Advancing Diagnostic Accuracy: EUS-Confocal Endomicroscopy for Pancreatic Cysts in the Era of Cyst Fluid Glucose Analysis and Current Standards of Care

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INTRODUCTION

- **Pancreatic adenocarcinoma** arises from mucinous pancreatic cysts in 15% of cases. Challenges in discerning **mucinous** from **non-mucinous cysts** results in unnecessary highly-morbid surgical procedures in 20% of cases.
- **EUS-guided needle-based confocal laser endomicroscopy (EUS-nCLE)** is a novel technique that offers real-time microscopic imaging of cyst epithelium enabling virtual biopsies with high resolution. However, with ever-evolving techniques and fluid sampling analysis (i.e. cyst glucose and CEA), the role of EUS-nCLE in PCL diagnosis has yet to be determined in the latest standards of care.
- This study aimed to **assess the diagnostic value of EUS-nCLE** when utilized with current standard of care in a well-characterized cohort of patients.

METHODS

- Subjects were selected from an ongoing multi-center prospective study (2020–2024, NCT03492151) evaluating the use of EUS-nCLE for diagnosing PCLs (The Confocal Laser Endomicroscopy as an Imaging Biomarker for the Diagnosis of Pancreatic Cystic Lesions [CLIMB]).
- **Fifteen endosonographers, naïve to EUS-nCLE, underwent a 2-hour didactic session** and then reviewed 66 cases with and without EUS-nCLE videos to arrive at diagnoses with histopathologic data serving as gold standard.

METHODS (Cont.)

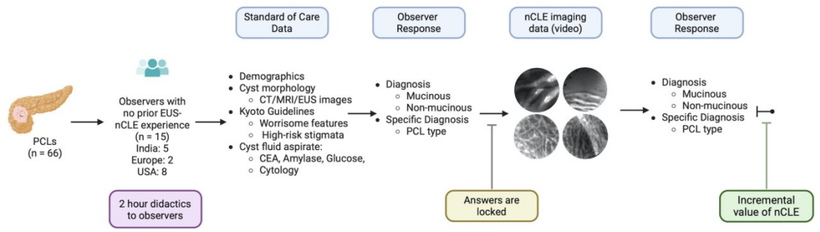

Figure 1. Study design mimicking the application of EUS-nCLE with current standards of care in PCL diagnosis.

RESULTS

- The study included 66 patients (56% female with a mean age of 65.0 ± 13.9 years) with PCLs. The mean cyst size was 4.3 ± 1.9 cm.
- **In the observer cohort, classification accuracy for differentiating mucinous from non-mucinous lesions significantly improved with nCLE, increasing from 90 ± 6% pre-nCLE to 96.1 ± 3.43% post-nCLE (p <0.01; McNemar's test).**
- **Diagnostic accuracy for IPMNs increased from 88% to 92% (p <0.01) and for MCNs increased from 87% to 91% (p <0.01).**
- **Diagnostic accuracy for SCAs increased from 88% to 93% (p <0.01), cystic-NET/SPN increased from 91% to 93% (p=0.016), and pseudocysts increased from 92% to 99% (p <0.01)**.

RESULTS (Cont.)

- The addition of EUS-nCLE to standard of care characteristics **improved diagnostic accuracy across all PCLs types compared to pre-nCLE evaluation (Table 1).**
- Overall, diagnostic accuracy for PCL subtypes increased from 72.8 ± 13.2% pre-nCLE to 84.6 ± 7.98% post-nCLE (p <0.01).

Cyst Type	Accuracy % (95% CI) (Pre-nCLE)	Accuracy % (95% CI) (Post-nCLE)	p-value
Mucinous vs. Non-mucinous	89.9 (87.9–91.7)	96.1 (94.7–97.2)	< 0.001
IPMN (n = 23 [34.8%])	87.6 (85.4–89.6)	91.9 (90.0–93.5)	< 0.001
MCN (n = 7 [10.6%])	87.2 (84.9–89.2)	91.1 (89.2–92.8)	< 0.001
SCA (n = 28, [42.4%])	88.4 (86.2–90.3)	93.4 (91.7–94.9)	< 0.001
PNET (n = 4 [6.1%])	90.9 (88.9–92.6)	93.3 (91.6–94.8)	0.016
Pseudocyst (n = 4 [6.1%])	91.6 (89.7–93.3)	99.3 (98.5–99.7)	< 0.001

DISCUSSION

- **When combined with standard-of-care testing, EUS-nCLE significantly improves diagnostic accuracy for classifying and diagnosing specific PCL types**.
- This is particularly relevant for larger PCLs (>3 cm), where management decisions become critical.
- These findings underscore the potential to refine diagnostic algorithms and integrate novel tools like nCLE into clinical practice.