Pancreatology

Pancreatology 2011;11(suppl 2):40–46
DOI: 10.1159/000323502

Published online: April 5, 2011

Current Concept of Endoscopic Ultrasound-Guided Fine Needle Aspiration for Pancreatic Cancer

Nobumasa Mizuno[a] Kazuo Hara[a] Susumu Hijioka[a] Vikram Bhatia[d]
Yasuhiro Shimizu[b] Yasushi Yatabe[c] Kenji Yamao[a]

Departments of [a]Gastroenterology, [b]Gastroenterological Surgery, [c]Pathology and Molecular Diagnostics, Aichi Cancer Center Hospital, Nagoya, Japan; [d]Department of Medical Hepatology, Institute of Liver and Biliary Sciences, New Delhi, India

Key Words
Endoscopic ultrasound · Fine needle aspiration · Non-invasive methods · Preoperative tissue diagnosis

Abstract
Endoscopic ultrasound (EUS) provides detailed, high-resolution images of the pancreas. However, whether a lesion is malignant or benign cannot be diagnosed solely from its imaging features on EUS. The introduction of EUS-guided fine needle aspiration (EUS-FNA) offers the possibility to obtain a cytological or histological diagnosis of pancreatic lesions with a high sensitivity and specificity. Although the clinical utility of EUS-FNA for pancreatic diseases is widely accepted, the indication for preoperative tissue diagnosis of pancreatic lesions suspected to be malignant is still controversial. This review highlights the diagnostic potential of EUS-FNA, as well as its current indications and contraindications, complications, and techniques.

Introduction

A variety of imaging modalities, such as ultrasonography (US), computed tomography (CT), magnetic resonance imaging (MRI), and endoscopic ultrasonography (EUS), have been developed to assess pancreatic lesions and have remarkably improved visualization of small lesions. Although these modalities allow the detection of small pancreatic lesions <2 cm, differentiation between benign and malignant lesions remains difficult based on their morphological appearance alone. Thus, a tissue sampling method that is accurate, safe, and easy is required.

There are several tissue sampling methods for pancreatic lesions, such as (1) a core or wedge biopsy [1], (2) fine needle aspiration (FNA) [2], and (3) collection of pancreatic juice by direct suction, washing, or brushing during endoscopic retrograde cholangiopancreatography (ERCP) [1, 3, 4]. Among these sampling methods, FNA of the pancreas under US, CT, or EUS guidance has become established as the most reliable and safe procedure. The ability of EUS to guide a biopsy needle into lesions that are too small to be identified by CT or US, or too closely related to surrounding vascular structures to allow a percutaneous biopsy, secures its role in a variety of clinical settings [5]. In the following, we describe EUS-guided FNA (EUS-FNA) for pancreatic disorders.

KARGER

Fax +41 61 306 12 34
E-Mail karger@karger.ch
www.karger.com

1424–3903/11/0118–0040$38.00/0

Accessible online at:
www.karger.com/pan

Nobumasa Mizuno, MD, PhD
Department of Gastroenterology
Aichi Cancer Center Hospital
1-1 Kanokoden, Chikusa-ku, Nagoya 464-8681 (Japan)
Tel. +81 52 762 6111, Fax +81 52 762 2947, E-Mail nobumasa@aichi-cc.jp

Indications

A fundamental principle of EUS-FNA is that the information obtained should have the potential to affect patient management [6]. In addition, the indications for EUS-FNA should be guided by its diagnostic accuracy, cost effectiveness, and patient comfort and safety [7]. EUS-FNA is indicated for the cytopathological diagnosis of lesions of the gastrointestinal tract (and adjacent tissue) and of the lymph nodes in its vicinity, when these lesions cannot be sampled by less invasive methods, or if other sampling methods have failed.

Contraindication

EUS-FNA is contraindicated in all conditions in which the risks of the procedure outweigh the expected benefits of the diagnostic information obtained. These situations would include all conditions where the FNA result would not affect patient management, when the lesion cannot be clearly visualized or a tumor mass or vessel is interposed between the needle-to-target path, in the presence of bleeding diathesis, and in the presence of the risk of tumor seeding [6–8].

Complications

EUS-FNA of the pancreas is considered a safe technique, with major complications observed in 1–2.5% of patients, and minor self-limiting complications occurring in up to 6% [9, 10]. The most common complications are bleeding and acute pancreatitis. Bleeding is usually self-limited and seldom requires transfusion. Although in most cases acute pancreatitis is mild, it may delay surgery and render a formerly resectable tumor unresectable [11]. Possible risk factors for acute pancreatitis are cystic lesions and benign pancreatic diseases [11, 12].

Another serious complication of EUS-FNA is tumor seeding. Four recent case reports have raised concerns that this risk may have been underestimated so far. In 3 of the cases, gastrointestinal wall implantation occurred as a consequence of EUS-FNA of malignant perigastric and mediastinal lymph node metastases [13, 14], and of a small pancreatic tail cancer [15]. The potential risk of peritoneal carcinomatosis due to transgastric sampling of pancreatic malignancies was highlighted by a case of peritoneal dissemination of an intraductal papillary mucinous neoplasm following EUS-FNA [16]. However, in comparison with percutaneous biopsy guided by US or CT, the risk of tumor seeding with EUS-FNA is reported to be very low (16.3 vs. 2.2%, respectively) [17]. This may be explained by the close proximity of the endoscope to the pancreatic lesion, without traversing several layers of other tissue structures, as in the percutaneous approach.

Thus, EUS-FNA of the pancreas should be carefully performed with special regard to complications peculiar to a pancreatic biopsy, such as acute pancreatitis and tumor seeding.

Needle Size and Needle Type

Several needles are available for performing EUS-FNA, each of which uses a spiral-wire-protected catheter assembly with an attached handle mechanism that secures to the luer lock adaptor on the US endoscope. Needles range from 19 to 25 gauges with a depth of penetration of up to 10 cm [18, 19]. The 19-gauge needle is quite stiff and can be difficult to manipulate in the duodenum with a sharply curved endoscope [18].

EUS-guided Trucut needle biopsy (TCB) overcomes some of the shortcomings of EUS-FNA by acquiring larger tissue samples while preserving tissue architecture [20]. TCB may be most useful in patients with autoimmune pancreatitis (AIP) [21]. An advantage of EUS-TCB for cystic pancreatic lesions has been described. However, whether TCB from the cyst wall could additionally help to guide clinical management requires further investigation [22].

On-Site Cytology

It has been recommended that a cytopathologist should be available on site to provide an immediate interpretation of the cytological specimen (fig. 1a). Although controlled studies are still lacking, immediate interpretation increases the sensitivity of the biopsy by 10–15%, shortens the procedure time, and minimizes the number of attempts required to obtain a representative diagnostic specimen [23, 24].

Training

The skills and experience of the EUS examiner as well as of the cytopathologist play a key role for the diagnostic yield of EUS-FNA. Acquiring the necessary skills for per-

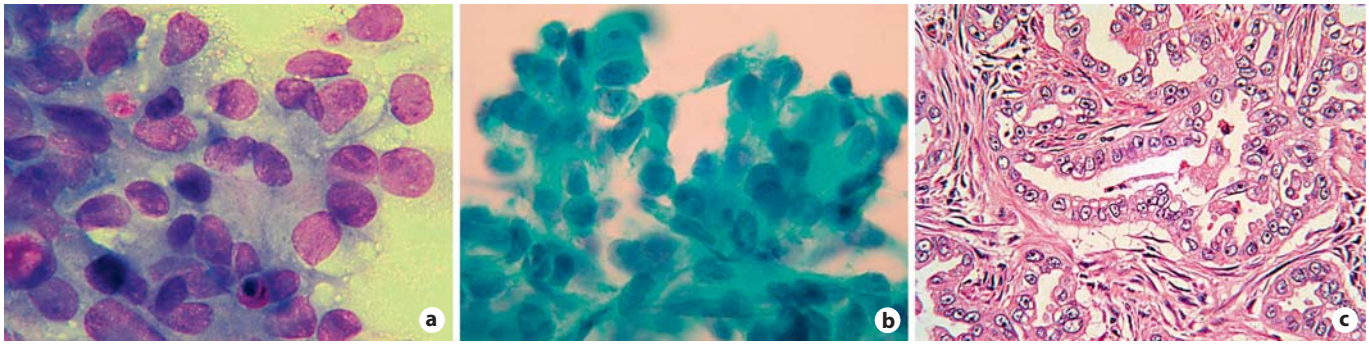

Fig. 1. Moderately differentiated tubular adenocarinima. **a** Diff-Quik stain (×400). **b** Papanicolaou stain (×400). **c** HE (×200).

forming EUS-FNA depends upon the fundamental understanding of normal and abnormal EUS anatomy to avoid inadvertent sampling of structures that should not be biopsied. Training should begin with relatively easily accessible lesions, such as paraesophageal or perigastric lymph nodes, followed by more difficult lesions, such as those arising from the pancreas.

EUS-FNA for Pancreatic Disease

Based on the high diagnostic accuracy, low complication rates, and a lack of other effective and less invasive alternatives, EUS-FNA is one of the best approaches to obtain a pathological diagnosis of pancreatic lesions. EUS-FNA has several advantages over CT- or US-guided biopsies [25]: (1) the ability to sample smaller lesions, (2) the ability to biopsy the lesion through a segment of the intestinal wall, which typically becomes part of the resection specimen, thereby minimizing the risk of needle tract seeding, and (3) the ability to provide additional information about disease staging. EUS-FNA can also target peripancreatic lymph nodes. This approach is useful for making a tissue diagnosis, determining nodal stage and obtaining a diagnosis when alternate biopsy results of the tumor are inconclusive.

Diagnostic Yield of EUS-FNA for Pancreatic Carcinoma

EUS-FNA has a sensitivity of approximately 75–90% and a specificity of virtually 100% for solid pancreatic mass lesions [26]. Although molecular analysis should not be considered as a routine component of the diagnostic evaluation for pancreatic masses, the addition of molecular genetic analysis (e.g. assay for k-ras gene mutations) to cytological or histological examination may improve sensitivity, especially in patients with small primary tumors [27]. On the other hand, one recent study of 230 patients with EUS-FNA positive or suspicious for pancreatic carcinoma undergoing surgery in the absence of neoadjuvant therapy identified 6 false-positive cases (4%) [28]. Therefore, the possibility of false-positive results of EUS-FNA should always be considered.

Role of EUS-FNA in Various Pancreatic Pathologies

Pancreatic Adenocarcinoma

EUS-FNA of a suspected pancreatic malignancy is indicated for treatment planning if there is systemic spread of disease, local evidence of unresectability, if the patient is unfit for surgery, or if neoadjuvant treatment is being contemplated. In the NCCN (National Comprehensive Cancer Network) guidelines for pancreatic adenocarcinoma [29], it is strongly recommended that all patients with unresectable pancreatic cancer should have cancer confirmation before non-surgical treatment is initiated (fig. 1a–c).

However, whether a preoperative diagnostic biopsy is needed in a fit patient with a potentially resectable pancreatic lesion suspicious for malignancy is controversial. While a positive biopsy can confirm the suspected diagnosis, a benign sample does not exclude the presence of malignancy. In one systematic review of 53 studies addressing this issue, the negative predictive value of EUS-FNA was only 60–70% [26]. In addition, the risk of tumor seeding caused by EUS-FNA is strongly stressed in the dissenting opinions against this indication. However, tu-

mor seeding was found in only 1 of 10,766 cases, based on a worldwide experience with percutaneous imaging-guided FNA [30]. The risk of tumor seeding with EUS-FNA of the pancreas is smaller than with the percutaneous approach [17]. Moreover, establishing a histological diagnosis may influence the treatment and operative procedure even when surgery is planned. Some patients, especially those at high surgical risk, as well as many surgeons would like to know the histological diagnosis before a major surgery.

In cases with suspected resectable pancreatic adenocarcinoma [31], EUS-FNA is currently indicated (1) to rule out other types of pancreatic malignancies that can mimic adenocarcinomas (e.g. lymphomas, small cell carcinomas, metastatic diseases, and neuroendocrine tumors), as well as non-malignant diseases such as AIP or chronic pancreatitis, (2) to assist in surgical planning (e.g. a more limited resection may be possible in patients with neuroendocrine tumors), and (3) to confirm the diagnosis in patients who want tissue verification prior to surgery.

Neuroendocrine Tumors

Generally, neuroendocrine tumors of the pancreas are characterized by a better prognosis and later symptomatic dissemination than ductal adenocarcinomas. As surgical resection is the only curative treatment, precise preoperative localization of the tumor is important. In contrast to CT or MRI, EUS is able to detect small lesions <10 mm suitable for a limited resection (fig. 2). EUS-FNA can provide pathological information with additional immunohistochemical staining [32, 33] (fig. 3). However, the preoperative distinction between a benign and malignant tumor is still challenging.

Pancreatic Cystic Lesions

Pancreatic cystic lesions may be inflammatory or neoplastic (benign, premalignant, or malignant). Among them, the diagnosis of intraductal papillary mucinous neoplasms and mucinous cystic neoplasms is especially important, because of their malignant or premalignant nature. These tumors have been traditionally diagnosed by a combination of CT, MRI, EUS, and ERCP [34]. Recently, estimation of tumor markers such as CEA levels in cyst fluid have been reported to be useful for differentiating a malignant/potentially malignant cystic tumor from a benign cystic tumor [35]. According to the International Consensus Guidelines [36], it is not enough only to make a differential diagnosis between mucinous and non-mucinous neoplastic cysts, it is also necessary to make a diagnosis of the degree of malignancy for treatment management. Complications such as bleeding, pancreatitis, and infection after EUS-FNA are more frequently encountered in cystic than solid pancreatic lesions [12, 26]. Furthermore, tumor seeding after FNA may occur more frequently in mucinous cystic lesions, especially those located in the body or tail of the pancreas, than after FNA of solid lesions [8, 12, 26]. A case report of tumor dissemination in a patient with an intraductal papillary mucinous neoplasm after EUS-FNA supports this apprehension [16]. Further studies are required to confirm the usefulness of cyst fluid analysis for the diagnosis of pancreatic cystic tumors versus the risk of tumor seeding by EUS-FNA.

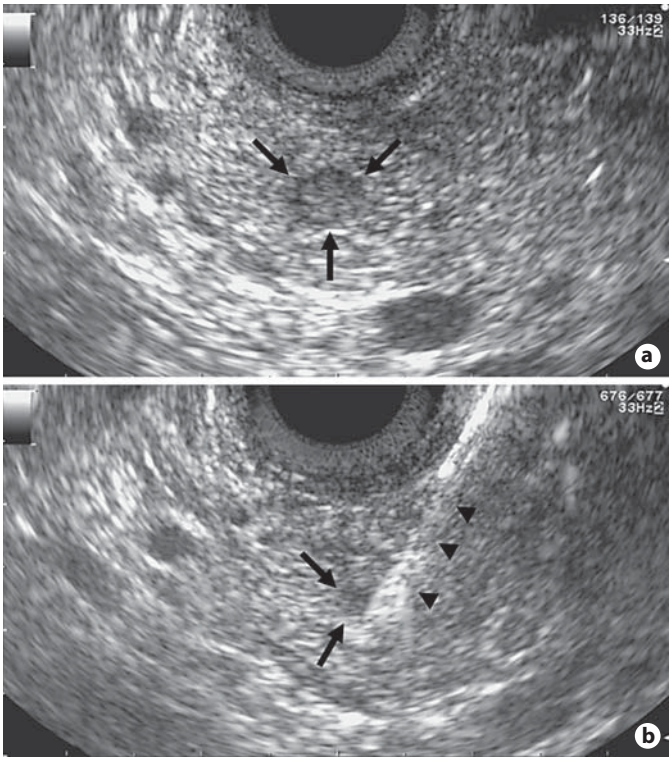

Fig. 2. Small neuroendocrine tumor of the pancreas. **a** EUS revealed a small low-echoic tumor (arrows, diameter: 6 mm) at the pancreatic head. **b** EUS displaying a fine needle (arrow heads) puncturing a tumor (arrows).

Autoimmune Pancreatitis

Based on cross-sectional imaging, AIP is often misdiagnosed as pancreatic carcinoma, with patients then being referred for surgical exploration [37, 38]. As non-surgical treatment with corticosteroids is effective, surgery should be avoided [39]. In recent studies, the diagnostic

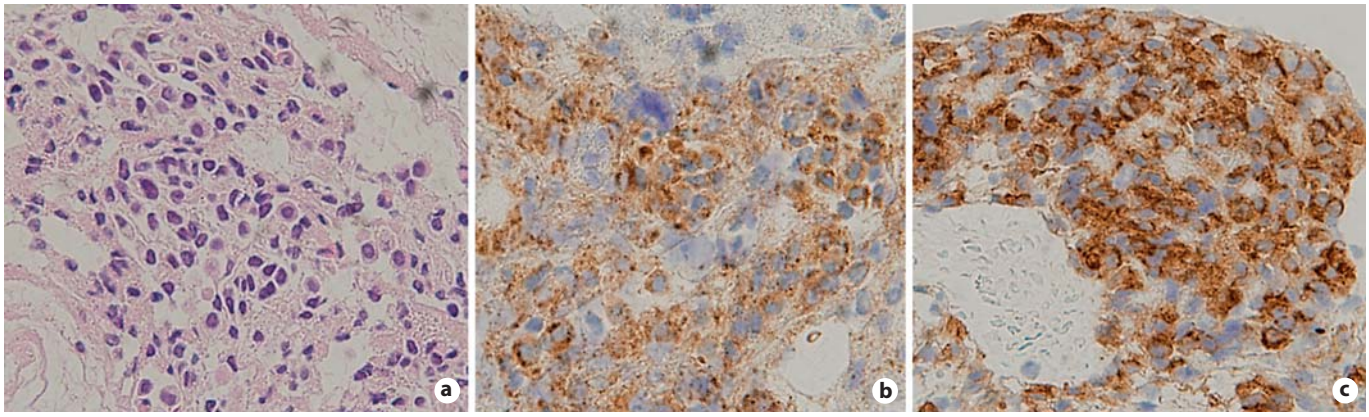

Fig. 3. Histology of a neuroendocrine tumor of the pancreas. **a** HE. **b** Chromogranin A. **c** Synaptophysin.

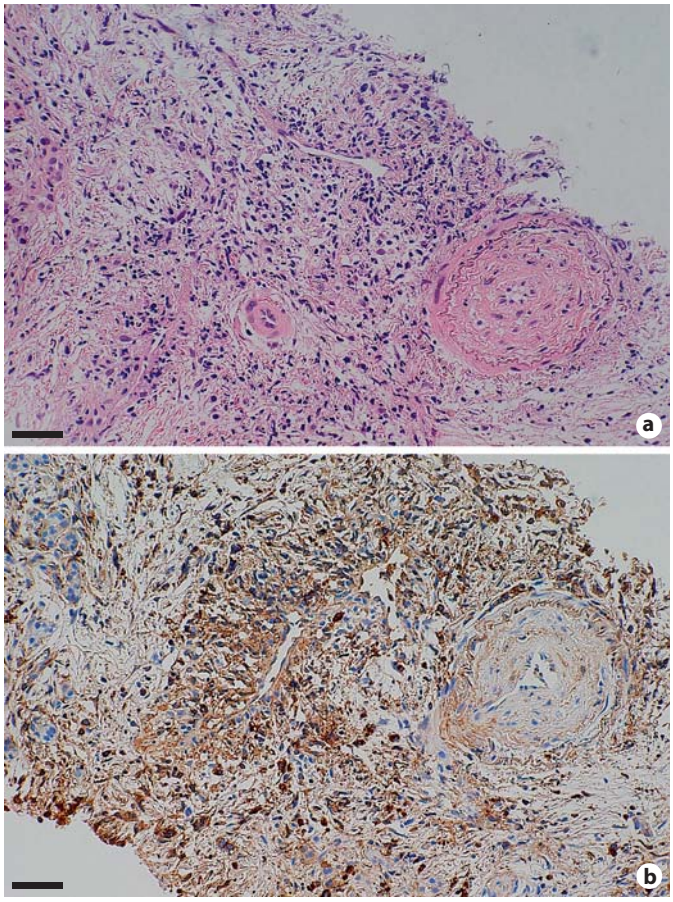

Fig. 4. Histopathology of AIP. Bar: 50 μm. **a** Consistent with lymphoplasmacytic sclerosing pancreatitis with storiform fibrosis, lymphoplasmacytic infiltration and obliterative phlebitis. **b** Numerous plasma cells show positive immunoreactivity for IgG4.

criteria for AIP [40–42] and the diagnostic utility of serum IgG4 levels have been established [43]. However, differentiating between AIP and pancreatic carcinoma is still challenging. Although EUS-FNA is the best modality to distinguish AIP from pancreatic carcinoma because of its high diagnostic accuracy for the latter condition, it is insufficient to diagnose AIP due to the small sample volume and absence of tissue architecture. EUS-TCB provides a core of pancreatic tissue, which can be diagnostic of AIP [20, 21] (fig. 4). Further studies are required to confirm the utility of EUS-TCB in the diagnosis of AIP.

Conclusion

EUS-FNA is minimally invasive and effective for sampling of malignant and benign lesions of the pancreas. The procedure has been well accepted worldwide and is being increasingly utilized. However, some of the issues related to the indications for EUS-FNA remain controversial and will have to be resolved in the near future.

Acknowledgements

This work was supported by grants from the Ministry of Health, Labour and Welfare of Japan (to N.M.) and the Japanese Society of Gastroenterology (to N.M.).

Disclosure Statement

The authors disclose no conflicts.

References

1 Kloppel G: Pancreatic biopsy; in Kloppel G, Heitz PU (eds): Pancreatic Pathology. Edinburgh, Churchill Livingstone, 1984, pp 114–122.

2 Hajdu SI, Ehya H, Frable WJ, Geisinger KR, Gompel CM, Kern WH, Lowhagen T, Oertel YC, Ramzy I, Rilke FO, et al: The value and limitations of aspiration cytology in the diagnosis of primary tumors. A symposium. Acta Cytol 1989;33:741–790.

3 Goodale RL, Gajl-Peczalska K, Dressel T, Samuelson J: Cytologic studies for the diagnosis of pancreatic cancer. Cancer 1981;47:1652–1655.

4 Osnes M, Serck-Hanssen A, Kristensen O, Swensen T, Aune S, Myren J: Endoscopic retrograde brush cytology in patients with primary and secondary malignancies of the pancreas. Gut 1979;20:279–284.

5 Vilmann P, Jacobsen GK, Henriksen FW, Hancke S: Endoscopic ultrasonography with guided fine needle aspiration biopsy in pancreatic disease. Gastrointest Endosc 1992;38:172–173.

6 Hawes RH: Indications for EUS-directed FNA. Endoscopy 1998;30(suppl 1):A155–A157.

7 Erickson RA: EUS-guided FNA. Gastrointest Endosc 2004;60:267–279.

8 Yamao K, Sawaki A, Mizuno N, Shimizu Y, Yatabe Y, Koshikawa T: Endoscopic ultrasound-guided fine-needle aspiration biopsy (EUS-FNAB): past, present, and future. J Gastroenterol 2005;40:1013–1023.

9 Chang KJ, Nguyen P, Erickson RA, Durbin TE, Katz KD: The clinical utility of endoscopic ultrasound-guided fine-needle aspiration in the diagnosis and staging of pancreatic carcinoma. Gastrointest Endosc 1997;45:387–393.

10 Eloubeidi MA, Tamhane A, Varadarajulu S, Wilcox CM: Frequency of major complications after EUS-guided FNA of solid pancreatic masses: a prospective evaluation. Gastrointest Endosc 2006;63:622–629.

11 Eloubeidi MA, Gress FG, Savides TJ, Wiersema MJ, Kochman ML, Ahmad NA, Ginsberg GG, Erickson RA, Dewitt J, Van Dam J, Nickl NJ, Levy MJ, Clain JE, Chak A, Sivak MV Jr, Wong R, Isenberg G, Scheiman JM, Bounds B, Kimmey MB, Saunders MD, Chang KJ, Sharma A, Nguyen P, Lee JG, Edmundowicz SA, Early D, Azar R, Etemad B, Chen YK, Waxman I, Shami V, Catalano MF, Wilcox CM: Acute pancreatitis after EUS-guided FNA of solid pancreatic masses: a pooled analysis from EUS centers in the United States. Gastrointest Endosc 2004;60:385–389.

12 Jenssen C, Dietrich CF: Endoscopic ultrasound-guided fine-needle aspiration biopsy and trucut biopsy in gastroenterology – an overview. Best Pract Res Clin Gastroenterol 2009;23:743–759.

13 Doi S, Yasuda I, Iwashita T, Ibuka T, Fukushima H, Araki H, Hirose Y, Moriwaki H: Needle tract implantation on the esophageal wall after EUS-guided FNA of metastatic mediastinal lymphadenopathy. Gastrointest Endosc 2008;67:988–990.

14 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.

15 Paquin SC, Gariepy 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.

16 Hirooka Y, Goto H, Itoh A, Hashimoto S, Niwa K, Ishikawa H, Okada N, Itoh T, Kawashima H: Case of intraductal papillary mucinous tumor in which endosonography-guided fine-needle aspiration biopsy caused dissemination. J Gastroenterol Hepatol 2003;18:1323–1324.

17 Micames C, Jowell PS, White R, Paulson E, Nelson R, Morse M, Hurwitz H, Pappas T, Tyler D, McGrath K: Lower frequency of peritoneal carcinomatosis in patients with pancreatic cancer diagnosed by EUS-guided FNA vs. percutaneous FNA. Gastrointest Endosc 2003;58:690–695.

18 Itoi T, Itokawa F, Sofuni A, Nakamura K, Tsuchida A, Yamao K, Kawai T, Moriyasu F: Puncture of solid pancreatic tumors guided by endoscopic ultrasonography: a pilot study series comparing Trucut and 19- and 22-gauge aspiration needles. Endoscopy 2005;37:362–366.

19 Sakamoto H, Kitano M, Komaki T, Noda K, Chikugo T, Dote K, Takeyama Y, Das K, Yamao K, Kudo M: Prospective comparative study of the EUS guided 25-gauge FNA needle with the 19-gauge Trucut needle and 22-gauge FNA needle in patients with solid pancreatic masses. J Gastroenterol Hepatol 2009;24:384–390.

20 Levy MJ: Endoscopic ultrasound-guided trucut biopsy of the pancreas: prospects and problems. Pancreatology 2007;7:163–166.

21 Mizuno N, Bhatia V, Hosoda W, Sawaki A, Hoki N, Hara K, Takagi T, Ko SB, Yatabe Y, Goto H, Yamao K: Histological diagnosis of autoimmune pancreatitis using EUS-guided trucut biopsy: a comparison study with EUS-FNA. J Gastroenterol 2009;44:742–750.

22 Levy MJ, Smyrk TC, Reddy RP, Clain JE, Harewood GC, Kendrick ML, Pearson RK, Petersen BT, Rajan E, Topazian MD, Wang KK, Wiersema MJ, Yusuf TE, Chari ST: Endoscopic ultrasound-guided trucut biopsy of the cyst wall for diagnosing cystic pancreatic tumors. Clin Gastroenterol Hepatol 2005;3:974–979.

23 Erickson RA, Sayage-Rabie L, Beissner RS: Factors predicting the number of EUS-guided fine-needle passes for diagnosis of pancreatic malignancies. Gastrointest Endosc 2000;51:184–190.

24 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.

25 Wiersema MJ, Norton ID: Endoscopic ultrasound-guided fine-needle aspiration biopsy in the gastrointestinal tract. UpToDate, 18.2.2010, http://www.uptodate.com/patients/content/topic.do?topicKey=~iIxncz_GU9HgNi.

26 Hartwig W, Schneider L, Diener MK, Bergmann F, Buchler MW, Werner J: Preoperative tissue diagnosis for tumours of the pancreas. Br J Surg 2009;96:5–20.

27 Takahashi K, Yamao K, Okubo K, Sawaki A, Mizuno N, Ashida R, Koshikawa T, Ueyama Y, Kasugai K, Hase S, Kakumu S: Differential diagnosis of pancreatic cancer and focal pancreatitis by using EUS-guided FNA. Gastrointest Endosc 2005;61:76–79.

28 Gleeson FC, Kipp BR, Caudill JL, Clain JE, Clayton AC, Halling KC, Henry MR, Rajan E, Topazian MD, Wang KK, Wiersema MJ, Zhang J, Levy MJ: False positive endoscopic ultrasound fine needle aspiration cytology: incidence and risk factors. Gut 2010;59:586–593.

29 NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™). Pancreatic Adenocarcinoma, v 1. 2010, www.nccn.org.

30 Bhutani MS: Interventional endoscopic ultrasonography: state of the art at the new millenium. Endoscopy 2000;32:62–71.

31 Saftoiu A, Vilmann P: Role of endoscopic ultrasound in the diagnosis and staging of pancreatic cancer. J Clin Ultrasound 2009;37:1–17.

32 Hosoda W, Takagi T, Mizuno N, Shimizu Y, Sano T, Yamao K, Yatabe Y: Diagnostic approach to pancreatic tumors with the specimens of endoscopic ultrasound-guided fine needle aspiration. Pathol Int 2010;60:358–364.

33 Imaoka H, Yamao K, Bhatia V, Shimizu Y, Yatabe Y, Koshikawa T, Kinoshita Y: Rare pancreatic neoplasms: the utility of endoscopic ultrasound-guided fine-needle aspiration – a large single center study. J Gastroenterol 2009;44:146–153.

34 Yamao K, Nakamura T, Suzuki T, Sawaki A, Hara K, Kato T, Okubo K, Matsumoto K, Shimizu Y: Endoscopic diagnosis and staging of mucinous cystic neoplasms and intraductal papillary-mucinous tumors. J Hepatobiliary Pancreat Surg 2003;10:142–146.

35 Brugge WR, Lewandrowski K, Lee-Lewandrowski E, Centeno BA, Szydlo T, Regan S, del Castillo CF, Warshaw AL: Diagnosis of pancreatic cystic neoplasms: a report of the cooperative pancreatic cyst study. Gastroenterology 2004;126:1330–1336.
36 Tanaka M, Chari S, Adsay V, Fernandez-del Castillo C, Falconi M, Shimizu M, Yamaguchi K, Yamao K, Matsuno S: International consensus guidelines for management of intraductal papillary mucinous neoplasms and mucinous cystic neoplasms of the pancreas. Pancreatology 2006;6:17–32.
37 Abraham SC, Wilentz RE, Yeo CJ, Sohn TA, Cameron JL, Boitnott JK, Hruban RH: Pancreaticoduodenectomy (Whipple resections) in patients without malignancy: are they all 'chronic pancreatitis'? Am J Surg Pathol 2003;27:110–120.
38 Weber SM, Cubukcu-Dimopulo O, Palesty JA, Suriawinata A, Klimstra D, Brennan MF, Conlon K: Lymphoplasmacytic sclerosing pancreatitis: inflammatory mimic of pancreatic carcinoma. J Gastrointest Surg 2003; 7:129–137, discussion 137–139.
39 Ko SB, Mizuno N, Yatabe Y, Yoshikawa T, Ishiguro H, Yamamoto A, Azuma S, Naruse S, Yamao K, Muallem S, Goto H: Corticosteroids correct aberrant CFTR localization in the duct and regenerate acinar cells in autoimmune pancreatitis. Gastroenterology 2010;138:1988–1996.
40 Okazaki K, Kawa S, Kamisawa T, Naruse S, Tanaka S, Nishimori I, Ohara H, Ito T, Kiriyama S, Inui K, Shimosegawa T, Koizumi M, Suda K, Shiratori K, Yamaguchi K, Yamaguchi T, Sugiyama M, Otsuki M: Clinical diagnostic criteria of autoimmune pancreatitis: revised proposal. J Gastroenterol 2006;41: 626–631.
41 Otsuki M, Chung JB, Okazaki K, Kim MH, Kamisawa T, Kawa S, Park SW, Shimosegawa T, Lee K, Ito T, Nishimori I, Notohara K, Naruse S, Ko SB, Kihara Y, Research Committee of Intractable Pancreatic Diseases provided by the Ministry of Health, Labour and Welfare of Japan and the Korean Society of Pancreatobiliary Diseases: Asian diagnostic criteria for autoimmune pancreatitis: consensus of the Japan-Korea Symposium on Autoimmune Pancreatitis. J Gastroenterol 2008;43:403–408.
42 Chari ST, Takahashi N, Levy MJ, Smyrk TC, Clain JE, Pearson RK, Petersen BT, Topazian MA, Vege SS: A diagnostic strategy to distinguish autoimmune pancreatitis from pancreatic cancer. Clin Gastroenterol Hepatol 2009;7:1097–1103.
43 Hamano H, Kawa S, Horiuchi A, Unno H, Furuya N, Akamatsu T, Fukushima M, Nikaido T, Nakayama K, Usuda N, Kiyosawa K: High serum IgG4 concentrations in patients with sclerosing pancreatitis. N Engl J Med 2001;344:732–738.