https://doi.org/10.31689/rmm.2024.31.1.13

ORIGINAL PAPERS

The Role of Spectral Focused Imaging (SFI) in Diagnosing Subtle Mucosal Changes in Patients with Ulcerative Colitis

Andreea DOBROMIRESCU[1,2], Simona-Andreea BALOSU[1,2], Adrian DUMITRU[1,3], Lucian NEGREANU[1,2]

Abstract

Background: Due to the rapid development of new diagnostic and therapeutic endoscopic techniques, there has been a gap between their development and implementation in daily practice, as well as in their uptake in guideline recommendations[1]. We investigated the effectiveness of spectral focused imaging (SFI), a new optical chromoendoscopy system (SonoScape, Shenzhen, China)2, in diagnosing subtle mucosal changes in patients with inactive ulcerative colitis. **Materials and Methods:** A group of 12 patients with quiescent ulcerative colitis were randomly assigned at a 1:1 ratio to undergo colonoscopy with high-definition white light (group A) or SFI (group B). The mucosal pattern, location of the mucosal changes (measured in centimeters from the anal verge), morphology, size and duration of the endoscopic procedure were recorded, while the disease activity was established following the Mayo endoscopic score for ulcerative colitis. Subsequent to the endoscopic characterization, targeted biopsies (or random biopsies in a case of normal colonic mucosa) were obtained from every segment for histopathological follow-up analysis. **Results:** The median endoscopic activity index, based on the Mayo ulcerative colitis endoscopic score, was 1 for both groups of patients. Taking into account the duration of the examination, the median value was 17.3 minutes in group A and 18.5 minutes in group B. Upon examining the concordance between the endoscopic prediction of disease activity and the histological findings, we obtained a 55% degree of conformity in group A, compared to 90% in group B. **Conclusions:** This pilot study showed that image-enhanced endoscopy using SFI might increase the rate of detection and demarcation for subtle inflammatory changes in the mucosa, correlating with potential histologic activity. Furthermore, this diagnostic tool could provide a more accurate and earlier identification of areas of minimal inflammation than conventional techniques.

Keywords: inflammatory bowel disease, ulcerative colitis, virtual chromoendoscopy, spectral focused imaging, high-definition white light endoscopy, mucosal healing

Rezumat

Introducere: Datorită dezvoltării rapide a noilor tehnici endoscopice diagnostice și terapeutice, a existat un decalaj între dezvoltarea și implementarea acestora în practica zilnică, precum și în adoptarea lor în recomandările ghidurilor[1]. Am investigat eficacitatea imagistică focalizată spectrală (SFI), un nou sistem de cromoendoscopie optică (SonoScape, Shenzhen, China)[2], în diagnosticarea modificărilor subtile ale mucoasei la pacienții cu colită ulceroasă inactivă. **Material și metode:** Un grup de 12 pacienți cu colită ulcerativă inactivă au fost repartizați aleatoriu într-un raport de 1:1 pentru a fi supuși colonoscopiei cu lumină albă de înaltă

[1]University of Medicine and Pharmacy "Carol Davila", Bucharest, Romania
[2]Gastroenterology II Department, Bucharest Emergency University Hospital, Romania
[3]Pathology Department, Bucharest Emergency University Hospital, Romania

***Corresponding author:**
Simona-Andreea BALOSU, University of Medicine and Pharmacy "Carol Davila", Bucharest, Romania
E-mail: simonaat93@gmail.com

definiție (grupul A) sau SFI (grupul B). Aspectul mucoasei, localizarea modificărilor mucoasei (măsurată în centimetri de la marginea anală) si morfologia acestora, precum și durata procedurii endoscopice au fost evaluate, în timp ce activitatea bolii a fost stabilită în urma scorului endoscopic Mayo. După caracterizarea endoscopică, biopsii țintite (sau biopsii aleatorii în caz de mucoasă colonică normală) au fost obținute din fiecare segment pentru analiza histopatologică. **Rezultate:** Indicele median al activității endoscopice, bazat pe scorul endoscopic al colitei ulcerative Mayo, a fost 1 pentru ambele grupuri de pacienți. Luând în considerare durata examinării, valoarea mediană a fost de 17,3 minute în lotul A și de 18,5 minute în lotul B. La examinarea concordanței dintre predicția endoscopică a activității bolii și constatările histologice, am obținut un grad de conformitate de 55% în grupul A, comparativ cu 90% din grupul B. **Concluzii:** Acest studiu pilot a arătat că tehnica de cromoendoscopie SFI ar putea crește rata de detectare și demarcare a modificărilor inflamatorii subtile ale mucoasei, corelându-se cu activitatea histologică potențială. În plus, acest instrument de diagnostic ar putea oferi o identificare mai precisă și mai timpurie a zonelor cu inflamație minimă decât tehnicile convenționale în lumină albă. Este nevoie de studii suplimentare pentru validare.
Cuvinte cheie: Boli inflamatorii intestinale, colită ulcerativă, cromoendoscopie virtuală, imagistică focalizată spectrală, colonoscopie cu lumină albă de înaltă definiție, vindecare mucosală.

INTRODUCTION

Ulcerative colitis (UC) is a chronic inflammatory disease involving the gastrointestinal tract, characterized by a relapsing and remitting course[3]. The therapeutic management of UC is constantly changing, and now a new concept known as "deep remission" might be the ideal therapeutic goal for this type of patient. Although the definition of a "deep remission" has not been validated, current studies have defined it as a profound remission without clinical symptoms or biological activity, with complete mucosal healing and the disappearance of histological inflammatory changes (histological healing)[4,5]. The evaluation of mucosal healing and its correlations with histological healing could be realized with high-definition white-light endoscopy, dye-based chromoendoscopy (CE) and virtual chromoendoscopy (VCE). Other less accessible techniques that deserve mentioning are autofluorescence imaging, confocal laser endomicroscopy, endocytoscopy and molecular imaging[6].

Endoscopy has an essential role in UC management, from the initial diagnosis to guiding and tailoring medical and surgical therapy, as well as in treating disease-related complications and assisting in the early detection of dysplasia (which can lead to colorectal cancer)[1]. The debate over the best method and intervals for colonoscopic surveillance in patients with longstanding UC is still ongoing. Currently, dye-based chromoendoscopy and virtual chromoendoscopy with targeted biopsies are recommended by the European Society of Gastrointestinal Endoscopy (ESGE) for neoplasia surveillance in patients with longstanding UC[7].

The aim of this pilot study was to determine whether virtual chromoendoscopy, represented by SFI, has the potential to enhance the rate of detection of subtle mucosal lesions in patients with inactive UC in comparison to high-definition white light endoscopy (HD-WLE), as WLE is the most widely used standard procedure in daily practice[8.] However, WLE has some weak points, namely, the fact that subtle and mild residual signs of inflammation cannot be highlighted and the results obtained cannot always be correlated with the histopathological aspects in terms of mucosal healing. These observations have been proven by Baars in a study of 152 patients with IBD, 65% of whom had ulcerative colitis[9]. Of the 152 patients, all in clinical remission, 31% had no evidence of endoscopic inflammation. Among the remaining 69%, 34% had both endoscopic and histological inflammation, 34% had only histopathologically evident inflammation, and 1% had an endoscopic inflammatory appearance but were unconfirmed histopathologically[9.] Therefore, even though WLE is extremely useful in evaluating active disease and its extension and severity, detailed images of the mucosa, especially of the vascular pattern, cannot be obtained in patients with mild or inactive forms

because the mucosal healing described by WLE might miss minimal inflammatory lesions, which can influence the evolution of the disease in terms of the risk of relapse and long-term complications[8].

The new HD-WLE has additional benefits in terms of mucosal visualization, but nevertheless, its ability to assess vascular patterns and mucosal surface characteristics is still limited[10]. New advanced techniques, such as virtual chromoendoscopy, have provided an enhanced visualization of mucosal and vascular patterns, allowing for targeted biopsies without the need for additional dyes or special equipment. Virtual CE is divided into two categories: optical chromoendoscopy and digital chromoendoscopy. Optical CE technology uses optical lenses that selectively filter white light, resulting in narrow-band light, and in this category, we have narrow-band imaging (NBI, Olympus, Japan) and linked color imaging (LCI, Fujifilm, Japan). Digital chromoendoscopy is based on the reflection of photons to reconstruct virtual images using a real-time digital video processor and it includes technologies such as i-Scan (Pentax) and flexible imaging color enhancement (FICE, Fujinon, Japan). The new SFI (SonoScape, China) combines both optical and digital chromoendoscopy into a single system, with the advantage that it preserves the original color while highlighting the mucosal structure and vascular distribution[11,12,13,2,14].

Given that we have a specific challenge in diagnosing lesions of chronically inflamed mucosa (IBD patients), there is a strong need for advanced endoscopic techniques for both the detection and characterization of colorectal lesions. Thus, virtual CE, due to its promising results in improving the accuracy of diagnosis in patients with IBD and because it sometimes provides additional information with images that beforehand suggested endoscopic healing, seems to be the future gold standard for surveillance colonoscopy in IBD patients[4].

With the use of these novel techniques, a new endoscopic semiology has emerged, including crypt architecture, microerosions, fine vascular changes around the crypts and a distinction between intramucosal and luminal bleeding[15,16]. There is also a virtual chromoendoscopy dedicated score, the PiCaSSo score (Paddington International Virtual ChromoendoScopy Score), which was shown in a study conducted by Iaccuci et al. to have the same degree of accuracy between observers, regardless of their experience, and a very good correlation with the histopathological examination of the identified lesions[17]. Another strong point of virtual chromoendoscopy is the fact that it can be easily introduced into current practice, as it is elegant, less cumbersome and easy to apply[17].

MATERIALS AND METHODS

A total of 12 patients with quiescent UC were randomized at a 1:1 ratio to undergo HD-WLE (group A) or SFI colonoscopy (group B). The procedures were performed with high-definition systems (the SonoScape HD-550 processor with a 4-LED light source and the SonoScape 550 colonoscope) following standard bowel preparation using a polyethylene glycol–electrolyte lavage solution. The procedures were carried out under conscious sedation with propofol, assisted by an anesthesiologist. All colonoscopies were performed strictly under either white light HD or spectral focused imaging (SFI) mode. In group B, the colonoscope was inserted under SFI mode, thereby excluding potential bias from the findings of HD-WL during insertion. All procedures were performed by a single experienced endoscopist blinded to the patients' history and their current medication.

The parameters assessed were the mucosal pattern, the location of any mucosal changes (measured in centimeters from the anal verge), their morphology and size, and the duration of the endoscopic procedure. Endoscopic disease activity was recorded by the endoscopist following the Mayo Endoscopic Score for UC. All patients with moderate or severe endoscopic activity (Mayo Endoscopic Score ≥2) involving at least one colonic segment were excluded.

Regarding the biopsy protocol, in group A, biopsies were taken from the most distal part of the area of mucosal inflammation as determined by the HD-WLE. In cases of normal colonic mucosa, random biopsies (2-4 non-targeted biopsies from every 10 cm of the colon) were taken to determine the histological extent and severity of any inflammation. The same biopsy protocol was used for the patients in group B.

The biopsy specimens were fixed with 10% neutral buffered formalin and sent for histopathological (HP) processing by the conventional method using paraffin embedding and hematoxylin-eosin (HE) staining. The pathologist was blinded to the identity and clinical history of the subjects. The histologic disease activity was determined using the Geboes score (GS). This is

a widely used 6-grade scoring system that evaluates the crypt architecture, lamina propria chronic inflammation, lamina propria neutrophils and eosinophils, intraepithelial neutrophils, crypt destruction and surface epithelial injury.

Data were analyzed by using SPSS Windows 15 version. Regarding the descriptive statistics, we used the mean and standard deviation (SD) to analyze the parametric data; the median and interquartile range (IQR) to analyze the non-parametric data; and the percentile (%) to analyze the qualitative data. To compare the parametric data, we used Student's t-test.

RESULTS AND DISCUSSION

We examined a group of 12 ulcerative colitis patients considered to be in endoscopic remission. Their mean age was 46.41 years (SD= 11.91), and the majority of the subjects were males (n= 9; 75%). The median C-reactive protein level was 0.88 (IQR = 0.81), while the median calprotectin level was 65.7 (IQR = 20.3). Fifty percent (n=6) of our patients presented with inflammation (C-reactive protein value > 0.5 mg/dL), and 16.67% (n=2) of them had mild anemia (defined as a hemoglobin value < 12 g/dL) (Table 1). Among the 12 patients, 4 were undergoing treatment with infliximab (33.33%), 2 with adalimumab (16.67%), 2 with vedolizumab (16.67%), 2 with mesalazine (16.67%), 1 with vedolizumab following infliximab and adalimumab failures (8.33%), and 1 with ozanimod after infliximab and adalimumab failures (8.33%).

Table 1. Characteristics of the included patients

n	12	
Age, Mean (SD)	46.41 (11.91)	
Sex	Male % (n)	75 (9)
	Female % (n)	25 (3)
C-reactive protein, Median (IQR)	0.88 (0.81)	
Calprotectin, Median (IQR)	65.7 (20.3)	
Inflammation % (n)	50% (6)	
Anemia % (n)	16.67% (2)	

The median endoscopic activity index, based on the Mayo UC endoscopic score, was 1 in group A (with 50%, n=3 of the patients scoring 1 point) and 1 in group B (with 66.67%, n=4 of the subjects scoring 1 point) (Figures 1, 2).

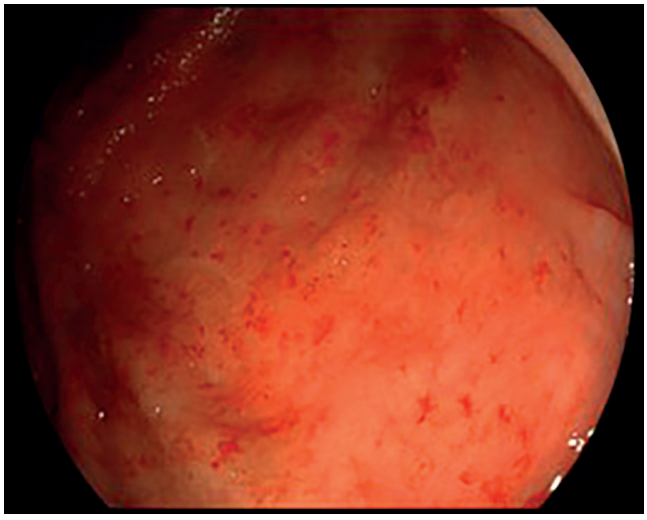

Figure 1. High-definition white-light endoscopy demonstrates minimal erosions and erythema; slight mucosal friability is visible

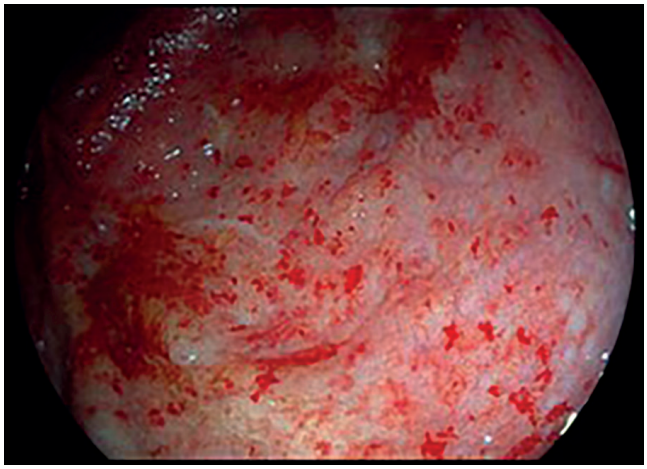

Figure 2. SFI considerably enhances the mucosal vascular pattern, more accurately revealing the extent of the mucosal lesions

Upon examining the concordance between endoscopic predictions of disease activity and histological findings (Figures 3, 4), we obtained a 55% degree of conformity in group A compared to a degree of 90% in group B (Table 2).

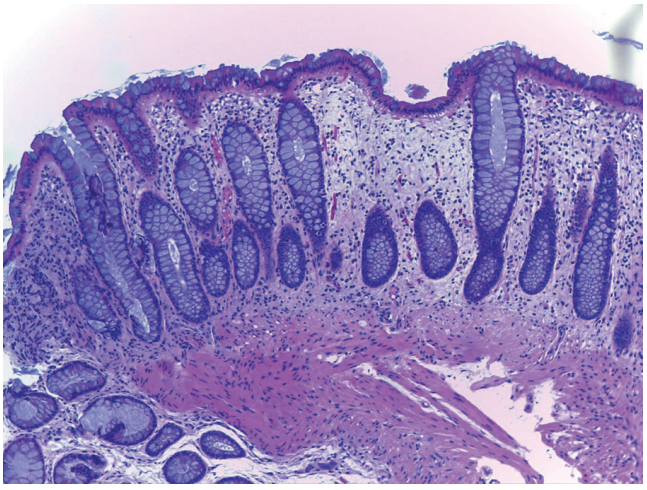

Figure 3. Chronic ulcerative colitis in remission (Geboes 1.1). Note the mild architectural glandular disarray (branching and irregular glands, not evenly spaced with an irregular luminal border), few reactive epithelial changes and a hypertrophic muscularis mucosa. Hematoxylin eosin staining, ob, 10x

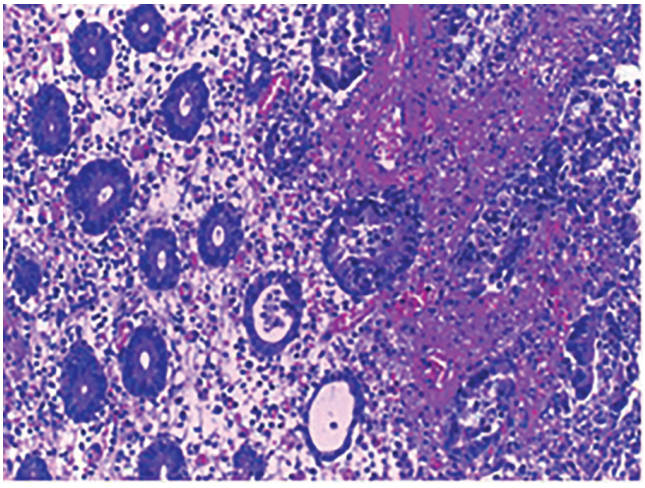

Figure 4. Active ulcerative colitis (Geboes 4.0): crypt abscesses, cryptitis and reduced intraepithelial mucin; note the edema, hemorrhagic areas and granulation tissue in the lamina propria. Hematoxylin eosin staining, ob, 10x

Table 2. Study results

N=12	Group A (n=6)	Group B (n=6)
Mayo score, Median (% patients with 1 point, n)	1 (50%, 3)	1 (66.67%, 4)
Duration of exam, Median (IQR)	17.3 (1.83)	18.5 (2.32)
Endoscopy and histology conformity, %	55	90

Taking into consideration the duration of the examination, including the time for cecal intubation and the total withdrawal time of the endoscope, the median value (minutes ± IQR) for the UC patients in the HD-WLE group was 17.3 ± 1.83 minutes versus 18.5 ± 2.32 minutes in the SFI group.

The current pilot study aimed to demonstrate the utility of SFI, a newly introduced optical and digital chromoendoscopic tool, for diagnosing subtle mucosal changes in patients with IBD. By direct comparison of white light endoscopy and in vivo dye-less chromoendoscopy results with the subsequent histology of the biopsy specimens, we demonstrated that SFI achieves a significant improvement in the prediction of disease extent and severity when compared with HD-WLE, although the use of virtual chromoendoscopy prolonged the procedure by approximately 1.2 minutes.

Possible limitations of our preliminary study need to be brought up for discussion. The study was performed in a tertiary IBD center by a single experienced endoscopist, which could introduce potential bias. Additionally, the number of patients enrolled was too small to draw definite conclusions. The differences in disease activity, endoscopically and histologically, were directly assessed with both diagnostic techniques, considering an agreement when a patient with mild endoscopic appearance (Mayo score 0 or 1) had mild inflammation on histology (Geboes score <3.). The clinical significance of histologically mild mucosal

inflammation is unclear. Recent data support the fact that persistent histological inflammation with apparently normal mucosa on endoscopic evaluation can be a criterion for disease relapse, justifying a more aggressive therapy to prevent recurrence[18].

However, the aim of this study was to assess the feasibility of SFI in diagnosing subtle inflammatory lesions and disease extension in patients with quiescent and inactive ulcerative colitis (defined by WLE). The SFI findings were confirmed by histology, and this new simple endoscopic tool may play a role in further adjusting the therapy in these patients. Future large prospective studies need to evaluate interobserver variation among IBD endoscopists with various levels of experience.

Taking into account the novelty of this technique, the information provided by the literature is scarce for SFI in this specific setting. The results of our study are in line with previously published data describing comparable success rates for similar devices, such as NBI and LCI. A prospective randomized crossover study including 42 patients with longstanding UC compared a first-generation NBI system with conventional colonoscopy. Although the degree of neoplasia detection seemed similar, more suspicious lesions were identified with the use of optical chromoendoscopy, which demonstrates (comparable to the current study) the superiority of the diagnostic method[19].

Leifeld et al. performed a prospective multicenter study enrolling 159 patients with longstanding UC. The team found statistically equivalent numbers of lesions using both WLE and NBI, but with fewer biopsy specimens needed for optical chromoendoscopy. However, the research team associated a shorter withdrawal time with the use of NBI, not consistent with our findings[20].

Kudo and colleagues conducted a study on 30 patients with asymptomatic or mildly active UC, focusing on the mucosal vascular pattern (MVP). They discovered that, when compared to conventional colonoscopy, NBI yielded a more precise assessment of inflammation in quiescent UC, correlating well with the histological findings, data supported by our study[21]. Additionally, a pilot trial performed by Danese et al. on 14 IBD patients proved the potential of optical chromoendoscopy for in vivo identification of intestinal angiogenesis, as areas that appeared normal on WLE but altered on NBI had an increased leucocyte infiltrate and microvessel density when examined histologically[22].

In contrast to these findings, a randomized crossover trial involving 48 patients with UC comparing HD colonoscopy with NBI demonstrated that optical chromoendoscopy does not improve the detection of neoplasia in this type of patient. Furthermore, NBI showed unsatisfactory results in discriminating neoplastic mucosa from the nonneoplastic type[23]. In addition, a crossover study performed by Sussman et al. of 29 patients with IBD compared WLE, dye-based CE (indigo carmine) and NBI, proving the superiority in inflammation and pseudopolyp histological prediction of the first two, as opposed to optical chromoendoscopy (64% WLE and 63% CE versus 42% NBI)[24].

The efficiency of the recently introduced LCI chromoendoscopy technique was assessed by Uchiyama and his colleagues in a study involving 52 UC patients. LCI significantly improved the diagnosis of subtle inflammation, correlating strongly with Matts' histopathological score[25]. Moreover, a trial performed by Paggi et al. on 649 patients compared the adenoma detection ability of LCI and HD-WLE in an organized colorectal cancer screening program, demonstrating a 2-20% increase in the detection rate when using bright chromoendoscopy[26].

An alternative digital chromoendoscopic technique that uses real-time virtual video postprocessing is i-Scan[11]. Similar to our study, Neumann et al. assigned 78 IBD patients to undergo HD-WLE (n=39) and computed virtual chromoendoscopy (i-Scan; n=39). Compared to our results, the average duration of the procedure was slightly higher in the i-Scan group (18 versus 20.5 minutes, without any statistical significance). Furthermore, while evaluating the inflammatory extent and activity in comparison to histopathological analysis, digital chromoendoscopy proved superior (48.71% and 53.85% versus 92.31% and 89.74%, differences that are statistically significant)[27]. In addition, in a randomized non-inferiority trial comprising 270 individuals, Iacucci et al. proved that i-Scan or HD-WLE was not inferior in comparison to dye-based chromoendoscopy in terms of detection tools for colonic neoplastic lesions when applied for IBD patient surveillance[28].

Although the data provided by the literature concerning virtual chromoendoscopy remain in conflict, this novel diagnostic tool is slowly but surely proving its considerable potential. There is still a need for additional studies involving larger groups of patients.

CONCLUSIONS

Overall, literature data evaluating the use of virtual chromoendoscopy as a monitoring strategy for patients with UC remain scarce. This pilot study demonstrated that image-enhanced endoscopy using SFI might increase the rate of detection and the demarcation of subtle mucosal inflammatory changes, correlating with potential histologic activity and having implications for future therapy and the follow-up of patients. SFI could provide more accurate and earlier identification for areas of minimal inflammation than conventional techniques. Additional studies on larger groups of patients are needed to support these findings.

CONFLICT OF INTERESTS

None to declare. All authors participated in the care of the patients and documentation, writing and corrections of the article.

ETHICAL STANDARDS

The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all of the patients included in this study.

References

1. Negreanu L, Voiosu T, State M, Voiosu A, Bengus A, Mateescu BR. Endoscopy in inflammatory bowel disease: from guidelines to real life. Therap Adv Gastroenterol. 2019;12:1-10. PMID: 31384307. doi:10.1177/ 1756284819865153.
2. https://www.prnewswire.com/news-releases/sonoscape-flagship-4-led-equipped-fhd-endoscopy-system-was-seen-in-live-demo-at-conference-endoscopy-on-air-301087983.html.
3. Boal Carvahlo P, Cotter J. Mucosal healing in ulcerative colitis: a comprehensive review. Drugs 77. 2017:159–173. PMID: 28078646. doi:https://doi.org/10.1007/s40265-016-0676-y.
4. Nardone OM, Cannatelli R, Zardo D, Ghosh S, Iacucci M. Can advanced endoscopic techniques for assessment of mucosal inflammation and healing approximate histology in inflammatory bowel disease? Ther Adv Gastroenterol. 2019;12:1756284819863015. PMID: 31360224. doi:10.1177/1756284819863015.
5. Pineton de Chambrun G, Blanc P, Peyrin-Biroulet L. Current evidence supporting mucosal healing and deep remission as important treatment goals for inflammatory bowel disease. Expert Rev Gastroenterol Hepatol. 2016:915-927. PMID: 27043489. doi:https://doi.org/10.1586/17474124.2016.1174064.
6. Beintaris I, Rutter M. Advanced imaging in colonoscopy: contemporary approach to dysplasia surveillance in inflammatory bowel disease. Front Gastroenterol. 2016;7(4):308–315. PMID: 28839872. doi:10.1136/flgastro-2016-100735.
7. Bisschops R, East JE, Hassan C et al. Advanced imaging for detection and differentiation of colorectal neoplasia: European Society of Gastrointestinal Endoscopy (ESGE) Guideline – Update 2019. Endoscopy. 2019;51:9-10.
8. Laine L, Kaltenbach T, Barkun A, et al. SCENIC international consensus statement on surveillance and management of dysplasia in inflammatory bowel disease. Gastroenterology. 2015;148(3):639-651.e28. PMID: 25702852. doi:10.1053/j.gastro.2015.01.031.
9. Baars J, Nuij V, Oldenburg B, Kuipers E, van der Woude CJ. Majority of patients with inflammatory bowel disease in clinical remission have mucosal inflammation. Inflamm Bowel Dis. 2012;18:1634-1640. PMID: 22069022. doi:10.1002/ibd.21925.
10. Subramanian V, Mannath J, Hawkey CJ, Ragunath K. High definition colonoscopy vs. standard video endoscopy for the detection of colonic polyps: a meta-analysis. Endoscopy. 2011;43(6):499-505. PMID: 21360420. doi:10.1055/s-0030-1256207.
11. Sikka S, Ringold DA, Jonnalagadda S, Banerjee B. Comparison of white light and narrow band high definition images in predicting colon polyp histology, using standard colonoscopes without optical magnification. Endoscopy. 2008;40(10):818–822. PMID: 18668472. doi:10.1055/s-2008-1077437.
12. Sano Y, Ikematsu H, Fu KI, Emura F et. al. Meshed capillary vessels by use of narrow-band imaging for differential diagnosis of small colorectal polyps. Gastrointest Endosc. 2009;69(2):278-283. PMID: 18951131. doi:https://doi.org/10.1016/j.gie.2008.04.066.
13. Kodashima S, Fujishiro M. Novel image-enhanced endoscopy with i-scan technology. World J Gastroenterol. 2010;16(9):1043-1049. PMID: 20205272. doi:10.3748/wjg.v16.i9.1043.
14. https://www.fujifilm.eu/eu/products/medical-systems/endoscopy/technology/lci.
15. Iacucci M, Panaccione R, Ghosh S. Advances in novel diagnostic endoscopic imaging techniques in inflammatory bowel disease. Inflamm Bowel Dis. 2013;19(4):873-880. PMID: 23448788. doi:10.1097/mib.0b013e318280143f.
16. Sivanathan V, Tontini GE, Möhler M, Galle PR, Neumann H. Advanced endoscopic imaging for diagnosis of inflammatory bowel diseases: Present and future perspectives. Dig Endosc. 2018;30(4):441-448. PMID: 29360261. doi:10.1111/den.13023.
17. Trivedi PJ, Kiesslich R, Hodson J, Bhala N et al. The Paddington International Virtual Chromoendoscopy Score in ulcerative colitis exhibits very good inter-rater agreement after computerized module training: a multicenter study across academic and community practice (with video). Gastrointest Endosc. 2018;88(1):95-106.e2. PMID: 29548940. doi:10.1016/j.gie.2018.02.044.
18. Neurath MF, Travis SPL. Mucosal healing in inflammatory bowel diseases: a systematic review. Gut. 2012;61(11):1619-1635. PMID: 22842618. doi:10.1136/gutjnl-2012-302830.
19. Dekker E, van den Broek FJ, Reitsma JB et al. Narrow-band imaging compared with conventional colonoscopy for the detection of dysplasia in patients with longstanding ulcerative colitis. Endoscopy. 2007;39(3):216-221. PMID: 17385106. doi:10.1055/s-2007-966214.
20. Leifeld L, Rogler G, Stallmach A et al. White-Light or Narrow-Band Imaging Colonoscopy in Surveillance of Ulcerative Colitis: A Prospective Multicenter Study. Clin Gastroenterol Hepatol. 2015;13(10):1776-1781.e1. PMID: 25952309. doi:10.1016/j.cgh.2015.04.172.
21. Kudo T, Matsumoto T, Esaki M, Yao T, Iida M. Mucosal vascular pattern in ulcerative colitis: observations using narrow band imaging colonoscopy with special reference to

histologic inflammation. Int J Color Dis. 2009;24(5):495-501. PMID: 19145441. doi:10.1007/s00384-008-0631-9.
22. Danese S, Fiorino G, Angelucci E, et al. Narrow-band imaging endoscopy to assess mucosal angiogenesis in inflammatory bowel disease: A pilot study. World J Gastroenterol. 2010;16(19):2396–2400. PMID: 20480525. doi:10.3748/wjg.v16.i19.2396.
23. van den Broek FJC, Fockens P, van Eeden S, et al. Narrow-band imaging versus high-definition endoscopy for the diagnosis of neoplasia in ulcerative colitis. Endoscopy. 2011;43(2):108-115. PMID: 21165822. doi:10.1055/s-0030-1255956.
24. Sussman DA, Barkin JA, Martin AM, et al. Development of Advanced Imaging Criteria for the Endoscopic Identification of Inflammatory Polyps. Clin Transl Gastroenterol. 2015;6(11):e128. PMID: 26583503. doi:10.1038/ctg.2015.51.
25. Uchiyama K, Takagi T, Kashiwagi S, Toyokawa Y, Tanaka M et. al. Assessment of Endoscopic Mucosal Healing of Ulcerative Colitis Using Linked Colour Imaging, a Novel Endoscopic Enhancement System. J Crohns Colitis. 2017;11(8):963-969. PMID: 28333209. doi:10.1093/ecco-jcc/jjx026.
26. Paggi S, Radaelli F, Senore C, Maselli R, Amato A, Andrisani G et al. Linked-color imaging versus white-light colonoscopy in an organized colorectal cancer screening program. Gastrointest Endosc. 2020;92(3):723-730. PMID: 32502550. doi:10.1016/j.gie.2020.05.044.
27. Neumann H, Vieth M, Günther C et al. Virtual chromoendoscopy for prediction of severity and disease extent in patients with inflammatory bowel disease: a randomized controlled study. Inflamm Bowel Dis. 2013;19(9):1935-1942. PMID: 23839228. doi:10.1097/MIB.0b013e318290550e.
28. Iacucci M, Kaplan GG, Panaccione R et al. A Randomized Trial Comparing High Definition Colonoscopy Alone With High Definition Dye Spraying and Electronic Virtual Chromoendoscopy for Detection of Colonic Neoplastic Lesions During IBD Surveillance Colonoscopy. Am J Gastroenterol. 2018;133(2):225-234. PMID: 29134964. doi:10.1038/ajg.2017.417.