# 2025 AUG. 30, PM 13:20-16:45 1st TIPES Conference



### Optimize the tissue diagnosis of pancreatobiliary diseases

Briefing Room, 2<sup>nd</sup> Floor New Taipei Municipal TuCheng Hospital (Operated by Chang Gung Medical Foundation)

TIME	TOPIC	SPEAKER	CHAIR
13:00~13:20	Registration		
13::20~13:30	Welcome and Opening	Ming-Yao Su New Taipei Municipal TuCheng Hospital Hsiu-Po Wang, President, TIPES	
13:30~13:50	EUS-guided tissue acquisition for genetic analysis – current status and prospects	Joo Kyung Park Samsung Medical Center	Chien-Jui Huang National Cheng Kung University Hospital Jiann-Hwa Chen Taipei Tzu Chi Hospital
13:50~13:55	Q&A Abstract		
13:55~14:10	The application of DNA nanomachines for detecting microRNA in blood for the diagnosis of pancreatic cancer	Weng -Fai Wong National Taiwan University Hospital	
14:10~14:15	Q&A Abstract		
14:15~14:35	Diagnosis of indeterminate biliary stricture - Bench & Al	Phonthep Angsuwatcharakon Chulalongkorn University	Yu-Ting Kuo National Taiwan University Hospital Nai-Jen Liu Linkou Chang-Gung Memorial Hospital
14:35~14:40	Q&A Abstract		
14:40~15:00	From Needle to Nucleotide: EUS-FNB for Next-Generation Sequencing in Pancreatic Neoplasms	Chi-Huan Wu Linkou Chang-Gung Memorial Hospital	
15:00~15:05	Q&A Abstract		
15:05~15:25	Coffee Break DM		
15:25~15:45	Does Cytological Evaluation of EUS-guided tissue acquisition still have value in the fine needle biopsy era?	Hsiang Yao Shih Kaohsiung Medical University Hospital	Szu-Chia Liao Taichung Veterans General Hospital Jui-Hsing Tang New Taipei Municipal TuCheng Hospital
15:45~15:50	Q&A Abstract		
15:50~16:10	In-room cytologic evaluation by trained endosonographers for determination of the procedure end in endoscopic ultrasound-guided fine needle biopsy of solid pancreatic lesions	Weng -Fai Wong National Taiwan University Hospital	
16:10~16:15	Q&A Abstract		
16:15~16:35	Adequate pancreatic tissue acquisition by EUS-guided procedure	Yin-Yi Chu New Taipei Municipal TuCheng Hospital	
16:35~16:45	Q&A Abstract	Jiann-Hwa Chen Taipei Tzu Chi Hospital Jui-Hsing Tang New Taipei Municipal TuCheng Hospital	
16:45~16:50	Closing		

On-site and overseas Attendance: free Online Attendance: 500











#### EUS-guided Tissue Acquisition for Genetic Analysis-Current Status and Prospects

Joo Kyung Park

Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine,
Seoul, Republic of Korea

Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) and fine-needle biopsy (EUS-FNB) are crucial minimally invasive techniques for obtaining tissue samples from pancreatic and other gastrointestinal masses for diagnosis and molecular analysis. Recent advancements, such as the slowpull with fanning technique, have significantly improved diagnostic accuracy and reduced blood contamination in EUS-FNA of pancreatic masses. These EUS-derived tissue samples are increasingly vital for comprehensive genetic analysis, including whole-genome sequencing (WGS) and RNA **sequencing (RNA-seq)**. A key challenge in molecular profiling of pancreatic ductal adenocarcinoma (PDAC) has been low tumor cellularity and extensive stromal infiltration. This is being overcome by techniques like laser capture microdissection (LCM), which purifies tumor epithelium, enabling highresolution genomic analysis even from small biopsy samples. Studies like the COMPASS trial have demonstrated the feasibility of obtaining robust WGS and RNA-seq results for advanced PDAC within a clinically meaningful turnaround time of eight weeks. Beyond direct genetic sequencing, EUS-guided biopsies serve as a critical source for generating patient-derived organoids (PDOs), which are threedimensional cell cultures that closely mimic the architecture, physiology, and genetic characteristics of the original tumor. This capability is particularly significant for pancreatic cancer, where the majority of patients are not candidates for surgical resection, making biopsy-derived tissue the

primary source for personalized cancer models. Organoids offer several advantages over traditional 2D cell lines and patient-derived xenografts (PDXs), including rapid generation, long-term expansion potential, and the preservation of patient-specific genetic and phenotypic traits. They are instrumental in:

- Modeling cancer progression: CRISPR-Cas9 genome editing allows researchers to introduce
  specific oncogenic mutations (e.g., in APC, SMAD4, TP53, KRAS, PIK3CA) into normal or tumor
  organoids, thereby mimicking multi-step tumorigenesis and studying the functional
  contribution of driver genes. This also includes studying mutational signatures.
- Personalized drug screening: PDOs can be used for high-throughput drug sensitivity testing, allowing for the identification of effective therapeutic agents for individual patients. This enables a precision medicine approach, predicting differential responses to chemotherapy based on molecular profiles.
- **Creating living biobanks**: Collections of well-characterized PDOs serve as invaluable resources for academic studies, drug discovery, and preclinical screening.

Organotypic models of patient-specific tumors are revolutionizing our understanding of cancer heterogeneity and its implications for personalized medicine. The study's aims were as follows: 1) to establish a PDAC patient-derived organoid (PDO) model obtained from various PDAC specimens. 2) to find out clinicogenomic factors affecting patients' outcomes.

Methods: The SMC PDAC Cohort Patients were prospectively enrolled and underwent EUS-guided FNB, metastatic sites (such as liver, ascites, lung, and bone), and surgical resection. PDAC PDOs were comprehensively analyzed for histology, genomic sequencing, and high-throughput screening (HTS) drug sensitivity tests.

Results: The 650 PDAC patients were prospectively enrolled in this study. PDAC PDO platform has been trying to establish from the following cancer specimens: ascites, biopsies from bone, liver, lung, and pancreas, or surgical resection. The success rate was as follows according to the source of

obtaining site; ascites due to peritoneal seeding (2/2: 100%), bone metastases (1/1: 0%), primary PDAC mass via EUS FNB (156/183:85.2%), liver mets (3/4: 75%), lung metastases (1/1: 100%), surgical PDAC specimens (353/459: 76.9%) and PDO was successfully established within 8.2±2.6 days. It took approximately 3 weeks to acquire each specimen and generate sufficient PDAC PDOs for the simultaneous HTS drug sensitivity test and genomic sequencing. The whole-exome sequencing showed an almost identical concordance between original PDAC tissues and matched PDOs and the increased frequency of genetic alterations in PDOs. The HTS drug sensitivity test revealed the clinical correlation between the PDO response and the actual chemotherapeutic response of the study patients in both palliative and adjuvant in real-world settings (ranging from 84.0~ to 91.2%). In addition, whole-transcriptome sequencing identified candidate genes associated with nab-paclitaxel resistance, such as ITGB7, ANPEP, and ST3GAL1.

Conclusions: The PDAC PDO platform may become a valuable tool for personalized medicine and may give us insights into tumor biology. The successful and rapid creation of PDAC organoids from EUS-FNB samples has been establishing this as a safe and feasible approach. Future prospects include achieving near 100% success rates for organoid generation and further integrating EUS-guided tissue acquisition with advanced genomic and organoid-based platforms to enable truly personalized treatment strategies for a broader range of cancers.

**Keywords:** Patient-Derived Organoid (PDO), Pancreatic ductal adenocarcinoma (PDAC), Precision medicine, High-throughput screening (HTS) drug test

#### Topic

The application of DNA nano machines for detecting microRNA in blood for diagnosis of pancreatic cancer

黃永輝

#### **Abstract**

Pancreatic cancer is highly lethal and carries a dismal prognosis. A practical, cost-effective screening tool is urgently needed. Unlike neoplasms arising from hollow organs (e.g., the esophagus, stomach, or colon), endoscopic luminal screening is not feasible for pancreatic cancer, and cross-sectional imaging has limited sensitivity for subtle epithelial lesions within the pancreatic duct. Consequently, early detection is relied on biomarker-based screening. The biomarker most commonly used in clinical practice, CA19-9, has disappointing sensitivity and specificity, underscoring the unmet need for novel markers that enable early diagnosis. MicroRNAs (miRNAs)—small, single-stranded, noncoding RNAs that mediate RNA silencing and post-transcriptional regulation—are promising candidates; aberrant miRNA expression can be detected in serum, tissue, or urine from patients with cancer. However, conventional detection typically requires qPCR, which requires thermal cycling and specialized instrumentation. We have developed a novel DNA nanomachine–based assay for blood-borne miRNA detection that operates at room temperature without thermocycling. This platform has the potential to facilitate the widespread adoption of miRNA-based screening for the early detection of pancreatic cancer.

### <u>Diagnosis of Indeterminate Biliary Stricture: From Bench Research to Artificial Intelligence-Enhanced</u> Clinical Practice



Phonthep Angsuwatcharakon, MD, MSc.

Faculty of Medicine, Chulalongkorn University

#### Abstract:

The evaluation of indeterminate biliary strictures remains one of the most persistent dilemmas in gastroenterology. Traditional diagnostic tools—including ERCP with brush cytology, forceps biopsy, cross-sectional imaging, and endoscopic ultrasound (EUS)-guided sampling—often fail to provide definitive answers, with sensitivities for malignancy frequently below 60%. The consequences are significant: delayed detection of cholangiocarcinoma in its potentially curable stages, or unnecessary surgical resections for benign strictures.

From the bench side, advances in molecular science have begun to illuminate new diagnostic avenues. Multi-omics profiling has revealed candidate biomarkers in serum, bile, and urine, including proteomic signatures, bile acid metabolite patterns, and mutational profiles from cell-free DNA. These markers hold promises for earlier and more accurate discrimination between benign and malignant etiologies, especially when integrated with histopathology and imaging data.

In parallel, endoscopic innovation has expanded our visualization capabilities. Probe-based confocal laser endomicroscopy (pCLE), intraductal ultrasound (IDUS), cholangioscopy, and molecular fluorescence imaging offer real-time, high-resolution assessments of mucosal and submucosal structures. These tools generate rich datasets that surpass human capacity for manual interpretation—opening the door for artificial intelligence (AI)—driven analysis.

Al is poised to transform indeterminate biliary stricture diagnosis through three main pathways:

- 1. **Imaging Analysis** Convolutional neural networks trained on ERCP cholangiograms, EUS images, and cholangioscopy videos can detect malignant patterns with greater sensitivity and consistency than human observers.
- 2. **Multimodal Data Integration** Machine learning models that combine imaging features with molecular biomarkers, histology, and clinical data can generate individualized malignancy risk scores, guiding biopsy targeting and management decisions.

3. **Digital Pathology** – Al-enhanced cytology and histology slide interpretation increases detection of subtle atypia, reduces interobserver variability, and supports real-time feedback during endoscopic procedures.

By bridging molecular-level discoveries with computational precision, this may offer a path toward resolving one of the most intractable challenges in hepatobiliary medicine.

## From Needle to Nucleotide: EUS-FNB for Next-Generation Sequencing in Pancreatic Neoplasms

吳季桓

#### Abstract

ancreatic cancer(PC) remains one of the most lethal malignancies worldwide, with limited survival despite advances in systemic therapies. Precision oncology offers a promising avenue for improving outcomes, particularly through the identification of actionable molecular alterations via next-generation sequencing (NGS). Endoscopic ultrasound-guided fine-needle biopsy (EUS-FNB) has emerged as a reliable method for acquiring tissue suitable for NGS, with higher success rates compared to traditional fine-needle aspiration. This presentation explores the integration of EUS-FNB into the diagnostic and therapeutic workflow for PC, emphasizing specimen eligibility criteria, optimal timing for tissue acquisition, and the impact of treatment-induced changes on sequencing success.

Emerging data suggest that early, targeted EUS-FNB sampling prior to chemotherapy or radiotherapy may enhance NGS success and facilitate personalized treatment strategies. As molecular profiling becomes increasingly central to PC management, optimizing biopsy techniques and timing is critical. Further research is needed to validate novel EUS approaches and establish standardized protocols for NGS acquisition in pancreatic cancer.

Does Cytological Evaluation of EUS-guided Tissue Acquisition Still Have Value in The Fine Needle Biopsy Era?

Hsiang Yao Shih

Division of Gastroenterology, Department of Internal Medicine, Kaohsiung Medical University Hospital, Taiwan

Endoscopic ultrasound-guided tissue acquisition (EUS-TA) is the mainstay for obtaining specimens from lesions adjacent to the digestive tract, particularly pancreatic solid lesions. Traditionally, endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) was primarily used to obtain cytological specimens. With the introduction of biopsy needles, endoscopic ultrasound-guided fine needle biopsy (EUS-FNB) has enabled the acquisition of histological samples, ushering in the era of fine-needle biopsy. However, in clinical practice, non-conclusive diagnoses can still occur with EUS-FNB, even after multiple passes. In such situations, does cytological evaluation remain helpful for achieving a definitive diagnosis? Current evidence suggests that EUS-FNA provides a diagnostic yield comparable to that of FNB for pancreatic solid lesions. Moreover, combining cytological and histological evaluations improves sensitivity and specificity.

Another important category is pancreatic cystic lesions. Obtaining adequate histological samples from cystic lesions via FNB is particularly challenging, and cytological evaluation of cyst fluid often remains unsatisfactory. In these cases, biochemical analysis of cyst fluid—such as amylase, glucose, and carcinoembryonic antigen (CEA)—is useful for differentiating between cystic lesion types. Except for biochemical analysis we also could use molecular analysis- such as KRAS, GNAS to differentiate from types of pancreatic cystic lesions. In addition to biochemical analysis, molecular testing—such as KRAS and GNAS mutation analysis—can further aid in the classification of pancreatic cystic lesions.

Although we are now in the era of fine needle biopsy, cytological evaluation continues to play a valuable role in achieving definitive diagnoses.

#### Topic

In-room cytologic evaluation by trained endosonographers for determination of the procedure end in endoscopic ultrasound-guided fine needle biopsy of solid pancreatic lesions

#### 黃永輝

#### Abstract

Endoscopic ultrasound-guided fine needle biopsy (EUS-FNB) is an essential tool for tissue acquisition in pancreatic solid tumors. Rapid on-site evaluation (ROSE) by cytologists can ensure the diagnostic accuracy. However, universal application of ROSE is limited by its availability. Therefore, we want to investigate the feasibility of determination of procedure end according to the results of in-room cytologic evaluation by trained endosonographer (IRCETE). A training course focusing on cytology interpretation of common pancreatic tumors had been provided to three endosonographers. After training, the decision to terminate EUS-FNB was made based on IRCETE results. Diagnostic accuracy, concordance rate of diagnostic category and sample adequacy assessment were compared with those determined by board-certified cytologists and macroscopic on-site evaluation (MOSE). We enrolled 65 patients with solid pancreatic tumors, with the majority being malignant cases (86%). The diagnostic accuracy was 90.8% when the procedure end was determined based on IRCETE, compared to 87.7% and 98.5% when determined by MOSE and cytologists, respectively (P = 0.060). Based on the results from cytologists, the accuracy of IRCETE in diagnostic category interpretation was 97.3%. Therefore, IRCETE can serve as a supplementary alternative alongside MOSE for determining the end of tissue sampling in the absence of ROSE.

#### Adequate Pancreatic Tissue Acquisition by EUS-guided Procedure

#### 朱允義

#### **Abstract**

Endoscopic ultrasound (EUS)-guided tissue acquisition has become a cornerstone in the diagnosis and management of pancreatic diseases. Obtaining adequate tissue samples is essential for accurate cytopathological and histological evaluation, which directly influences therapeutic decision-making. Several factors contribute to the diagnostic yield, including needle type and size, number of passes, suction technique, and the use of rapid on-site evaluation (ROSE). Recent evidence suggests that fine-needle biopsy (FNB) needles provide superior histological core samples compared with fine-needle aspiration (FNA), particularly in cases requiring molecular profiling. Technical refinements such as the fanning technique, slow-pull suction, and optimal puncture site selection further enhance sample adequacy. Additionally, operator expertise and multidisciplinary collaboration between endoscopists and cytopathologists remain critical. Despite significant progress, challenges persist in small or fibrotic lesions, and standardized consensus guidelines are still evolving. This review highlights current strategies, consensus recommendations, and future perspectives to optimize pancreatic tissue acquisition through EUS-guided procedures, aiming to improve diagnostic precision and patient outcomes.