Original Article

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대한영상의학회지

Fine Needle Aspiration Cytology vs. Core Needle Biopsy for Thyroid Nodules: A Prospective, Experimental Study Using Surgical Specimen

갑상선 결절에 대한 세침 흡인 세포 검사와 중심부 바늘 생검의 비교: 수술 검체를 기반으로 한 전향적, 실험적 비교 연구

Hyuk Kwon, MD[1], Jandee Lee, MD[2], Soon Won Hong, MD[3], Hyeong Ju Kwon, MD[4], Jin Young Kwak, MD[1], Jung Hyun Yoon, MD[1]*

Departments of [1]Radiology, Research Institute of Radiological Science and [2]Surgery, Severance Hospital, Yonsei University, College of Medicine, Seoul, Korea
[3]Department of Pathology, Yongin Severance Hospital, Yonsei University, College of Medicine, Yongin, Korea
[4]Department of Pathology, Wonju Severance Christian Hospital, Yonsei University Wonju College of Medicine, Wonju, Korea

Purpose To evaluate and compare the diagnostic outcomes of ultrasonography (US)-guided fine needle aspiration (FNA) and core needle biopsy (CNB) performed on the same thyroid nodule using a surgical specimen for direct comparison.

Materials and Methods We included 89 thyroid nodules from 88 patients from February 2015 to January 2016. The inclusion criterion was thyroid nodules measuring ≥ 20 mm (mean size: 40.0 ± 15.3 mm). Immediately after surgical resection, FNA and subsequent CNB were performed on the surgical specimen under US guidance. FNA and CNB cytopathologic results on the specimen were compared with the surgical diagnosis.

Results Among the 89 nodules, 30 were malignant and 59 were benign. Significantly higher inconclusive rates were seen in FNA for malignant than benign nodules (80.0% vs. 39.0%, $p < 0.001$). For CNB, conclusive and inconclusive rates did not differ between benign and malignant nodules ($p = 0.796$). Higher inconclusive rates were seen for FNA among cancers regardless of US features, and in the subgroup of size ≥ 40 mm (62.5% vs. 22.9%, $p = 0.028$). Eleven cancers were diagnosed with CNB (36.7%, 11/30), while none was diagnosed using FNA.

Conclusion In this experimental study using surgical specimens, CNB showed a potential to provide improved diagnostic sensitivity for thyroid cancer, especially when a conclusive diagnosis is limited with FNA.

Index terms Thyroid Nodule; Thyroid Cancer; Fine Needle Aspiration; Core Needle Biopsy

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***Corresponding author**
Jung Hyun Yoon, MD
Department of Radiology, Research Institute of Radiological Science, Severance Hospital, Yonsei University, College of Medicine, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 03722, Korea.

Tel 82-2-2228-7400
Fax 82-2-2227-8337
E-mail lvjenny@yuhs.ac

ORCID iDs
Hyuk Kwon
https://orcid.org/0000-0001-7018-6363
Jandee Lee
https://orcid.org/0000-0003-4090-0049
Soon Won Hong
https://orcid.org/0000-0002-0324-2414
Hyeong Ju Kwon
https://orcid.org/0000-0002-3603-5032
Jin Young Kwak
https://orcid.org/0000-0002-6212-1495
Jung Hyun Yoon
https://orcid.org/0000-0002-2100-3513

INTRODUCTION

Currently, ultrasonography (US)-guided fine needle aspiration (FNA) is commonly recommended for the preoperative diagnosis of thyroid nodules (1). Studies have shown that 89%–95% of FNA samples are of satisfactory quality for cytologic interpretation (1), and report diagnostic accuracy of 72%–93% for thyroid malignancy (2-4). However, inconclusive cytology results such as non-diagnostic (ND) or atypia of undetermined significance/follicular lesion of undetermined significance (AUS/FLUS) is a major limitation of FNA, that consists of approximately 3%–25% and 6%–18% of all FNA results, respectively (5-9). In nodules with such inconclusive results, repeat US-FNA is recommended for a definitive diagnosis (1), but studies have reported that repeated ND or AUS/FLUS cytology occurs in approximately 17%–47% and 19%–31% of nodules with initial inconclusive diagnosis, respectively (9).

To overcome this limitation of FNA, core needle biopsy (CNB) has been introduced and applied to the diagnosis of thyroid nodules. Studies have reported lower inconclusive rates for CNB compared to repeat FNA (2, 10-13). CNB has higher conclusive rates of 87.9% for initially ND and 68.4% for initial AUS/FLUS nodules compared to repeat FNA (14). Prior studies compared the diagnostic performances between FNA and CNB using outcomes from different study samples, mainly because of difficulties in performing both procedures simultaneously on the same nodule in the clinical setting. One recent study performed both repeat FNA and CNB on the same thyroid nodules, but they had only included nodules that were initially diagnosed as ND or AUS (2), and in which only 48.4% of the study samples were pathologically confirmed by surgery.

With this background, we hypothesized that using surgical specimens after diagnostic lobectomy for simultaneous FNA and CNB would enable us to do a direct comparison between the two diagnostic methods according to final pathology. The purpose of this study was to prospectively evaluate and compare the diagnostic outcomes of FNA and CNB performed on the same thyroid nodule detected on the US using surgical specimens.

MATERIALS AND METHODS

This prospective study was approved by the Institutional Review Board of Severance Hospital, Seoul, Korea (IRB No. 4-2014-1006). Informed consent was obtained from all patients included in this study.

PATIENTS

As US-FNA or CNB was performed on surgical specimens obtained just after lobectomy procedures, we included thyroid nodules more than 20 mm in size since 1) CNB would be appropriate for the diagnosis of large thyroid nodules than small ones, 2) it would be difficult to localize small thyroid nodules in surgical specimens with the US, and 3) nodules of large size would be less affected by surgical procedures such as frozen sections. From February 2015 to January 2016, 89 thyroid nodules fulfilling the size criteria described above from 88 patients were included. Among the 88 patients, 68 (77.3%) were female and 20 (22.7%) were male. The mean age of the 88 patients was 47.9 ± 14.6 years old (range, 17–76 years). The mean size of

the 89 thyroid nodules was 40.0 ± 15.3 mm (range, 20–100 mm). Preoperative *in vivo* FNA or CNB was done in all patients, in which 29 had procedures performed at local clinics. Reasons for surgery were cytopathologic results suggestive or confirming follicular neoplasm (FN), suspicious malignancy, or malignancy on preoperative FNA or CNB, for diagnostic purposes after recurrent inconclusive cytopathology results, large size (over 40 mm) or interval growth on serial studies, symptoms related to the thyroid nodule, and patients' preference to surgery.

PREOPERATIVE US FEATURES

All patients underwent preoperative US evaluation at our institution using a 5–12-MHz linear transducer (iU22 or Epiq 5, Philips Medical Systems, Bothell, WA, USA). US examinations were performed on thyroid nodules and their US features were prospectively recorded into our institutional database by 11 radiologists dedicated to thyroid imaging (4 staff, 7 fellows) with 1–15 years of experience.

The following US features were recorded (15, 16): composition, echogenicity, margin, calcification, and shape. Composition was classified as solid, predominantly solid (solid contents ≥ 50%), or predominantly cystic (solid contents < 50%). Echogenicity was classified as hyperechoic (compared to the surrounding thyroid parenchyma), isoechoic (compared to the surrounding thyroid parenchyma), hypoechoic (compared to the surrounding thyroid parenchyma), or markedly hypoechoic (compared to the strap muscles). Margin was classified as well-circumscribed, microlobulated, or irregular. Calcifications were classified as macrocalcifications, microcalcifications, mixed calcifications, or no calcification. Shape was classified as parallel or non-parallel (when the anteroposterior diameter was greater than the transverse diameter, also called the taller than wide shape). Microlobulated or irregular margins, micro- or mixed calcifications, and the non-parallel shape were considered as suspicious US features. Nodules showing one or more suspicious US features were assessed as 'suspicious malignant', and nodules showing no suspicious US features were assessed as 'probably benign' (1, 16).

ACQUISITION OF FNA AND CNB FROM SURGICAL SPECIMENS

After the thyroid gland with the nodule requiring biopsy was extracted, an US examination was performed to localize the targeted nodule. After the nodule initially detected on the preoperative US examinations was identified on the extracted thyroid gland, FNA and subsequent CNB were performed under US guidance. FNA/CNB was performed by 1 radiologist with 15 years of experience in thyroid imaging (J.Y.K.). FNA was performed twice for each thyroid nodule using a 23-gauge needle attached to a 2 mL syringe. Direct smears were made and immediately placed in 95% alcohol for Papanicolaou staining (17). CNB was performed using an 18-gauge semi-automated core biopsy needle (Stericut biopsy needle, co-axial type; TSK Laboratory, Tochigi, Japan). CNB was performed twice, and core specimens were immediately placed and fixed with formalin solution.

CYTOPATHOLOGIC INTERPRETATION

FNA cytology and CNB pathology slides were reviewed by a cytopathologist (H.J.K.) specializing in thyroid cytopathology with 6 years of experience. The cytopathologist was blind-

ed to the final pathologic diagnosis during the review. FNA cytology was classified into six categories according to the Bethesda system for reporting thyroid cytopathology (18). Because there is no standard reporting system for CNB pathology, the pathologist classified each CNB slide into one of six categories according to the guidelines published by the Korean Endocrine Pathology Thyroid Core Needle Biopsy Study Group (19). The definitions of each diagnostic category for CNB are summarized in Supplementary Table 1 in the online-only Data Supplement.

DATA AND STATISTICAL ANALYSIS

Final surgical pathology was considered as the standard reference for each nodule. For statistical analysis, the diagnostic categories of the Bethesda System were dichotomized into 'conclusive', which included the benign, FN or suspicious FN, suspicious for malignancy, and malignancy categories since subsequent management after these cytologic diagnoses is either follow-up or surgery, and 'inconclusive', which included the ND and AUS/FLUS or indeterminate categories because repeat FNA is usually recommended after these cytologic diagnoses (18). Independent two-sample *t* test was used for continuous variables, and the chi-square test or Fisher's exact test was used for categorical variables. Diagnostic performances including sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were calculated. McNemar's test was used to compare the diagnostic performances between FNA and CNB using SPSS (ver. 26.0, IBM Corp., Armonk, NY, USA) program. *p* values < 0.05 indicated statistical significance.

RESULTS

Among the 89 thyroid nodules, 30 (33.7%) were malignant and 59 (66.3%) were benign. Among the 30 malignant nodules, 5 were conventional papillary thyroid carcinomas (PTCs), 10 follicular variant PTCs, 1 solid variant PTC, 1 diffuse sclerosing variant PTC, 10 minimally invasive follicular carcinomas, 2 medullary carcinomas, and 1 poorly differentiated carcinoma. Among the 59 benign nodules, 34 were adenomatous hyperplasias, 23 follicular adenomas, 1 lymphocytic thyroiditis, and 1 benign nodular hyperplasia. The mean size of the malignant nodules was 34.7 ± 13.1 mm (range, 20–66 mm), and the mean size of the benign nodules was 42.6 ± 15.7 mm (range, 20–100 mm). Mean nodule size was significantly smaller for the malignant nodules than benign nodules ($p = 0.020$). Among the 89 nodules, 46 (51.7%) were more than 20 mm and less than 40 mm in size, and 43 (48.3%) were larger than 40 mm. Based on US features, 65 (73.0%) were assessed as 'probably benign' and 24 (27.0%) were assessed as 'suspicious malignant'.

COMPARISON OF FNA AND CNB RESULTS ACCORDING TO FINAL PATHOLOGY

Table 1 compares FNA and CNB results according to final pathology. None of the nodules was classified as suspicious for malignancy or malignancy using FNA, and none of the nodules was classified into FN or suspicious FN using CNB. With FNA, significantly higher rates of AUS/FLUS (76.7% vs. 27.1%) and FN or suspicious for FN (10.0% vs. 1.7%) were seen in

Table 1. FNA vs. CNB Results according to the Final Pathology for 89 Thyroid Nodules

Final Pathology	Benign (*n* = 59)	Malignancy (*n* = 30)	*p*-Value	Benign (*n* = 59)	Malignancy (*n* = 30)	*p*-Value
Biopsy method	FNA			CNB		
Cytopathology			< 0.001			< 0.001
ND	7 (11.9)	1 (3.3)		2 (3.4)	0 (0.0)	
Benign	35 (59.3)	3 (10.0)		20 (33.9)	0 (0.0)	
AUS/FLUS or indeterminate	16 (27.1)	23 (76.7)		37 (62.7)	19 (63.3)	
FN or suspicious FN	1 (1.7)	3 (10.0)		0 (0.0)	0 (0.0)	
Suspicious for malignancy	0 (0.0)	0 (0.0)		0 (0.0)	7 (23.4)	
Malignancy	0 (0.0)	0 (0.0)		0 (0.0)	4 (13.3)	
Dichotomized cytopathologic categories			< 0.001			0.796
Conclusive	36 (61.0)	6 (20.0)		20 (33.9)	11 (36.7)	
Inconclusive	23 (39.0)	24 (80.0)		39 (66.1)	19 (63.3)	

Percentages are in parentheses.
AUS/FLUS = atypia or follicular lesion of undetermined significance, CNB = core needle biopsy, FN = follicular neoplasm, FNA = fine needle aspiration, ND = non-diagnostic

Table 2. Diagnostic Performance for Malignancy of FNA and CNB in the Surgical Specimen

	FNA (%)	CNB (%)	*p*-Value
Sensitivity	0.0 (0/30)	36.7 (11/30)	-
Specificity	100.0 (59/59)	100.0 (59/59)	-
Negative predictive value	66.3 (59/89)	75.6 (59/78)	0.294
Positive predictive value	-	100.0 (11/11)	-
Accuracy	66.3 (59/89)	78.7 (70/89)	0.381

Raw data are in parentheses.
CNB = core needle biopsy, FNA = fine needle aspiration

malignant nodules than benign nodules. With CNB, higher rates of indeterminate results were observed in malignant nodules than benign nodules (63.3% vs. 62.7%). When assessments were dichotomized into conclusive and inconclusive results, there were significantly higher rates of inconclusive FNA results in malignant nodules than benign nodules (80.0% vs. 39.0%, $p < 0.001$). As for CNB specimens, no significant differences were seen between the conclusive and inconclusive rates for benign and malignant nodules ($p = 0.796$). Diagnostic performances of FNA and CNB on the surgical specimen are summarized in Table 2.

Among the 50 nodules diagnosed as either FN ($n = 33$) or PTC variants ($n = 17$), significantly higher inconclusive rates were seen in PTC variants than FN with FNA (88.2% vs. 57.6%, $p = 0.028$), and in FN than PTC variants with CNB (87.9% vs. 52.9%, $p = 0.006$) (Supplementary Table 2 in the online-only Data Supplement).

COMPARISON OF FNA AND CNB ACCORDING TO US ASSESSMENT

Table 3 compares FNA and CNB results according to US assessment. Among the 65 nodules assessed as probably benign on the preoperative US, 46 were pathologically benign and 19 were malignant. Both FNA and CNB had significantly higher rates of AUS/FLUS (63.1% vs. 21.7%) or indeterminate results (78.9% vs. 54.3%) in malignant nodules compared to benign

Table 3. FNA vs. CNB Results according to the Final Pathology for US Assessments

Probably Benign US Assessment (*n* = 65)						
Final Pathology	Benign (*n* = 46)	Malignancy (*n* = 19)	*p*-Value	Benign (*n* = 46)	Malignancy (*n* = 19)	*p*-Value
Biopsy method	FNA			CNB		
Cytopathology			< 0.001			< 0.001
ND	5 (10.9)	1 (5.3)		2 (4.4)	0 (0.0)	
Benign	31 (67.4)	3 (15.8)		19 (41.3)	0 (0.0)	
AUS/FLUS or indeterminate	10 (21.7)	12 (63.1)		25 (54.3)	15 (78.9)	
FN or suspicious FN	0 (0.0)	3 (15.8)		0 (0.0)	0 (0.0)	
Suspicious for malignancy	0 (0.0)	0 (0.0)		0 (0.0)	4 (21.1)	
Malignancy	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	
Dichotomized cytopathologic categories			0.008			0.120
Conclusive	31 (67.4)	6 (31.6)		19 (41.3)	4 (21.1)	
Inconclusive	15 (32.6)	13 (68.4)		27 (58.7)	15 (78.9)	
Suspicious Malignant US Assessment (*n* = 24)						
Final Pathology	Benign (*n* = 13)	Malignancy (*n* = 11)		Benign (*n* = 13)	Malignancy (*n* = 11)	
Biopsy method	FNA			CNB		
Cytopathology			0.039			0.008
ND	2 (15.4)	0 (0.0)		0 (0.0)	0 (0.0)	
Benign	4 (30.8)	0 (0.0)		1 (7.7)	0 (0.0)	
AUS/FLUS or indeterminate	6 (46.1)	11 (100.0)		12 (92.3)	4 (36.4)	
FN or suspicious FN	1 (7.7)	0 (0.0)		0 (0.0)	0 (0.0)	
Suspicious for malignancy	0 (0.0)	0 (0.0)		0 (0.0)	3 (27.2)	
Malignancy	0 (0.0)	0 (0.0)		0 (0.0)	4 (36.4)	
Dichotomized cytopathologic categories			0.021			0.004
Conclusive	5 (38.5)	0 (0.0)		1 (7.7)	7 (63.6)	
Inconclusive	8 (61.5)	11 (100.0)		12 (92.3)	4 (36.4)	

Percentages are in parentheses.
AUS/FLUS = atypia or follicular lesion of undetermined significance, CNB = core needle biopsy, FN = follicular neoplasm, FNA = fine needle aspiration, ND = non-diagnostic, US = ultrasonography

nodules. With FNA, 3 nodules were classified as FN or suspicious FN, and all 3 were finally diagnosed as malignant: 1 solid variant PTC, 1 follicular variant PTC, and 1 minimally invasive follicular carcinoma. When results were dichotomized as conclusive and inconclusive, malignant nodules had significantly higher rates of inconclusive results than benign nodules (68.4% vs. 32.6%) with FNA ($p < 0.001$). As for CNB, no significant differences were seen between the conclusive and inconclusive rates for benign and malignant nodules ($p = 0.120$).

Among the 24 nodules assessed as suspicious malignant on the preoperative US, 13 were pathologically benign and 11 were malignant. With FNA, significantly higher rates of AUS/FLUS (100.0% vs. 46.1%) were observed in malignant nodules than benign nodules while with CNB, significantly higher rates of indeterminate results (92.3% vs. 36.4%) were observed in benign nodules than malignant nodules. In the dichotomized cytopathologic categories, significantly higher inconclusive FNA rates were seen in malignant nodules than benign nod-

Table 4. FNA vs. CNB Results according to the Final Pathology for Each Size Range

Size ≥ 20 mm, < 40 mm (*n* = 46)						
Final Pathology	Benign (*n* = 24)	Malignancy (*n* = 22)	*p*-Value	Benign (*n* = 24)	Malignancy (*n* = 22)	*p*-Value
Biopsy method	FNA			CNB		
Cytopathologic categories			0.031			0.003
ND	4 (16.7)	1 (4.5)		1 (4.1)	0 (0.0)	
Benign	9 (37.5)	2 (9.1)		7 (29.2)	0 (0.0)	
AUS/FLUS or indeterminate	11 (45.8)	18 (81.9)		16 (66.7)	14 (63.6)	
FN or suspicious FN	0 (0.0)	1 (4.5)		0 (0.0)	0 (0.0)	
Suspicious for malignancy	0 (0.0)	0 (0.0)		0 (0.0)	5 (22.7)	
Malignancy	0 (0.0)	0 (0.0)		0 (0.0)	3 (13.7)	
Dichotomized cytopathologic categories			0.066			0.603
Conclusive	9 (37.5)	3 (13.6)		7 (29.2)	8 (36.4)	
Inconclusive	15 (62.5)	19 (86.4)		17 (70.8)	14 (63.6)	
Size ≥ 40 mm (*n* = 43)						
Final Pathology	Benign (*n* = 35)	Malignancy (*n* = 8)		Benign (*n* = 35)	Malignancy (*n* = 8)	
Cytopathologic categories			0.001			0.003
ND	3 (8.6)	0 (0.0)		1 (2.9)	0 (0.0)	
Benign	26 (74.3)	1 (12.5)		13 (37.1)	0 (0.0)	
AUS/FLUS or indeterminate	5 (14.3)	5 (62.5)		21 (60.0)	5 (62.5)	
FN or suspicious FN	1 (2.8)	2 (25.0)		0 (0.0)	0 (0.0)	
Suspicious for malignancy	0 (0.0)	0 (0.0)		0 (0.0)	2 (25.0)	
Malignancy	0 (0.0)	0 (0.0)		0 (0.0)	1 (12.5)	
Dichotomized cytopathologic categories			0.028			0.985
Conclusive	27 (77.1)	3 (37.5)		13 (37.1)	3 (37.5)	
Inconclusive	8 (22.9)	5 (62.5)		22 (62.9)	5 (62.5)	

Percentages are in parentheses.
AUS/FLUS = atypia or follicular lesion of undetermined significance, CNB = core needle biopsy, FN = follicular neoplasm, FNA = fine needle aspiration, ND = non-diagnostic, US = ultrasonography

ules (100.0% vs. 61.5%, $p = 0.021$). As for CNB in nodules with suspicious US features, benign nodules had significantly higher rates of inconclusive results than malignant nodules (92.3% vs. 36.4%, $p = 0.004$).

COMPARISON OF FNA AND CNB ACCORDING TO SIZE RANGE

Table 4 compares FNA and CNB results according to the size range. Among 46 nodules that were ≥ 20 mm and < 40 mm in size, 24 were pathologically benign and 22 were malignant. With FNA, significantly higher rates of AUS/FLUS (81.9% vs. 45.8%) were observed in malignant nodules than benign nodules. With CNB, higher rates of indeterminate results were observed for benign nodules than malignant nodules (66.7% vs. 63.6%). No significant differences were seen between the conclusive and inconclusive cytopathologic categories according to final pathology for both FNA and CNB ($p = 0.066$ and 0.603, respectively).

Among the 43 nodules that were larger than 40 mm, 35 were pathologically benign and 8

were malignant. With FNA, significantly higher rates of AUS/FLUS were seen in malignant nodules compared to benign nodules (62.5% vs. 14.3%). With CNB, higher rates of indeterminate results were seen in malignant nodules compared to benign nodules (62.5% vs. 60.0%). For the dichotomized conclusive and inconclusive cytopathologic categories, malignant nodules showed a significantly higher rate of inconclusive results than benign nodules with FNA (62.5% vs. 22.9%, $p = 0.028$). No significant differences were seen between the conclusive and inconclusive results according to final pathology for CNB ($p = 0.985$).

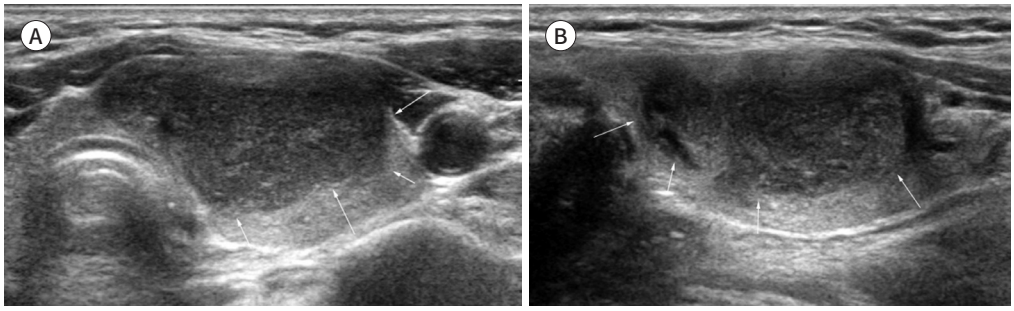
DISCUSSION

In our experimental study using surgical specimens, higher inconclusive rates were observed in malignant nodules with FNA while there was no statistical difference in the results with CNB according to final pathology. Similar trends persisted even when nodules were subgrouped according to preoperative US assessment or nodule size, i.e., a higher inconclusive rate was seen in malignant nodules for FNA, especially for the size larger than 40 mm, but not for CNB. Using CNB, no significant differences were seen between subgroups according to final pathology, except for nodules assessed as suspicious malignant by US features that had a significantly higher rate of inconclusive results in benign nodules.

Our results showing higher inconclusive rates for FNA are consistent with the results of prior studies that also reported higher ND or AUS/FLUS rates for FNA (2, 3, 11-13). In addition, among the 30 cancers in our study sample, none were classified as suspicious for malignancy or malignancy by FNA, while 11 (7 suspicious for malignancy, and 4 malignancy) were classified as these categories by CNB. One hypothesis for the high inconclusive rate for FNA in our study is the experimental setting using surgical specimen in which vascular supply is cut off, and changes in the microenvironment may have interfered with cell retrieval in FNA. Immediate postsurgical changes in the specimen did not critically affect CNB specimen retrieval, supporting that CNB can be considered over FNA when looking for possible ways to improve diagnostic sensitivity for thyroid cancers. Past studies have presented similar results to our findings with CNB showing higher sensitivity over FNA in the diagnosis of thyroid cancer (2, 3, 20, 21). In contrast to FNA, CNB enables a histopathologic diagnosis that explains its higher sensitivity in cancer diagnosis, supported with the higher sensitivity in our results.

For the subgroups divided according to the preoperative US assessment, significantly higher rates of inconclusive results with FNA were seen in malignant nodules than benign nodules (68.4% vs. 32.6%, $p = 0.008$) in nodules with the probably benign US assessment while no significant differences were seen for CNB results according to final pathology ($p = 0.120$). Similar trends were seen for FNA in nodules with suspicious malignant US assessment. But for CNB in nodules with the suspicious malignant US assessment, significantly higher rates of inconclusive results were seen for benign nodules (92.3% vs. 36.4%, $p = 0.004$). Among the 13 benign nodules with suspicious US features, 12 were diagnosed as indeterminate by CNB and the final pathology of all these nodules was benign follicular adenoma (Fig. 1). Although CNB has the potential to improve diagnostic sensitivity for thyroid cancer, higher rates of inconclusive results for thyroid nodules with suspicious US features may lead to more diagnostic surgeries to reach a confirmative benign diagnosis. Pathologic features of FN might con-

Fig. 1. US images of a 56-year-old female.
A, B. A 27-mm-sized thyroid nodule is seen in the left thyroid (A: transverse, B: longitudinal scan), which was assessed as suspicious of malignancy due to the microlobulated margins (arrows) observed on the preoperative US examination. The patient underwent surgery, and FNA/CNB was performed simultaneously on the surgical specimen under US guidance. The FNA result was atypia of undetermined significance, and the CNB result was indeterminate. Based on the final pathology, the nodule was diagnosed as adenomatous hyperplasia.
CNB = core needle biopsy, FNA = fine needle aspiration, US = ultrasonography



tribute to these findings (20, 22), in which CNB cannot provide an accurate differential diagnosis. Given that CNB is mostly performed in clinical situations where the presence of malignancy is suspected and a conclusive diagnosis is required, we need to acknowledge the issues that can occur when diagnosing benign nodules before we choose a biopsy method.

As for nodule size, no significant differences were seen in the conclusive and inconclusive rates for both FNA and CNB in nodules in the 20–40 mm size range. But in nodules larger than 40 mm, a significantly higher inconclusive rate was seen in malignant nodules with FNA while no significant differences were seen between malignant and benign nodules with CNB. High false-negative rates have been reported for FNA in large thyroid nodules (23-27), leading to more surgeries for diagnostic purposes. Based on our findings, CNB shows potential as a tool that allows clinicians to make more conclusive preoperative diagnoses of large thyroid nodules that can guide clinicians when they are deciding on how to approach patient management.

One interesting finding is that none of the 89 nodules were classified as FN or suspicious FN with CNB. Definitions of FN or suspicious for follicular neoplasm for CNB specimens according to the Korean Endocrine Pathology Thyroid Core Needle Biopsy Study Group (19) (Supplementary Table 1 in the online-only Data Supplement) are based on follicular proliferation with the presence of a fibrous capsule, which is relatively hard to include with the limited biopsy angle for US-CNB (28), and this may explain why there were no cases of FN or suspicious FN in the CNB group. Approximately 87.9% of FN had indeterminate CNB results (Supplementary Table 2 in the online-only Data Supplement) and that was the cause for the significantly higher inconclusive CNB results in FN compared to PTC variants. The role of CNB in the diagnosis of FN still needs further investigation.

There are several limitations to this study. First, a relatively small number of patients were included and the inclusion criteria for thyroid nodules was size $\geq$ 20 mm. This size criteria was used since CNB is mostly recommended for large thyroid nodules than subcentimeter nodules and since small nodules would be difficult to localize on the surgical specimen. Second, we used surgically resected specimens for obtaining FNA and CNB cytopathology,

which is quite different from the *in vivo* environment. Also, FNA was evaluated in direct smear during the study period and not in liquid-based preparation. Third, diagnostic sensitivity and rate of the conclusive result of FNA and CNB were lower than generally expected (5-9). Other than using surgical specimen, the inclusion criteria of size ≥ 20 mm may have resulted in the lower diagnostic sensitivity. The risk of follicular cancers and other rare thyroid malignancies which are difficult to diagnose with cytology (29), are known to increase with nodule size (30) as seen by the predominant number of follicular or other cancer types in this study, and this differs from the general population where PTC predominates (31-33). Finally, we used the guidelines published by the Korean Endocrine Pathology Thyroid Core Needle Biopsy Study Group for the pathologic classification of CNB in this study. The diagnostic sensitivity of both FNA and CNB varies depending on what cytopathological criteria is chosen (34), but we did not compare different criteria in this study.

Based on our experimental study, we conclude that CNB has the potential to provide improved diagnostic sensitivity for thyroid cancer, especially where conclusive diagnosis is limited with FNA.

Supplementary Materials

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Author Contributions

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Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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대한영상의학회지

갑상선 결절에 대한 세침 흡인 세포 검사와 중심부 바늘 생검의 비교: 수술 검체를 기반으로 한 전향적, 실험적 비교 연구

권 혁[1] · 이잔디[2] · 홍순원[3] · 권형주[4] · 곽진영[1] · 윤정현[1]*

목적 수술 검체를 사용하여 동일한 갑상선 결절에 시행한 세침 흡인 세포검사와 중심부 바늘 생검의 진단 결과를 비교 평가하고자 하였다.

대상과 방법 2015년 2월부터 2016년 1월까지 88명의 20 mm 이상 크기의 89개의 갑상선 결절이 연구에 포함되었다(평균 크기: 40.0 ± 15.3 mm). 갑상선이 적출된 후 검체에 초음파 보조하에 세침 흡인 검사와 중심부 바늘 생검을 차례대로 시행하였다. 세포 병리 검사 결과는 수술 병리 진단 결과와 비교하였다.

결과 89개의 결절 중 30개는 악성, 59개는 양성이었다. 악성 결절에서 양성 결절보다 유의하게 비진단적 세침 흡인 검사 결과율이 높았다(80.0% vs. 39.0%, $p < 0.001$). 중심부 바늘 생검의 경우 양성과 악성 결절 사이에 결과의 유의한 차이가 없었다($p = 0.796$). 크기가 40 mm 이상인 결절과(62.5% vs. 22.9%, $p = 0.028$) 초음파 소견과는 상관없이, 악성 결절에서 비진단적 세침 흡인 검사 결과율이 높았다. 30개의 갑상선암 중 11개(36.7%)가 중심부 바늘 생검으로 진단되었으나, 세침 흡인 검사에서는 진단된 검체가 없었다.

결론 수술 검체를 이용한 본 실험 연구에서, 중심부 바늘 생검은 갑상선암에 대한 진단적 민감도를 높일 수 있는 가능성이 있는 것으로 생각된다.

연세대학교 의과대학 세브란스병원 [1]영상의학과, [2]외과,
[3]연세대학교 의과대학 용인세브란스병원 병리과,
[4]연세대학교 원주의과대학 원주세브란스기독병원 병리과