Cytopathology in Focus—Endoscopic ultrasound-guided FNA and core biopsy: Are we progressing to a best practice?

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August 2016—Endoscopic ultrasound (EUS) is a safe and effective procedure for visualizing and screening for lesions within and in the vicinity of the upper gastrointestinal tract, liver, pancreas and peri-pancreatic lymph nodes, and soft tissues. In addition to the detection and imaging of these lesions, endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) allows for concomitant sampling of visualized lesions for tissue diagnosis. Over the past two decades, EUS-FNA has emerged as the preferred method of sampling accessible masses in the abdomen, most successfully of the pancreas and peripancreatic lymph nodes. In the latter instance, a combination of endoscopic ultrasound and FNA/fine needle (core or cutting) biopsy (FNB) will often eliminate the need for surgical interventions in patients who have advanced pancreatic cancer. In addition, staging of cancer, through direct sampling of lymph nodes for metastases, can help triage patients into the most appropriate treatments.

EUS is considered a minimally invasive procedure. The potential advantages of an EUS-guided procedure (versus conventional biopsy) are that it is a lower-cost procedure and safer and more comfortable for the patient, and it uses fewer expensive hospital resources. For solid pancreatic masses (most primary adenocarcinomas and non-cystic neoplasms), FNA performs very well as an initial procedure for obtaining a tissue diagnosis. The technical expertise of the ultrasonographer/endoscopist, the size and location of the lesion sampled, and the presence or absence of rapid on-site evaluation (ROSE) to evaluate specimen adequacy are factors associated with increased accuracy of EUS-FNA. The addition of ROSE to an endoscopic procedure has been estimated to raise the accuracy rate by up to 10 percent.[1]

The diagnostic accuracy of EUS-FNA ranges from 70 to 98 percent depending on the location of the lesion and operator experience.[2,3] A recent meta-analysis of EUS-FNA for solid pancreatic lesions with appropriate clinical follow-up (surgery or clinical observation) found the following: pooled sensitivity of 86.8 percent (95 percent confidence interval, 85.5–87.9) with a pooled specificity of 95.8 percent (95 percent CI, 94.6–96.7).[4] These results would indicate that EUS-FNA represents a highly reliable first-line method for the diagnosis of solid pancreatic neoplasms.

Despite the overall success of EUS-FNA in the diagnosis of primary pancreatic cancer, there are many settings in which FNA alone appears to underperform other diagnostic alternatives. Submucosal and intramural gastrointestinal tumors such as gastrointestinal stromal tumor are often difficult to diagnose with FNA alone. In this setting, the addition of a fine needle (core or cutting) biopsy appears to be the technique of choice.[5] The addition of the FNB allows for better sampling of dense tissue than aspiration alone. In addition, gastrointestinal stromal tumors are routinely evaluated with immunohistochemical markers such as CD117 for diagnostic and potentially therapeutic purposes. In this setting, cell blocks prepared from aspirated material alone are often insufficient to perform essential ancillary studies. Likewise, accurate and complete diagnoses of other lesions such as metastases or lymphoma require additional tissue sampling.

To overcome some of the limitations of FNA alone, endoscopists have introduced small-gauge cutting needle biopsies in conjunction with or as an alternative to FNA. Early experience with EUS-guided Trucut biopsy (EUS-TCB) needles compared with EUS-guided FNA found a slightly higher accuracy in EUS-TCB than EUS-FNA, although the difference did not reach statistical significance in side-by-side clinical studies.[6] However, the nominal increase in accuracy was also associated with a decrease in the number of EUS-TCB passes needed to obtain a diagnostically adequate specimen. This particular feature makes the use of the cutting-type needles attractive to endoscopists.

ProCore FNB needle (Cook Medical, Bloomingdale, Ind.) is one of the modified or next-generation ultrasound needles. It is a high-definition ultrasound biopsy needle that uses a unique reverse bevel technology to collect a cytology specimen through FNA and a histology sample through FNB. The reverse bevel on the lateral aspect of the ProCore needle tip facilitates collection of the FNB sample via retrograde movement of the needle through the target lesion. A recent study evaluated the performance of EUS-guided Echo Tip ProCore FNB of solid intra-abdominal masses, including the pancreas, and compared its diagnostic utility with that of matched FNA.[7] This study showed no statistical difference in the yield of adequate specimens but did note that specimens from FNB tended to have a higher cellular yield. Similar studies comparing these two techniques are also inconclusive regarding accuracy, with recommendations that additional information and study are needed before conclusions can be drawn about the superiority of either method.[8,9]

As demands increase to do more with less on cytologic samples, clinicians and pathologists need to evaluate the optimal paradigm for tissue acquisition. Where traditional FNA (with ROSE) offers the advantage of an immediate evaluation of specimen adequacy, proponents of FNB claim that one advantage of this procedure is that it works satisfactorily “ROSE-less” and, as such, frees up valuable professional resources (cytotechnologist and pathologist time). In addition, there may be added value in sequential sampling with FNA followed by FNB. While this would seem to be optimal, additional considerations must be weighed against a slight increase in sensitivity. For one, the next-generation cutting needles are more expensive. These newer sampling devices are an estimated one and a half times the cost of their predecessors.[7] In addition, the increase in needle punctures using a sequential FNA then FNB tissue acquisition scheme could potentially lead to an increase in patient complications.

While it remains clear that EUS-guided tissue acquisition will remain the preferred option for first-line diagnosis of pancreatic and other intra-abdominal malignancies, the superiority of FNA over FNB is unclear. As new therapies evolve, more information will be needed from a given specimen. For example, individuals with pancreatic cancer are now being evaluated as candidates for neoadjuvant therapy, with preliminary results showing some survivorship benefit.10 If patients proceed to resection after neoadjuvant therapy, it is conceivable that the only sample of their original malignancy will be the cellular material from the EUS-guided procedure. As treatments evolve further in the targeted or molecularly based era, pathologists will be called on to provide even more information from these small specimens.

Pathologists must be prepared to move from rendering a diagnosis to providing added value by using available material to facilitate individual patient personalized treatment plans. All pathologists, including those who interpret FNA or FNB exclusively, need to be active participants in designing the most appropriate tissue acquisition models.

1. Schmidt RL, Witt BL, Matynia AP, Barraza G, Layfield LJ, Adler DG. Rapid on-site evaluation increases endoscopic ultrasound-guided fine-needle aspiration adequacy for pancreatic lesions. *Dig Dis Sci.* 2013;58(3):872–882.
2. Hasan MK, Hawes RH. EUS-guided FNA of solid pancreas tumors. *Gastrointest Endosc Clin N Am.* 2012;22(2):155–167.
3. Bluen BE, Lachter J, Khamaysi I, et al. Accuracy and quality assessment of

EUS-FNA: a single-center large cohort of biopsies. *Diagn Ther Endosc.* 2012;(2012):article ID 139563. doi:101155/2012/139563.

4. Puli SR, Bechtold ML, Buxbaum JL, Eloubeidi MA. How good is endoscopic ultrasound-guided fine-needle aspiration in diagnosing the correct etiology for a solid pancreatic mass?: A meta-analysis and systematic review. *Pancreas.* 2013;42(1):20–26.
5. Webb K, Hwang JH. Endoscopic ultrasound-fine needle aspiration versus core biopsy for the diagnosis of subepithelial tumors. *Clin Endos.* 2013;46(5):441–444.
6. Levy MJ, Jondal ML, Clain J, Wiersema MJ. Preliminary experience with a EUS-guided trucut biopsy needle compared with EUS-guided FNA. *Gastrointest Endosc.* 2003;57(1):101–106.
7. Dwyer J, Pantanowitz L, Ohori NP, et al. Endoscopic ultrasound-guided FNA and ProCore biopsy in sampling pancreatic and intra-abdominal masses. *Cancer Cytopathol.* 2016;124(2):110–121.
8. Witt BL, Adler DG, Hilden K, Layfield LJ. A comparative needle study: EUS-FNA procedures using the HD ProCore and EchoTip 22-gauge needle types. *Diagn Cytopathol.* 2013;41(12):1069–1074.
9. Bang JY, Hawes R, Varadarajulu S. A meta-analysis comparing ProCore and standard fine-needle aspiration needles for endoscopic ultrasound-guided tissue acquisition. *Endoscopy.* 2016;48(4):339–349.
10. Sherman WH, Chu K, Chabot J, et al. Neoadjuvant gemcitabine, docetaxel, and capecitabine followed by gemcitabine and capecitabine/radiation therapy and surgery in locally advanced, unresectable pancreatic adenocarcinoma. *Cancer.* 2015;121(5):673–680.

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