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# Endoscopic ultrasound-guided fine needle aspiration and biopsy using a 22-gauge needle with side fenestration in pancreatic cystic lesions

Luca Barresi[a,*], Ilaria Tarantino[a], Mario Traina[a], Antonino Granata[a], Gabriele Curcio[a], Neville Azzopardi[a], Paola Baccarini[b], Rosa Liotta[c], Adele Fornelli[b], Antonella Maimone[d], Elio Jovine[e], Vincenzo Cennamo[d], Carlo Fabbri[d]

[a] Gastroenterology and Endoscopy Unit, ISMETT, Palermo, Italy
[b] Pathology Unit, AUSL Bologna Bellaria-Maggiore Hospital, Bologna, Italy
[c] Pathology Unit, ISMETT, Palermo, Italy
[d] Unit of Gastroenterology and Digestive Endoscopy, AUSL Bologna Bellaria-Maggiore Hospital, Bologna, Italy
[e] Department of General Surgery, AUSL Bologna Bellaria-Maggiore Hospital, Bologna, Italy

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ABSTRACT

*Background:* Cytologic diagnosis by endoscopic ultrasound-guided fine needle aspiration is associated with low sensitivity and adequacy. A newly designed endoscopic ultrasound-guided fine needle biopsy device, endowed with a side fenestration, is now available.
*Aims:* We carried out a study with the aim of evaluating the feasibility, safety, and diagnostic yield of the 22-gauge needle with side fenestration for endoscopic ultrasound fine needle aspiration and biopsy of pancreatic cystic lesions.
*Methods:* 58 patients with 60 pancreatic cystic lesions consecutively referred for endoscopic ultrasound guided-fine needle aspiration were enrolled in a prospective, dual centre study, and underwent fine needle aspiration and biopsy with the 22-gauge needle with side fenestration.
*Results:* Fine needle aspiration and biopsy was technically feasible in all cases. In 39/60 (65%) pancreatic cystic lesions, the specimens were adequate for cyto-histologic assessment. In lesions with solid components, and in malignant lesions, adequacy was 94.4% ($p = 0.0149$) and 100% ($p = 0.0069$), respectively. Samples were adequate for histologic evaluation in 18/39 (46.1%) cases. There were only 2 (3.3%) mild complications.
*Conclusions:* Fine needle aspiration and biopsy with the 22-gauge needle with side fenestration is feasible, and superior to conventional endoscopic ultrasound-guided fine needle aspiration cytology from cystic fluid, particularly in pancreatic cystic lesions with solid component or malignancy, with a higher diagnostic yield and with no increase in complication rate.


## 1. Introduction

Pancreatic cystic lesions (PCLs) are increasingly found in clinical practice because of the widespread use of imaging modalities [1–3].

Pancreatic cysts are a complex group of benign, premalignant and malignant lesions with diverse clinical, radiologic and pathologic features [4]. However, diagnosis and classification remain a challenge despite advances in diagnostic tools.

Radiologic and endosonographic morphologic features alone are not accurate enough for arriving at a final diagnosis in all cases [5–8]. However endoscopic ultrasound (EUS) has the advantage of allowing fine needle aspiration (FNA), with cystic fluid analysis and cytological characterization.

In cystic fluid, the most widely used test to distinguish mucinous from non-mucinous lesions is carcinoembryonic antigen (CEA) and more recently K-ras mutation, but the accuracy of these tests is only moderate [8–10], and neither test is useful in identifying malignant lesions [8,10].

Pathologic analysis is the most reliable diagnostic test, but while cytology obtained by EUS-FNA from cystic fluid has a high specificity for identification of malignancy and PCL type, it has a low sensitivity [8,9], due to the small number of cells present in the aspirate, particularly in small PCLs [11]. Several studies have explored the possibility of obtaining a better cyto-histological sample with new devices such as the Echobrush (Cook Endoscopy, Winston-Salem, NC, USA) [12–14], or new techniques of FNA like cystic wall punctures (CWP) using a standard EUS-FNA needle [11,15] or

* Corresponding author at: Gastroenterology and Endoscopy Unit, ISMETT, Via Tricomi 1, Palermo 90127, Italy. Tel.: +39 331 1718159; fax: +39 091 2192400.
*E-mail address:* lbarresi@ismett.edu (L. Barresi).

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EUS-trucut biopsy needle (Quick-Core; Cook Endoscopy, Winston-Salem, NC, USA) [16].

A newly designed EUS-guided fine needle biopsy was released on the market, featuring ProCore reverse bevel technology (EchoTip ProCore High Definition Ultrasound Biopsy Needle, Cook Endoscopy Inc., Limerick, Ireland), and equipped with a side fenestration that is 2 mm in length for the 22-gauge needle, and in which the tissue sample is embedded during puncture. With this new device, histological samples of the target organs can be obtained effectively and safely in different solid lesions [17,18].

The aim of this study was to evaluate the feasibility, safety, and diagnostic yield of this newly developed needle in pancreatic cystic lesions.

## 2. Patients and methods

### 2.1. Patient inclusion and exclusion criteria

All patients with PCLs observed at two referral centres (Gastroenterology and Endoscopy Unit, ISMETT, Palermo and Unit of Gastroenterology and Digestive Endoscopy, AUSL Bologna Bellaria-Maggiore Hospital, Bologna) were evaluated for inclusion in this prospective, observational study.

All patients underwent abdominal MRI or if contraindicated, CT scan. Patients with a clear diagnosis of pancreatic pseudocysts (round, non-septated lesions, presence of internal debris, recent acute pancreatitis or radiologic imaging of chronic pancreatitis) were excluded from the study.

Inclusion criteria were: (1) PCLs in patients fit for surgery or where cyto-histological diagnosis was requested for oncologic treatments, (2) PCLs $\geq$1.5 cm, and (3) PCLs of any size with worrisome features (thickened enhanced cyst walls, non-enhanced mural nodules, mean pancreatic duct (MPD) size of 5–9 mm, abrupt change in the MPD calibre with distal pancreatic atrophy, and lymphadenopathy). Exclusion criteria included: (1) patients <18-years old, (2) Severe haemorrhagic risk (platelet count <50,000 per μL or prothrombin activity <50%), and (3) interposed vessels or EUS-procedure considered risky by endosonographer.

A PCL diameter of 1.5 cm was considered the minimum size required to obtain useful information for diagnosis from FNA and cystic fluid analysis, as previously described [19].

Written informed consent was obtained from all patients and the study protocol was approved by the institutional review board.

A dedicated database was created to record clinical characteristics of patients, endoscopy reports, cystic fluid analysis, pathologic results, surgery and surgical diagnosis and follow-up.

### 2.2. EUS-guided FNA/B techniques

All patients underwent standard sedation with propofol under anesthesiologic monitoring. Prophylactic antibiotics were administered intravenously once before the procedure (piperacillin–tazobactam 4.5 mg or ciprofloxacin 400 mg) and orally (amoxicillin–clavulanic acid 1 g or ciprofloxacin 500 mg twice a day) for 5 days after the procedure. The exams were done by three experienced endosonographers (LB, IT, CF), all with at least 5 years of experience in pancreatic EUS (about 3000 EUS each). The instruments used were linear echoendoscopes (Olympus UCT-140; Olympus America, Inc., Melville, NY or Fujinon, Inc., Saitama, Japan). A cytopathologist experienced in pancreatic cytology was present in the EUS room for rapid on site evaluation during the exams.

The morphologic evaluation of the PCLs and evaluation of findings suspicious for malignancy were done during the EUS procedure.

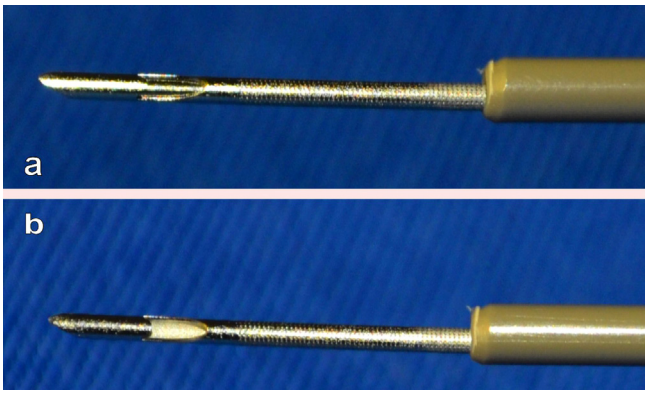


**Fig. 1.** (a) The 22-gauge needle with the side fenestration, 2 mm in length; with stylet and (b) without stylet.

Presence of solid components was defined at EUS as the presence of a solid cystic wall nodule, pericystic solid lesions, thickened wall or intracystic septa. All these aspects are associated with an increased risk of malignancy and so were considered together for the analysis.

The PCL puncture was made with the 22-gauge, Echotip Ultra FNB needle, featuring ProCore reverse bevel technology, with side fenestration (Cook Medical, Ireland) (Fig. 1a and b). Because of the particular characteristics of this needle we called our technique fine needle aspiration and biopsy (FNA/B). The technique used was the so-called cystic wall puncture (CWP), previously described in the literature [15], and modified for our study based on the characteristics of the new needle. After the target lesion was endosonographically visualized, and under colour doppler control, FNA/B was performed either from the duodenum or from the stomach. The needle was advanced into the PCL under EUS guidance. Once the lesion was penetrated, the stylet was removed (Fig. 2a), and suction was applied using a 10-mL syringe to aspirate all the intra-cystic liquid.

If at least 1 ml of intracystic fluid was obtained, a sample for CEA and amylase was first sent and if more fluid was available another 0.5 ml was sent for verification of K-*ras* mutation. The molecular analysis of K-*ras* oncogene (exon 2 and exon 3) was done by direct sequencing, using 3500 Genetic Analyzer (Applied Biosystems). A CEA value of $\geq$192 ng/ml was considered suggestive of mucinous PCLs [8]. Any additional fluid aspirated was sent for cytology.

When the cystic walls collapsed on the needle (Fig. 2b), aspiration was continued for about 30 s to allow cystic wall tissue to enter the side fenestration of the needle. The needle was then moved 3–4 times about 5–10 mm back and forth within the lesion. If intracystic septae were present and the fluid was impossible to aspirate due to its density, we performed the FNA/B on the septae; otherwise we performed a smear with the few drops of cystic fluid aspirated for cytologic evaluation.

If there was a solid component, FNA/B was performed directly on it by inserting the needle and leaving the aspiration open for 30 s and then moving 3–4 times about 5–10 mm back and forth within the lesion. Thereafter we waited for on-site evaluation by the pathologist to assess sample adequacy. If the sample was considered adequate the procedure was stopped; otherwise we performed further FNA/B on the solid component.

### 2.3. Cyto-histological analysis

For each PCL, two or three smears were stained with Hemacolor or Papanicolau for cytological analysis. Small visible pieces were stored in formalin. Finally we pushed the stylet through the