

---

# Fine Needle Aspiration of the Thyroid Gland

JONGKOLNEE SETTAKORN, M.D.\*,  
KAMTHORN THAMPRASERT, M.D.\*,  
SAMREUNG RANGDAENG, M.D.\*

BENJAPORN CHAIWUN, M.D.\*,  
WATTANAPORN WISEDMONGKOL, B.B.A.\*

## Abstract

Fine needle aspiration (FNA) has become a major diagnostic triage for clinical management of patients with a thyroid mass. Diagnostic accuracy of this procedure can be evaluated by cyto-histologic correlation. Out of 1,761 fine needle aspirates of thyroid glands performed from January 1996 to December 1999, 230 satisfactory specimens contained respective histologic correlates. Using histologic diagnoses as the gold standard, the overall accuracy, sensitivity and specificity for cytologic diagnoses of thyroid neoplasm were 90.4 per cent, 85.7 per cent, and 92.5 per cent respectively. The positive predictive value for diagnosing thyroid neoplasm was 83.3 per cent while the negative predictive value was 93.7 per cent. The common pairs of cyto-histological diagnostic discrepancy included adenomatous goiter vs follicular neoplasm, adenomatous goiter vs papillary carcinoma, and thyroiditis vs follicular neoplasm. In conclusion, FNA is a rapid, reliable and safe diagnostic tool to distinguish non-neoplastic from neoplastic lesions in patients with thyroid masses.

**Key word :** FNA, Cytology, Thyroid Gland

SETTAKORN J, CHAIWUN B,  
THAMPRASERT K, WISEDMONGKOL W, RANGDAENG S  
J Med Assoc Thai 2001; 84: 1401-1406

Northern Thailand is an area in South East Asia in which endemic goiter is prevalent<sup>(1)</sup>. Headington et al<sup>(2)</sup> studied thyroid glands from surgical removal in this area and were able to demonstrate that there was a higher incidence of nodular goiters,

adenomas, and carcinomas compared with that in the United States. In the United States, the prevalence of thyroid nodules varied from 4 to 7 per cent in the general population<sup>(3-5)</sup> and only a few of these nodules became malignant lesions<sup>(3)</sup>. While only a

---

\* Department of Pathology, Faculty of Medicine, Chiang Mai University, Chiang Mai 50200, Thailand.

few patients with thyroid nodule require surgical intervention, it is the physician's responsibility to filter these patients from a large pool of others with thyroid masses who need only medical treatment. Radioisotope scanning, ultrasonography, and fine needle aspiration (FNA) have been used as the diagnostic triage of thyroid nodules<sup>(6)</sup>. Cytological diagnosis based on FNA material is believed to be the most sensitive and specific test as well as being a safe, simple and cost-effective procedure. Hence, it is widely used as the diagnostic test of choice for evaluating thyroid nodules worldwide<sup>(6)</sup>. FNA was introduced in our institute almost ten years ago. In this study, we analyzed the overall diagnostic efficacy and accuracy of thyroid FNA in our institute during the past four years. The major diagnostic discrepancies were scrutinized and compared with studies from other parts of the world.

## MATERIAL AND METHOD

From January 1996 through December 1999, 1,761 FNA procedures were performed on thyroid lesions. The patient selection was based upon the clinician's discretion. Clinical experience varied from first year resident physicians to senior faculty members. The procedure was done either in the outpatient department or in-patient floors. Specimen procurement and smear preparations were performed by all the mentioned clinicians. The smears were sent to the Department of Pathology, Faculty of Medicine, Chiang Mai University for evaluation. The smears were fixed by isopropanol-based spray fixative with or without accompanying air-dried slides. The fixed slides were stained with Papanicolaou's stain while air-dried specimens were processed under Romanowsky's or Diff-Quik<sup>®</sup> method. A total of 415 FNA patients subsequently underwent thyroidectomy. The decision to perform surgery again was based upon either surgical or cosmetic reasons.

The aspirates from these 415 patients included 185 unsatisfactory and 230 satisfactory cytologies. The histologic diagnoses of those with satisfactory cytology were reviewed and correlated with previous FNA cytological diagnoses that were roughly classified as non-neoplastic and neoplastic groups. Subsequently, each diagnostic group was stratified into specific diagnoses based upon the standard criteria in the literature<sup>(7)</sup>. The "suspicious" lesions were included in the neoplastic group according to the studies of Cersosimo<sup>(8)</sup> and Hersoulis<sup>(9)</sup> that suspicious thyroid cytology yielded 50 per cent and 64.3 per cent malignant histology, respectively.

The diagnostic efficacy of FNA cytological diagnoses including accuracy, sensitivity, specificity, positive predictive value, negative predictive value, false positive rate (FP), and false negative rate (FN) were calculated from these 230 patients using histological diagnoses as the gold standard. The cyto-histological diagnostic discrepancies were divided into major and minor categories. The major discrepancy was defined as non-neoplastic cytologic diagnosis vs neoplastic histological lesion or vice versa, that, inadvertently, led to improper clinical management. The minor discrepancy was clarified as incorrect cytologic diagnosis within groups of non-neoplastic or neoplastic lesions.

## RESULTS

Out of 1,761 aspirates, 389 (22.1%) were considered unsatisfactory or insufficient for cytological diagnosis. A summary of the results is shown in Table 1 and 2, respectively. Using histological diagnosis as the gold standard, those contributing to thyroid nodules included 160 non-neoplastic lesions (NNS) and 70 thyroid neoplasms (TNS). There were 12 false positive cases leading to 92.5 per cent specificity and 83.3 per cent positive predictive value for diagnosis of thyroid neoplasm by FNA. Ten false

Table 1. FNA thyroid glands during 1996-1999, 230 cases.

Cytology	Histology		Total
	Non-neoplasm	Neoplasm	
Non-neoplasm	148	10	158
Neoplasm	12	60	72
Total	160	70	230

**Table 2. Cyto-histocorrelation of FNA thyroid glands during 1996-1999, 230 cases.**

Histology	ADG	DHP*	TDI	FNS	HNS	PTC	MTC	ATC	OMS	Total
Cytology										
ADG	133	3	6	6	-	4	-	-	-	152
DHP	1	-	-	-	-	-	-	-	-	1
TDI	2	-	3	-	-	-	-	-	-	5
FNS	2	1	5	11	1	3	-	-	-	23
HNS	-	-	-	2	2	3	-	-	1**	8
PTC	3	-	-	-	-	19	1	1	-	24
MTC	-	-	-	-	-	-	4	-	-	4
ATC	-	-	1	-	-	-	-	3	-	4
OMS	-	-	-	-	-	1***	-	-	8	9
Total	141	4	15	19	3	30	5	4	9	230

\* Diffuse thyroid hyperplasia \*\* Rhabdomyosarcoma \*\*\* Squamous cell carcinoma

□ Major discrepancy

negative cases yielded 85.7 per cent sensitivity and 93.7 per cent negative predictive value of diagnosis of non-neoplastic lesions. The false positive and false negative rates were 16.7 per cent and 6.3 per cent, respectively.

Among NNS; there were 141 goiters, 4 hyperplasia, and 15 thyroiditis. By FNA, two and three cases of goiter were misdiagnosed as follicular neoplasms (FNS) and papillary thyroid carcinomas (PTC), respectively. One hyperplasia was misdiagnosed as FNS. Five cases of Hashimoto's thyroiditis were misdiagnosed as FNS, whereas, a single case of subacute granulomatous thyroiditis (de Quervian's thyroiditis) was incorrectly classified as anaplastic thyroid carcinoma (ATC).

Among the TNS; there were 19 FNS, including 12 adenomas and 7 carcinomas, 3 Hurthle cell neoplasms (HNS), 30 PTC, 5 medullary carcinomas (MTC), 4 ATC, and 9 other malignant lesions (OMS). Six cases of FNS and four cases of PTC were misclassified as adenomatous goiters by FNA.

The OMS group included two Hodgkin's lymphomas, two metastatic squamous cell carcinomas, one Non-Hodgkin's lymphoma, one meta-

static malignant melanoma, one metastatic adenocarcinoma, one metastatic undifferentiated carcinoma from the nasopharynx, and one rhabdomyosarcoma. There were two interesting cases in this group. The first was a rhabdomyosarcoma misdiagnosed as HNS and the second was one PTC misdiagnosed as squamous cell carcinoma.

## DISCUSSION

The incidence of unsatisfactory or inadequate aspirates in our institute was 22.1 per cent which is higher than reports in the literature that varied from 4.7-18 per cent<sup>(9-12)</sup>. However, Rosen<sup>(13)</sup> and Hatada<sup>(14)</sup> demonstrated even worse unsatisfactory rates of 32 per cent and 30 per cent, respectively. The high unsatisfactory rates usually occurred when the cytopathologists were not the ones who performed the procedure. Hence, it was difficult to judge the specimen adequacy in certain circumstances<sup>(15)</sup>. Although considerable experience is required to obtain adequate material with consistency, it is the intensity of experience rather than the duration of FNA practice that is more important<sup>(16)</sup>. If the tumor is less than 2 cm in diameter, the

Table 3. Diagnostic efficacy of FNA thyroid glands in other countries.

Author	Year	Country	No. of case	Sense (%)	Spec (%)	PV+ (%)	PV- (%)	Acc (%)
Norton LW(17)	1982	USA	21	90.0	77.0	31.0	99.0	79.0
Harsoulis P(9)	1986	Greece	213	89.2	95.4	82.5	97.3	94.2
Rosen IB(13)	1993	Canada	59	90.0	100	100	80.0	85.0
Vargas-Dominguez A(18)	1994	Mexico	107	94.4	53.9	81.0	87.0	85.5
Pomata M(19)	1997	Italy	85	51.8	96.0	87.5	78.6	80.5
Lin JD(20)	1997	Taiwan	378	79.8	98.7	96.3	91.7	92.9
Lopez LH(21)	1997	Mexico	136	90.0	99.8	98.0	99.0	99.0
Leonard N(10)	1997	UK	184	88.0	78.0	46.0	97.0	80.0
Hatada T(14)	1998	Japan	94	45.0	51.0	96.0	55.0	48.0
Al-Rikabi AC(11)	1999	Saudi Arabia	125	78.0	100	100	93.0	94.4
Ersoy E(22)	1999	Turkey	100	45.5	100	100	93.7	94.0
Mikosch P(12)	2000	Austria	718	87.8	78.5	33.5	98.1	79.5
Settakorn J	2000	Thailand	230	85.7	92.5	83.3	93.7	90.4

ultrasound-guided FNA can increase the satisfactory rate and diagnostic accuracy(14).

The efficacy of FNA for diagnosing thyroid lesions in our institute was comparable with that reported by others(9-14,17,19-22) as shown in Table 3. The study of Hatada(14) yielded low efficacy because inadequate cytologic smears were not excluded from the analysis.

The NNS such as goiter, hyperplasia and even thyroiditis can be misinterpreted as a neoplastic lesion if the smear contained highly cellular materials and/or numerous Hurthle cells within a scant colloid background. The high false positive rate in our study (16.7%) arose from inclusion of "suspicious cases" within the neoplastic group. Unlike breast FNA, we feel that it might be safer to have a slightly higher false positive rate in problematic cases for thyroid FNA since thyroidectomy is a relatively safe procedure. Immediate or late surgical treatment for patients with "suspicious" thyroid cytologic results was recommended(8). Patients with a positive FNA can be correctly diagnosed by an intra-operative frozen section and adequately treated while still in the operating room(21).

False negative diagnosis may occur because of sampling error or interpretive error(21). Smears from TNS may contain low cellularity from many causes, such as inexperienced aspirators, massive tumor fibrosis, or cystic degeneration, which may lead to the interpretative error. The experience of the

cytopathologist is also of prime importance. It is thought that examination of 30 to 40 FNA annually should be required to maintain interpretative proficiency(7). FN rates have been reported between 1 per cent to 45 per cent(9-14,17,19-22). Our FP rate, 6.3 per cent, may be high but is better than one half of the previous studies.

Cytologic features of rhabdomyosarcoma in our study were similar to those of HNS. The tumor cells stayed singly and were of oval or round shape. They contained eccentrically located round nuclei and prominent nucleoli. The clue to correct diagnosis was presence of spindle or bizarre malignant cells in rhabdomyosarcoma. The case of papillary carcinoma that was misdiagnosed as squamous cell carcinoma was solely due to an interpretative error.

Our study supports the contention that FNA of the thyroid gland is a reliable method to select or deselect patients with thyroid nodule for surgery. The efficacy of the tool could be improved if the errors were eliminated. The clinicians should frequently practice the procedure to gain more experience. The cytopathologists should be aware of possible diagnostic pitfalls. Of the utmost importance, teamwork of clinicians and pathologists will alleviate misdiagnosis or mismanagement of problematic cases.

#### ACKNOWLEDGEMENT

The authors wish to thank Mr. Sarayut Natri for the collection of the glass slides.

## REFERENCES

1. Nontasuta A. Use of iodate salt in control in endemic goiter. Annual Report of Chiang Mai Division of Public Health 1966; 82-9.
  2. Headington JT, Tantajumroon T. Surgical thyroid disease in Northern Thailand. *Arch Surg* 1967; 95: 157-61.
  3. Rojeski MT, Gharib H. Nodular thyroid disease: evaluation and management. *N Engl J Med* 1985; 313: 428-36.
  4. Van Herle AJ, Rich P, Ljung B-ME, Ashcraft MW, Solomon DH, Keeler EB. The thyroid nodule. *Ann Intern Med* 1982; 96: 221-32.
  5. Vander JB, Gston EA, Dawber TR. The significance of nontoxic thyroid nodules: Final report of a 15-year study of the incidence of thyroid malignancy. *Ann Intern Med* 1968; 69: 537-40.
  6. Gharib H. Fine needle aspiration biopsy of thyroid nodules: Advantages, limitations, and effect. *Mayo Clin Proc* 1994; 69: 44-9.
  7. The Papanicolaou society of cytopathology task force on standards of practice. Guidelines of the Papanicolaou society of cytology for the examination of fine-needle aspiration specimens from thyroid nodules. *Diag Cytopathol* 1996; 15: 84-9.
  8. Cersosimo E, Gharib H, Suman VJ, Goellner JR. "Suspicious" thyroid cytology findings: Outcome in patients without immediate surgical treatment. *Mayo Clin Proc* 1993; 68: 343-8.
  9. Harsoulis P, Leontsini M, Economou A, Gerasimidis T, Smbarounis C. Fine needle aspiration cytology in the diagnosis of thyroid cancer: Comparative study of 213 operated patients. *Br J Surg* 1986; 73: 461-4.
  10. Leonard N, Melcher DH. To operate or not to operate? The value of fine needle aspiration cytology in the assessment of thyroid swelling. *J Clin Pathol* 1997; 50: 941-3.
  11. Al-Rikabi AC, Al-Omran M, Cheema M, El-Khwsy F, Al-Nuaim A. Pattern of thyroid lesions and role of fine needle aspiration cytology (FNA) in the management of thyroid enlargement: A retrospective study from a teaching hospital in Riyadh. *Acta Pathol Mikrobiol Immunol Scand* 1998; 106: 1069-74.
  12. Mikosch P, Gallowitsch HJ, Kresnik E, et al. Value of ultrasound-guided fine-needle aspiration biopsy of thyroid nodules in an endemic goiter area. *Eur J Nucl Med* 2000; 27: 62-9.
  13. Rosen IB, Azadian A, Walfish PG, Salem S, Lansdown E, Bedard YC. Ultrasound-guided fine needle aspiration biopsy in the management of thyroid disease. *Am J Surg* 1993; 166: 346-9.
  14. Hatada T, Okada K, Ishii H, Ichii S, Utsunomiya J. Evaluation of ultrasound-guided fine needle aspiration biopsy for thyroid nodules. *Am J Surg* 1998; 175: 133-6.
  15. Altavilla G, Pascale M, Nenci I. Fine needle aspiration cytology of the thyroid gland diseases. *Acta Cytol* 1990; 34: 251-6.
  16. Hall TL, Layfield LJ, Philippe A, Rosenthal DI. Sources of diagnostic error in fine needle aspiration of the thyroid. *Cancer* 1989; 63: 718-25.
  17. Norton LW, Wangenstein SL, Davis JR, Paplanus SH, Werner SC. Utility of thyroid aspiration biopsy. *Surgery* 1982; 92: 700-5.
  18. Vargas-Dominguez A, Arellano S, Alnoso P, Viramontes Madrid JL. Sensitivity, specificity and predictive values of fine-needle biopsy in thyroid cancer. *Gac Med Mex* 1994; 130: 55-8.
  19. Pamata M, Pisano G, Pili A, Daniele GM. Results of a cytological study of needle aspiration in 85 cases of nodular pathology of the thyroid gland, surgically controlled. *Ann Ital Chir* 1997; 68: 29-34.
  20. Lin JD, Huang BY, Weng HF, Jeng LB, Hsueh C. Thyroid ultrasonography with fine needle aspiration cytology for diagnosis of thyroid cancer. *J Clin Ultrasound* 1997; 25: 111-8.
  21. Lopez LH, Canto JA, Herrera MF, et al. Efficacy of fine-needle aspiration biopsy of thyroid nodules: Experience of a Mexican institution. *World J Surg* 1997; 21: 408-11.
  22. Ersoy E, Taneri F, Tekin E, et al. Pre-operative fine-needle aspiration cytology *versus* frozen section in thyroid surgery. *Endocr Regul* 1999; 33: 141-4.
-

## การใช้เข็มเล็กเจาะดูดต่อมธัยรอยด์

จกกลณี เศรษฐกร, พ.บ.\*, เบญจพร ไชยวรรณ, พ.บ.\*,  
ก่าธร ธรรมประเสริฐ, พ.บ.\*, วัฒนาพร วิเศษมงคล, บ.ธ.บ.\*, สำเริง รวงแดง, พ.บ.\*

เพื่อที่จะประเมินความถูกต้องแม่นยำของเซลล์วิทยาวินิจฉัยจากการเจาะดูดด้วยเข็มเล็ก ในการวินิจฉัยรอยโรคที่ต่อมธัยรอยด์ของผู้ป่วยโรงพยาบาลมหาราชนครเชียงใหม่ จึงได้รวบรวมผลการวินิจฉัยทางเซลล์วิทยาจากการเจาะดูดด้วยเข็มเล็กของผู้ป่วยจำนวน 1,761 ราย ระหว่างเดือนมกราคม 2539 ถึง เดือนธันวาคม 2542 ในจำนวนนี้มีผู้ป่วย 230 ราย ที่ได้รับการรักษาด้วยการผ่าตัดต่อมธัยรอยด์ เมื่อใช้การวินิจฉัยทางฮิสโตโลยีของต่อมธัยรอยด์เป็นมาตรฐาน พบว่า ค่าความถูกต้อง ความแม่นยำและความเฉพาะเจาะจง ของเซลล์วิทยาวินิจฉัยจากการเจาะดูดด้วยเข็มเล็ก ในการวินิจฉัยโรคเนื้องอกที่ต่อมธัยรอยด์ มีค่า 90.4%, 85.7% และ 92.5% ตามลำดับ ส่วนความแม่นยำในการทำนายผลบวกและผลลบ มีค่า 83.3% และ 93.7% ตามลำดับ รอยโรคที่พบบ่อยกว่าการวินิจฉัยทางเซลล์วิทยาไม่ตรงกับฮิสโตโลยีได้แก่ adenomatous goiter กับ follicular neoplasm, adenomatous goiter กับ papillary carcinoma, และ thyroiditis กับ follicular neoplasm โดยสรุป เซลล์วิทยาวินิจฉัยจากการเจาะดูดด้วยเข็มเล็ก เป็นวิธีที่สะดวก รวดเร็ว น่าเชื่อถือ และปลอดภัย สำหรับวินิจฉัยแยกโรคเนื้องอกออกจากโรคที่ไม่ใช่เนื้องอกของต่อมธัยรอยด์

**คำสำคัญ :** การเจาะดูดด้วยเข็มเล็ก, เซลล์วิทยาวินิจฉัย, ต่อมธัยรอยด์

จกกลณี เศรษฐกร, เบญจพร ไชยวรรณ,

ก่าธร ธรรมประเสริฐ, วัฒนาพร วิเศษมงคล, สำเริง รวงแดง

จดหมายเหตุมหาวิทยาลัยฯ 2544; 84: 1401-1406

\* ภาควิชาพยาธิวิทยา, คณะแพทยศาสตร์ มหาวิทยาลัยเชียงใหม่, เชียงใหม่ 50200