# Fifty Percent Increase in Low-Grade Dysplasia Detection Using Probe-Based Confocal Endomicroscopy in a Metropolitan Veteran Cohort Undergoing Short Segment Barrett's Esophagus Surveillance

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## Introduction

Barrett's esophagus (BE) is the finding of intestinal metaplasia of the distal esophagus and is the predominant risk factor of esophageal adenocarcinoma (EAC). When a segment of BE is suspected, the Seattle protocol (SP) is typically performed to confirm and evaluate for the presence of dysplasia. Despite this rigorous biopsy protocol, only a small fraction of the affected mucosa is randomly screened. An accurate assessment of the Barrett's mucosa can be more challenging in the setting of short segment BE (SSBE), defined as BE length ≤ 3 cm.

Probe-based confocal endomicroscopy (pCLE) has previously been shown to increase detection of BE in vivo when used with high-definition white light endoscopy (HD-WLE). When used during endoscopy, pCLE can help target specific areas within the Barrett's mucosa that are suspicious for metaplasia, thereby increasing the diagnostic yield.

The aim of this study was to compare the accuracy of pCLE in diagnosing dysplastic short-segment BE in a surveillance population.

## Methods and Materials

Patients undergoing surveillance endoscopy for an established diagnosis of SSBE between January 1, 2018 and January 1, 2021 at the VA Loma Linda Healthcare System (VALLHCS) were included in this study.

Patients who underwent pCLE + HD-WLE were compared to those undergoing SP + HD-WLE.

All pCLE examinations were performed by two gastroenterologists (C.S.J & N.S)

All endoscopic biopsies consistent with dysplastic BE were reviewed and confirmed by two pathologists.

Age, sex, BMI, CCI score, smoking status, use of PPI or H2 antagonist, and length of Barrett's segment were compared in the two groups.

Continuous variables were compared using a Fisher's exact test with p≤0.05 as statistically significant.

## Results

A total of sixty-seven patients were identified as having SSBE. Fifty-one patients underwent the Seattle protocol (SP group) biopsy method using cold forceps to sample the Barrett's segment, while sixteen patients underwent pCLE-targeted biopsies (pCLE group).

The mean age of the pCLE group was 64 years and 65.9 years for those who underwent SP.

There was no difference in age, BMI, smoking status, statin, H2 blocker or PPI use between the two groups.

Low-grade dysplasia was detected in a total of 17 patients (25.3%). Of these 17 patients, 11 were detected using pCLE, and 6 using the SP biopsy method.

The use of pCLE was significantly associated with the detection of low-grade dysplasia (11/16, 68.7%) compared to Seattle protocol (6/51, 11.7%) with a p-value of < 0.001.

**Table 1.** Comparisons between Seattle protocol and pCLE groups

| | Seattle protocol | pCLE | P-value |
|---|---|---|---|
| LGD detected | 11.7% | 68.7% | <0.001 |
| Age | 62.3 ± 7.9 | 65.9 ± 9.3 | 0.55 |
| BMI (kg / m$^2$) | 28.6 ± 4.3 | 27.0 ± 4.6 | 0.61 |
| CCI score | 4.8 ± 2.1 | 5.1 ± 1.8 | 0.68 |
| | **Seattle protocol** | **pCLE** | **P-value** |
| PPI use | 72% | 75% | 0.73 |
| H2 antagonist use | 5.8% | 17.6% | 0.63 |
| Current smoker | 15.4% | 17.6% | 0.49 |

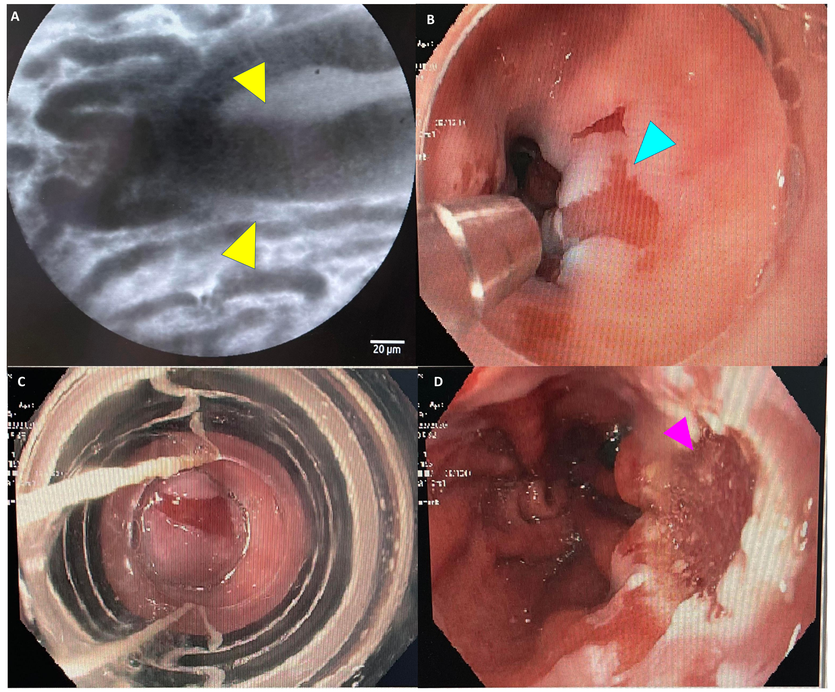


Figure 1: A) probe-based confocal endomicroscopy image of low-grade Barrett's esophagus. Arrows: rows of non-equidistant glands, unequal size and shape of glands which are suspicious for LGD. B) High-definition white light endoscopy (HD-WLE) of (arrow) the same area of LGD. C) Banding of the same area of LGD, in preparation for endoscopic mucosal resection. D) Arrow: the same area of LGD, now status post-EMR.

## Conclusions

Several studies have demonstrated a low rate of detecting dysplastic Barrett's using the Seattle protocol. Furthermore, the rate of adherence to the Seattle protocol has a wide variation among practicing gastroenterologists (25-80%) based on several studies (1, 2, 3).

Low-grade dysplasia (LGD) is more common than high-grade dysplasia (HGD) or EAC. The rate of progression of LGD to EAC is estimated to be approximately 0.7% to 5% per year (4,5). Ensuring the accuracy of this diagnosis is crucial as it directly impacts management. Endoscopic eradication therapy can be considered in patients with histologically confirmed LGD, thereby preventing progression to EAC.

Probe-based confocal endomicroscopy can be useful to increase the yield of diagnosing dysplastic SSBE in the high-risk surveillance population.

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