学位論文

「Effectiveness of Endoscopic Ultrasound-guided Tissue Acquisition with Stereomicroscopic On-site Evaluation for Preoperative Diagnosis of Resectable or Borderline Resectable Pancreatic Cancer」

（切除可能膵癌および切除可能境界膵癌に対するEUS-TAによる術前診断における実体顕微鏡を用いた迅速評価の有用性の検証）

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著者の宣言

本学位論文は、著者の責任において実験を遂行し、得られた真実の結果に基づいて正確に作成したものに相違ないことをここに宣言する。

論文要旨

論文題目「Effectiveness of Endoscopic Ultrasound-guided Tissue Acquisition with Stereomicroscopic On-site Evaluation for Preoperative Diagnosis of Resectable or Borderline Resectable Pancreatic Cancer」

（切除可能膵癌および切除可能境界膵癌に対するEUS-TAによる術前診断における実体顕微鏡を用いた迅速評価の有用性の検証）

【背景】

endoscopic ultrasound-guided tissue acquisition（EUS-TA）は膵癌の病理診断を得る上で一般的に実施されている検査法である．近年，resectable pancreatic cancer（R-PC）やborder-line resectable pancreatic cancer（BR-PC）において，術前の補助治療を行うことによって生存率が改善することが明らかになったため，術前に膵癌の病理学的確定診断を得ることの重要性が増している．一方で，EUS-TA による術後の穿刺経路播種（Needle tract seeding，NTS）が懸念されている．

EUS-TA で得られた検体の適正性を現場で迅速評価する手法として stereomicroscopic on-site evaluation（SOSE）の有効性が報告されている．SOSE はEUS-TA で得られた検体を実体顕微鏡により拡大視野下に迅速評価し，stereomicroscopically visible white core（SVWC）がcutoff値（SVWC 11mm以上）を満たすかを判定する．SVWC cutoff値を満たす場合には高い感度を示すことから，SOSE により必要穿刺回数を最小限にすることができる可能性があるが，対象をR-PC やBR-PC に限定した場合のSOSE の有用性を検討した報告はない．そのため我々はR-PC およびBR-PC に対するEUS-TA において，SOSE の結果に基づき規定される必要最少回数の穿刺によって得られる診断成績を前向き介入研究によって検証した．

【方法】

本研究は2021年5月から2023年3月の間に北里大学病院，JCHO相模野病院の2施設にて事前の画像検査でR-PC もしくはBR-PC が疑われた78例を登録し，研究プロトコールに従い実施された SOSE 併用下の EUS-TA の成績を前向きに検証した．主要評価項目はSOSE併用下のEUS-TAにおいてSVWC cutoff 値が得られた検体の悪性診断の感度とした．副次評価項目は SVWC cutoff 値が得られた検体の割合，細胞診と組織診を組み合わせたEUS-TA の感度，特異度，陽性的中率，陰性的中率および正診率，EUS-TA 後 30 日までに発生した偶発症とした．

EUS-TA は 22-gauge 針（Acquire; Boston Scientific Corporation, Marlborough, MA, USA）が全例で用いられ，日本内視鏡学会指導医 4名と日本内視鏡学会専門医4名，計8名の内視鏡医によって実施された．SVWC cutoff値が得られた時点で穿刺を終了し（最少穿刺回数は 1 回），最大穿刺回数は（SVWC cutoff 値の有無にかかわらず）2 回と規定した．

EUS-TA は 20mL の吸引法を用いて実施され，病変内で穿刺針を 20 回ストロークした．

【結果】

R-PC は 56 例，BR-PC は 22 例であった．最大腫瘍径中央値は 19mm（4-45mm）で，最大腫瘍径が 20mm 未満の症例は 42 症例（53.1%）であった．最終診断は膵癌 74 例，神経内分泌腫瘍 2 例，腫瘤形成性膵炎 1 例，自己免疫性膵炎 1 例であった．

EUS-TA の技術的成功率は 100%であった．78 症例に対し全 99 検体を採取した．1 穿刺目で SVWC cutoff 値が得られたのは 57 検体（73.1%）であった．EUS-TA に関連した偶発症は認めなかった．

EUS-TA の感度，特異度，陽性的中率，陰性的中率，正診率はそれぞれ 90.8%，100%，100%，22.2%，91.0%であった．最終診断で良性腫瘍と判断された 2 例を除いた 76 例 95 検体において SVWC cutoff 値に基づく 1 穿刺目と 2 穿刺目の悪性診断の感度はそれぞれ 89.5%，93.8%であり，全検体の悪性診断の感度は 90.4%であった． SVWC cutoff 値を満たした検体と満たさなかった検体を比較すると，悪性診断の感度に有意差は認めなかった（90.4% 対 86.4%）．

【考察】

初回穿刺で SVWC cutoff 値を満たした検体の悪性診断の感度は本研究で 89.5%，先行研究では 94.4%であった．その差は 4.9%（95%CI：-8.37~18.17）であり，同等性の証明には至らなかった．この要因の 1 つは対象病変の腫瘍径が小さいことが影響したと推測する．先行研究における母集団の最大腫瘍径（中央値 35mm）と比較して，本研究の母集団は最大腫瘍径が有意に小さかった（$p < 0.01$）．2 つ目は本研究で用いられた SOSE は，検体の適正性を間接的に評価する手法の 1 つであり，細胞検査士や病理医が検査に帯同して実施する rapid on-site evaluation（ROSE）のように標的病変の病理診断に寄与し得る検体の適正を直接評価しているわけではないという点である．以上より，我々の研究で得られた新たな知見としては，R-PC や BR-PC など小さな腫瘍が多く含まれる病変を対象とした場合，特に体尾部に局在し経胃的に穿刺を行うことで術後の NTS が危惧される例においては，間接的な検体評価法である SOSE ではなく検体の適正を直接評価する ROSE を実施することにより最小穿刺回数の EUS-TA でより高い精度の病理診断が得られる可能性がある．

本研究では，悪性診断の感度において SVWC cutoff 値を満たした検体と満たさなかった検体では有意差は認めなかった．この要因の 1 つは SVWC cutoff 値を満たさなかった検体が少なかったこと，もう 1 つは本研究で用いた SVWC cutoff 値が，対象の多くが進行癌であった先行研究に基づき算出されたことが影響していたと考える．以上から腫瘍径の小さな病変を対象として新たな cutoff 値を算出することが望まれるが，本研究で得られた悪性診断の感度は決して低くなく，SOSE は ROSE の実施が困難な施設において EUS-TA の必要穿刺回数の判定に寄与するものであると考える．

目次

Introduction

Endoscopic ultrasound-guided tissue acquisition (EUS-TA) is a safe and standard procedure for pathologically diagnosing pancreatic cancer.[1-4] Preoperative adjuvant treatment improves the survival of patients with resectable pancreatic cancer (R-PC) and those with borderline resectable pancreatic cancer (BR-PC).[5-9] Therefore, obtaining a definitive pathological diagnosis of pancreatic cancer before surgery is crucial. However, most studies on EUS-TA for radically resectable R-PC and BR-PC or small pancreatic masses have been retrospective,[10-14] and prospective studies are scarce. Improvements are required in the diagnostic yield and safety of EUS-TA for small solid pancreatic lesions; furthermore, investigations are also required into the optimal needle and technique for the procedure.[15] This is particularly important because of the recently reported cases of needle tract seeding (NTS);[16-18] almost all occurrences of NTS are noted to have been preceded by several punctures during EUS-TA.

Rapid on-site (ROSE),[19] macroscopic on-site (MOSE),[20] sample isolation processing by stereomicroscopy,[21] and stereomicroscopic on-site (SOSE)[22] evaluations can be performed to assess the quality of specimens obtained on-site via EUS-TA. ROSE is the most common among these procedures, but it requires an on-site cytopathologist; this may be feasible for most hospitals in the United States, but not for approximately 50% of the hospitals in Europe and Asia.[23] Conversely, SOSE does not require a cytopathologist, and specimens are diagnosed when a stereomicroscopically visible white core (SVWC) cutoff value of ≥11 mm is obtained.[22] The adequacy of specimens obtained using EUS-TA can be directly or indirectly determined using on-site evaluation, and the procedure can be terminated. Thus, the number of punctures can be minimized. However, the relevance of SOSE in terms of R-PC and BR-PC has not been determined.

Therefore, this prospective interventional study on R-PC and BR-PC (at a clinical stage where their radical resection was possible) aimed to verify the diagnostic SOSE findings of specimens obtained using the minimum number of punctures during EUS-TA.

Methods

Study design

This prospective interventional study was performed at two medical centers. The primary endpoint was the diagnostic sensitivity of EUS-TA combined with SOSE for malignant specimens based on an SVWC cutoff value. The secondary endpoints were the ratio of specimens meeting the cutoff values, sensitivity of EUS-TA combined with cytology and histology, specificity, positive and negative predictive values (PPV and NPV, respectively), accurate diagnosis rates (ADRs), and EUS-TA-associated events that occurred within 30 days of the procedure.

Patient eligibility

Patients who underwent an EUS-TA-based assessment of pancreatic tumors suspected to be pancreatic cancer at the Kitasato University Hospital and the Japan Community Health Care Organization Sagamino Hospital were enrolled between March 2021 and January 2023.

The inclusion criteria were as follows: age ≥20 years, suspicion of R-PC or BR-PC based on the General Rules for the Study of Pancreatic Cancer published by the Japan Pancreas Society (fourth English Edition), presence of pancreatic tumors that required EUS-TA for pathological diagnosis, adequate organ functions, and provision of written informed consent. The exclusion criteria comprised allergies or renal dysfunction that contraindicated the use of iodine-containing contrast agents.

EUS-TA procedure

After conscious sedation with midazolam, EUS-TA was performed by eight endoscopists comprising four fellows and four trainers who were board-certified by the Japan Gastroenterological Endoscopy Society. A GF-UCT260 linear scanning video echoendoscope (Olympus Medical, Tokyo, Japan), an EU-ME2 Premier Plus dedicated ultrasound processor (Olympus Medical), and an Acquire 22-gauge biopsy needle (Boston Scientific Corp., Marlborough, MA, USA) were used for the procedure. The endoscopists used a 20 mL syringe for aspiration, and the needle was stroked approximately 20 times within the lesion. The procedure was terminated when the SVWC cutoff was met following a single puncture or when the maximum number of punctures was two (irrespective of whether the SVWC cutoff was met or not). The incidence of adverse events within 30 days after EUS-TA was evaluated at the outpatient clinics.

SOSE

Two designated evaluators (K.O and M.W) conducted SOSE using protective gloves, glasses, and clothing in a well-ventilated environment. The specimens obtained via EUS-TA were evaluated using a stereomicroscope under a magnified field of view, as described previously.[22] Both of these evaluators had also participated as evaluators in a previous study.[22] As a rule, SVWCs and blood clots were differentiated on the basis of coloration under the stereomicroscope. Furthermore, brittle white specimens identified using the injection needles were considered necrotic tissues and not SVWCs. The tissue sections obtained via EUS-TA were immersed in 10% neutral buffered formalin and submitted to the pathology laboratory.

Pathological diagnosis

Pathologists stained the specimens with hematoxylin and eosin and with papanicolaou hematoxylin for histological and cytological diagnoses, respectively.

In cases of patients treated surgically during the observation period, the diagnosis was considered valid if the pathological findings of the surgical specimen and those obtained with EUS¬-TA were consistent. In cases wherein tumors were deemed unresectable after EUS-TA, we first confirmed whether the clinical course and imaging findings for >6 months from the date of EUS-TA were consistent with the pathological diagnosis obtained with EUS-TA; we then determined the validity of the diagnosis.

Statistical analysis

Based on a previous study, we assumed that the frequency of meeting the SVWC cutoff value would be 66.7% and that the sensitivity of a malignant diagnosis based on that value would be 94.4%.[22] We determined that 65 specimens were required to satisfy the SVWC cutoff at the first puncture (one-sided α, 0.05). We also considered a detection power of 80% and an equivalence tolerance margin of 10% for the sensitivity of malignant diagnosis. Hence, the number of patients required to achieve the required number of specimens with up to two punctures each was 74. After assuming a dropout rate of approximately 5%, the target number of patients was set at 78.

The presence of SVWC and the tissue sampling rate were classified as positive if white samples were visible using stereomicroscopy and if the lesion tissues were visible using optical microscopy, respectively. Accuracy was based on combined cytological and histological diagnoses.

The 95% confidence interval (CI) was calculated by analyzing the differences in the population ratio. Categorical variables were compared using Fisher's exact probability

tests, and values with two-tailed $P < 0.05$ were considered statistically significant. Data were statistically analyzed using R version 3.2.4 (R Foundation for Statistical Computing, Vienna, Austria) and BellCurve for Excel version 4.03 (Social Survey Research Information Co., Ltd., Tokyo, Japan).

Ethical statements

This study complied with the principles of the Declaration of Helsinki (2013 amendment) and was approved by the Ethics Review Boards of the Kitasato University School of Medicine and the Japan Community Health Care Organization Sagamino Hospital on the basis of ethical, scientific, and medical validity (approval numbers: C21 -018, 202101). All patients provided written informed consent to participate. This study was registered at http://www.umin.ac.jp (UMIN 000044023).

Results

Patient characteristics

Table 1 presents the patient characteristics (median age, 73 [40–85] years; men, n = 45 [57.7%]). Overall, 47 of the 78 included patients had pancreatic head tumors (60.3%). The median maximum diameter of the pancreatic tumors was 19 (4–45) mm; the maximum tumor diameter was <20 mm in 42 patients (53.8%). Among the tumors, 56 (71.8%) and 22 (28.2%) were of R-PC and BR-PC, respectively. Additionally, BR-PC invaded the portal vein and abutted the major arteries in 16 and 6 patients, respectively. The final diagnoses were pancreatic ductal adenocarcinomas (n = 74), neuroendocrine neoplasms (n = 2), tumor-forming pancreatitis (n = 1), and autoimmune pancreatitis (n = 1).

EUS-TA procedure

Table 2 shows the EUS-TA results. The technical success rate was 100%; 99 punctures were required for 78 lesions. The median number of punctures was 1 (1–2), and the procedure was completed with only one puncture in 57 (73.1%) lesions based on the SOSE results. The puncture routes were transgastric, transduodenal (descending), and via the transduodenal bulb in 32 (41.0%), 36 (46.2%), and 10 (12.8%) patients, respectively. No complications associated with EUS-TA were observed.

Diagnostic yields of EUS-TA with SOSE

Table 3 shows the results of rapid specimen evaluation via SOSE for the entire cohort. Overall, 73.7% of specimens met the SVWC cutoff value. More specifically, among the 78 and 21 specimens collected during the first and second punctures, 73.1% and 76.2% met the SVWC cutoff values, respectively. The median time required for evaluation using SOSE was 32 (4–126) seconds. The collection rate was 100% (99/99). The sensitivity, specificity, PPV, NPV, and ADR for EUS-TA were 90.8%, 100%, 100%, 22.2%, and 91.0%, respectively (Table 4). For 95 specimens from 76 lesions (excluding those from two patients diagnosed with benign tumors during the observation period), the sensitivities for malignant diagnosis at the first and second punctures based on the SVWC cutoff value were 89.5% and 93.8%, respectively; the overall sensitivity was 90.4%. The diagnosis rate did not show a significant difference between specimens that met and did not meet the SVWC cutoff value (90.4% versus 86.4%).

Discussion

NTS after EUS-TA was first established for lymph node metastases of melanomas.[24] Thereafter, NTS was identified in pancreatic cancer.[25] A recent retrospective survey of 12,109 primary pancreatic tumors across 235 facilities in Japan found an NTS incidence of 0.330%, which increased to 0.409% when limited to pancreatic cancer.[16] Another retrospective study limited to pancreatic body and tail cancer found an NTS incidence of 3.4%.[17] The authors of that study concluded that preoperative EUS-TA for pancreatic body and tail cancer does not adversely affect the long-term prognosis; however, NTS developed in a small proportion of patients. NTS associated with EUS-TA typically presents with a submucosal tumor-like morphology. Therefore, its spread to the gastrointestinal wall in surgically resected pancreatic body and tail cancer followed up for a certain period after the surgery can be proven; iatrogenic dissemination into the abdominal cavity due to EUS-TA and metastasis are otherwise difficult to differentiate. As such, the frequency of NTS or dissemination might be higher. The origin of NTS remains unknown. However, it is speculated that malignant cells isolated upon puncturing a pancreatic tumor with a needle migrate to the gastrointestinal tract walls.[26,27] Furthermore, the microscopic bleeding resulting from a puncture and the consequent reactive changes may promote tumor cell survival in the gastrointestinal wall.[18] Thus, NTS can be caused by a single puncture.[24,28] Kurosu et al. prospectively investigated whether cells derived from pancreatic cancers adhered to the puncture needle's external surface after EUS-TA; they found that the rate of positive lavage cytology for the needle's external surface was 20%.[29] Thus, multiple punctures would naturally increase the risk of NTS. Accordingly, where postoperative NTS is a concern, EUS-TA should be completed within a minimum number of punctures.

In the present study, the sensitivity for malignant diagnosis in specimens that met the SVWC cutoff value at the first puncture was 89.5%, as compared with the 94.4% determined in a previous study.[22] With a difference of 4.9% (95% CI: −8.37 to 18.17), the findings of the present study are inconsistent with those of the previous study. The first reason may be the small diameters of the target lesions in the present study. The aforementioned previous study verified the usefulness of SOSE in 58 patients with unresectable PC and 12 patients with BR-PC; the median maximum tumor diameter in that study was 35 (26–44) mm.[22] The maximum tumor diameter was significantly smaller in the present study ($P < 0.01$). Small tumors might affect the diagnostic performance of EUS-TA. In a retrospective analysis of EUS-TA in 159 patients with pancreatic masses, ADRs of 97% and 64% were observed when the tumor diameters

were ≥10 and <10 mm, respectively.[10] Moreover, in another retrospective analysis of EUS-TA in 944 patients with pancreatic masses, ADRs of 82.5%, 83.5%, and 93.4% were observed when the tumor diameters were ≤10, 10–20, and ≥20 mm, respectively.[11] The authors of that study also noted that the ADRs decreased when the lesions were <20 mm and when ROSE was not included in the multivariate analysis. In the present study on small-sized tumors of R-PC and BR-PC, EUS-TA similarly yielded diagnostic results that were inferior to those obtained by EUS-TA for unresectable PC in a previous study.[22] The second reason may be that SOSE allows an indirect assessment of the adequacy of the specimens, similar to MOSE.[20] The diagnostic sensitivity of SOSE was high when the SVWC cutoff value was met. However, unlike ROSE, SOSE does not allow a rapid and direct evaluation of the adequacy of specimens (i.e., whether they contain atypical cells) that could contribute to the pathological diagnosis of the target lesions. Therefore, the novel finding of the present study is that for small tumors (such as those of R-PC and BR-PC), especially when postoperative NTS is a concern owing to transgastric puncture of the body and tail, ROSE might provide a more accurate pathological diagnosis with EUS-TA with fewer punctures than SOSE (which allows indirect evaluation of the specimens). However, ROSE is not feasible in several medical facilities.[23] We suggest that in such cases, SOSE may serve as an alternative for determining and minimizing the number of punctures according to the SVWC cutoff value.

In this study, the diagnosis rate showed no significant difference between specimens that met and did not meet the SVWC cutoff value. We attribute one reason for this lack of significance to the small number of samples that did not meet the SVWC cutoff value. Another reason is that the SVWC cutoff values employed in this study were set based on the results of previous studies in which the majority of the patients had advanced cancer.[21,22] Potentially, the SVWC cutoff value may need to be adjusted for smaller tumors, including R-PC and BR-PC. Nevertheless, the high sensitivity for a malignant diagnosis based on the SVWC cutoff value can serve as a reference for determining the number of punctures required for EUS-TA in medical facilities where ROSE is not feasible.

This study had some limitations. First, we only included two facilities; a multicenter study would be ideal. Second, this study did not compare SOSE and ROSE; therefore, further prospective studies are required to determine the degree of the additional effect of ROSE on the diagnostic results of SOSE.

In conclusion, EUS-TA with SOSE for small lesions of R-PC and BR-PC has decent, although somewhat insufficient, sensitivity for diagnosing malignancies based on the SVWC cutoff value. Developing an EUS-TA device and technique might be crucial to

further improving our results.

References

1. Chen G, Liu S, Zhao Y, Dai M, Zhang T. Diagnostic accuracy of endoscopic ultrasound-guided fine-needle aspiration for pancreatic cancer: a meta-analysis. Pancreatology 2013;13:298–304.
2. Bhatia V, Varadarajulu S. Endoscopic ultrasonography-guided tissue acquisition: how to achieve excellence. Dig Endosc 2017;29:417–430.
3. Kanno A, Yasuda I, Irisawa A, et al. Adverse events of endoscopic ultrasound-guided fine-needle aspiration for histologic diagnosis in Japanese tertiary centers: multicenter retrospective study. Dig Endosc 2021;33:1146–1157.
4. Wang KX, Ben QW, Jin ZD, et al. Assessment of morbidity and mortality associated with EUS-guided FNA: a systematic review. Gastrointest Endosc 2011;73:283–290.
5. Kato H, Usui M, Isaji S, et al. Clinical features and treatment outcome of borderline resectable pancreatic head/body cancer: a multi-institutional survey by the Japanese Society of Pancreatic Surgery. J Hepatobiliary Pancreat Sci 2013;20:601–610.
6. Ielpo B, Caruso R, Duran H, et al. A comparative study of neoadjuvant treatment with gemcitabine plus nab-paclitaxel versus surgery first for pancreatic adenocarcinoma. Surg Oncol 2017;26:402–410.
7. Fujii T, Satoi S, Yamada S, et al. Clinical benefits of neoadjuvant chemoradiotherapy for adenocarcinoma of the pancreatic head: an observational study using inverse probability of treatment weighting. J Gastroenterol 2017;52:81–93.
8. Jang JY, Han Y, Lee H, et al. Oncological benefits of neoadjuvant chemoradiation with gemcitabine versus upfront surgery in patients with borderline resectable pancreatic cancer: a prospective, randomized, open-label, multicenter phase 2/3 trial. Ann Surg 2018;268:215–222.
9. Motoi F, Satoi S, Honda G, et al. A single-arm, phase II trial of neoadjuvant gemcitabine and S1 in patients with resectable and borderline resectable pancreatic adenocarcinoma: PREP-01 study. J Gastroenterol 2019;54:194–203.
10. Takahashi K, Yasuda I, Hanaoka T, et al. Diagnostic fine-needle biopsy of small solid pancreatic lesions using a franseen needle during endoscopic ultrasound examination. Diagnostics (Basel) 2020;11:27.
11. Haba S, Yamao K, Bhatia V, et al. Diagnostic ability and factors affecting accuracy of endoscopic ultrasound-guided fine needle aspiration for pancreatic solid lesions: Japanese large single center experience. J Gastroenterol 2013;48:973–981.

12. Crinò SF, Conti Bellocchi MC, Bernardoni L, et al. Diagnostic yield of EUS-FNA of small (≤15 mm) solid pancreatic lesions using a 25-gauge needle. Hepatobiliary Pancreat Dis Int 2018;17:70–74.
13. Li HZ, Peng CY, Shen SS, et al. Factors affecting the accuracy of endoscopic ultrasound-guided fine needle aspiration for the diagnosis of small (≤20 mm) pancreatic lesions. J Dig Dis 2020;21:416–421.
14. Park JS, Lee JH, Song TJ, et al. The impact of preoperative EUS-FNA for distal resectable pancreatic cancer: is it really effective enough to take risks? Surg Endosc 2022;36:3192–3199.
15. Nakai Y, Hamada T, Hakuta R, et al. Endoscopic ultrasonography-guided tissue acquisition for small solid pancreatic lesions: does the size matter? DEN Open 2021;2:e52.
16. Kitano M, Yoshida M, Ashida R, et al. Needle tract seeding after endoscopic ultrasound-guided tissue acquisition of pancreatic tumors: a nationwide survey in Japan. Dig Endosc 2022;34:1442–1455.
17. Yane K, Kuwatani M, Yoshida M, et al. Non-negligible rate of needle tract seeding after endoscopic ultrasound-guided fine-needle aspiration for patients undergoing distal pancreatectomy for pancreatic cancer. Dig Endosc 2020;32:801–811.
18. Nakatsubo R, Yamamoto K, Itoi T, et al. Histopathological evaluation of needle tract seeding caused by EUS-fine-needle biopsy based on resected specimens from patients with solid pancreatic masses: an analysis of 73 consecutive cases. Endosc Ultrasound 2021;10:207–213.
19. Klapman JB, Logrono R, Dye CE, Waxman I. Clinical impact of on-site cytopathology interpretation on endoscopic ultrasound-guided fine needle aspiration. Am J Gastroenterol 2003;98:1289–1294.
20. Iwashita T, Yasuda I, Mukai T, et al. Macroscopic on-site quality evaluation of biopsy specimens to improve the diagnostic accuracy during EUS-guided FNA using a 19-gauge needle for solid lesions: a single-center prospective pilot study (MOSE study). Gastrointest Endosc 2015;81:177–185.
21. Masutani H, Okuwaki K, Kida M, et al. On-site stereomicroscope quality evaluations to estimate white core cutoff lengths using EUS-FNA biopsy sampling with 22-gauge needles. Gastrointest Endosc 2019;90:947–956.
22. Watanabe M, Okuwaki K, Kida M, et al. Multicenter prospective study of the efficacy of stereomicroscopic on-site evaluation in endoscopic ultrasound-guided tissue acquisition in patients with pancreatic cancer. Pancreatology 2022;22:311–316.
23. Van Riet PA, Cahen DL, Poley JW, Bruno MJ. Mapping international practice

patterns in EUS-guided tissue sampling: outcome of a global survey. Endosc Int Open 2016;4:E360–E370.

24. Shah JN, Fraker D, Guerry D, Feldman M, Kochman ML. Melanoma seeding of an EUS-guided fine needle track. Gastrointest Endosc 2004;59:923–924.
25. Paquin SC, Gariépy G, Lepanto L, Bourdages R, Raymond G, Sahai AV. A first report of tumor seeding because of EUS-guided FNA of a pancreatic adenocarcinoma. Gastrointest Endosc 2005;61:610–611.
26. Levy MJ, Gleeson FC, Campion MB, et al. Prospective cytological assessment of gastrointestinal luminal fluid acquired during EUS: a potential source of false-positive FNA and needle tract seeding. Am J Gastroenterol 2010;105:1311–1318.
27. Levy MJ, Kipp BR, Milosevic D, et al. Analysis of cell-free DNA to assess risk of tumoremia following endoscopic ultrasound fine-needle aspiration of pancreatic adenocarcinomas. Clin Gastroenterol Hepatol 2018;16:1632–1640.e1
28. Doi S, Yasuda I, Iwashita T, et al. Needle tract implantation on the esophageal wall after EUS-guided FNA of metastatic mediastinal lymphadenopathy. Gastrointest Endosc 2008;67:988–990.
29. Kurosu T, Kida M, Okuwaki K, et al. Pancreatic cancer cells may adhere to the external surface of the puncture needle after endoscopic ultrasound-guided fine-needle aspiration. Pancreas 2023;52:e298–e304.

Tables

Table 1. Characteristics of the patients and lesions.

Median age, years [range]	73 [40–85]
Sex, *n* (%)	
Male	45 (57.7%)
Female	33 (42.3%)
Pancreatic tumor location, *n* (%)	
Head	47 (60.3%)
Body/tail	31 (39.7%)
Median maximum lesion diameter, mm [range]	19 [4–45]
<20	42 (53.8%)
≥20	36 (46.2%)
Clinical stage, *n* (%)	
R	56 (71.8%)
BR-A	6 (7.7%)
BR-PV	16 (20.5%)
Final diagnosis, *n* (%)	
Malignancy	76 (97.4%)

PDAC	74 (94.9%)
PNEN	2 (2.6%)
Benign	2 (2.6%)
Tumor-forming pancreatitis	1 (1.3%)
AIP	1 (1.3%)

AIP, autoimmune pancreatitis; BR-A, borderline resectable-abutting major arteries; BR-PV, borderline resectable-invading the portal vein; PDAC, pancreatic ductal adenocarcinoma; PNEN, pancreatic neuroendocrine neoplasm; R, resectable.

Table 2. Results of EUS-TA (n = 78).

Technical success, *n* (%)	78 (100%)
Total passes, *n*	99
Passes per lesion, *n* (%)	
1	57 (73.1%)
2	21 (26.9%)
Puncture site, *n* (%)	
Stomach	32 (41.0%)
D1	10 (12.8%)
D2	36 (46.2%)
Adverse events, *n* (%)	0 (0%)

D1, bulb of the duodenum; D2, second portion of the duodenum; EUS-TA, endoscopic ultrasound-guided tissue acquisition.

Table 3. Assessment of the 78 stereomicroscopic on-site evaluations.

Meeting the SVWC cutoff value, *n* (%)	
First pass	57/78 (73.1%)
Second pass	16/21 (76.2%)
All passes	73/99 (73.7%)
Median time of evaluation required for SOSE, seconds [range]	32 [4–126]

Abbreviations: SOSE, stereomicroscopic on-site evaluation; SVWC, stereomicroscopically visible white core.

Table 4. Diagnostic yields of EUS-TA with SOSE.

Overall diagnostic yield (n = 78)	
Per lesion analysis, %	
Sensitivity	90.8%
Specificity	100%
PPV	100%
NPV	22.2%
Accuracy	91.0%
Sensitivity for malignant diagnoses based on the SVWC cutoff value	
First pass, n (%), (n = 57)	
Cytology	42 (73.7%)
Histology	49 (86.0%)
Cytology and histology	51 (89.5%)
Second pass, n (%), (n = 16)	
Cytology	11 (68.8%)
Histology	15 (93.8%)
Cytology and histology	15 (93.8%)
All passes, n (%), (n = 73)	

Cytology	53 (72.6%)
Histology	64 (87.7%)
Cytology and histology	66 (90.4%)

EUS-TA, endoscopic ultrasound-guided tissue acquisition; NPV, negative predictive value; PPV, positive predictive value; SOSE, stereomicroscopic on-site evaluation; SVWC, stereomicroscopically visible white core.

業績目録

（Ⅰ）原　著

◎1．Ishizaki J, Okuwaki K, Watanabe M, Imaizumi H, Iwai T, Hasegawa R, Kurosu T, Tadehara M, Matsumoto T, Adachi K, Hanaoka T, Kida M, Kusano C. Effectiveness of Endoscopic Ultrasound-guided Tissue Acquisition with Stereomicroscopic On-site Evaluation for Preoperative Diagnosis of Resectable or Borderline Resectable Pancreatic cancer: a prospective study. Clin Endosc, 2024.（in press）

○2．Okuwaki K, Watanabe M, Yoshida T, Tamaki A, Iwai T, Adachi K, Ishizaki J, Hanaoka T, Imaizumi H, Kida M, Kusano C. Efficacy of endoscopic ultrasound-guided tissue acquisition using stereo-microscopic on-site evaluation for possible comprehensive genome profile in patients with advanced pancreatic cancer. J Gastroenterol Hepatol, 39(4):740-745, 2024.

○3．Nakatani S, Okuwaki K, Watanabe M, Imaizumi H, Iwai T, Matsumoto T, Hasegawa R, Masutani H, Kurosu T, Tamaki A, Ishizaki J, Ishizaki A, Kida M, Kusano C. Stereomicroscopic on-site evaluation in endoscopic ultrasound-guided tissue acquisition of upper gastrointestinal subepithelial lesions. Clin Endosc, 57(1):89-95, 2024

○4．Ishizaki A, Okuwaki K, Kida M, Imaizumi H, Iwai T, Yamauchi H, Kaneko T, Hasegawa R, Watanabe M, Kurosu T, Ishizaki J, Kusano C. Implication of Skeletal Muscle Loss in the Prognosis of Patients with Pancreatic Ductal Adenocarcinoma Receiving Chemotherapy. Intern Med, 62(19):2783-2793, 2023

○5．Watanabe M, Okuwaki K, Kida M, Imaizumi H, Matsumoto T, Iwai T, Hasegawa R, Masutani H, Kurosu T, Minato N, Tamaki A, Ishizaki J, Kusano C. Multicenter prospective study of the efficacy of stereomicroscopic on-site evaluation in endoscopic ultrasound-guided tissue acquisition in patients with pancreatic cancer. Pancreatology, 22(2):311-316, 2022

（Ⅱ）著　書

なし

（Ⅲ）総説・講座

なし

（Ⅳ）症例・臨床治験・その他

なし