Comparison of Probe-Based Confocal Laser Endomicroscopy With Virtual Chromoendoscopy for Classification of Colon Polyps

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BACKGROUND & AIMS: Probe-based confocal laser endomicroscopy (pCLE) allows in vivo imaging of tissue at micron resolution. Virtual chromoendoscopy systems, such as Fujinon intelligent color enhancement and narrow band imaging, also have potential to differentiate neoplastic colorectal lesions. The accuracy of these systems in clinical practice is, however, unknown. Our primary aim was to compare sensitivity and specificity of pCLE to virtual chromoendoscopy for classification of colorectal polyps using histopathology as a gold standard. A secondary aim was to compare sensitivity and specificity of pCLE to virtual chromoendoscopy using a modified gold standard that assumed that all polyps ≥10 mm had malignant potential and were considered neoplastic or high risk. **METHODS:** Patients underwent colonoscopy using high-resolution colonoscopes. The surface pit pattern was determined with NBI or FICE in all patients. Confocal images were recorded and subsequently analyzed offline, blinded to the endoscopic characteristics and histopathology. Each polyp was diagnosed as benign or neoplastic based on confocal features according to modified Mainz criteria. **RESULTS:** A total of 119 polyps (81 neoplastic, 38 hyperplastic) from 75 patients was assessed. The pCLE had higher sensitivity compared to virtual chromoendoscopy when considering histopathology as gold standard (91% vs 77%; $P = .010$) and modified gold standard (88% vs 76%; $P = .037$). There was no statistically significant difference in specificity between pCLE and virtual chromoendoscopy when considering histopathology or modified gold standard. **CONCLUSIONS: Confocal endomicroscopy demonstrated higher sensitivity with similar specificity in classification of colorectal polyps. These new methods may replace the need for ex vivo histological confirmation of small polyps, but further studies are warranted.**

Keywords: Confocal Endomicroscopy; Colonoscopy; Colorectal Neoplasia; Chromoendoscopy.

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Colorectal cancer has been recognized as the second most common cause of cancer-related death in the United States.[1] It progresses through various morphological stages, including polyp formation and malignant transformation. There are different types of colonic polyps, including hyperplastic, traditionally considered with no significant malignant potential and adenomatous polyps with truly malignant potential. Standard colonoscopy has been used for identification of colonic lesions. However, standard endoscopic inspection by itself cannot reliably distinguish between neoplastic and non-neoplastic lesions.[2-4] Thus, all visualized lesions need to be removed during colonoscopy to be evaluated by histopathology. This approach remains the gold standard for final diagnosis.[5]

With almost half of all polyps being hyperplastic,[6] the standard approach results in a large proportion of unnecessary polypectomies, which increases time, risk, and cost of colonoscopy with unnecessary follow-up.

Various trials have investigated the role of advanced endoscopic imaging techniques, such as dye-based chromoendoscopy and digital chromoendoscopy with narrow band imaging and Fujinon intelligent color enhancement in neoplastic lesion detection. They have been shown to improve the in vivo diagnostic accuracy of neoplasia, especially with the use of pit pattern characterization.[7-13] This, however, did not eliminate the need for ex vivo histopathology because these techniques were shown to

Abbreviation used in this paper: pCLE, probe-based confocal laser endomicroscopy.

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lack specificity, despite an increased sensitivity of diagnosing neoplasia in some trials.[7,12] With dye-based chromoendoscopy, the prolonged procedure times, variability in dyes staining, and washing techniques have also played a role in their overall limited application. The new techniques of "virtual" chromoendoscopy, such as narrow band imaging (NBI) or Fujinon intelligent color enhancement (FICE) overcome this limitation, but accuracy has been variable.

Extremely high-resolution confocal laser endomicroscopy techniques have been developed and integrated into a dedicated endoscope (eCLE; Pentax Corp, Japan) or a through-the-endoscope probe (pCLE; Mauna Kea Technologies, France).

The primary aim of this study was to assess the clinical applicability and overall diagnostic sensitivity and specificity of a pCLE system for diagnosing neoplasia during colonoscopy and to compare sensitivity and specificity between pCLE and a virtual chromoendoscopy system (FICE and NBI). Long-term aims are to determine if gastroenterologists can make accurate and reliable diagnoses of pathology in vivo without removal of tissue.

Material and Methods

Patients

The study was approved by Mayo Clinic Institutional Review Board, and full informed consent was obtained from all study participants. Patients were enrolled if they were due for surveillance or screening colonoscopies, evaluation of known or suspected polyps on other imaging modalities, and endoscopic mucosal resection of larger flat colorectal neoplasia. Exclusion criteria were patients with noncorrected coagulopathy, women who were pregnant or breast feeding, documented allergy to fluorescein, and patients with no colorectal lesions found during a study colonoscopy. Between November 2007 and March 2009, 78 patients were enrolled in the study, of which 3 patients without polyps were excluded from the study. Twenty-four hours before the procedure, patients were prepped with 2−4 L polyethylene glycol solution. Conscious sedation was performed with intravenous administration of midazolam and meperidine.

Endoscopy Equipment and Procedure

All procedures were performed using a high-definition colonoscope (Fujinon EC450HL5 or 490 ZW, Fujinon, Ft Wayne, NJ; Olympus CFH180, Olympus, Center Valley, NY). The system was equipped with the EPX 4400 processor (Fujinon Inc) or (CV 180 Exera, Olympus, Co). The white-light, high-definition colonoscopy was always used as the primary screening method, whereas the FICE or NBI modes, followed by confocal imaging, were used after detection of a suspicious lesion. Assignment to FICE or NBI was not formally randomized but was dictated by random availability of endoscopy rooms. These systems are not capable of optical zoom.

All examinations were performed by the 2 experts in pCLE and advanced imaging methods (MBW, AMB).

Prior to pCLE imaging, either FICE mode 4 with Fujinon colonoscope or NBI with Olympus 180 series scope was used to characterize lesions in all patients. The surface pit pattern of the lesion was classified according to Kudo criteria, where pit pattern round and stellate (1−2) represented benign, hyperplastic lesion; and villiform, gyrus-like irregular patterns (3−5) represented neoplastic lesions. The anatomical site and morphological class of lesions was recorded during the procedure in accordance with the Paris classification.[14] Protruded colorectal lesions were defined either as sessile (1s) or polypoid (1p), and flat colorectal lesions were defined as either flat elevated lesions (IIa) or flat elevated with central depression (IIa/c) lesions vs flat lesions (II b) and flat depressed lesions (IIc).[14] Fluorescein sodium 2.5−5.0 mL 10% (AK Fluor, Akorn Pharmaceutical, Lake Forest, IL) solution was administered intravenously after the first polyp was identified. Immediately after fluorescein injection, the confocal probe was passed through the scope and confocal video sequences of the lesions were obtained and recorded.

Then appropriate procedures—simple polypectomies, biopsies, or complex endoscopic mucosal resection of lesions—were performed.

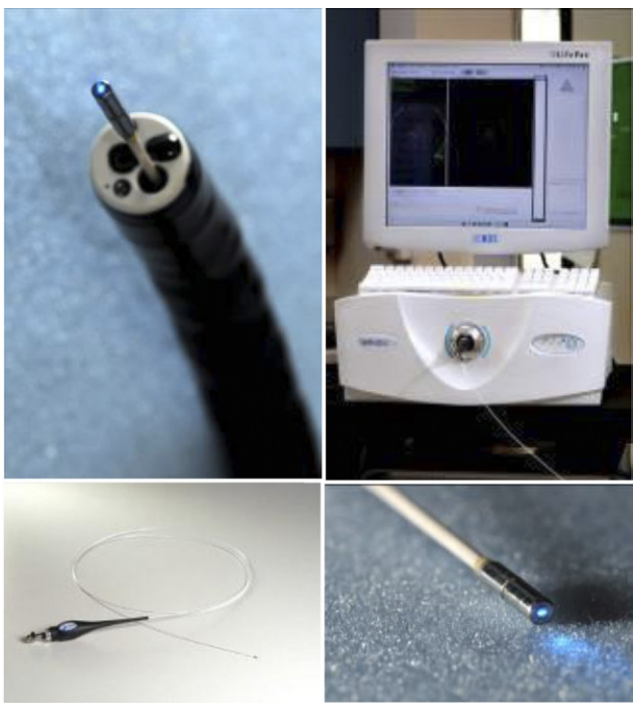

Figure 1. Confocal microscopy probe based system (Cellvizio).