

# Prospective evaluation of 25-gauge Franseen needles for endoscopic ultrasound-guided fine-needle biopsy of solid pancreatic masses



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## Bibliography

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## ABSTRACT

**Background and study aims** The ideal puncture needle for endoscopic ultrasound (EUS)-guided sampling is maneuverable and easy to puncture with, and can obtain sufficient

material in almost one pass. The novel 25-gauge Franseen needle may provide a good balance between maneuverability and sample yield.

**Patients and methods** Between July 2017 and December 2018, 116 patients with solid pancreatic masses were prospectively enrolled and investigated. We evaluated the diagnostic yield associated with using the 25-gauge Franseen needle for EUS-guided sampling of pancreatic masses.

**Results** The technical success rate was 100% (116/116). The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy for malignancy were 98% (105/107), 100% (9/9), 100% (105/105), 82% (9/11), and 98% (114/116), respectively. Cumulative sensitivities for malignancy were 87% (93/107) on pass 1, 97% (104/107) on pass 2, and 98% (105/107) on pass 3, respectively, with no increase in sensitivity after 4 or more. An adequate specimen for histological assessment was obtained in 79% (92/116) of cases. Multivariate logistic analyses showed that lesion size smaller than 13 mm was a risk factor for failure of obtaining an adequate specimen for histological assessment ( $P=0.010$ ).

**Conclusions** The novel 25-gauge Franseen needle showed excellent diagnostic yield for solid pancreatic masses. However, its ability to obtain an adequate specimen for histological assessment may still be insufficient, especially when dealing with small lesions.

## Introduction

Endoscopic ultrasound (EUS)-guided sampling is an established method for pathological diagnosis of pancreatic masses. The diagnostic performance of EUS-guided sampling for pancreatic masses is good, with sensitivity rates of about 90% reported [1]. However, the amount of tissue obtained by EUS-guided sampling is very small because only 19- to 25-gauge needles can be used, and the diagnostic yield still depends on endoscopic and pathological skills. Therefore, further improvement of needles was expected and needed. The ideal needle is maneuverable and easy to puncture with, and can obtain sufficient

material in almost one pass.

The Franseen needle, which has three symmetric heels at the tip [2], was recently developed to improve the quantity and quality of the samples obtained, and subsequently diagnostic yields, by preserving the structural integrity of the tissues. An experimental study in an animal model [3] showed that the Franseen needle has better tissue acquisition abilities than conventional needles, and clinical studies on 22-gauge needles have also shown good results [2,4–11]. However, it is sometimes relatively difficult to obtain a puncture with the Franseen needle because of the unique design of the tips. Generally, a

25-gauge needle can penetrate the mass more easily, but obtains inferior amounts of the specimen compared to 19- to 22-gauge needles [1]. We hypothesized that the 25-gauge Franseen needle can strike a good balance between technical maneuverability and obtaining sufficient tissue, resulting in improved diagnostic ability. The present study aimed to evaluate the diagnostic ability of 25-gauge Franseen needles for EUS-guided sampling of solid pancreatic masses.

## Patients and methods

### Study design and patients

This was a prospective single-center observational study conducted at Aichi Medical University Hospital between July 2017 and December 2018. Consecutive patients who were 20 years or older and had a solid pancreatic mass requiring EUS-guided sampling were enrolled. Exclusion criteria were (1) severe comorbidity in any other organ; (2) a performance status of 4; (3) inability to undergo an endoscopic approach; (4) coagulopathy; (5) pregnancy; and (6) inability to provide informed consent. Whether the mass was solid, was judged by EUS with/without magnetic resonance cholangiopancreatography.

Our hospital's institutional review board approved this study in accordance with the principles of the Declaration of Helsinki (approval number: 2017-H147). The study protocol was registered in the University Hospital Medical Information Network Clinical Trial Registry database (identifier: UMIN000028273).

### Procedural technique

A linear-array echoendoscope (GF-UCT260; Olympus Medical Systems Corp., Tokyo, Japan) was used with an EU-ME2 processor (Olympus Medical Systems Corp.). Contrast-enhanced EUS was used if required. The target lesion was punctured under EUS guidance using 25-gauge Franseen needles (Acquire; Boston Scientific Corporation, Marlborough, MA). After puncturing the target lesion, the stylet was removed and suction was applied using a 10-mL syringe. Subsequently, about 10 to 20 strokes were performed within each lesion. All procedures were performed by experienced endoscopists who were skilled at performing EUS-guided sampling.

### Pathological assessment

After the needle was removed from the lesion and the endoscope, the stylet was inserted into the needle again and the sample was expelled onto a tray. Aspirated specimens were smeared using slides and air-dried. Then, air-dried smears were subjected to May-Giemsa staining and rapid onsite cytological evaluation (ROSE) was performed to assess sample adequacy. Punctures were repeated until ROSE determined that the tissue obtained was satisfactory; however, the maximum number of passes was set at 5. If the residual sample after ROSE seemed inadequate for histological examination, one more puncture was performed. The specimen was fixed in formalin, embedded in paraffin, and sectioned for histopathological analysis. Tissues were processed by experienced cytotechnologists,

and all samples were assessed by experienced cytopathologists.

### Outcomes and definitions

The primary outcomes were sensitivity for malignancy, number of needle passes required to reach a plateau of sensitivity, and rate of obtaining adequate specimens for histological assessment. Furthermore, the predictive factors that affected adequate specimen acquisition were evaluated, including sex, age, lesion location and size, puncture route, number of passes, and type of lesion.

The plateau of number of needle passes was defined as the point at which increasing needle passes cease to improve sensitivity. Histological adequacy was determined, by experienced cytopathologists, based on whether samples allowed adequate histological interpretation. Lesion size was defined as the length of the lesion on the ultrasonographic images within the field of view of the puncture site, that is, the maximum length of the needle's penetration rather than the maximum diameter of the lesion.

The final pathological diagnoses were based on the surgical specimens obtained from those patients who underwent surgery. For patients who did not undergo surgery, final diagnoses were based on disease clinical course, which was evaluated for at least 6 months and included repeated imaging assessments.

Definitions and severity of adverse events (AEs) were classified according to the lexicon of the American Society for Gastrointestinal Endoscopy [12].

### Statistical analyses

The target sample size was set to 100, based on the number of patients we could enroll within a 1.5-year period. The differences in categorical variables were evaluated using Fisher's exact tests. Continuous variables were compared using the Mann-Whitney U-test. To evaluate the factors that affected adequate specimen acquisition, multivariate analyses were carried out using logistic regression analyses of the variables with values of  $P < 0.2$  in the univariate analyses.  $P < .05$  was considered to indicate statistical significance. All statistical analyses were performed using R version 3.4.1 (The R Foundation for Statistical Computing, Vienna, Austria).

## Results

### Patient characteristics

During the study period, 116 patients met the eligibility criteria for study inclusion. ► **Table 1** presents the patients' characteristics, including sex, age, lesion location and size, puncture route, number of passes, and final diagnosis. The final diagnosis was benign disease in nine patients and malignancy in 107, 98 of which had pancreatic adenocarcinoma.

### Diagnostic performance

► **Table 2** presents the outcomes. The technical success rate was 100% (116/116), and diagnostic adequacy on ROSE was 98% (114/116). The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy for

► **Table 1** Baseline patient characteristics (n = 116).

Characteristics	
Sex, (male/female), n	62/ 54
Median age (range), years	72 (42–92)
Location of lesion, n (%)	
▪ Head	51 (44)
▪ Body	46 (40)
▪ Tail	19 (16)
Median lesion size (range), mm	15 (5–31)
Puncture route, n (%)	
▪ Transgastric	67 (58)
▪ Transduodenal	49 (42)
Median number of passes (range), n	2 (1–5)
Final diagnosis, n (%)	
▪ Adenocarcinoma	98 (85)
▪ Metastatic cancer	4 (3)
▪ Neuroendocrine carcinoma	2 (2)
▪ Intraductal papillary mucinous carcinoma	2 (2)
▪ Acinar cell carcinoma	1 (1)
▪ Neuroendocrine tumor	4 (3)
▪ Chronic pancreatitis	4 (3)
▪ Solid pseudopapillary neoplasm	1 (1)

malignancy were 98 % (105/107), 100 % (9/9), 100 % (105/105), 82 % (9/11), and 98 % (114/116), respectively. Cumulative sensitivity for malignancy was 87 % (93/107) on pass 1, 97 % (104/107) on pass 2, and 98 % (105/107) on pass 3, within no increase in sensitivity after four or more passes. Subgroup analyses based on lesion location and size are shown in ► **Table 3**, where patients were divided into four groups according to location in the head or body/tail, and size above or below the median. The number of passes required to reach a plateau of sensi-

► **Table 2** Outcomes of endoscopic ultrasound-guided sampling using 25-gauge Franseen needles.

Technical success, % (n)	100 (116/116)
Diagnostic adequacy on ROSE, % (n)	98 (114/116)
Adequate specimen for histological assessment, % (n)	79 (92/116)
Adverse events, % (n)	1 (1/116)
▪ Pancreatitis, n	1
Sensitivity, % (n)	98 (105/107)
Specificity, % (n)	100 (9/9)
Positive predictive value, % (n)	100 (105/105)
Negative predictive value, % (n)	82 (9/11)
Accuracy, % (n)	98 (114/116)
ROSE, rapid onsite cytological evaluation	

tivity were two, two, two, and three in the head lesion < 15 mm, head lesion ≥ 15 mm, body/tail lesion < 15 mm, and body/tail lesion ≥ 15 mm subgroups, respectively.

An adequate specimen for histological assessment was obtained in 79 % of patients (92/116). With regard to AEs, mild pancreatitis was observed in one patient, which improved with conservative management.

### Factors affecting adequate specimen acquisition

Sex, age, lesion location and size, puncture route, number of passes, and type of lesion were assessed as predictive factors for obtaining adequate specimens for histological assessment (► **Table 4**). Univariate analyses determined that the median lesion size was significantly smaller in the failed cases (10 mm) than in successful cases (15 mm) ( $P = 0.035$ ). The receiver operating characteristic curve analysis of lesion size revealed an area under the curve of 0.638. The optimal cutoff for prediction of successful adequate histological specimen acquisition was calculated to be 13 mm, with a sensitivity of 67 % and specificity of 63 %. Multivariate logistic regression analyses determined that

► **Table 3** Cumulative sensitivities for malignancy.

		Cumulative sensitivity, % (n)		
		Pass 1	Pass 2	Pass 3
Location of lesion	Lesion size			
Head	< 15 mm	90 % (18/20)	95 % (19/20) <sup>1</sup>	
Head	≥ 15 mm	81 % (22/27)	100 % (27/27) <sup>1</sup>	
Body/tail	< 15 mm	90 % (18/20)	100 % (20/20) <sup>1</sup>	
Body/tail	≥ 15 mm	88 % (35/40)	95 % (38/40)	98 % (39/40) <sup>1</sup>
Total		87 % (93/107)	97 % (104/107)	98 % (105/107) <sup>1</sup>

<sup>1</sup> Diagnostic sensitivity did not increase with additional needle passes

► **Table 4** Univariate analysis of the factors associated with acquisition of adequate histological samples.

	Successful acquisition of adequate histological sample (n = 92)	Failure to obtain adequate histological sample (n = 24)	P value
Sex, n (%)			0.068
▪ Male	45 (49)	17 (71)	
▪ Female	47 (51)	7 (29)	
Median age (range), years	73 (42–92)	70 (48–85)	0.611
Location of lesion, n (%)			0.645
▪ Head	39 (42)	12 (50)	
▪ Body/tail	53 (58)	12 (50)	
Median lesion size (range), mm	15 (5–31)	10 (5–28)	<b>0.035</b>
Puncture route, n (%)			0.817
▪ Transgastric	54 (59)	13 (54)	
▪ Transduodenal	38 (41)	11 (46)	
Median number of passes (range)	2 (1–4)	2 (1–5)	0.164
Type of lesion, n (%)			0.390
▪ Malignant	86 (93)	21 (88)	
▪ Benign	6 (7)	3 (13)	

► **Table 5** Multivariate analysis of the factors associated with acquisition of adequate histological samples.

	Odds ratio	95% CI	P value
Sex (male)	0.368	0.135–1.01	0.052
Lesion size (<13 mm)	0.282	0.107–0.738	<b>0.010</b>
Number of passes	1.520	0.818–2.840	0.184
CI, confidence interval			

lesion size smaller than 13 mm was a predictive factor that was significantly associated with failure of obtaining adequate specimen for histological assessment (odds ratio, 0.282; 95% confidence interval, 0.107–0.738;  $P = 0.010$ ) (► **Table 5**).

## Discussion

The current study showed that the sensitivity of the 25-gauge Franseen needle for solid pancreatic masses was very high at 98%, in which plateaued at three passes. However, the rate of obtaining adequate specimen for histological assessment was 79%, and was particularly low for small lesions.

The Franseen needle's tips are uniquely structured with three-symmetric heels to improve the quantity and quality of the samples obtained, and subsequently the diagnostic yields, by preserving the structural integrity of the tissue. Some studies have already investigated the utility of 22-gauge Franseen needles, showing very good results with a pooled diagnostic yield rate of 92.7% [11].

Higher sample quality and presence of histology are associated with enhanced diagnostic performance and agreement among pathologists of varying expertise [13]. Although thick needles are generally superior for obtaining histologic cores, a 25-gauge may be sufficient to collect samples of adequate quality if the Franseen needle is used. If the diagnostic yields among different sized needles are equal, a thinner needle would be preferable in terms of operation and reducing tissue injuries. The 25-gauge Franseen needle may achieve a good balance between maneuverability and amount of sample obtained.

However, to our knowledge, only one study [14] on the 25-gauge Franseen needle has been reported. The study comprised 100 varying lesions including the pancreas, lymph nodes, and subepithelial tumors, and showed that the sensitivity, specificity, and accuracy was 87%, 100%, and 88%, respectively, at only one pass. Our study is the first to focus on the effectiveness of the 25-gauge Franseen needle for pancreatic masses only. We were able to report sensitivity, specificity, and accuracy rates of 98%, 100%, and 98%, respectively, using multiple passes and with ROSE available. Both our own and the aforementioned report showed very good diagnostic results, with technical success rates of 100% in both. Conversely, technical failure has been reported when using the 22-gauge Franseen needle [2]. Although the unique structure of the tip leads to a lower penetrative ability than conventional needles, this may not be an issue when a 25-gauge needle is used.

The rate of adequate specimen acquisition for histological assessment using the 25-gauge Franseen needle was 82% in the aforementioned report [14]. The present study showed a rate of 79%. Both studies reported results superior to recent

large-scale studies of conventional 25-gauge needles, which reported rates of 44–67% [15, 16]. However, the rates were lower than those of 22-gauge Franseen needle, which were reported as 94–100% [2, 4, 6, 9–10]. If a disease that requires an adequate histologic specimen for immunohistological evaluation, such as neuroendocrine tumors, is suspected before EUS-guided sampling, use of a 22-gauge or thicker needle may be preferable.

Regarding the number of passes, a previous study of EUS-guided sampling for pancreatic lesions using conventional needle reported that the number of needle passes to reach a plateau for head lesions < 15 mm, head lesions > 15 mm, body/tail lesions < 15 mm, and body/tail lesions > 15 mm was four, four, three, and four, respectively [17]. In the current study, the number of passes required was two, two, two, and three, respectively. Since the sensitivity did not increase with the use of four or more passes, it may be better to limit the number of passes when using a Franseen needle to a maximum of three.

An increase in AEs associated with use of the Franseen needle is a matter of concern because the structure of the tip may cause tissue injuries. In previous studies, bleeding [2, 7], pancreatitis [10], and pancreatic fistula [14] were reported as AEs. In the present study, pancreatitis occurred in one patient. Because evidence regarding AEs associated with the Franseen needle is lacking, more careful monitoring after procedures involving Franseen needles is desirable.

The results of the current study should be considered in the context of its limitations, which include its nonrandomized design and single-center setting. Furthermore, only experienced endoscopists, cytotechnologists, and cytopathologists were involved in EUS-guided sampling. Therefore, multicenter, randomized, controlled trials are warranted before drawing definitive conclusions.

## Conclusion

In conclusion, the 25-gauge Franseen needle showed excellent technical success rates and diagnostic sensitivity for solid pancreatic masses. Although the ability to obtain adequate histological samples was also good compared to conventional needles, it may still be insufficient, especially when dealing with small lesions.

## Competing interests

The authors declare that they have no conflict of interest.

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