**22G Acquire vs. 20G Procore needle for endoscopic ultrasound-guided biopsy of pancreatic masses: a randomized study comparing histologic sample quantity and diagnostic accuracy**

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**ABSTRACT**

**Background** Endoscopic ultrasound-guided fine-needle biopsy (EUS-FNB) has been suggested for obtaining high quality tissue samples from pancreatic tumors. We performed a multicenter randomized crossover trial comparing EUS-FNB with a 20G Procore needle vs. a 22G Acquire needle. The aims were to compare the quantity of targeted tissue (pancreas) and diagnostic accuracy for the two needles.

**Methods** 60 patients admitted for EUS-FNB in three endoscopy units were included. One pass was performed consecutively with each needle, in a randomized order. Histologic material was studied in a blinded manner with respect to the needle. The primary end point was mean cumulative length of tissue core biopsies per needle pass.

**Results** Final diagnosis was adenocarcinoma (n=46; 77 %), neuroendocrine neoplasm (n=11; 18 %), autoimmune pancreatitis (n=2), and mass-forming chronic pancreatitis (n=1). The mean cumulative length of tissue core biopsies per needle pass was significantly higher with the 22G Acquire needle at 11.4 mm (95 % confidence interval [CI] 9.0–13.8) vs. 5.4 mm (95 %CI 3.8–7.0) for the 20G Procore needle (P<0.001), as was the mean surface area (3.5 mm² [95 % CI 2.7–4.3] vs. 1.8 mm² [95 %CI 1.2–2.3]; P<0.001). Diagnostic adequacy and accuracy were 100 % and 87 % with the 22G Acquire needle, and 82 % and 67 % with the 20G Procore needle (P=0.001 and P=0.02, respectively).

**Conclusions** EUS-guided biopsy of pancreatic masses with the 22G Acquire needle provided more tissue for histologic evaluation and better diagnostic accuracy than the 20G Procore needle.

**Introduction**
Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) is the gold-standard method for histologic diagnosis of pancreatic masses [1–4]. Although diagnosis is achieved in 64%–95% of cases with cytologic samples obtained using a 22G EUS-FNA needle [1–4], histologic samples may be preferable. Not only do histologic samples enable more accurate tumor characterization, but they also allow molecular characterization of the pancreatic tumor, which will soon be needed for...
personalized therapy. Accordingly, medical device companies have recently marketed needles for endoscopic ultrasound-guided fine-needle biopsy (EUS-FNB) featuring a larger caliber and/or new cutting devices (Fig. 1) [5, 6]. Owing to the variability of the histologic samples obtained by EUS-FNB [6], many series have, however, hitherto failed to convincingly demonstrate that EUS-FNB is more effective than EUS-FNA [7–9].

Two different needle technologies have recently been developed for histologic sampling. The first of these, the 20G Procore needle (Wilson Cook Medical, Winston-Salem, North Carolina, USA), combines a lateral bevel technology with a relatively large caliber. Two recent meta-analyses on the first generation of the bevel system did not confirm a benefit in terms of diagnostic yield, but did do so in reducing the number of needle passes required to reach a diagnosis [7–9]. The second technology, the 22G Acquire needle (Boston Scientific Natick, Massachusetts, USA), features a cutting device that has already proven its efficacy for obtaining good-quality histologic specimens in percutaneous biopsies [10–15], along with a standard diameter.

A previous pilot observational study comparing the two needles suggested that the 22G Acquire needle was more effective than the 20G Procore needle for pancreatic tumors in terms of the quantity of the histologic sample, as evaluated by a simple, reliable, and reproducible histologic criterion, namely the cumulative length of the tissue core biopsies per needle pass [16].

To determine with which type of needle it is possible to obtain the largest quantity of histologic material, we performed a multicenter randomized crossover trial comparing EUS-FNB with a 20G Procore needle vs. a 22G Acquire needle. The primary end point was the mean cumulative length of tissue core biopsies per needle pass. The secondary end points were the surface area of the core fragments, the diagnostic adequacy (core biopsy obtained), and the diagnostic accuracy with each needle.

Methods
This multicenter randomized crossover study was conducted in three expert tertiary endoscopy centers from 1 June 2018 to 1 November 2018. Written informed consent for the EUS procedure was obtained from all patients. The study was carried out in accordance with the Helsinki Declaration and was approved by the Ouest III ethics committee of the University Hospital of Poitiers, France (number 18.03.22) and the French National Agency for the Safety of Medicines and Health Products (ANSM 2018-A00276-49). It was registered in the ClinicalTrials.gov database (NCT03567863) and followed the STARD and CONSORT statements. All authors had full access to the study data.

Patients
The study included all consecutive patients aged ≥ 18 years who were referred to one of the participating expert tertiary endoscopy centers for EUS-guided sampling of a solid pancreatic mass. The physicians made the decision on whether or not to proceed based on whether or not the presence of a pancreatic tissue mass was confirmed on EUS. Contraindications to puncture with the EUS-FNB needle were predefined as follows: non-accessible pancreatic mass owing to history of Billroth II or Roux-en-Y reconstruction, coagulation disorder (such as partial thromboplastin time > 42 seconds, prothrombin time [Quick value] < 50%, or platelet count < 50 000/mm³), treatment with clopidogrel, or pregnancy.

Groups and randomization
Computer-generated randomization assignments establishing the order of needle use were placed in sealed envelopes and opened locally during the procedure when the patient matched the inclusion criteria. Both needles were used in each patient. The 20G Procore needle was used first in group A, and the 22G Acquire needle first in group B.

EUS-FNB procedure
All the EUS-FNB procedures included within this study were performed by three expert endoscopic physicians (one per center [D.K., L.P., and B.N.]), who annually perform more than 150 EUS-guided sampling procedures each. During the procedures, the patients were under propofol-induced general anesthesia and lying in the supine or left lateral position. The following convex-array echoendoscopes were used: (i) the GF-UCT180 Olympus (Olympus Europe Inc., Hamburg, Germany) with a channel diameter of 3.7 mm; and (ii) the Fujinon EG-580UT (Fujifilm France [Medical Systems], Asnières, France) with a working channel diameter of 3.8 mm. Once an optimal puncture site had been determined and any vascular interposition had been eliminated by Doppler examination, a puncture was made using the two needles according to the randomization instruction.

Following puncture under EUS control, the stylet was entirely removed. The needle was subsequently moved back and forth five times within the lesion, before suction was applied with a 10-mL syringe while moving the needle back and forth a
further five times, using the fanning method [17]. The needle was gently flushed with air after withdrawal and the aspirated material was placed in formalin solution for histologic examination. The same procedure was systematically repeated once with the second needle and the material was flushed into a second sample pot.

The aspirated material was assessed macroscopically by the endosonographer. If the size or quality of the specimens were judged insufficient on visual examination of the sample pots, further passes could be made as many times as needed with either needle and placed into a third sample pot. In this case, the specimen obtained with the additional (third and subsequent) passes was processed separately and was not used for the comparison of the needles.

The tissue fragments obtained were fixed in formalin prior to delivery to each cytopathology unit within 2 days. None of the pathologic request forms indicated the type of needle used. If required, an endoscopic retrograde cholangiopancreatography (ERCP) could be performed after the EUS-FNB procedure.

Histologic preparations and analysis

The tissue fragments obtained were secured in low melting agarose (Histogel) prior to paraffin embedment and hematoxylin, eosin, and saffron staining. A standardized procedure was developed for all three pathology departments for the cell block. Briefly, all the fragments were fixed in buffered formalin (minimum 30 minutes) and gently spun down (600 g for 10 minutes). After removal of the fixative agent, the pellet was embedded using the CYTOBLOCK reagent (Thermo Scientific, USA), transferred into a fine mesh cassette, and processed through the routine paraffin embedment procedure. All the examined sections were cut at 4 μm. A core fragment was defined microscopically as a fragment of tissue measuring at least 1 mm in its greatest diameter.

One expert physician in pancreatic pathology in each unit (J. Z., J. C., and A.-I. L.) examined the samples of histologic material obtained by EUS-FNB in a manner that was blinded with regards to the type of needle and their order of use. However, they evaluated the specimens from both needles with the knowledge that they had been obtained from the same patient.

The following pathologic criteria were assessed:
- presence of core biopsies on histologic sampling
- cumulative length of targeted tissue (pancreas) core biopsies per needle pass (sum of all the targeted tissue core lengths, as measured manually with a graduated ruler under microscopy on the best cell block section) (Fig. 2)
- pancreatic mass characterization.

Slides were digitalized (Aperio-Leica) for the computer-assisted analyses. For each slide, all of the core fragments were manually circled and the cumulative surface area of all cores was computed using the positive pixel algorithm v1 (Aperio-Leica) (Fig. 2).

Data collection and post-procedure management

We collected patient characteristics (sex, age, American Society of Anesthesiologists [ASA] score, and current treatment with acetylsalicylic acid), pancreatic mass characteristics (size and location), and puncture characteristics (transduodenal or transgastric access and final number of passes), and recorded any endoscopic biliary drainage procedures that had to be performed at the same time as the EUS-FNB.

Depending on the center and on the other procedures performed, patients were discharged within 4 hours of the endoscopic procedure or remained in hospital for at least 24 hours. Before discharge, patients were examined to ensure that they were not displaying any signs of perforation, bleeding, acute pancreatitis, sepsis, or other complications. Laboratory blood tests (liver function tests, amylase, creatinine, blood count, and C-reactive protein) were performed either if patients were experiencing symptoms or in all cases if they had undergone an ERCP.

The patient and the referring physicians notified any delayed adverse events within 1 week. Serious adverse events were defined as complications resulting in a new hospital admission or an extension of an existing hospital stay, or a significant disability or death [18]. Complications and deaths were recorded for both groups. Morbidities due to ERCP (when performed) were defined and graded according to the modified 1991 consensus guidelines [15].

Repeat and/or alternative procedures were performed in patients where false-negative diagnoses were suspected. Additional physical and computed tomography (CT) examinations were made at least 12 months after the procedure on patients who were negative for malignancy.

End point definitions

The primary end point was the quantity of histologic sample obtained, as evaluated by the mean cumulative length of tissue core biopsies per needle pass.

The secondary end points were: (i) the quantity of histologic sample obtained, as evaluated by the computer-assisted measurement of the core fragment surface area; (ii) diagnostic ade-
quacy, meaning the proportion of patients in whom an adequate histologic sample for diagnosis was obtained based on the presence of a core biopsy of pancreatic tissue; and (iii) diagnostic accuracy, meaning the proportion of correct diagnoses (malignant vs. benign and/or diagnosis of a specific tumor type) based on histologic diagnosis obtained by EUS-FNB or by surgical resection and/or on tumor evolution after more than 12 months of follow-up.

Statistical analyses

Given a previous comparative pilot study, we hypothesized a 4-mm difference in the length of the tissue core biopsies obtained by the two needles [16]. The sample size was calculated with a type I error of 0.05 (two-sided) and a power of 0.9, therefore the study required a total of 60 patients.

Quantitative variables were expressed as mean and 95% confidence interval (95%CI) or median and interquartile range (IQR), while qualitative variables were expressed as numbers and percentages. The correlation between the core length and the core surface area was estimated using the Spearman coefficient.

For the primary end point, an analysis of variance (ANOVA) was conducted to test for potential order and period effects. The effect of the type of needle was assessed by a paired t test, with the significance level set to 5%. Statistical analyses were performed using Stata 15.1 software (StataCorp LP, College Station, Texas, USA).

Results

A total of 60 patients (38 men and 22 women, with a median age of 69 years [IQR 63–74]) were enrolled in the study and randomized (▶ Fig. 3).

The patient demographic, treatment, and tumor data are presented in ▶ Table 1. The median tumor size was 30 mm (IQR 25–45), with a large majority of the lesions being 2 cm or larger (53/60; 88%). The two groups were well matched in terms of baseline characteristics (▶ Table 2).

EUS-FNB was feasible in all patients, with one pass per needle. A third pass was almost systematically performed by one operator (16/20 patients), but never yielded a different diagnosis. ERCP was performed during the same procedure in 15 patients and was successful in 13 (87%). One early biliary stent obstruction was noted in one of the 15 patients on whom ERCP was performed during the same endoscopic procedure. No other adverse effects were noted in the 60 patients, and in particular there was no acute pancreatitis.

Primary end point

The ANOVA did not show either a significant order effect (P = 0.31) or a significant period effect (P = 0.70). The mean cumulative length of tissue core biopsies per needle pass was significantly higher with the 22G Acquire needle at 11.4 mm (95%CI 9.0–13.8) vs. 5.4 mm (95%CI 3.8–7.0) for the 20G Procore needle (P<0.001) (▶ Table 3). The difference remained significant if only patients with positive core biopsy were considered (P<0.01). The difference of means was 5.9 (95%CI 3.6–8.3; P<0.001).

Secondary end points

The computer-assisted measurement of the mean cumulative surface area of tissue core biopsies per needle pass was significantly higher with the 22G Acquire needle at 3.5 mm² (95%CI
2.7–4.3) vs. 1.8 mm² (95% CI 1.2–2.3) for the 20G Procore needle (P < 0.001) (Table 3). The difference of means was 1.7 (95% CI 0.9–2.6; P < 0.001). In addition, the correlation between the core length and the core surface area was excellent in the whole cohort (r = 0.92 [95%CI 0.89–0.95]; P < 0.001), validating the “manual” assessment of the core length (Fig. 4).

Diagnostic adequacy was 100% with the 22G Acquire needle and 82% (49/60) with the 20G Procore needle (P = 0.001) (Table 3). The final diagnoses included 57 lesions (95%) classified as definitively malignant and three lesions (5%) classified as definitively benign. Pathologic analysis for both needles allowed final diagnosis (malignant or benign) in 54 patients (90%). In the remaining six negative cases, malignant diagnosis was made by another EUS-FNB, performed during a new procedure.

Among the three patients with benign disease, two were diagnosed as autoimmune pancreatitis by the EUS-FNB analysis (confirmed by ampullary biopsies and response to treatment) and one as a mass-forming chronic pancreatitis. Owing to the possibility of malignant transformation of the latter diagnosis, another EUS-FNB was performed during a new procedure.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Comparison of demographic, treatment, tumor, and endoscopic procedure data between the two groups of patients.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group A¹ (n = 34)</td>
</tr>
<tr>
<td>Age, median (IQR), years</td>
<td>67 (62–73)</td>
</tr>
<tr>
<td>Sex, male/female, n</td>
<td>22/12</td>
</tr>
<tr>
<td>Acetylsalicylic acid treatment, n (%)</td>
<td>5 (14.7%)</td>
</tr>
<tr>
<td>Tumor size, median (IQR), mm</td>
<td>30 (21–45)</td>
</tr>
<tr>
<td>Transduodenal/transgastric access, n</td>
<td>14/20</td>
</tr>
<tr>
<td>Synchronous metastasis, n (%)</td>
<td>9 (26.5%)</td>
</tr>
<tr>
<td>ERCP for biliary stenting in the same procedure, n (%)</td>
<td>5 (14%)</td>
</tr>
<tr>
<td>Morbidity, n (%)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Pancreatic carcinoma/other diagnosis, n</td>
<td>25/9</td>
</tr>
</tbody>
</table>

¹ Group A, Procore 20G first. ² Group B, Acquire 22G first.

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Comparison of quantity of histologic material obtained, and diagnostic adequacy and accuracy between a single pass with the two needles.</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Acquire 22G¹ (n = 60)</td>
</tr>
<tr>
<td>Cumulative length of tissue core biopsies per needle pass, mean (95% CI), mm</td>
<td>11.4 (9.0–13.8)</td>
</tr>
<tr>
<td>Cumulative surface area of tissue core biopsies per needle pass, mean (95% CI), mm²</td>
<td>3.5 (2.7–4.3)</td>
</tr>
<tr>
<td>Diagnostic adequacy² (95% CI), %</td>
<td>100 (94–100)</td>
</tr>
<tr>
<td>Diagnostic accuracy (95% CI), %</td>
<td>87 (75–94)</td>
</tr>
<tr>
<td>Sensitivity for adenocarcinoma (95% CI), %</td>
<td>83 (59–92)</td>
</tr>
<tr>
<td>Sensitivity for neuroendocrine neoplasm (95% CI), %</td>
<td>100 (72–100)</td>
</tr>
<tr>
<td>Sensitivity for autoimmune pancreatitis (95% CI), %</td>
<td>100 (16–100)</td>
</tr>
<tr>
<td>Sensitivity for chronic pancreatitis (95% CI), %</td>
<td>100 (3–100)</td>
</tr>
</tbody>
</table>

¹ One pass per needle. ² Core biopsy obtained.

CI, confidence interval.
a second concurring EUS-FNB and the absence of mass progression on CT after more than 12 months of follow-up completed the diagnosis.

The final diagnosis was adenocarcinoma in 46 patients (77%), neuroendocrine neoplasm in 11 patients (18%), autoimmune pancreatitis in two patients, and a mass-forming chronic pancreatitis in one patient (Table 1). Diagnostic accuracy for the specific diagnosis was 87% (52/60 patients) with the 22G Acquire biopsy sample and 67% (40/60 patients) with the 20G Procore (P = 0.02) (Table 3). Among the 20 patients with negative sampling with the 20G Procore needle, 17 were negative for adenocarcinoma, two for neuroendocrine neoplasm, and one for autoimmune pancreatitis. All eight patients with negative sampling with the 22G Acquire needle were negative for adenocarcinoma (Table 3).

Sensitivity for the diagnosis of adenocarcinoma was 83% (38/46 patients) with the 22G Acquire needle and 63% (29/46 patients) with the 20G Procore needle (P = 0.06) (Table 3).

Discussion

The results of this randomized crossover trial comparing two needles for pancreatic EUS-FNB show that the 22G Acquire needle achieves a significantly higher quantity of histologic core biopsy sample compared with the 20G Procore needle, as well as achieving a higher diagnostic accuracy for pancreatic masses.

Optimal sampling beyond diagnostic accuracy will likely become increasingly crucial in the coming years as demand from oncologists for more personalized therapy grows [19]. Better histologic and molecular characterization of the pancreatic tumor can be obtained with a histologic tissue core sample. New biopsy needles for EUS-FNB have been developed and marketed by device manufacturers but, although some data are available on the rates of core biopsy obtained by those needles [7–9], there are very few data on the quantity of the obtained samples [14, 16]. In addition, their price is roughly the same in France, with an Acquire needle costing less than 7% more than the Procore (250 euros vs. 234 euros).

First, our study has confirmed that the two needles are safe and can duly be called EUS-FNB needles, especially the 22G Acquire needle, whose 100% rate for obtaining core biopsies (diagnostic adequacy) is much higher than the 82% rate of the 20G Procore needle. Our data are consistent with the first published data on the 22G Acquire needle [14, 15]. Either of the needles could therefore potentially help to reduce the number of needle passes and eliminate the need for rapid onsite evaluation (ROSE) to reach the diagnosis. Macroscopic onsite evaluation (MOSE) could also limit needle passes by accurately estimating the quantity of histologic core fragments [15].

Second, in addition to being useful for personalized therapy [19], the longer histologic core specimens were able to improve the diagnostic accuracy in this study. Third, although we might have expected the larger needle to have yielded more tissue than the finer one, as has already been published [5, 20, 21], our study found that EUS-FNB performed with the 22G Acquire needle provided more than double the quantity of tissue compared with the 20G Procore needle. Our data confirm the findings of a previous pilot study [16]. The lower quantity of tissue with the 20G Procore needle could be explained by the fact that a needle with a larger diameter is more rigid, making positioning the needle in the tumor more difficult, particularly if being used for transduodenal access [16, 20]; however, no puncture failures were noted with the 20G Procore needle in our study, which is in line with recently published data on the high technical success rate of EUS-FNB with the 20G Procore needle through the duodenum [22].

Therefore, our findings suggest that not only the needle diameter but also the cutting system affects the quantity of the histologic tissue sample obtained. The core-trap system of the new 20G Procore needle draws the tissue into the needle through a window, to be cut by a bevel. Perhaps because the bevel shreds the tissue, however, the core biopsies obtained are not always of high quality. The 22G Acquire needle features a cutting system with a sharper tip (Franseen) that seems to be more effective in terms of the histologic material and core histologic specimens obtained, which is consistent with two recent retrospective comparative studies [23, 24]. In line with our data for pancreatic tumors, a very recent study compared the two needles specifically for the diagnosis of type 1 autoimmune pancreatitis, with the Acquire needle outperforming the Procore needle in terms of diagnostic accuracy (78% vs. 45%; P = 0.001) [25].

Our study has some limitations. First, the primary end point of the study, as evaluated by the mean cumulative length of tissue core biopsies per needle pass, has only recently been described and has never been used in a randomized study; however, the very low inter- and intraobserver variability make the criterion highly reliable and reproducible [16]. Moreover, the results were confirmed by the more reliable computer-assisted measurement of the surface area of the histologic samples, which has already been used in previous studies [26, 27], with a perfect correlation between length and surface area. Additionally, any potential bias due to the measurement technique would have affected both groups and therefore should have been balanced.

Second, the randomized crossover method chosen for this study imposed a single pass per needle type. It is, however, not uncommon to perform at least two passes in current practice and, as we know, the diagnostic performance of a needle increases with the number of passes. The difference in diagnostic accuracy should probably be less significant if there are multiple passes per needle, as was the case in the preliminary comparative study; however, we did not evaluate the previously reported technical failure of a second pass with the same needle due to stylet re-insertion difficulties as part of this study [16].

Third, we analyzed the length of the targeted tissue (pancreas) and not the length of the tumor itself. The paucity of tumor cells in the stroma of some pancreatic tumors explains our choice. It was more reliable to compare the pancreas (including the tumor) than the tumor alone. The difference in diagnostic accuracy between the two needles indirectly proves that the
length of tumor tissue was higher with the Acquire needle than with the Procore needle.

In conclusion, this randomized crossover study shows that the 22G Acquire needle is more effective than the 20G Procore needle for pancreatic tumors in terms of the quantity of histologic sample obtained and both diagnostic adequacy and accuracy.

Clinical trial

Trial Registration: ClinicalTrials.gov | Registration number (trial ID): NCT03567863 | Type of study: Multicenter randomized crossover trial

Competing interests

Bertrand Napoleon has received teaching sessions fees from Boston Company.

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