

Frozen section in thyroid surgery: Is it a necessity?

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Introduction: Many surgeons use intraoperative frozen-section (FS) biopsy of thyroid nodules to predict malignant disease, but the findings are often not in agreement with those of fine-needle aspiration (FNA) biopsy. Our objective in this study was to assess the value of intraoperative FS biopsy in patients with nodular disease of the thyroid gland. **Methods:** In this study, 203 patients underwent thyroid surgery at the Ankara Oncology Hospital. Nodules were assessed by FNA biopsy preoperatively, by FS intraoperatively and by histologic examination of the excised specimen. Sensitivity, specificity and accuracy were determined for FS and FNA with respect to the histologic findings. **Results:** The sensitivity, specificity and accuracy rates for FNA, excluding occult cancers, were 74.1%, 100% and 95.2%, respectively, and for FS were 87.1%, 100% and 97.8%, respectively. FS influenced operative decisions in 0.6% of nodules found to be benign by FNA and in 20% of nodules found to be suspicious by FNA. FS contributed nothing for FNA-malignant disease since all the results in this group were true positive. **Conclusions:** Intraoperative FS was most helpful when the FNA findings were suspicious for malignant disease. FS does not seem to be necessary when FNA indicates malignant or benign disease. Both FNA and FS failed to detect occult thyroid carcinomas.

Introduction : Beaucoup de chirurgiens utilisent la biopsie sur coupe congelée (CC) de nodules thyroïdiens pendant l'intervention pour prédire l'existence d'une tumeur maligne, mais il arrive souvent que les constatations ne concordent pas avec ceux d'une biopsie par aspiration à l'aiguille fine (AAF). Cette étude visait à évaluer la valeur de la biopsie CC intraopératoire chez les patients ayant des nodules à la thyroïde. **Méthode :** Au cours de cette étude, 203 patients ont subi une intervention chirurgicale à la thyroïde à l'Hôpital d'oncologie d'Ankara. Les nodules ont été évalués par biopsie AAF avant l'intervention, par biopsie CC pendant l'intervention et par examen histologique du spécimen excisé. On a déterminé la sensibilité, la spécificité et l'exactitude des techniques CC et AAF par rapport aux résultats histologiques. **Résultats :** La sensibilité, la spécificité et la précision de la technique AAF, sauf dans le cas des cancers occultes, se sont établies à 74,1 %, 100 % et 95,2 % respectivement, et à 87,1 %, 100 % et 97,8 % respectivement dans le cas de la technique CC. La technique CC influé sur la décision d'opérer dans 0,6 % des cas de nodules jugés bénins par la technique AAF et dans 20 % de ceux que l'on a jugés douteux par la même technique. La technique CC n'a apporté aucune contribution dans le cas de la tumeur maligne déterminée par AAF puisque tous les résultats de ce groupe étaient réellement positifs. **Conclusions :** La technique CC intraopératoire s'est révélée des plus utiles lorsque les résultats de la technique AAF laissaient soupçonner une tumeur maligne. La technique CC ne semble pas nécessaire lorsque la technique AAF indique l'existence d'une tumeur maligne ou bénigne. Les deux techniques, soit AAF et CC, n'ont pas détecté de cancer occulte de la thyroïde.

Thyroid nodules, a feature of many thyroid disease processes, are mostly benign and are discovered by the patient or during a medical examination. Often these nodules can be managed conservatively. The clinical problem is to identify malignant lesions that require surgical excision. The most cost-effective test for evaluating thyroid masses is fine-needle aspiration (FNA) biopsy, the accuracy of which exceeds 80% in most series.¹ Many surgeons use intraoperative frozen-section (FS) biopsy to confirm the FNA biopsy findings

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Accepted for publication Nov. 3, 2003.

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and to guide the extent of thyroidectomy.² Surgeons may be faced with a difficult decision when the FNA and FS diagnoses are discordant. The role of FS has been criticized by some authors who have found no or little difference in sensitivity, specificity and accuracy between FS and FNA biopsies, and some have recommended against the routine use of FS due to cost-ineffectiveness.³ The purpose of our study was to assess the value of FS in predicting malignancy in patients with nodular thyroid disease.

Patients and methods

Between July 1990 and December 2001, 203 patients underwent surgery for thyroid nodules at the Ankara Oncology Hospital. Most patients had thyroid goitre and were referred because malignant disease was suspected on clinical grounds. The diagnosis was made both by FNA preoperatively and by FS intraoperatively. FNA biopsies were obtained with the use of 24-gauge needles; the specimens were stained and interpreted in the conventional manner.⁴ The prominent nodule of multinodular goitre or a solitary nodule was sampled by FNA and FS. The final histopathological diagnosis of thyroidectomy specimens was available in all patients. The cytologic findings for FNA were classified as follows: 1, benign; 2, suspicious; 3,

malignant; and 4, inadequate for evaluation. FS biopsy findings were categorized as 1, benign; 2, malignant; and 3, deferred. All FS and histologic diagnoses were from our laboratory; fine-needle aspirates were evaluated by several pathologists at our hospital and outside.

Sensitivity, specificity and diagnostic accuracy were assessed for FNA and FS procedures. The results were given as follows.

- True positive: a result positive for malignancy with subsequent final histopathological confirmation
- True negative: a result negative for malignancy with definitive histopathological confirmation
- False positive: a result that was positive for malignancy but with no evidence of carcinoma on histopathological examination
- False negative: a result that was negative for malignancy but with a diagnosis of malignant disease on histopathological assessment

Sensitivity was defined on the basis of thyroid cancer detected with FNA or FS technique: true positive/[true positive + false negative]. Specificity was defined on the basis of the detection of benign thyroid disease: true negative/[true negative + false positive]. Diagnostic accuracy represented the combination of sensitivity and specificity: [true positive + true negative]/[true positive + false positive +

true negative + false negative].

Minimal or occult microcarcinomas of the thyroid are defined as tumours 1 cm or smaller in dimension without evidence of capsular invasion and not associated with lymph-node metastases. They are nonpalpable and usually found incidentally at surgery or on pathological examination. There is controversy about their management and the importance of identifying them.^{5,6} Sensitivity, specificity and diagnostic accuracy of FNA and FS biopsies were assessed separately, including and excluding occult carcinomas.

Results

The series comprised 157 women (77.3%) and 46 men (22.7%); the mean (and standard deviation) age was 46.1 (13.5), ranging from 13 to 76 years. Malignant disease was encountered in 48 patients (23.6%). The final or definitive histopathological diagnoses are shown in Table 1.

Fine-needle aspiration biopsy

On the basis of the FNA biopsy, 23 (11.3%) patients had findings of malignant disease, 152 (74.9%) had a benign specimen, 20 (9.8%) had findings that suggested malignant disease, and 8 (3.9%) had inadequate findings. Table 2 shows FNA results

Table 1

Final Histopathological Diagnosis in 203 Patients With Thyroid Nodular Disease

Diagnosis	Patients, no. (and %)
Malignant	48 (23.6)
Papillary carcinoma	23 (11.3)
Follicular carcinoma	4 (2.0)
Follicular variant of papillary carcinoma	6 (3.0)
Hürthle cell carcinoma	1 (0.5)
Anaplastic carcinoma	8 (3.9)
Thyroid lymphoma and others	6 (3.0)
Benign	155 (76.4)

Table 2

Results of Preoperative Fine-Needle Aspiration (FNA) Biopsy and Frozen-Section Biopsy in 203 Patients With Thyroid Nodular Disease and Correlation With the Final Histopathological Findings

FNA biopsy, no. (and %) of patients	Frozen-section biopsy, no. of patients	Final histopathological findings, no. of patients
23 (11.3) malignant	22 malignant 1 deferred	22 malignant 1 malignant
152 (74.8) benign	1 malignant 145 benign 6 deferred	1 malignant 138 benign, 7 malignant (4 OPC) 5 malignant (1 OPC), 1 benign
20 (9.9) suspicious	4 malignant 11 benign 5 deferred	4 malignant 10 benign, 1 malignant 5 malignant
8 (3.9) inadequate	7 benign 1 deferred	5 benign, 2 malignant (2 OPC) 1 benign

OPC = occult papillary carcinoma.

and their correlation with the FS and histopathological diagnoses. In all 23 patients reported to have malignant disease by FNA, the malignancy was confirmed by final pathological examination (i.e., there was no false-positive FNA result). Their FS diagnoses were malignant for 22 patients and deferred for 1.

Among the 152 patients classified as having benign nodules by FNA biopsy, the final histopathological examination diagnosed malignant disease in 13 (8.6%); of these, occult papillary carcinoma was diagnosed in 5, papillary carcinoma in 2, a follicular variant of papillary carcinoma in 5 and follicular carcinoma in 1. In the FNA-benign group, FS biopsy reported only 1 (0.6%) patient with malignant disease (a papillary carcinoma) out of the 13 patients. FS diagnosis was deferred for 6 patients. The final histopathological diagnosis was malignant disease in 5 of these of whom 1 had occult papillary carcinoma (Table 2).

FS biopsy of the 20 patients with FNA-suspicious nodules revealed 4 (20%) cases of malignant disease, which was confirmed by postoperative histopathological diagnosis (1 follicular, 1 medullary, 2 anaplastic carcinomas). In 11 patients whose specimen was reported as benign by FS, 1 had a papillary carcinoma. In 5 patients, the FS diagnosis was deferred, and the histopathological examination revealed that all had malignant disease (1 papillary carcinoma, 1 follicular carcinoma, 1 papillary carcinoma follicular variant, 1 medullary carcinoma, 1 Hürthle cell carcinoma) (Table 2).

Although we repeated the FNA, the biopsy specimen was inadequate for a diagnosis in 8 patients; 2 of them were found to have occult papillary carcinoma on histopathological examination. For these 8 patients, the FS biopsy specimen was reported as benign in 7, and the diagnosis was deferred for 1 patient, whose tissue was benign on histopathological examination.

Frozen-section biopsy

FS biopsy results showed malignant disease in 27 (13.3%) of the 203 patients (the diagnosis was confirmed by histopathological examination), as benign disease in 173 (85.2%), but in 10 (5.8%) of these histopathological examination diagnosed malignant disease (6 occult papillary carcinomas, 2 papillary carcinomas, 1 follicular variant of papillary carcinoma and 1 follicular carcinoma). When the occult cancers are excluded, the rate drops to 2.3%. The preoperative FNA results in these 4 patients reported benign disease in 3 patients and “suspicious” in 1.

FS biopsy recognized malignant disease in 22 (95.6%) of 23 patients reported to have malignant disease by FNA biopsy, in 1 (0.6%) of 152 with FNA-benign disease and in 4 (20%) of 20 patients with FNA-suspicious disease. In other words FS biopsy recognized 4 suspicious specimens and 1 false-negative FNA biopsy specimen as malignant. Seven patients in this series had occult papillary thyroid carcinomas, and neither FNA nor FS could reveal them.

Overall sensitivities for FNA and FS were 63.8% and 72.9% respectively; specificities were 100% for both and diagnostic accuracy was 92.5% and 94.4% respectively. When occult carcinomas were excluded, sensitivity, specificity and accuracy rates for FNA reached 74.1%, 100% and 95.2%, re-

spectively and for FS 87.1%, 100% and 97.8%, respectively (Table 3).

Discussion

FNA cytology of thyroid nodules has been shown to be safe, accurate and superior to clinical assessment in cases of malignant thyroid disease.^{2,7} Many surgeons prefer to confirm all diagnoses of neoplasia made by FNA biopsy by intraoperative FS examination,⁸ but the role of FS has been debated in the literature; some authors have found no or little difference in sensitivity, specificity or accuracy between the 2 techniques^{3,6} (Table 3). FS increases operating time and expenditure, and its necessity is still uncertain.⁹ The surgeon may be faced with a difficult decision when the results of FNA and FS biopsies are discordant.⁸

In this study, FNA biopsy results in 23 (11.3%) patients were reported to be malignant and malignancy was confirmed by final pathological examination in all; FS reported 22 of them as malignant. FS sensitivity for the FNA-malignant group was 100%, but FNA was always correct and FS contributed nothing and did not alter surgical decisions in this group.

Thirteen of 152 patients who were reported to have benign disease by FNA were confirmed to have malignant disease by histopathological examination. FS reported only 1 patient with malignant disease out of

Table 3
Sensitivity, Specificity and Diagnostic Accuracy of Fine-Needle Aspiration Biopsy and Frozen-Section Biopsy in Patients With Thyroid Nodular Disease Compared With That in the Literature

Biopsy technique	Sensitivity, %	Specificity, %	Accuracy, %
Fine-needle aspiration			
Present series, overall	63.8	100	92.5
Present series, excluding occult carcinomas	74.1	100	95.2
Range in the literature	80-93.5	56-94	79.6-92
Frozen section			
Present series, overall	72.9	100	94.7
Present series, excluding occult carcinomas	87.1	100	97.8
Range in the literature	60-93	97-100	92-97

these 13 patients and diagnosis was deferred for 6 cases. The sensitivity of FS for the FNA-benign group was 25% even when 5 occult cancers were excluded, so the contribution of FS in this group was also small. This could be explained by the fact that in follicular neoplasms and Hürthle cell neoplasms diagnosis depends on demonstrating capsular or vascular invasion, which is not possible by FNA and FS.¹⁰⁻¹² There is also difficulty in diagnosing the follicular variants of papillary carcinoma by FNA and FS biopsy because its cytomorphic features overlap with those of benign and neoplastic follicular lesions; the follicular variant contains very few of the nuclear features characteristic of papillary carcinoma and may be missed by both techniques.¹³ Freezing may induce cellular distortion making differentiation even more difficult.¹²

FNA biopsy findings showed that 20 patients had specimens that were suspicious for malignant disease, and 4 of these were reported to be malignant by FS. FS sensitivity for the FNA-suspicious group was 80%, which was parallel to that reported in the medical literature³ (Table 3 and Table 4). For the present series FS influenced the operative decision in 20% of cases. From these results we concluded that FS was most helpful in recognizing malignancy when the FNA results were suggestive of malignancy.

In the inadequate FNA group of 8 patients, in which 2 were eventually found to have occult papillary carcinoma, FS biopsy reported 7 benign

results and 1 deferred result. The small group size and lack of invasive cancer prevented any conclusion as to the need for FS biopsy. Most authors recommend either FS or touch imprint cytology if FNA is inadequate.¹⁴⁻¹⁶

In this series, neither FNA nor FS demonstrated the 7 cases of occult thyroid carcinoma. Occult carcinomas are difficult to diagnose by cytologic methods and some recommend ultrasound-guided FNA biopsy.¹⁷

Overall FNA sensitivity in our series was lower than that reported in the literature (63.8%), whereas FS sensitivity (72.9%) was within the reported range³ (Table 3 and Table 4). In the present study, suspicious findings were considered separately from clearly malignant and benign FNA findings, and when occult carcinomas were excluded, sensitivity rates for FNA reached 74.1% and FS, 87.1%.

Many recent papers report results similar to ours; i.e., when FNA was sufficient (benign or malignant), FS did not contribute more.^{18,19} Some prefer to add intraoperative touch imprint cytology to FS; others suggest imprint cytology as an alternative to FS and recommend it especially for small hospitals lacking the facilities for FS examination.¹⁵

Conclusions

FNA and FS were found to be specific, accurate and sensitive diagnostic procedures in evaluating thyroid nodules. Intraoperative FS biopsy was most helpful for patients with suspicious FNA biopsy findings. Pres-

ent data also suggest that FS biopsy is not necessary when FNA biopsy gives a malignant or benign diagnosis. Both techniques fail to reveal occult carcinomas of the thyroid.

Competing interests: None declared.

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Table 4

Sensitivity, Specificity and Diagnostic Accuracy of Frozen-Section Biopsy in Patients With Thyroid Nodular Disease Relative to Fine-Needle Aspiration Biopsy

Fine-needle aspiration biopsy	Frozen-section biopsy; %			
	Malignant	Benign	Suspicious	Inadequate
Sensitivity	100	12.5/25*	80	—
Specificity	—	100	100	100
Accuracy	100	95.2/97.8*	93.3	71.4/100*

*When occult thyroid carcinomas were excluded.

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CLINICAL PRACTICE GUIDELINES FOR THE CARE AND TREATMENT OF BREAST CANCER



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- Guideline 3: Mastectomy or lumpectomy? The choice of operation for clinical stages I and II breast cancer [July 23, 2002]
- Guideline 5: The management of ductal carcinoma in situ [Oct. 2, 2001]
- Guideline 6: Breast radiotherapy after breast-conserving surgery [Feb. 18, 2003]
- Guideline 7: Adjuvant systemic therapy for women with node-negative breast cancer [Jan. 23, 2001]
- Guideline 8: Adjuvant systemic therapy for women with node-positive breast cancer [Mar. 6, 2001]
- Guideline 10: The management of chronic pain in patients with breast cancer [Oct. 30, 2001]

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- Guideline 11: Lymphedema [Jan. 23, 2001]
- Guideline 12: Chemoprevention [June 12, 2001]
- Guideline 13: Sentinel node biopsy [July 24, 2001]
- Guideline 14: The role of hormone replacement therapy in women with a previous diagnosis of breast cancer [April 16, 2002]