

# Diagnostic yield of Franseen and Fork-Tip biopsy needles for endoscopic ultrasound-guided tissue acquisition: a meta-analysis




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## Bibliography

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 Supplementary Tables 1–5, Supplementary Figs. 1–6  
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## ABSTRACT

**Background and study aims** Although newer needle designs are thought to improve diagnostic outcomes of endo-

scopic ultrasound-guided fine-needle biopsy, there is limited evidence on their diagnostic performance. The aim of this meta-analysis was to provide a pooled estimate of the diagnostic performance and safety profile of Franseen and Fork-tip fine-needle biopsy needles.

**Patients and methods** Computerized bibliographic search on the main databases was performed through March 2019. The primary endpoint was sample adequacy. Secondary outcomes were diagnostic accuracy, optimal histological core procurement, mean number of needle passes, pooled specificity and sensitivity. Safety data were also analyzed.

**Results** Twenty-four studies with 6641 patients were included and pancreas was the prevalent location of sampled lesions. Overall sample adequacy with the two newer needles was 94.8% (93.1%–96.4%), with superiority of Franseen needle over Fork-tip (96.1% versus 92.4%,  $P < 0.001$ ). Sample adequacy in targeting pancreatic masses was 95.6% and both needles produced results superior to fine-needle aspiration (FNA) (odds ratio 4.29, 1.49–12.35 and 1.79, 1.01–3.19 with Franseen and Fork-tip needle, respectively). The rate of histological core procurement was 92.5%, whereas diagnostic accuracy and sensitivity were 95% and 92.8%, again with no difference between the two needles. Number of needle passes was significantly lower in comparison to FNA (mean difference: –0.42 with Franseen and –1.60 with Fork-tip needle). No significant adverse events were registered.

**Conclusion** Our meta-analysis speaks in favor of use of newer biopsy needles as a safe and effective tool in endoscopic ultrasound-guided tissue acquisition.

## Introduction

Among the main advantages of endoscopic ultrasound (EUS), tissue acquisition (TA) represents a valuable and accurate diagnostic technique for cytopathological and histological characterization of several abdominal lesions such as pancreatic masses, lymph nodes, or subepithelial lesions (SELs).

In spite of good results observed with EUS-guided fine-needle aspiration (EUS-FNA) and recent developments in this field,

such as use of rapid on-site evaluation (ROSE) [1], contrast-enhanced guided FNA or tissue elastography [2], diagnostic sensitivity still remains an issue. Thus, the most important pitfall associated with this procedure is false-negative diagnosis, which has the potential to delay patient care and negatively affect patient outcomes.

Development of EUS-guided fine-needle biopsy (EUS-FNB) needles has generated a great deal of interest in the field of EUS-TA primarily based on proposed advantages over EUS-FNA

needles concerning diagnostic accuracy. Furthermore, EUS-FNB seems to improve procurement of samples with preserved tissue architecture, thus allowing for immunohistochemistry required for certain diagnoses, obviating ROSE and obtaining results in fewer passes [2].

Two recent meta-analyses reached the conclusion that EUS-FNB performed with the reverse bevel needle (ProCore, Cook Medical, Limerick, Ireland) shows comparable diagnostic accuracy and sample adequacy in comparison to EUS-FNA [3, 4]; even the previous finding of a lower number of passes through the lesion needed to obtain adequate samples with FNB was recently challenged [4].

Two newer FNB needles were recently introduced in endoscopic practice: one with fork-tip design with two leading sharp tips on the opposite side of the lumen (SharkCore, Medtronic, Minneapolis, Minnesota, United States), and another with Franseen tip design with three symmetric cutting edges (Acquire, Boston Scientific Corp, Natick, Massachusetts, United States).

Although these novel needle designs are thought to improve tissue capture and several studies have been published testing these novel devices, there is limited evidence on their diagnostic performance in terms of diagnostic yield and histology core procurement; hence the pressing need to systematically assess the increasing body of evidence in the field to better define their optimal role and safety in endoscopy.

The aim of this meta-analysis was to provide a pooled estimate of the diagnostic performance and safety profile of these two newer needles, namely Franseen and Fork-tip, thus attempting to determine their comparative efficacy and potential utility in EUS-TA.

The primary endpoint was sample adequacy. Secondary outcomes were diagnostic accuracy, optimal histological core procurement, mean number of needle passes, pooled specificity and sensitivity. Safety data were also analyzed.

## Patients and methods

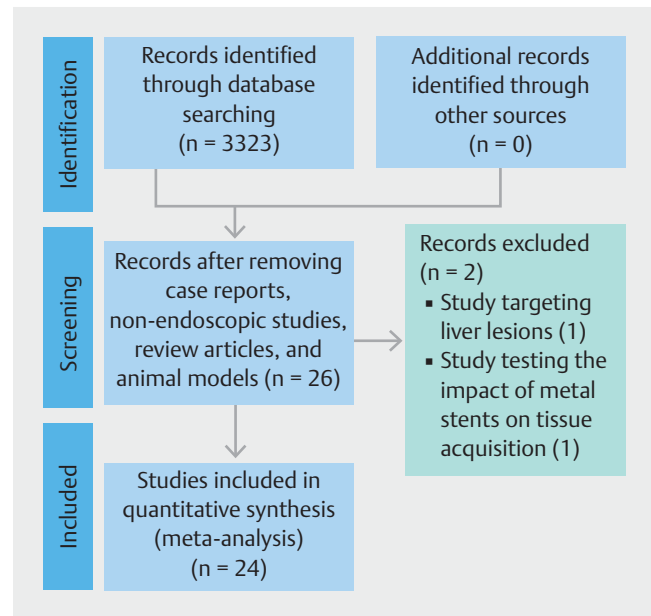
### Inclusion and exclusion criteria

Only studies meeting the following criteria were included: 1) full-text articles recruiting patients undergoing EUS-TA of solid lesions with Franseen or Fork-tip needles; 2) studies published in English; and 3) articles reporting at least one of the following data: sample adequacy, diagnostic accuracy (or data useful for its calculation), histologic core procurement. Case reports, non-endoscopic studies, review articles, and animal models were excluded.

### Search strategy

► **Fig. 1** reports the search strategy followed in the meta-analysis. Bibliographic research was conducted on PubMed, EMBASE, Cochrane Library and Google Scholar including all studies fulfilling inclusion criteria published until March 2019. Details of the search strategy adopted are reported in **Supplementary Table 1**.

Relevant reviews and meta-analyses on use of EUS-TA with newer biopsy needles were examined for potential suitable



► **Fig. 1** Flowchart of included studies.

studies. Authors of included studies were contacted to obtain full text or further information when needed.

Data extraction was conducted by two reviewers (AF and VDP) using a standardized approach (PRISMA Statement). The quality of included studies was assessed by two authors independently (AF, VDP) according to the Cochrane Collaboration's tool for assessing risk of bias [5] for randomized controlled trials (RCTs) and the Newcastle-Ottawa scale [6] for non-randomized studies. Disagreements were solved by discussion and following a third opinion (NM).

## Outcomes

The primary outcome was sample adequacy, defined as ability to procure cytological and/or histological samples adequate for interpretation; secondary outcomes were diagnostic accuracy (defined as true positive + true negative/total number of patients), optimal core histological tissue (defined as samples with high cellularity and quality enabling appropriate core assessment in terms of tissue architecture), specificity (true negative/true negative + false positive), sensitivity (true positive/true positive + false negative), number of needle passes, and safety.

### Statistical analysis

Diagnostic outcomes were computed overall and then separately pooled for each needle through a random-effects model based on DerSimonian and Laird test, and summary estimates were expressed in terms of rate and 95% Confidence Interval (CI). Chi-square and  $I^2$  tests were used for across studies comparison of the percentage of variability attributable to heterogeneity beyond chance.  $P < 0.10$  for chi-square test and  $I^2 < 20\%$  were interpreted as low-level heterogeneity.

Probability of publication bias was assessed using funnel plots and with Begg and Mazumdar's test.

Safety data were inconsistently reported, hence they were analyzed descriptively.

Pooled diagnostic outcomes of the two needles were compared using the bivariate approach [7].

Sensitivity analysis was conducted according to location of the lesion sampled (pancreas vs lymph nodes vs SEL), quality of included studies, use of ROSE, and study design (single-cohort versus comparative). A separate comparative analysis was conducted with studies directly comparing newer needles to a control device (FNA or reverse-bevel FNB).

All statistical analyses were conducted using RevMan version 5 from the Cochrane collaboration and OpenMeta[Analyst] software. For all calculations a two-tailed *P* value of less than 0.05 was considered statistically significant.

## Results

### Characteristics of included studies

As shown in ► **Fig. 1**, of 3323 studies initially identified, after preliminary exclusion of papers not fulfilling inclusion criteria, 26 potentially relevant articles were examined. Among these studies, two were excluded because they were focused exclusively on liver lesions [8] or tested the impact of metal stents on tissue acquisition [9].

Finally, 24 studies [10–33] with 6641 patients were included in the meta-analysis. Main characteristics of included studies are reported in ► **Table 1**. Four RCTs were conducted in Asia [14, 17–19] and all comparative studies presented two well-balanced arms in terms of lesion size and clinical-demographical characteristics (► **Table 1**). Quality was deemed mainly moderate/high with only three studies assessed as low-quality articles [21, 24, 31].

Details on methodological characteristics and quality of included articles are shown in **Supplementary Table 2**.

### Sample adequacy

As reported in ► **Table 2** and **Supplementary Fig. 1**, overall sample adequacy with the two newer needles was 94.8% (93.1%–96.4%;  $I^2=87\%$ ). Subanalysis performed according to needle design showed superiority of Franseen needle over Fork-tip (96.1%, 93.7% to 98.4% versus 92.4%, 88.8% to 96%;  $P<0.001$ ), although this finding should be interpreted with caution due to the high heterogeneity observed ( $I^2=82.9\%$  and 88%, respectively; ► **Table 2** and **Supplementary Fig. 2a** and **Supplementary Fig. 2b**). There was no evidence of publication bias (data not shown).

The findings of main analysis were confirmed in sensitivity analysis performed according location of sampled lesions, study quality and use of ROSE. Sample adequacy in targeting pancreatic masses was 95.6% (94%–97.3%;  $I^2=48.9\%$ ) with significantly higher rates of adequate samples obtained with Franseen needle (97%, 94.8% to 99.3% versus 92.6%, 88.8% to 96.4%;  $P=0.006$ ). Of note, there was evidence of only low-moderate heterogeneity in sensitivity analysis for pancreatic

masses ( $I^2=13.4\%$  and 34%, respectively; ► **Table 2** and ► **Fig. 2a** and ► **Fig. 2b**).

When considering lymph nodes and SELs, findings were in keeping with the aforementioned results (adequacy 97.2%, 94%–100% and 95.6%, 92.2%–98.9% with lymph nodes and SELs, respectively) with significant superiority of Franseen over Fork-tip needle (98.4%, 96%–100% versus 77.6%, 46.2%–100%,  $P<0.001$  for lymph nodes and 97.6%, 94%–100% versus 90.5%, 79.6%–100%,  $P=0.006$  for SELs). Heterogeneity was 0% and 39% with the two needles, respectively (► **Table 2**).

The above reported results were confirmed in sensitivity analysis restricted to high quality studies and those using ROSE (**Supplementary Table 3**). As depicted in **Supplementary Fig. 3a**, five studies [15–19] directly compared Franseen FNB needle to FNA, showing a clear advantage in terms of sample adequacy of Franseen needle (OR 4.29, 1.49–12.35;  $P=0.007$  and  $I^2=0\%$ ). Likewise, Fork-tip needle appeared to clearly overperform FNA in the pairwise meta-analysis of 5 studies [23–27] (OR 1.79, 1.01–3.19,  $P=0.05$  and  $I^2=0\%$ ; **Supplementary Fig. 3b**).

Technical details about handling of the sampled tissue are reported in **Supplementary Table 4**. Handling protocols were relatively homogeneous with no difference between Franseen and Fork-tip groups.

### Optimal histologic core procurement, diagnostic accuracy, sensitivity and specificity

The rate of histological optimal core procurement obtained with the new FNB needles was 92.5% (89.8%–95.3%) with evidence of high heterogeneity ( $I^2=79.8\%$ ). No difference between the two FNB needles was observed neither in main analysis (93.5%, 89.8%–97.2% versus 90.8%, 85.5%–96.2%;  $P=0.4$ , ► **Table 2** and **Supplementary Fig. 4**) nor in subanalysis restricted to pancreatic masses (94%, 89%–99% versus 93.1%, 87.3%–99%;  $P=0.7$ , ► **Table 2**).

Moderate evidence of heterogeneity ( $I^2=33\%$  to 35%) and no evidence of publication bias was observed, as confirmed with Begg and Mazumdar's test ( $P=0.64$ ). Overall diagnostic accuracy was 95% (93.5%–96.5%;  $I^2=11\%$ ) with no difference between Franseen and Fork-tip needle (95%, 92.5%–97.5% versus 94.4%, 92.3%–96.5%;  $P=0.71$ , ► **Table 2** and **Supplementary Fig. 5**). Similarly, subanalysis of pancreatic lesions confirmed the above reported findings (96.8%, 94.9%–98.7% versus 95.2%, 92.8%–97.6%;  $P=0.8$  and  $I^2=0\%$ ).

Overall sensitivity of new FNB needles was 92.8%, 89.8%–95.7%, again with no difference between Franseen and Fork-tip needles (93.3%, 89.2%–97.4% versus 92.2%, 87.9%–96.6%, respectively;  $P=0.3$ , ► **Table 2**). Similar results were registered in subanalysis of pancreatic masses (► **Table 2**). Heterogeneity was low to moderate (0% to 45.6%).

As expected, specificity was 100% with both needles.

► **Table 1** Characteristics of included studies.

Study	Needle	Sample size	Study period/design	Country	Age	Gender male	Lesion size (cm)	Location	ROSE
Fransen									
Adler 2018 [10]	Acquire	200	2016/Retrospective	USA	63 ± 14.5	121 (60.5%)	3.6 (0.3–10)	Pancreas: 55% Nodes: 23% SE: 17% Other: 4%	Yes
Bang 2017 [11]	Acquire	30	2016/Retrospective	USA	71.5 (56–79)	21 (70%)	3.4 (2.8–4)	Pancreas: 60% Nodes: 10% SE: 16.6% Other: 13.4%	Yes
Haseeb 2018 [12]	Acquire	132	2016–2017/Retrospective	USA	63.5 ± 13	87 (66%)	NR	Pancreas: 73% Nodes: 21% SE: 4% Other: 1%	Yes
Leung Ki 2019 [13]	Acquire	54	2016/Retrospective	France	70 (61–78)	34 (74%)	2.4 ± 1.38	Pancreas: 57% Nodes: 17% SE: 9% Other: 17%	No
Sugiura 2019 [14]	Acquire	100	2017–2018/Prospective	Japan	70 (31–87)	57 (57%)	2.3 (0.7–8.2)	Pancreas: 81% Nodes: 13% SE: 3% Other: 3%	No
Fransen versus FNA									
Bang 2017 [15]	Acquire FNA	46/46	NR/Crossover RCT	USA	67.9 ± 14.7	28 (60.9%)	2.9 ± 0.8	Pancreas: 100%	Yes
El Hajji 2018 [16]	Acquire Expect	51/50	2013–2017/Retrospective	USA	NR	NR	2.98/2.9	Pancreas: 45% Pancreas: 40%	Yes
Fujita 2018 [17]	Acquire Expect	17/44	2013–2017/Retrospective	Japan	72 (58.5–74.5) 67 (55–74.8)	10 (58.8%) 27 (61.3%)	2.67 (1.9–4) 2.39 (1.6–3)	SE: 100% SE: 100%	No
Ishikawa 2019 [18]	Acquire EZShot	50/36	2016–2018/Retrospective	Japan	70.5 (60–75) 65 (57–77)	30 (60%) 21 (58.3%)	3 (2–3.9) 2.3 (2.3–3.4)	Pancreas: 100% Pancreas: 100%	No
Mukai 2018 [19]	Acquire Expect	30/30	2016–2017/Retrospective	Japan	64.7 ± 12.5 69 ± 9.5	19 (63.3%) 20 (66.6%)	3 ± 1.07 2.7 ± 0.7	Pancreas: 100% Pancreas: 100%	No
Fork-Tip									
DiMaio 2016 [20]	Shark-Core	226	2014–2015/Retrospective	USA	66 (18–92)	113 (50%)	2.6 (0.2–15)	Pancreas: 60% Nodes: 22% SE: 12% Other: 6%	Yes
Ishikawa 2018 [21]	Shark-Core	85	2015–2016/Retrospective	Canada	62.3 ± 15	48 (60.7%)	3.8 ± 3.7	Pancreas: 56% Nodes: 15% SE: 26% Other: 3%	No
Larsen 2018 [22]	Shark-Core	41	2015–2016/Prospective	Denmark	68 ± 11	22 (54%)	2.8 ± 1.1	Pancreas: 100%	No

► **Table 1** (Continuation)

Study	Needle	Sample size	Study period/design	Country	Age	Gender male	Lesion size (cm)	Location	ROSE
Fork-Tip versus FNA									
El Chafic 2017 [23]	Shark-Core EchoTip Ultra/Expect	15 91	2011–2016/Retrospective	USA	65 ± 12.7 64.8 ± 15.7	9 (60%) 44 (48.3%)	2.5 ± 0.9 2.8 ± 1.65	SE: 100% SE: 100%	Yes
Jovani 2017 [24]	Shark-Core FNA	51 51	2015–2016/Retrospective	USA	63.5 ± 12.7 62.1 ± 11.6	22 (43.1%) 27 (52.9%)	3.16 ± 1.8 2.67 ± 1.1	Pancreas: 57% Pancreas: 57%	NR
Kandel 2016 [25]	Shark-Core FNA	39 117	2012–2015/Retrospective	USA	66 (26–85) 70 (17.91)	19 (49%) 65 (56%)	1.8 (0.2–20) 2.3 (0.4–11)	Pancreas: 56% Pancreas: 56%	NR
Naveed 2018 [26]	Shark-Core EchoTip	115 973	2009–2015/Retrospective	USA	66.1 66.7	57 (50%) 496 (51%)	2.75 2.59	Pancreas: 100% Pancreas: 100%	Yes
Song 2018 [27]	Shark-Core® Echo-Tip/Expect	139 42	2013–2017/Retrospective	USA	64.7 ± 11.9 61.2 ± 12.6	47.5% 54.8%	2.8 ± 1.44 2.8 ± 1.8	Pancreas: 78% Pancreas: 79%	No
Witt 2018 [28]	Shark-Core EchoTip	10 10	2015–2016/Retrospective	USA	NR	NR	NR	Pancreas: 100% Pancreas: 100%	Yes
Fork-Tip versus Reverse bevel									
Abdelfatah 2018 [29]	Shark-Core ProCore	162 139	2014–2016/Retrospective	USA	67 ± 12 67 ± 11.8	70 (49%) 65 (47%)	2.5 ± 1.4 2.4 ± 1.3	Pancreas: 66% Pancreas: 63%	77% 98.3%
Nayar 2016 [30]	Shark-Core ProCore	101 100	2013–2015/Retrospective	UK	66.4 68.1	58 (59%) 49 (49%)	3.4 (1.4–9) 3.3 (1–8.5)	Pancreas: 100% Pancreas: 100%	No
Franseen/Fork-Tip versus FNA									
Bang 2019 [31]	Acquire/Shark-Core Expect	938 2082	2014–2017/Retrospective	USA	67.1 ± 12.9 65.8 ± 13.7	510 (54.4%) 1181 (56%)	2.88 ± 1.32 2.69 ± 1.39	Pancreas: 73% Nodes: 9.4% Pancreas: 71% Nodes: 13%	Yes
Franseen versus Fork-Tip									
Abdelfatah 2018 [32]	Acquire Shark-Core	97 97	2015–2017/Retrospective	USA	63.7 ± 10.8 62.8 ± 15.5	47% 52%	2.4 ± 1.3 2.5 ± 1.4	Pancreas: 55% Pancreas: 48%	14.5%
Bang 2018 [33]	Acquire Shark-Core	50 50	2016–2017/Cross-over RCT	USA	71.3 ± 11	28 (56%)	2.4 ± 0.6	Pancreas: 100%	Yes

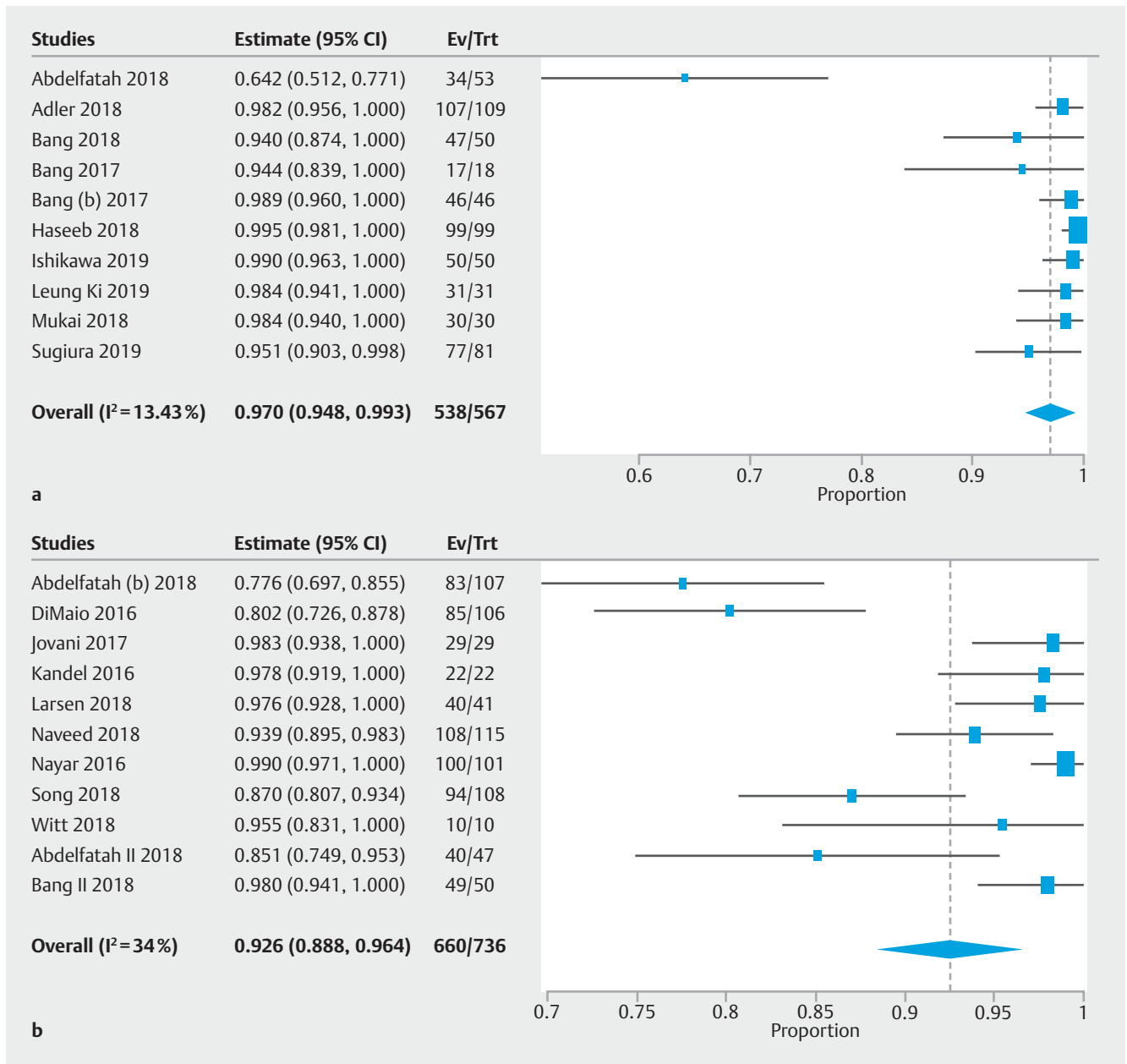
Data are reported as absolute numbers (percentages) or mean (± standard deviation or with interquartile range)  
FNA, fine-needle aspiration; NR, not reported; RCT, randomized controlled trial; ROSE, rapid on-site evaluation; SE: subepithelial lesion

► **Table 2** Overall and subgroup analysis of main diagnostic outcomes. Subgroup analysis was performed based on a) location of the target lesion (pancreas, nodes, subepithelial lesion), and b) needle used (Franseen versus Fork-Tip). Numbers in parentheses indicate 95 % confidence intervals.

Location	Needle	No. of Cohorts	No. of patients	Summary Estimate (95 % CI)	Within-group heterogeneity (I <sup>2</sup> )
Sample Adequacy					
Overall	Overall	25	2894	94.8% (93.1%-96.4%)	87%
	Franseen	12	857	96.1% (93.7%-98.4%)	82.9%
	Fork-Tip	13	1099	92.4% (88.8%-96%)	88%
Pancreas	Overall	22	1987	95.6% (94%-97.3%)	48.9%
	Franseen	10	567	97% (94.8%-99.3%)	13.4%
	Fork-Tip	11	736	92.6% (88.8%-96.4%)	34%
Nodes	Overall	8	223	97.2% (94%-100%)	52.6%
	Franseen	4	95	98.4% (96%-100%)	0%
	Fork-Tip	3	54	77.6% (46.2%-100%)	39%
Subepithelial Lesion	Overall	9	218	95.6% (92.2%-98.9%)	27%
	Franseen	5	68	97.6% (94%-100%)	0%
	Fork-Tip	4	64	90.5% (79.6%-100%)	38.9%
Histological Core Procurement					
Overall	Overall	17	1932	92.5% (89.8%-95.3%)	79.8%
	Franseen	7	455	93.5% (89.8%-97.2%)	65%
	Fork-Tip	9	539	90.8% (85.5%-96.2%)	84%
Pancreas	Overall	11	1192	93.7% (90.7%-96.8%)	35.3%
	Franseen	5	225	94% (89%-99%)	36.3%
	Fork-Tip	5	283	93.1% (87.3%-99%)	33.8%
Diagnostic Accuracy					
Overall	Overall	15	945	95% (93.5%-96.5%)	11%
	Franseen	8	492	95% (92.5%-97.5%)	37%
	Fork-Tip	7	453	94.4% (92.3%-96.5%)	0%
Pancreas	Overall	11	631	96.2% (94.7%-97.7%)	0%
	Franseen	7	324	96.8% (94.9%-98.7%)	0%
	Fork-Tip	4	307	95.2% (92.8%-97.6%)	0%
Diagnostic Sensitivity					
Overall	Overall	10	755	92.8% (89.8%-95.7%)	64.2%
	Franseen	4	255	93.3% (89.2%-97.4%)	45%
	Fork-Tip	6	500	92.2% (87.9%-96.6%)	73%
Pancreas	Overall	6	445	94.1% (90.7%-97.6%)	40.4%
	Franseen	2	81	95.3% (90.7%-99.9%)	0%
	Fork-Tip	4	364	93.4% (88.3%-98.4%)	45.6%

CI, confidence interval.

The study by Bang et al [31] did not report a subgroup analysis based on the needle design, therefore data from this study were considered only in the overall analysis.



► **Fig. 2** Pooled analysis assessing rates of sample adequacy of **a** Franseen and **b** Fork-tip fine-needle biopsy in targeting pancreatic lesions. Sample adequacy in targeting pancreatic masses was 95.6% (94%–97.3%;  $I^2=48.9\%$ ) with significantly higher rates of adequate samples obtained with Franseen needle (97%, 94.8% to 99.3% versus 92.6%, 88.8% to 96.4%;  $P=0.006$ ).

### Number of passes and adverse events

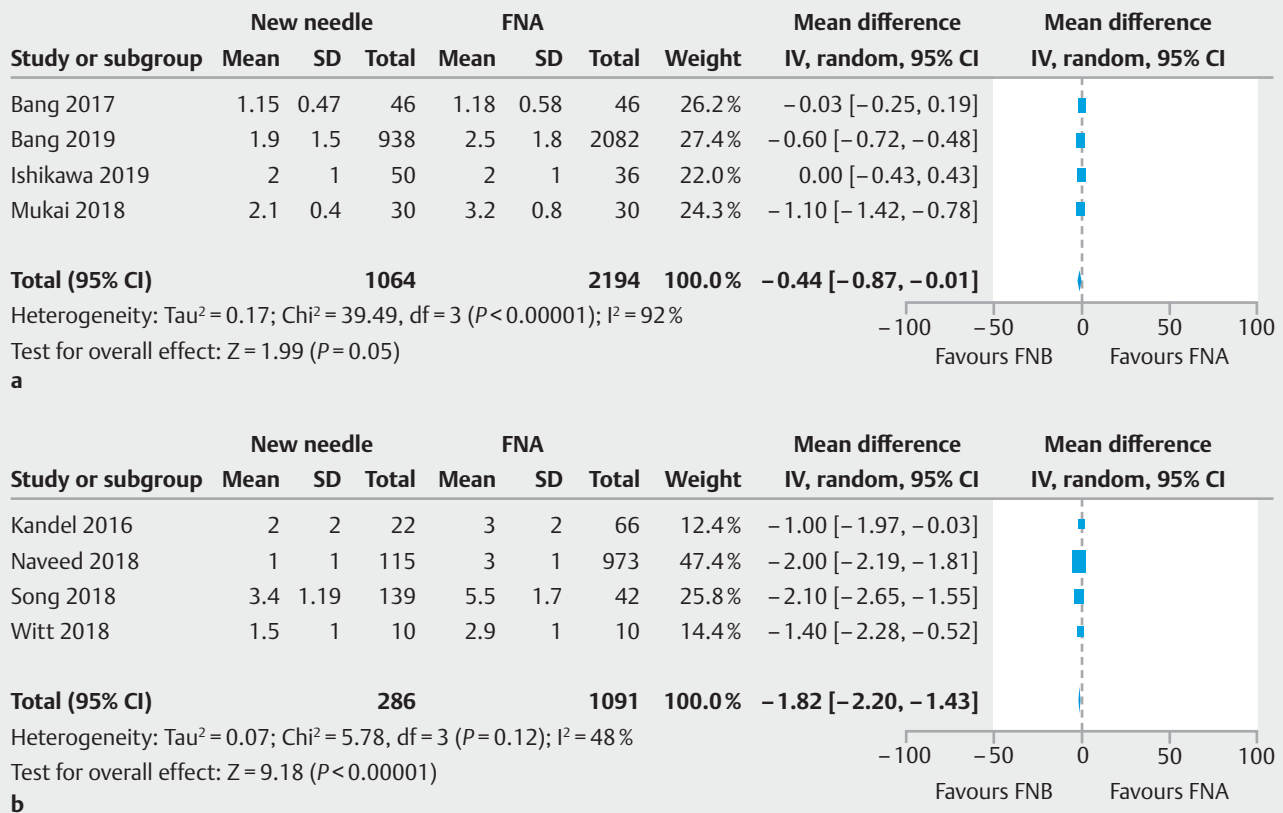
Analysis of number of needle passes needed to obtain adequate sample showed favorable results with the new needles in comparison to standard FNA (mean difference:  $-0.42$ ,  $-0.94$  to  $0.09$ , and  $-1.60$ ,  $-2.23$  to  $-0.98$  with Franseen and Fork-tip needle, respectively; **Supplementary Fig. 6**).

Both needles were significantly superior to FNA when restricting the analysis to pancreatic masses ( $-0.44$ ,  $-0.87$  to  $-0.01$ , and  $-1.82$ ,  $-2.20$  to  $-1.43$  with the two needles, respectively; ► **Fig. 3**). Heterogeneity was moderate to high ( $I^2=48\%$  to  $92\%$ ) and no evidence of publication bias was detected.

Details on safety profile of the two devices are reported in **Supplementary Table 5**. Of note, only a small number of patients experienced adverse events and all of these complications (mainly bleeding) were mild and did not impact on patient outcomes.

### Discussion

EUS-TA plays a pivotal role in the diagnostic algorithm of solid masses but its diagnostic accuracy is strictly dependent on a series of lesion-related features (such as size, number, histological type) and technical variables like needles adopted, number of



**► Fig. 3** Meta-analysis comparing mean number of needle passes of **a** Franseen and **b** Fork-tip needle in comparison to fine-needle aspiration. Both needles resulted in significantly superior to fine-needle aspiration (FNA) when restricting the analysis to pancreatic masses ( $-0.44$ ,  $-0.87$  to  $-0.01$ , and  $-1.82$ ,  $-2.20$  to  $-1.43$  with the two needles, respectively). Heterogeneity was moderate to high ( $I^2 = 48\%$  to  $92\%$ ).

passes or availability of ROSE. To at least partially overcome these limitations and given the pressing need for adequate histological samples for molecular analysis, biopsy needles have been developed and introduced in clinical practice [34].

Given recent development of novel FNB needle designs (such as Franseen and Fork-tip needles), there is a clear need to systematically evaluate the impact of these newer devices on EUS-TA. The current manuscript represents the first attempt to systematically assess diagnostic performance of newer FNB needles, namely Franseen and Fork-tip needles, in a variety of abdominal masses.

With a meta-analysis of 24 studies selectively evaluating Franseen and Fork-tip needles (alone or in comparison to a control group), we made several key observations.

First, the two newer needles showed striking results in terms of sample adequacy (94.8%), rate of histological optimal core procurement (92.5%), diagnostic accuracy (95%), and sensitivity (92.8%). Although a significant increase in sample adequacy was observed with Franseen needle as compared to Fork-tip (96.1% versus 92.4%,  $P < 0.001$ ), the other diagnostic outcomes were perfectly comparable between the two needle designs with no significant difference observed in terms of histological core procurement, diagnostic accuracy, or sensitivity. Second, all sensitivity analyses confirmed findings from the main analy-

sis, in particular both Franseen and Fork-tip needles performed well in targeting all abdominal lesions (sample adequacy 95.6% for pancreatic masses, 97.2% for lymph nodes, and 95.6% for SELs). As expected, use of ROSE did not impact significantly on diagnostic yield. Third, meta-analysis of head-to-head studies directly comparing FNB to FNA showed a clear advantage in terms of sample adequacy of both FNB needles ( $P = 0.007$  and  $P = 0.05$ , respectively). Fourth, as already pointed out in previous meta-analyses [3,4], FNB required a lower number of needle passes through the lesion to obtain adequate samples in comparison to standard FNA. Fifth, both FNB needles resulted to be safe with only a small number of patients experiencing mainly mild pancreatitis or bleeding events.

These findings, which are considerably more favorable as compared to those reported in previous meta-analyses on a reverse bevel FNB needle [3], are likely to be related to the different design of newer needles with higher number of cutting points (3 in Franseen and 6 in Fork-tip needle) designed to provide improved control at the puncture site and stability at the tip, allowing for enhanced penetration [35]. As tissue moves into the tip of the Franseen needle, suction is applied to push the tissue into three symmetrical cutting heels which cut tissue from three different angles to make a more circular cut. In the case of the Fork-tip device, two opposing catch beveled tips al-



low funneling of target tissue into the lumen of the needle, while a distal cutting design minimizes stacking and fracturing of collected samples to produce more intact tissue architecture [35].

As expected, the aforementioned results were not influenced by use of ROSE, a tool not routinely adopted in non-American centers, thus confirming that FNB may obviate the need for an on-site pathologist to obtain optimal diagnostic outcomes. Moreover, increased costs of newer needles may be at least partially compensated for by obviating the need for an on-site pathologist.

Because most of the included studies were single-cohort non-comparative series, results regarding the higher sample adequacy observed with the Franseen needle as compared to the Fork-tip device should be interpreted with caution, considering that the single head-to-head trial directly comparing the two newer FNB needles did not report significant differences between the two devices [15].

There are some limitations to our study. First, the limited number of case-control or randomized studies does not allow a strong comparison between newer needles and standard FNA or reverse bevel FNB. This aspect requires particular caution in interpreting our comparative findings due to the high risk of indirectness. In fact, the validity of indirect comparisons rests on the assumption that factors in the design of the included studies (patients, co-interventions, measurement of outcomes) and methodological quality are not sufficiently different to result in different effects (the so-called “similarity assumption” [36]). Because this assumption is always in some doubt, indirect comparisons always warrant rating down by one level in quality of evidence. Second, as most included studies used 22G needles, subanalysis based on needle caliber was not feasible. Therefore, absent of studies specifically testing different calipers, our results should be considered applicable only to the 22G FNB device, which is indeed the most frequently used FNB needle worldwide.

## Conclusion

In conclusion, despite these weaknesses, our meta-analysis speaks in favor of use of newer biopsy needles as safe and effective tools in EUS-guided tissue acquisition. In particular, based on the extremely high rates of optimal histological core procurement, they may represent a valuable option in conditions that require assessment of tissue architecture (for example, in oncologic studies that require core biopsies for personalized medicine or benign conditions such as autoimmune pancreatitis). Further RCTs comparing the two newer needles to reverse bevel FNB or each other are warranted to confirm these promising results.

## Competing interests

None

## References

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