



## Advanced endoscopy imaging in inflammatory bowel diseases

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**Background and Aims:** Rapid assessment of mucosal inflammation is of crucial importance for the initial diagnosis and the assessment of mucosal healing in inflammatory bowel disease (IBD). Moreover, the identification of intraepithelial neoplasias in IBD is of key relevance for clinical management. Here, we systematically analyzed the utility of advanced endoscopic imaging techniques for optimized diagnosis in IBD.

**Methods:** PubMed/Medline, Web of Knowledge, and Cochrane library were searched twice for diagnostic studies on advanced endoscopic imaging in IBD. Clinical and technical information was retrieved and subsequently analyzed. Main outcome parameters consisted of the quality of the results, adverse events, and diagnostic yield.

**Results:** Fifty-six clinical studies with a total of 3296 patients were selected for final analysis. Filter technologies permitted a more detailed analysis of mucosal inflammation in IBD. In spite of substantial heterogeneity across studies, dye-based chromoendoscopy with targeted biopsy sampling yielded higher detection rates of intraepithelial neoplasias in ulcerative colitis as compared with white-light endoscopy with random biopsy sampling. Moreover, endocytoscopy and endomicroscopy allowed subsurface imaging of inflamed or neoplastic mucosa in IBD at subcellular resolution. Finally, endomicroscopy-aided molecular imaging enabled the identification of membrane-bound tumor necrosis factor on mucosal cells as a potential driver of disease activity in Crohn's disease. No relevant adverse events were reported.

**Conclusions:** Advanced endoscopic imaging technologies are feasible, safe, and partially effective tools for detailed diagnosis of mucosal inflammation and detection of neoplasias in IBD. Results obtained from these advanced techniques may provide a rational basis for individualized, optimized therapy for IBD patients. (Gastrointest Endosc 2017;85:496-508.)

Although for many decades endoscopy was only considered as a useful tool for the initial diagnosis of inflammatory bowel disease (IBD), the identification of mucosal healing as a key therapeutic goal has led to a paradigm change. Indeed, mucosal healing on endoscopy has emerged as an important treatment goal in IBD that predicts sustained clinical

remission and resection-free survival of patients,<sup>1</sup> thereby highlighting the role of endoscopic monitoring of disease activity. Moreover, advanced imaging techniques such as chromoendoscopy (CE) have led to markedly improved possibilities for the endoscopic detection and characterization of intraepithelial neoplasias and colorectal

*Abbreviations:* AFI, autofluorescence imaging; CD, Crohn's disease; CE, chromoendoscopy; CLE, confocal laser endomicroscopy; GMP, good manufacturing practice; IBD, inflammatory bowel disease; iCE, indigo carmine-aided chromoendoscopy; iCLE, integrated confocal laser endomicroscopy; IN, intraepithelial neoplasia; mCE, methylene blue-aided chromoendoscopy; ME, magnifying endoscopy; NBI, narrow-band imaging; pCLE, probe-based confocal laser endomicroscopy; PSC, primary sclerosing cholangitis; UC, ulcerative colitis; WLE, white-light endoscopy.

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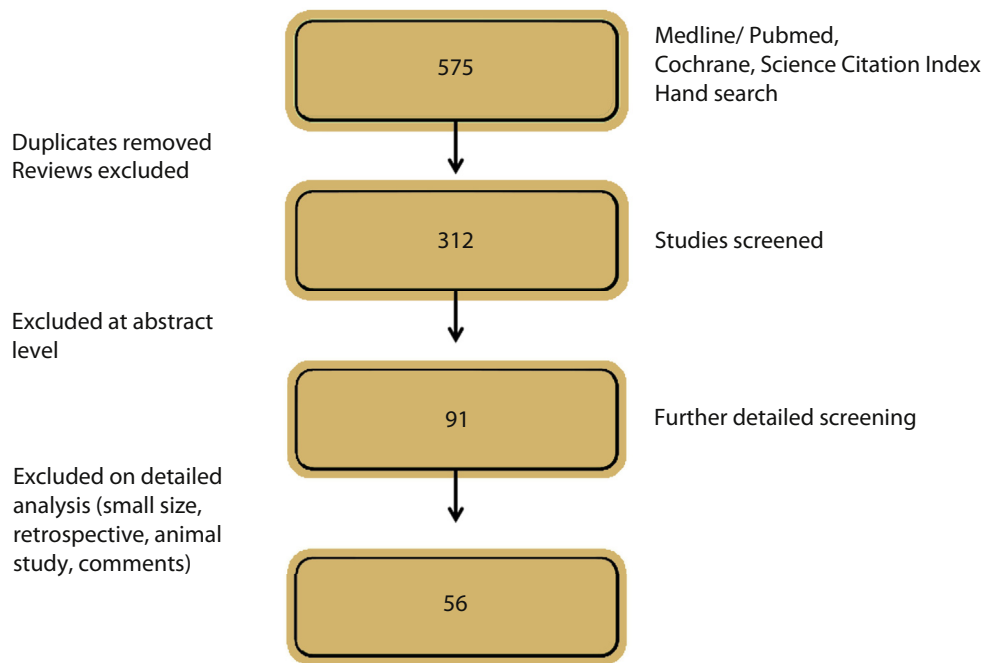
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**Figure 1.** Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flowchart for this review.

cancer in IBD. Finally, endomicroscopy has recently been used for subcellular imaging of the mucosa and for molecular imaging in IBD. Taken together, these developments have led to growing interest in the use of new imaging technologies in IBD. Here, we provide a systematic review on the use of currently available, advanced imaging technologies in IBD.

## METHODS

A Web of Knowledge search using the search term “endoscopy AND IBD” identified a more than 2-fold increase in the number of published studies per year since 2010 and more than 100 studies were published per year since 2011 (2010, n = 72; 2011, n = 136; 2012, n = 160; 2013, n = 145; 2014, n = 182; 2015, n = 157). Citation numbers per year showed an almost 3-fold increase since 2010 (citations 2010, n = 930; 2011, n = 1073; 2012, n = 1298; 2013, n = 1767; 2014, n = 2180; 2015, n = 2775). To further select clinical studies on advanced endoscopic imaging in IBD, we stratified studies with randomized controlled studies, large cohort studies, and case series with more than 9 patients.

The particular aim of this systematic review was to analyze the effects of advanced endoscopic imaging on the detection of mucosal inflammation in IBD. Additionally, this review aimed at highlighting the value of advanced endoscopic techniques for the identification of preneoplastic and neoplastic lesions in IBD that is of crucial relevance for the clinical management of patients.

Methods for generating inclusion criteria and analysis of data were based on PRISMA (Preferred Reporting System for Systematic Reviews and Meta-analyses) recommendations.<sup>2</sup> A literature search using Medline/PubMed, Cochrane library, and Science Citation Index was performed in May 2016 and July 2016. All studies in which endoscopy in IBD was studied that were published from 1979 to July 2016 were reviewed. Potential exclusion criteria to reduce risk of bias and unnecessary observations included case reports on single patients, small case series with less than 10 patients, small retrospective studies (n < 150), ethical concerns, and book chapters. In addition, review articles and animal studies in IBD models were excluded. Finally, publications on capsule endoscopy, optical coherence tomography, and balloon endoscopy of the small intestine were not considered.

Relevant publications were identified between 1979 and 2016. The medical terms “mucosal healing” (TI) and “endoscopy,” “advanced endoscopy and IBD,” “advanced endoscopy and Crohn’s disease,” “advanced endoscopy and ulcerative colitis,” “endomicroscopy and IBD,” “chromoscopy and colitis,” “endocytoscopy and IBD,” “chromoendoscopy and IBD,” “chromoendoscopy and colitis,” “methylene blue and colitis,” “indigo carmine and colitis,” “molecular imaging and IBD,” “FICE and IBD,” “NBI and IBD,” “NBI and colitis,” “AFI and IBD,” “FUSE and IBD,” and “I-Scan and IBD” were used in the search. Additional references were hand-searched. The full articles of all relevant studies were retrieved, and reference lists from identified articles were searched to identify any additional studies that may have been missed during the process.

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