assessment of endoscopic activity in IBD, virtual chromoendoscopy should be preferred over DCE
- To achieve an optimal direct assessment of histologic activity, the use of confocal laser endomicroscopy and endocytoscopy is currently limited to selected cases in high-expertise tertiary centers
- For the assessment of endoscopic and histologic activity in IBD, the use of AI might be considered in addition to the other endoscopic techniques to improve diagnostic reproducibility and accuracy.

DISCLOSURE

None to declare.

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