EDITORIAL

EUS-FNA and needle echogenicity in the age of personalized medicine

The concept of EUS-guided FNA (EUS-FNA) and a working prototype were introduced by Vilmann et al in 1992.[1] Since then, EUS-FNA has largely replaced histology and non–EUS-FNA obtained cytology for the diagnosis and characterization of suspected neoplasia in and around the GI and pulmonary tracts. EUS-FNA has met described criteria of a disruptive innovation.[2] This theory was originally described by Christensen et al[3] and consists of a process by which a small company, usually at the fringe and usually overlooked, is able to successfully challenge an established business model.[2] In one single-institution study, cytologic diagnosis improved with a sensitivity and specificity of 55% and 78% before, to 88% and 96% after, implementation of an EUS-FNA program. Unsatisfactory specimens also markedly decreased from 7% to 1%.[2] Unfortunately, despite progress in equipment, including needle technology, it is still far from 100% accurate to detect a malignancy. A meta-analysis showed a pooled sensitivity and specificity of 85% and 98%, respectively.[4] When EUS-FNA is not diagnostic, a repeat attempt revealed a malignancy in 37% of patients.[5]

Known factors affecting the outcome of EUS-FNA can be grouped into operator characteristics such as training[6] and current volume.[7] I believe these also apply to the cytology team. There are patient factors, such as type, location, and accessibility of the lesion and anesthesia tolerance. Intraprocedural factors include the presence of rapid on-site evaluation, which, in my experience, depends on whether it is done by a resident, fellow, technician, or attending physician. Evaluation by an experienced cytologist is especially important in a repeat procedure for a prior nondiagnostic FNA. Much has been written about technical factors, including the size and type of needle, number of passes (and number of actuations within a pass, although little is known about this), whether suction is applied, or a stylet is used, and whether "fanning" is used.[8]

Needle-related factors have also been extensively reviewed and include size and type of needle (standard vs fenestrated reverse beveled) and whether it is made of stainless steel or nitinol (which is more elastic and recovers its original shape). Less is known about echogenicity of the tip or internal friction of the needle components, especially in a torqued long position. There are also more subtle cognitive factors, which probably merit further study, such as the amount of time allotted for a procedure (is the physician in a rush?), whether an oncologic history was taken and shared with the cytologist performing rapid on-site evaluation (history of malignancy and what type), or are images, or even a radiology report, available for review. Finally, the work culture in the endoscopy unit also seems to be important (is the staff adequately trained and focused or easily distracted?) toward a successful EUS-FNA procedure.

> Needle-related factors are just one variable that can be controlled in the outcome of EUS-FNA. Because needle performance seems to have maxed-out, the goalpost is being moved again as we move toward molecular subclassification of tumors, including pancreatic tumors.

In this issue of *Gastrointestinal Endoscopy*, the Copenhagen group, the same group that described the first EUS-FNA, studied the echogenicity of currently available needles in a bench-top model.[9] Forty-three endosonographers and 17 radiologists from busy centers in Europe, Asia, South America, and the United States rated them. All needles commercially available and 2 prototypes were evaluated and ranked. One needle was found to be superior to the others by 10% to 40%. This needle was a prototype and the entire shaft has a proprietary echogenic polymer coating. They also found that being a senior or a junior endosonographer and personal needle preference did not influence the results. Interestingly, the needle was seen better at a sharper angle (50 vs 30 degrees), which is known as the HABE (higher angle, better echogenicity) effect. Needle-tip echogenicity is clinically important because it will likely allow for a more-confident and thus, successful, EUS-FNA pass, having made sure that the needle is indeed within the lesion. This study is also

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singular in that it is a bench-top study and hence more likely to be reproducible. This should serve as a template for further studies of needle characteristics and performance.

Needle-related factors are just one variable in the outcome of EUS-FNA that can be controlled. Just as needle diagnostic performance seems to have maxed out, the goalpost is being moved again as we move toward molecular subclassification of tumors, including pancreatic tumors, which likely require larger specimens. A recent multinational study classified pancreas cancer into 4 molecular pathway subtypes: squamous, pancreatic progenitor, immunogenic, and aberrantly differentiated endocrine exocrine.[10] This study used (presumably abundant) surgically resected tissue. Although not immediately translatable into clinical use, there will likely be implications for therapy if and when molecular classification becomes the standard of care. In the United States, as part of the National Institutes of Health personalized medicine initiative, the National Cancer Institute-Molecular Analysis for Therapy Choice, known as NCI-MATCH, study is ongoing and currently in the interim analysis period.[11] This study recommends at least 4 "core" biopsy samples, 16 to 18G in diameter, at least 1 cm in length, and obtained via interventional radiology. Unfortunately, 94 of 739 specimens collected so far have been inadequate for analysis. One can assume that an EUS needle would not perform better than a percutaneous larger-bore needle. In addition, in this trial, serial biopsy specimens are likely to be needed as treatment progresses because tumor genetics may change over time. It is unclear what type of specimens will be needed in the future, but the trend will likely be toward more tissue.

Twenty-four years after its introduction, EUS-FNA still follows the same general idea: a needle penetrates the lesion and by capillary action (probably) captures tissue in the lumen of the needle. Would better needle echogenicity alone make one choose a needle or change one's preferred needle? The answer is probably not. Although it is a desirable characteristic, experienced endosonographers likely can compensate for a less-echogenic but higher-yield needle. With the likely need to provide bigger and better samples for genomic analysis in the very near future, a disruptive innovation soon may be required to meet the tissue acquisition goals of the personalized medicine age.

DISCLOSURE

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Jorge V. Obando, MD
Department of Medicine
Duke University
Division of Gastroenterology
Durham, North Carolina, USA

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