Comparison of Cytopathologist-Performed Ultrasound-Guided Fine-Needle Aspiration With Cytopathologist-Performed Palpation-Guided Fine-Needle Aspiration

A Single Institutional Experience

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● *Context.*—Although fine-needle aspiration (FNA) practice by pathologists is now well established, it has been primarily performed by manual palpation. In recent years, pathologists have begun to venture into ultrasound-guided FNAs (UGFNAs). Reports on experiences with this relatively new technique for pathologists have shown promising results. However to date, there have been few studies in the literature comparing pathologist-performed UGFNA with the more traditional pathologist-performed palpation-guided FNA (PGFNA).

Objective.—To compare UGFNA to PGFNA by cytopathologists at an academic medical center.

Design.—A retrospective study of FNAs performed by cytopathologists within the University of California, Los Angeles (UCLA) pathology departmental FNA clinic was performed. Data collected included performance technique (UGFNA versus PGFNA), lesion site and size, adequacy status (nondiagnostic rate), and number of passes per procedure. Corresponding surgical pathology/flow cytometric/cytogenetic result follow-up was com-

pared to FNA results. Findings between UGFNA and PGFNA cases were compared.

Results.—Of 1029 FNA cases during the study period, there were 449 UGFNA cases (43.6%) and 580 PGFNA cases (56.4%). Nondiagnostic rates with UGFNA and PGFNA were 6.7% (30 of 449 cases) and 20.7% (120 of 580 cases), respectively. Nondiagnostic rate was also significantly lower with UGFNA than with PGFNA for lesions within the thyroid (6.0% versus 33.3%), head and neck (6.6% versus 21.2%), and salivary gland (6.2% versus 17.1%), and across all nodule sizes. A total of 495 of 1029 FNA cases (48.1%) had follow-up. Discordance rate was significantly lower with UGFNA than with PGFNA (5.4% versus 12.8%).

Conclusions.—This study shows improved performance characteristics of cytopathologist-performed UGFNA versus PGFNA.

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Fine-needle aspiration (FNA) originated in the 1930s, and since then it has evolved into a widely used, cost-effective, and minimally invasive diagnostic tool. Pathologist Heinz Grohs, MD, viewed the performance of FNAs "as a natural expansion of the pathologist's supportive role to clinicians in the selection of tests, procurement of specimens, interpretation of

results, and development and teaching of advance diagnostic modalities."[1]

Pathologists who perform FNAs act almost as a "single-operator" model because most are involved in gathering essential history, performing a focused physical exam, performing the aspiration procedure, preparing the slides with rapid on-site evaluation, and ultimately making the diagnosis. Although the practice of FNA by pathologists is now well established, this has been done primarily under palpation guidance on superficial palpable lesions. However, in recent years, increasing numbers of cytopathologists have begun to move beyond palpation-guided FNAs (PGFNAs) and perform ultrasound-guided FNAs (UGFNAs), the latter of which had mainly fallen under the realm of interventional radiologists. This is heralding a new evolution in the performance of FNAs by cytopathologists.

Ultrasound-guided FNA appears to have several advantages over PGFNA, including the ability to target nonpalpable and subcentimeter lesions, a more accurate sampling of heterogeneous lesions, and avoidance of nearby vessels, implants, and other important structures, such as

pleural surfaces. In a study of FNAs performed by head and neck surgeons in an office-based setting, the UGFNA of palpable head and neck lesions resulted in significantly higher diagnostic rates compared with PGFNA.[2] Some reports have discussed the relative ease by which pathologists can acquire the skills to perform UGFNA,[3–5] with some organizations now providing UGFNA courses for pathologists (eg, the College of American Pathologists, the American Society of Cytopathology, and the American Society for Clinical Pathology).[6] Furthermore, recent studies have shown that UGFNAs performed by cytopathologists can yield diagnostic material more often than those done by radiologists or clinicians, such as endocrinologists.[4,7] Although there have been several reports comparing the performance characteristics of FNAs performed by clinicians with versus without ultrasound guidance,[2,8–11] to date only a few studies have directly compared the performance of UGFNA and PGFNA in a setting where both techniques are done by cytopathologists.[12,13]

We report a single-institutional experience of cytopathologist-performed UGFNA and compare that to cytopathologist-performed PGFNA in a variety of anatomic sites. Features such as adequacy rates and discordance rates using primarily corresponding surgical pathology follow-up as the gold standard are evaluated.

MATERIALS AND METHODS

A retrospective study of all FNAs performed by cytopathologists at the University of California, Los Angeles (UCLA) Department of Pathology FNA clinic from January 1, 2010, to June 30, 2015, was performed. The departmental anatomic pathology computer database was searched for all such cases.

Data collected from the pathology reports included: (1) age and sex of patient; (2) location of lesion that underwent FNA; (3) size of lesion; (4) method of FNA performed (palpation guided or ultrasound guided); (5) FNA specimen adequacy status (diagnostic or inadequate/nondiagnostic); and (6) number of FNA passes performed for each procedure. The corresponding results from follow-up surgical pathology (biopsies or excisions), flow cytometry studies, or cytogenetics studies were also searched and, if available, used as the gold standard to determine discordance rate. These parameters for UGFNAs were compared to those for PGFNAs. For purposes of follow-up, the corresponding surgical pathology/flow cytometry/cytogenetics cases had to be performed concurrently or within 1 year after the FNA procedure. Fine-needle aspiration cases performed by nonpathologists were excluded from the study.

Discordance was classified as minor or major. Minor discordance encompassed the following situations: (1) FNA diagnosis of benign/low-grade neoplasm with corresponding surgical pathology/flow cytometry demonstrating a different but also benign/low-grade neoplasm (eg, FNA diagnosis of cellular pleomorphic adenoma and corresponding surgical pathology showing basal cell adenoma); (2) FNA diagnosis of malignant neoplasm with corresponding surgical pathology/flow cytometry/cytogenetics showing a different malignant neoplasm (eg, FNA diagnosis of "salivary gland carcinoma, favor acinic cell carcinoma," and corresponding surgical pathology showing salivary duct carcinoma); and (3) nondiagnostic FNA with corresponding surgical pathology showing benign lesion with inherent low cellularity (eg, pseudocyst). Major discordances included: (1) nondiagnostic FNA with corresponding surgical pathology/flow cytometry diagnosed as malignant; (2) nondiagnostic FNA with corresponding surgical pathology showing a cellular benign/low-grade lesion; (3) benign FNA diagnosis with corresponding surgical pathology/flow cytometry diagnosed as malignant neoplasm; and (4) malignant FNA diagnosis with corresponding surgical pathology/flow cytometry diagnosed as benign lesion. Fine-needle aspiration cases diagnosed as "atypical," without further qualifiers, such as "suspicious for,"

were categorized for concordance purposes as being benign. Fine-needle aspiration diagnoses of "atypical, suspicious for malignancy" or "suspicious for malignancy" were considered concordant with malignant surgical pathology/flow cytometry diagnoses.

The authors defined, a priori, a set of criteria with which to categorize nondiagnostic cases for concordance purposes, based on the "watchful waiting" assumption. We assumed that, in the absence of additional concerning symptoms and signs, a nondiagnostic FNA would likely be followed by a period of watchful waiting of a duration appropriate for each clinical context. Therefore, if an FNA was nondiagnostic and eventual surgical diagnosis was completely benign (no pathologic lesions), the case would be considered concordant, because a clinically reasonable period of watchful waiting following the FNA protected the patient from undergoing unnecessary invasive diagnostics tests. If the FNA was nondiagnostic and surgical diagnosis was a benign lesion with inherent low cellularity, we would categorize this as minor discordance, because the likelihood for the lesion to progress to more concerning pathology would generally be low. If the FNA was nondiagnostic and surgical diagnosis was a cellular benign/low-grade lesion, we would consider this a major discordance because the inherent neoplastic potential would warrant timely escalation to further invasive diagnostic measures. Finally, if the FNA was nondiagnostic and surgical diagnosis was malignant, this would be considered a major discordance. Our discordance analysis was conducted based on these above predefined rationales.

Prior to the introduction of ultrasound guidance into our departmental clinic, FNAs were performed by manual palpation. In 2011, ultrasound guidance began to be incorporated into our practice. Ultrasound-guided FNAs were performed in a dedicated clinic room with the aid of a portable Toshiba Xario (Toshiba America Medical Systems, Tustin, California) ultrasound instrument with a high-resolution linear array small parts transducer, with scanning done at a frequency of 14 MHz. This machine allows for lesion size measurements and for power and color Doppler flow analysis. After informed consent was obtained from patients, the procedures were carried out by cytopathology fellows and, infrequently, pathology residents, under active training and supervision mainly by 4 experienced cytopathology faculty members. (Two of the faculty members underwent certification by the College of American Pathologists Ultrasound-Guided Fine Needle Aspiration program. All 4 faculty members and all cytopathology fellows also shadowed a local pathologist with a successful freestanding FNA clinic and had continual practice with phantoms as part of their training in UGFNA.) Because 1 of these 4 cytopathologists was only present within the institution from the latter half of 2010 to 2011, most of the study period involved 3 cytopathology faculty members. There were also 2 to 3 additional faculty members who had only a few numbers of cases in the clinic.

The UGFNA procedures in our clinic were performed in accordance with the method described by Lieu.[14] Sizes of the FNA needles used ranged in gauge from 23G to 27G and from lengths of 1 inch to 1.5 inches. Prior to procedures, 1 to 1.5 mL of 1% lidocaine (with epinephrine if there were no contraindications) mixed with sodium bicarbonate in a 10:1 ratio was injected into the skin/subcutaneous tissue as local anesthetic.

Statistical analysis for the study was performed using Stata/SE 10.1 (College Station, Texas). Categoric variables were compared using a 2-tailed χ^2 test or Fisher exact test, as appropriate. Non–normally distributed continuous variables were compared using Wilcoxon-Mann-Whitney test. A P value $\leq.05$ was considered statistically significant.

This study was approved by the Institutional Review Board (IRB No. 14-000263).

RESULTS

From January 1, 2010, to June 30, 2015, a total of 1029 FNA cases were performed within the pathology department FNA clinic. Of these, 449 cases (43.6%) were done under ultrasound guidance and 580 (56.4%) were done by
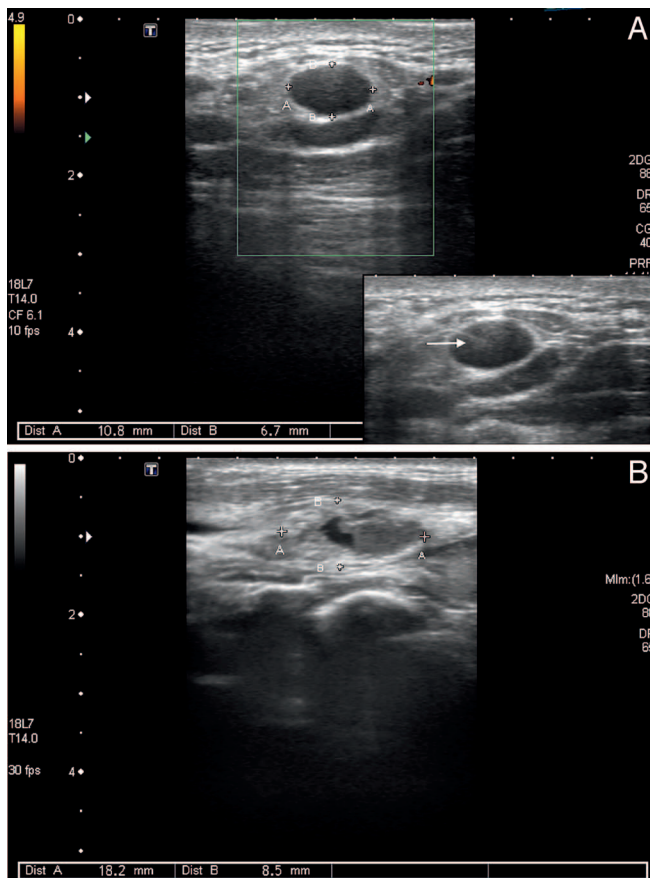
Figure 1. A, Ultrasound image of abnormal neck lymph node, showing loss of central echogenic hilum. Appearance was homogeneous. Inset showing fine-needle aspiration (FNA) needle (arrow) within the lymph node. Power Doppler—seen as a measure of degree of blood flow—showed a lack of signal, and therefore was inconsistent with a vessel. Final diagnosis was B-cell lymphoma. B, Ultrasound image of neck lesion with heterogeneous appearance, including possible central cystic area. Ultrasound allows for targeting of different solid regions of a lesion and avoidance of cystic-appearing areas, which would yield less material during FNA. Final diagnosis was metastatic squamous cell carcinoma.

only palpation guidance. In 2010, all FNAs were performed using only palpation guidance. Ultrasound guidance was incorporated into the clinic practice in 2011, with 29 of 179 FNA cases (16.2%) being performed using that technique

that year. Subsequently, the use of ultrasound guidance increased each year, with the percentage of cases with ultrasound guidance going from 48% (86 of 179) in 2012 to 97% (65 of 67) in the first half of 2015 (Figure 1; Table 1).

The demographics of study participants between those who underwent PGFNA and those who had UGFNA were similar. Of those who underwent PGFNA (580 cases), 277 (47.8%) were male, and of those who underwent UGFNA (449 cases), 195 (43.4%) were male ($P = .17$). In the palpation-guided group, median age was 54.5 years (range, 2–99 years), and in the ultrasound-guided group, median age was 56 years (range, 12–99 years; $P = .12$; Table 2).

In terms of lesion location, head and neck was the most common site that underwent FNAs (475 of 1027 total cases; 46.3%). This included cervical lymph nodes, neck cysts, face and scalp masses, and ear. This was followed by salivary gland (16.5% [169 of 1027] of cases), breast (11.9% [122 of 1027] of cases), and soft tissue lesions (11.1% [114 of 1027] of cases). The thyroid was the site of 9.0% (92 of 1027) of all FNAs. A total of 9 of 579 PGFNAs (1.6%) were from the thyroid, compared with 83 of 448 UGFNA cases (18.5%) being from the thyroid ($P < .001$, χ^2). A total of 85 (14.7%) of the PGFNA cases and 37 (8.3%) of the UGFNA cases were from breast lesions ($P = .002$, χ^2; Table 2). There was no significant difference between percentage of PGFNAs and percentage of UGFNAs that were for head and neck lesions (48.0% [278 of 579] and 44.0% [197 of 448], respectively; $P = .20$, χ^2) and for salivary gland lesions (15.2% [88 of 579] and 18.1% [81 of 448], respectively; $P = .22$, χ^2; Table 2).

Adequacy rates for PGFNAs and UGFNAs were calculated. Cases were classified as either adequate or nondiagnostic/inadequate. Nondiagnostic cases were those with findings that did not show lesional cells that would explain the mass or lesion identified by palpation or ultrasound, such as aspirates yielding only blood or scant incidental stromal fragments. There were a total of 150 nondiagnostic FNA cases (14.6% of total cases) during the study period. Overall, nondiagnostic rate was significantly lower for ultrasound-guided cases (30 of 449 cases; 6.7%) than for palpation-guided cases (120 of 580 cases; 20.7%; $P < .001$; Table 3). When further stratified by lesion site, nondiagnostic rates in ultrasound-guided cases remained significantly lower than in palpation-guided cases for thyroid (6.0% [5 of 83] versus 33.3% [3 of 9]; $P = .03$), head and neck (6.6% [13 of 197] versus 21.2% [59 of 278]; $P < .001$), and salivary gland (6.2% [5 of 81] versus 17.1% [15 of 88]; $P =$

Table 1. Temporal Trends of All Fine-Needle Aspirations (FNAs) Performed at the FNA Clinic					
Year	No. of FNAs Performed	No. (%) of FNA Cases That Are Thyroids[a]	No. (%) of FNAs With Ultrasound Guidance[a]	Nondiagnostic Rate, No. (%)[a]	Follow-up Rate— Includes Histologic/Flow Cytometry/ Cytogenetics, and Nondiagnostic FNA Cases, No. (%)[b]	Discordance Rate— Includes Major and Minor, and Nondiagnostic FNA Cases, No. (%)[c]
2010	260 (25.3)	7 (2.7)	0 (0)	60 (23.1)	114 (43.9)	15/114 (13.2)
2011	179 (17.4)	6 (3.4)	29 (16.2)	28 (15.6)	99 (55.3)	13/99 (13.1)
2012	179 (17.4)	16 (8.9)	86 (48.0)	25 (14.0)	84 (46.9)	5/84 (6.0)
2013	202 (19.6)	38 (18.8)	154 (76.2)	24 (11.9)	94 (46.5)	10/94 (10.6)
2014	142 (13.8)	17 (12.0)	115 (81.0)	8 (5.6)	77 (54.2)	4/77 (5.2)
2015	67 (6.5)	8 (11.9)	65 (97.0)	5 (7.5)	27 (40.3)	0/27 (0)
Overall	1029 (100)	92 (9.0)	449 (43.6)	150 (14.6)	495 (48.1)	47/495 (9.5)

[a] Between-year changes, $P < .001$, 2-tailed χ^2 test.
[b] Between-year changes, $P = .08$, 2-tailed χ^2 test.
[c] Between-year changes, $P = .20$, 2-tailed Fisher exact test.

Table 2. Patient and Lesion Characteristics by Palpation-Guided Fine-Needle Aspiration (FNA) Versus Ultrasound-Guided FNA

	Palpation Only	Ultrasound Guidance	Overall	P Value
Age, y, median (minimum, maximum)	54.5 (2, 99)	56 (12, 99)	55 (2, 99)	.12[a]
Male sex, No. (%)	277/580 (47.8)	195/449 (43.4)	472/1029 (45.8)	.17[b]
Nodule size ≥2 cm, No. (%)[c]	248/470 (52.8)	244/437 (55.8)	492/907 (54.2)	.35[b]
Nodule size ≥1 cm, No. (%)[c]	426/470 (90.6)	403/437 (92.2)	829/907 (91.4)	.40[b]
Body site[d]				Overall, <.001[b]
Head/neck[e]	278/579 (48.0)	197/448 (44.0)	475/1027 (46.3)	
Thyroid	9/579 (1.6)	83/448 (18.5)	92/1027 (9.0)	
Breast	85/579 (14.7)	37/448 (8.3)	122/1027 (11.9)	
Salivary gland[f]	88/579 (15.2)	81/448 (18.1)	169/1027 (16.5)	
Soft tissue[g]	83/579 (14.3)	31/448 (6.9)	114/1027 (11.1)	
Groin	20/579 (3.4)	9/448 (2.0)	29/1027 (2.8)	
Axilla	16/579 (2.8)	10/448 (2.2)	26/1027 (2.5)	

[a] Wilcoxon-Mann-Whitney test.
[b] Two-tailed χ^2 test.
[c] Nodule size was recorded for 907 of 1029 FNA cases.
[d] Body site was recorded for 1027 of 1029 FNA cases.
[e] Head/neck: includes face/scalp, ear, cervical lymph nodes, and neck cysts.
[f] Salivary: includes parotid and submandibular lesions.
[g] Soft tissue: includes from abdomen, chest, back, and extremities.

.03) lesions. A similar but nonsignificant trend was seen for breast lesions (5.4% [2 of 37] versus 18.8% [16 of 85]; P = .09).

Lesions were also assessed with regard to their size. For palpation-guided cases, lesion size was determined by external measurement, whereas for ultrasound-guided cases, lesion size was measured by ultrasound imaging. Of the 1029 total FNA cases performed, nodule size was documented for 907 cases (88.1%), of which 470 underwent only PGFNA and 437 underwent UGFNA. In the palpation-guided group, 426 of 470 cases (90.6%) involved nodules greater than or equal to 1 cm, compared with 403 of 437 cases (92.2%) in the ultrasound-guided group (P = .40; Table 2). Of the cases in which nodules were less than 1 cm in size, 44 underwent only PGFNA and 34 underwent UGFNA. Across all nodule sizes, UGFNA resulted in significantly higher adequacy rates. For nodules measuring less than 1 cm, 17 of 44 palpation-guided–aspirated cases (38.6%) were nondiagnostic, compared with 1 of 34

ultrasound-guided–aspirated cases (2.9%; P < .001). A total of 19.1% (34 of 178) of PGFNA cases versus 8.2% (13 of 159) of UGFNA cases for nodules measuring between 1 and 2 cm in size were nondiagnostic (P = .004). For lesions greater than or equal to 2 cm, 18.2% (45 of 248) of palpation-guided cases and 5.3% (13 of 244) of ultrasound-guided cases were nondiagnostic (P < .001; Table 3).

Inadequacy (nondiagnostic) rates for the cytopathologists were also investigated, showing a significant difference between the attendings (including ones with only a few cases; rates ranged from 9.9% to 37.0%; P < .001, Fisher exact test). For the 3 cytopathologists with the greatest number of cases, respective inadequacy rates were 18.4% (63 of 342), 10.0% (29 of 290), and 9.9% (15 of 152). Over time, these 3 pathologists significantly increased their adoption of ultrasound guidance. Conversely, inadequacy rates of 2 of these attendings significantly declined over time. The trend of decreasing nondiagnostic rate over time was also observed for the third attending, but this did not

Table 3. Sample Adequacy (Nondiagnostic Rate) by Fine-Needle Aspiration (FNA) Technique

Nondiagnostic Rate	Palpation-Guided FNA	Ultrasound-Guided FNA	Overall	P Value
All cases, No. (%)	120/580 (20.7)	30/449 (6.7)	150/1029 (14.6)	<.001[a]
Head/neck cases only	59/278 (21.2)	13/197 (6.6)	72/475 (15.2)	<.001[a]
Thyroid cases only	3/9 (33.3)	5/83 (6.0)	8/92 (8.7)	.03[b]
Breast cases only	16/85 (18.8)	2/37 (5.4)	18/122 (14.8)	.09[b]
Salivary gland cases only	15/88 (17.1)	5/81 (6.2)	20/169 (11.8)	.03[b]
Soft tissue cases only	17/83 (20.5)	4/31 (12.9)	21/114 (18.4)	.43[b]
Groin cases only	5/20 (25.0)	1/9 (11.1)	6/29 (20.7)	.63[b]
Axilla cases only	5/16 (31.3)	0/10 (0)	5/26 (19.2)	.12[b]
Nodule size ≥2 cm cases	45/248 (18.2)	13/244 (5.3)	58/492 (11.8)	<.001[a]
Nodule size ≥1 cm and <2 cm cases	34/178 (19.1)	13/159 (8.2)	47/337 (14.0)	.004[a]
Nodule size <1 cm cases	17/44 (38.6)	1/34 (2.9)	18/78 (23.1)	<.001[b]
FNA passes per case, median (IQR)	4 (3, 5)	5 (4, 6)	4 (3, 5)	<.001[c]

Abbreviation: IQR, interquartile range.

[a] Two-tailed χ^2 test.
[b] Two-tailed Fisher exact test.
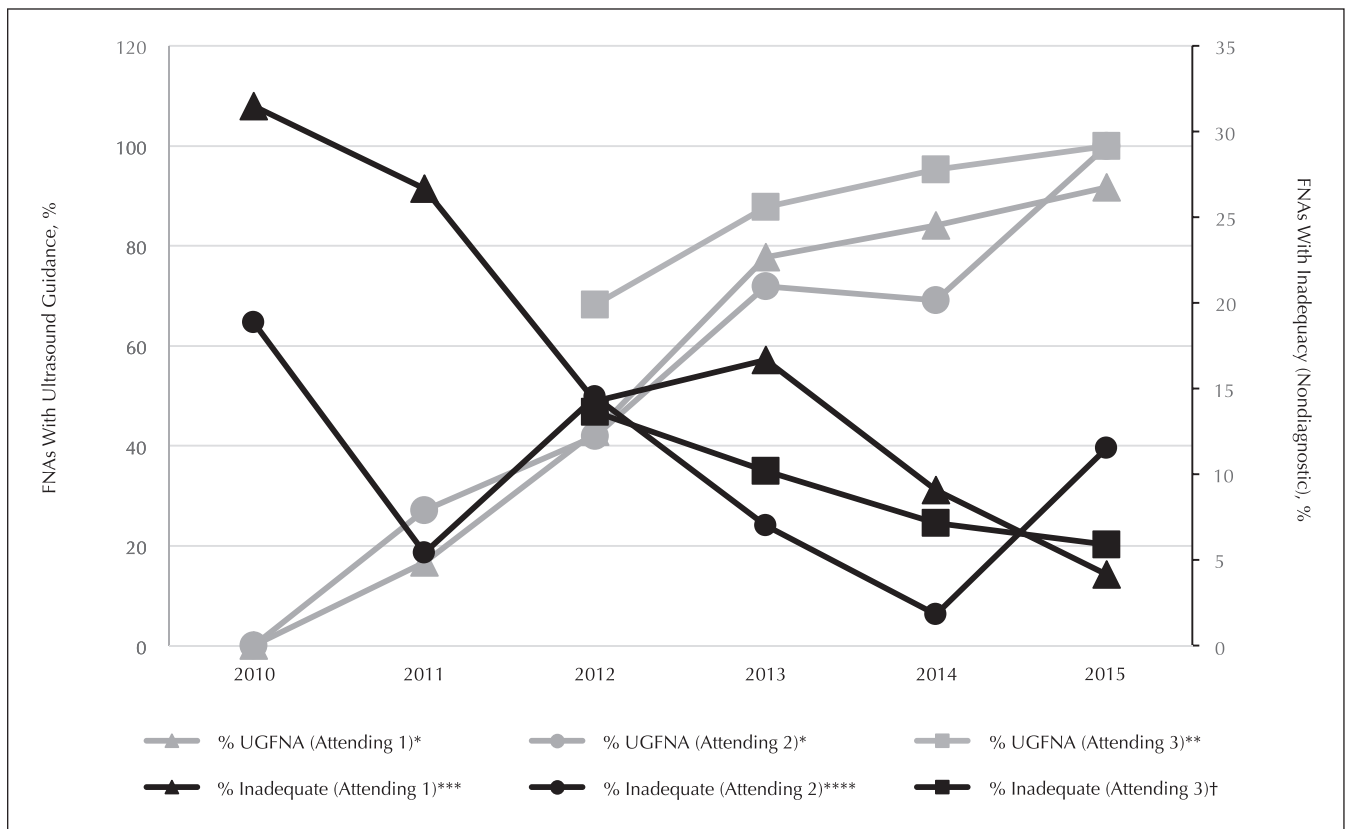[c] Wilcoxon-Mann-Whitney test.

Figure 2. *Trends in ultrasound guidance adoption and inadequacy (nondiagnostic) rates over time for the top 3 cytopathology attendings with the highest case volume. Abbreviations: FNA, fine-needle aspiration; UGFNA, ultrasound-guided FNA. *Between-year comparisons for each attending, P < .001, χ^2 test. **Between-year comparisons for each attending, P =.001, Fisher exact test. ***Between-year comparisons for each attending, P = .009, Fisher exact test. ****Between-year comparisons for each attending, P =.03, Fisher exact test. †Between-year comparisons for each attending, P =.77, Fisher exact test.*

reach statistical significance because this pathologist was part of the FNA clinic for only the last 3 years of the study period (Figure 2).

Surgical pathology (biopsies or excisions), flow cytometry, or cytogenetics follow-up was available for 495 of the 1029 FNA cases (48.1%), with follow-up seen for 273 of 580 palpation-guided cases (47.1%) and 222 of 449 ultrasound-guided cases (49.4%; P = .45). Among these 495 cases, 339 (68.5%) had follow-up in the form of surgical pathology (histology), whereas 155 (31.3%) had only flow cytometry follow-up. One case (0.2%), a biphenotypic leukemia involving left neck lymph node, had follow-up in the form of only cytogenetics testing. Using these follow-up modalities as the gold standard, discordance rates were calculated for PGFNAs and UGFNAs.

Of the 495 cases with follow-up, there were 47 discordant cases (9.5%), 32 of which showed major discordance and 15 of which showed minor discordance (Table 4). A total of 35 of 273 PGFNA cases with surgical/flow cytometry follow-up (12.8%) were discordant, compared with 12 of 222 UGFNA cases (5.4%) with similar follow-up (P = .005). Major discordance was seen in 26 of 273 palpation-guided cases with follow-up (9.5%), compared with 6 of 222 ultrasound-guided cases with follow-up (2.7%; P = .002; Table 4). When stratified by body site, for head and neck lesions, UGFNA cases had a significantly lower rate than PGFNA cases of having any discordance, either major or minor (3.8% [5 of 130] versus 11.0% [16 of 145], respectively; P = .04), and of

having a major discordance (3.1% [4 of 130] versus 9.0% [13 of 145], respectively; P = .048). There was a nonsignificant trend toward lower discordance rate for UGFNA cases compared with PGFNA cases for thyroid lesions (10.0% [1 of 10] versus 57.1% [4 of 7], respectively; P = .10). These trends were not seen for the other body sites (Table 4).

We also conducted a subset analysis to determine whether the differences in concordance rates between UGFNA and PGFNA cases were affected by the nondiagnostic cases. When the nondiagnostic cases were excluded, there remained a trend toward a lower major discordance rate among ultrasound-guided cases (2 of 217; 0.9%) compared with palpation-guided cases (7 of 251; 2.8%), although this trend was no longer statistically significant (P = .19, Fisher exact test). Among the small number of nondiagnostic cases with surgical follow-up (27 cases), the major discordance rate was slightly lower for UGFNA cases (4 of 5; 80.0%) than for PGFNA cases (19 of 22; 86.4%; P > .99, Fisher exact test).

DISCUSSION

Fine-needle aspirations done under ultrasound guidance have been primarily performed by interventional radiologists and endocrinologists. During the past several years, however, pathologists have begun to venture into the realm of UGFNA, with encouraging results. Several recent studies demonstrate that UGFNAs performed by cytopathologists result in greater specimen adequacy than those done by

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Table 4. Follow-up and Discordance Rate by Fine-Needle Aspiration (FNA) Technique Among the 495 Cases With Surgical/Flow Cytometry/Cytogenetics Follow-up, Including Nondiagnostic FNA Cases

	Palpation-Guided FNA (n = 580)	Ultrasound-Guided FNA (n = 449)	Overall (n = 1029)	P Value
Follow-up rate overall, No. (%)	273 (47.1)	222 (49.4)	495 (48.1)	.45[a]
Among those with follow-up, No. (%)				Overall, .07[b]
Surgical—histologic	177 (64.8)	162 (73.0)	339 (68.5)	
Flow cytometry only	95 (34.8)	60 (27.0)	155 (31.3)	
Cytogenetics only	1 (0.4)	0 (0)	1 (0.2)	
Discordance rate, No. (%)				
Any discordance	35/273 (12.8)	12/222 (5.4)	47/495 (9.5)	.005[a]
Major discordance	26/273 (9.5)	6/222 (2.7)	32/495 (6.5)	.002[a]
Minor discordance	9/273 (3.3)	6/222 (2.7)	15/495 (3.0)	.70[b]
By body site, any discordance				
Head/neck cases only	16/145 (11.0)	5/130 (3.8)	21/275 (7.6)	.04[b]
Thyroid cases only	4/7 (57.1)	1/10 (10.0)	5/17 (29.4)	.10[b]
Breast cases only	2/23 (8.9)	2/11 (18.2)	4/34 (11.8)	.58[b]
Salivary gland cases only	7/52 (13.5)	4/47 (8.5)	11/99 (11.1)	.53[b]
Soft tissue cases only	3/23 (13.0)	0/8 (0)	3/31 (9.7)	.55[b]
Groin cases only	1/14 (7.1)	0/8 (0)	1/22 (4.6)	>.99[b]
Axilla cases only	2/9 (22.2)	0/7 (0)	2/16 (12.5)	.48[b]

[a] Two-tailed χ^2 test.
[b] Two-tailed Fisher exact test.

radiologists or clinicians, at least in the setting of thyroid nodules and head and neck lesions.[4,7,15] Moreover, the burgeoning interest in UGFNA has led to reports by some pathology training programs and individual pathologists on their experiences with the technique in pathologist-led clinics.[12–14,16] Although there are studies comparing UGFNA and PGFNA by nonpathologists showing a decrease in specimen inadequacy rates[2,8–11] and increased accuracy rates[9,11] with UGFNA relative to PGFNA, there currently exist only a few such comparison studies for procedures done by cytopathologists.[12,13] The current study aims to further address this latter topic.

Our study demonstrates that for pathologists, one of the major advantages of the addition of ultrasound guidance in FNA performance is to significantly improve the adequacy of FNA specimens. As seen in Table 3, 20.7% (120 of 580) of PGFNA cases were nondiagnostic, compared with only 6.7% (30 of 449) of UGFNA cases ($P < .001$). This pattern was also seen in a similar pathologist study, where the nondiagnostic rate was 12.7% (17 of 134 cases) for the PGFNA cohort and 2.5% (3 of 118 cases) for the UGFNA cohort ($P = .004$).[13] The reduced nondiagnostic rate in our study with ultrasound-guided cases was also observed across all nodule sizes. As was expected, the nondiagnostic rate was highest (38.6% [17 of 44]) for lesions measuring less than 1 cm in size when only palpation guidance was performed. With UGFNAs of these subcentimeter lesions, however, the nondiagnostic rate was significantly lower, at 2.9% (1 of 34; $P < .001$). This illustrates the ability of ultrasound guidance to ensure sufficient evaluation of even the smallest lesions (Figure 3).

We also evaluated adequacy rates when lesions were further stratified by anatomic site. Many of the existing studies comparing PGFNA and UGFNA adequacy rates focused on only one site[8–11] or were limited to a single anatomic region, such as the head and neck.[2,12] In our study, we found that when stratified by lesion site, the trend of lower FNA nondiagnostic rates by UGFNA versus PGFNA

continued to be seen. For head and neck lesions, our study showed a significant reduction in nondiagnostic results with ultrasound guidance compared with manual palpation (21.2% [59 of 278] PGFNA nondiagnostic rate versus 6.6% [13 of 197] UGFNA nondiagnostic rate; $P < .001$). This was also seen with salivary gland lesions (17.1% [15 of 88] PGFNA nondiagnostic rate versus 6.2% [5 of 81] UGFNA nondiagnostic rate; $P = .03$) and for thyroid nodules (33.3% [3 of 9] PGFNA nondiagnostic rate versus 6.0% [5 of 83] UGFNA nondiagnostic rate; $P = .03$; Table 3). Similar low percentages of unsatisfactory/nondiagnostic cases with pathologist-performed UGFNA of thyroid were also reported in other studies, with nondiagnostic rates of 2.6% to 3.2%.[4,7,14]

Our study involved a situation whereby the earlier years comprised almost exclusively palpation-guided cases that gradually transitioned to almost exclusively ultrasound-guided cases by the end of the study period. During the transition period (the middle years of the study), factors such as lesion location, time constraints, and habit may have biased the method choice in favor of palpation guidance. If the lesion was in a location that initially seemed difficult—because of an initial lack of confidence—for needle placement in the presence of an ultrasound transducer or if multiple patients were scheduled one after another, then some of the cytopathologists may have decided to do PGFNA. Over time, these factors became less of a concern because of our increasing ease with UGFNA. The ability to perform FNA needle insertion and movement, smear preparation, and adequacy assessment remained fairly constant over time, however, because the cytopathologists at our institution already had ample experience with FNA performance prior to the study. Furthermore, the cytopathology fellows performed the bulk of the procedures during the academic year, once their attendings deemed them sufficiently capable. The attendings served in mostly a supervisorial role at that point. With each academic year, the same scenario repeated itself. Therefore, it appears that the

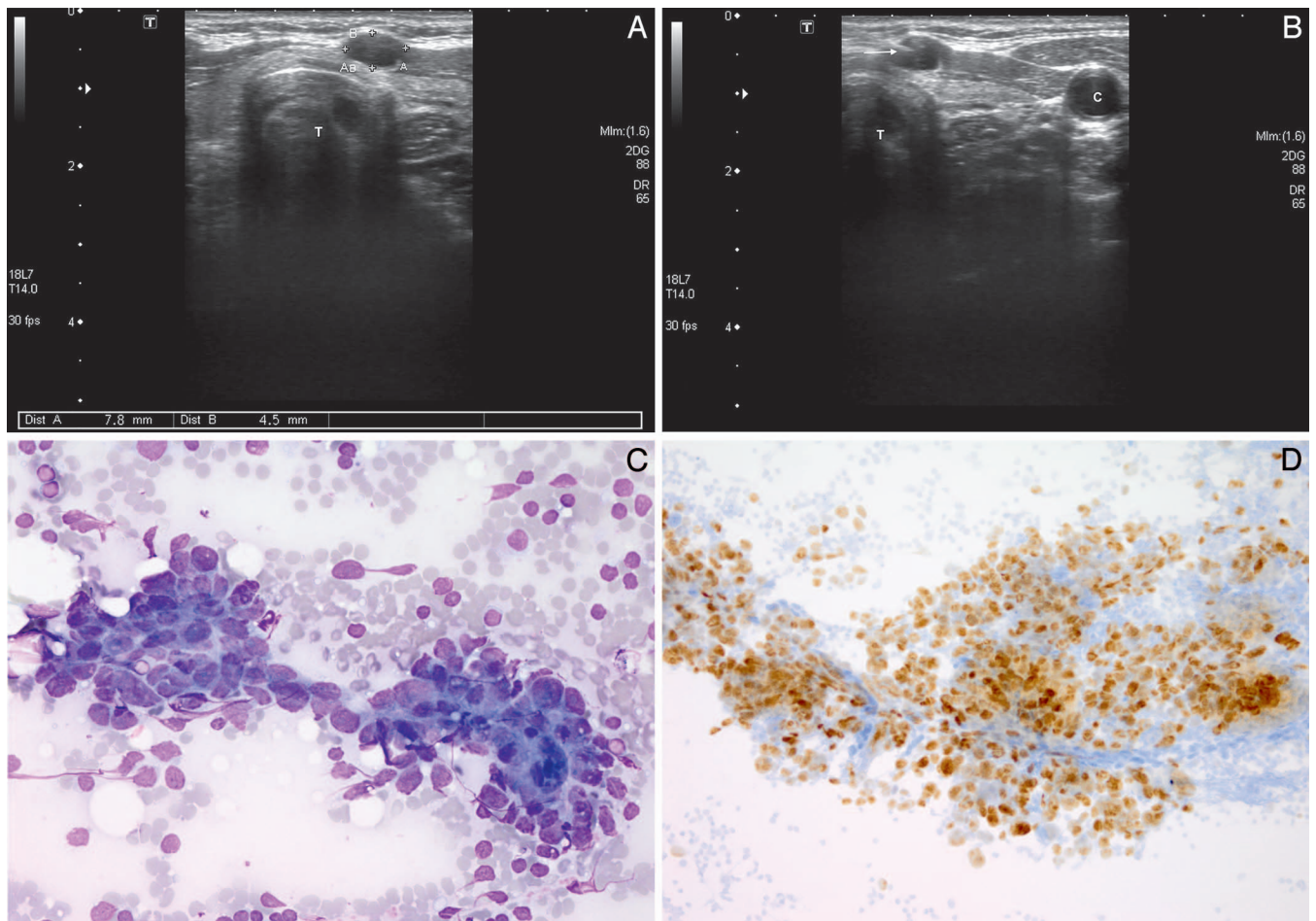*Ultrasound-Guided Versus Palpation-Guided FNA*—Conrad et al   **1265**

Figure 3. A, Ultrasound image showing a subcentimeter hypoechoic, homogeneous nodule at neck level 6, anterior to the trachea (T). Nodule measured 7.8 × 4.5 mm. B, Different ultrasound image of the nodule in A, with the trachea (T) to the left of the field and the carotid artery (C) to the right of the field. Fine-needle aspiration (FNA) needle (arrow) is seen within the nodule. C, Pleomorphic basaloid epithelial cells in cohesive sheet and singly, from ultrasound-guided fine-needle aspiration of the subcentimeter nodule shown in A and B. D, Malignant epithelial cells seen in C were positive for p63 immunohistochemical stain; final diagnosis was metastasis from nasopharyngeal nonkeratinizing squamous cell carcinoma (May-Grünwald Giemsa, original magnification ×400 [C]; original magnification ×200 [D]).

lower nondiagnostic rates with UGFNA compared with PGFNA are mostly attributable to the addition of ultrasound guidance, more than any possible gain in cytopathologist FNA experience over time.

Another issue we explored was whether differences between cytopathologist nondiagnostic/inadequacy rates were confounding factors in our results. When stratifying by the 3 cytopathologists with the greatest numbers of cases, we found that although their overall inadequacy rates differed (ranging from 9.9% to 18.4%), they demonstrated a significant trend toward decreased nondiagnostic rates over time with increasing adoption of ultrasound guidance (Figure 2). This trend is what appears to be driving our study results, regardless of inadequacy rate differences.

There are 2 likely mechanisms by which ultrasound guidance reduces nondiagnostic rates. One would be the ability of ultrasound to allow the FNA operator to visualize the needle to ensure that it is situated within the confines of the lesion during aspiration. This is as opposed to if the needle were situated in the nodule's surrounding soft tissues during the procedure, which may often occur during only palpation guidance. Aspiration of these adjacent soft tissues would very likely yield nondiagnostic specimens. Another

likely explanation for decreased nondiagnostic rates with UGFNAs is the ability of ultrasound to permit visualization and targeting of heterogeneous areas of a lesion. Areas suggestive of necrosis and cystic areas can be avoided, and solid areas of lesions can be preferentially targeted.

Another major advantage of the addition of ultrasound guidance to FNA is increased concordance between the FNA findings and final surgical pathology/flow cytometry/cytogenetic study findings. Our study showed that UGFNAs were associated with a significantly decreased number of discordances, specifically major discordances, between FNA and surgical/flow cytometry follow-up diagnosis (major discordance rate of 9.5% [26 of 273] with palpation versus only 2.7% [6 of 222] with ultrasound guidance; $P = .002$). A limitation in our study, however, was that some of our minor discordance cases (eg, benign/low-grade neoplasm FNA with different benign/low-grade neoplasm on follow-up) were likely due in part to interpretive issues and not solely to sampling issues, because the inability of cytology to completely classify certain neoplasms is well known. Nevertheless, there were only 15 minor discordance cases in our study, with no significant difference in minor discordance rates between UGFNA and PGFNA.

As mentioned earlier, nondiagnostic cases were included in our discordance analysis—27 of 150 nondiagnostic cases (18%) had corresponding follow-up and were included in the analysis. We believed that excluding such cases would result in loss of both patient data and the ability to consider how these cases may contribute to overall discordance rates. On subset analysis in which we excluded the nondiagnostic cases, we found that there remained a trend, albeit no longer statistically significant, toward lower major discordance rate for UGFNA versus PGFNA. This suggests that the differences in discordance rates between the 2 methods are due in part to clinical consequences secondary to reductions in nondiagnostic FNAs with ultrasound.

Another parameter reported in a few studies that examined pathologist-performed UGFNAs is the number of passes required to achieve adequacy. One study of 118 UGFNAs and 134 PGFNAs found that 22 (18.6%) of the UGFNAs were completed—in other words, achieved adequacy—after one pass, as opposed to 6 (4.5%) of the PGFNAs ($P < .001$).[13] Another study also showed favorable UGFNA pass number results, with the mean and median number of passes required to reach adequacy being 1.43 and 1.0, respectively.[16] This illustrates that with UGFNA one can achieve specimen adequacy with just a few passes. In our study, although we documented the number of passes performed per case (Table 3), we unfortunately did not record the pass number at which adequacy was achieved.

Areas of FNA that we did not explore but would be beneficial to investigate in future studies include: (1) performance of UGFNA versus PGFNA for obtaining material for ancillary testing, and (2) "costs" of UGFNA versus those of PGFNA. With regard to the first point, ancillary tests, such as molecular profiling and cytogenetics analyses, are increasingly being requested on cytology specimens to aid in prognostication and prediction of response to therapies. In order to achieve this purpose, cytologic material (smears and/or cell block) would need to have adequate tumor cellularity and purity. With respect to the second point, there are "costs" associated with any procedure, which include time needed to perform the procedure, complication rates, and financial expenses. From the authors' personal experiences, there did not appear to be any differences in degree and amount of procedural complications between UGFNA and PGFNA. For both modalities there seemed to be only a few minor complications, mostly limited to bruising and pain in very occasional cases.

In terms of financial costs, high-quality portable machines that allow for thorough examination of superficial lesions and image capturing have decreased in price and can be had for as little as $15,000.[17] One study that looked at cost considerations in a head and neck office found that offsetting a $30,000 ultrasound machine cost could be achieved with either 406 diagnostic ultrasound–only procedures or 119 UGFNA-only procedures.[18] Dependent on practice volume, this number of UGFNA procedures could potentially be achieved within 1 year. Importantly, one must properly document the FNA technique performed and use proper Current Procedural Terminology (CPT) codes in order to recoup costs. There is a difference in CPT coding between PGFNA (CPT 10021) and UGFNA (CPT 10022, which should be paired with CPT 76942 for ultrasound guidance of needle placement). The CPT code for the diagnostic ultrasound examination itself (eg, CPT 76536 for Head and Neck, which includes thyroid) may also be used in certain situations.[18] As for cost-efficiency, 1 study involving thyroid nodules found that, when taking into account the expense of repeat FNA for initial inadequate results and of surgery for repeat inadequate FNAs, UGFNA was more cost-effective than PGFNA.[9]

In summary, UGFNA is no longer a technique that only radiologists can perform. Pathologists, although they are latecomers to this field, are even better suited for the performance of UGFNA; they are already familiar with the performance of traditional PGFNA, subsequent FNA smear preparation, and on-site adequacy assessment. As shown in the current study and other recent studies by pathology institutions, through proper training, UGFNA in the hands of cytopathologists is relatively easy to implement, can result in increased specimen adequacy rates, and can result in greater concordance rates with the final follow-up pathology results. We are confident that in time, UGFNA will become an integral component of the cytopathologist's skill set.

References

1. Grohs HK. The interventional cytopathologist: a new clinician/pathologist hybrid. *Am J Clin Pathol*. 1988;90(3):351–354.
2. Robitschek J, Straub M, Wirtz E, Klem C, Sniezek J. Diagnostic efficacy of surgeon-performed ultrasound-guided fine needle aspiration: a randomized controlled trial. *Otolaryngol Head Neck Surg*. 2010;142(3):306–309.
3. Abele JS. The case for pathologist ultrasound-guided fine-needle aspiration biopsy. *Cancer*. 2008;114(6):463–468.
4. Bellevicine C, Vigliar E, Malapelle U, et al. Cytopathologists can reliably perform ultrasound-guided thyroid fine needle aspiration: a 1-year audit on 3715 consecutive cases. *Cytopathology*. 2016;27(2):115–121.
5. Jakowski JD, DiNardo LJ. Advances in head and neck fine-needle aspiration and ultrasound technique for the pathologist. *Semin Diagn Pathol*. 2015;32(4):284–295.
6. Lieu D. Breast imaging for interventional pathologists. *Arch Pathol Lab Med*. 2013;137(1):100–119.
7. Wu M, Choi Y, Zhang Z, et al. Ultrasound guided FNA of thyroid performed by cytopathologists enhances Bethesda diagnostic value. *Diagn Cytopathol*. 2016;44(10):787–791.
8. Can A, Peker K. Comparison of palpation-versus ultrasound-guided fine-needle aspiration biopsies in the evaluation of thyroid nodules. *BMC Res Notes*. 2008;1(1):12.
9. Can AS. Cost-effectiveness comparison between palpation- and ultrasound-guided thyroid fine-needle aspiration biopsies. *BMC Endocr Disord*. 2009;9(1):14.
10. Cesur M, Corapcioglu D, Bulut S, et al. Comparison of palpation-guided fine-needle aspiration biopsy to ultrasound-guided fine-needle aspiration biopsy in the evaluation of thyroid nodules. *Thyroid*. 2006;16(6):555–561.
11. Izquierdo R, Arekat MR, Knudson PE, et al. Comparison of palpation-guided versus ultrasound-guided fine-needle aspiration biopsies of thyroid nodules in an outpatient endocrinology practice. *Endocr Pract*. 2006;12(6):609–614.
12. Wu M. A comparative study of 200 head and neck FNAs performed by a cytopathologist with versus without ultrasound guidance: evidence for improved diagnostic value with ultrasound guidance. *Diagn Cytopathol*. 2011;39(10):743–751.
13. Dueber J, Pang JC, Lew M, et al. Value of ultrasound guidance in cytopathologist-performed fine-needle aspirations of palpable lesions. *J Am Soc Cytopathol*. 2015;4(4):195–202.
14. Lieu D. Cytopathologist-performed ultrasound-guided fine-needle aspiration and core-needle biopsy: a prospective study of 500 consecutive cases. *Diagn Cytopathol*. 2008;36(5):317–324.
15. Ganguly A, Burnside G, Nixon P. A systematic review of ultrasound-guided FNA of lesions in the head and neck–focusing on operator, sample inadequacy and presence of on-spot cytology service. *Br J Radiol*. 2014;87(1044):20130571.
16. DiMaggio PJ, Kutler DI, Cohen MA, Chen Z, Hoda RS. Cytopathologist-performed ultrasonography-guided fine-needle aspiration of head and neck lesions: the Weill Cornell experience. *J Am Soc Cytopathol*. 2015;4(6):313–320.
17. Lieu D. Ultrasound physics and instrumentation for pathologists. *Arch Pathol Lab Med*. 2010;134(10):1541–1556.
18. Akbar NA, Bodenner DL, Kim LT, Suen JY, Kokoska MS. Considerations in incorporating office-based ultrasound of the head and neck. *Otolaryngol Head Neck Surg*. 2006;135(6):884–888.