Accuracy and Consistency of Fine-Needle Aspiration Biopsy in the Diagnosis and Management of Solitary Thyroid Nodules

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Abstract
Background: Fine-needle aspiration biopsy has been well established as a diagnostic technique for selecting patients with thyroid nodules for surgical treatment, thereby reducing the number of unnecessary surgical procedures in cases of non-malignant tumors.
Objectives: To evaluate the sensitivity, specificity, accuracy, and positive and negative predictive values of FNAB in cases of a solitary thyroid nodule.
Methods: The preoperative FNAB results in 170 patients who underwent thyroidectomy due to a solitary thyroid nodule were compared retrospectively with the final postoperative pathologic diagnoses.
Results: In cases of a solitary thyroid nodule, FNAB had a sensitivity of 79%, specificity of 98.5%, accuracy of 87%, and positive and negative predictive values of 98.75% and 76.6% respectively. All cases of papillary carcinoma diagnosed by FNAB proved to be malignant on final histology, while 8 of 27 cases of follicular adenoma detected by preoperative FNAB were shown to be malignant on final evaluation of the surgical specimen.
Conclusions: FNAB cytology reduces the incidence of thyroidectomy since this method has excellent specificity and sensitivity and a low rate of false-negative results. It proved to be cost-effective and is recommended as the first test in the diagnostic workup in patients with thyroid nodules.

Preoperative fine-needle aspiration biopsy of thyroid nodules was pioneered by Martin in the 1930s [1], and since then has been well established as a diagnostic technique for selecting patients for surgical treatment. The utilization of FNAB, along with clinical, laboratory and imaging data, has reduced the number of thyroidectomies performed by 21% to 75% [2,3]. FNAB, with an accuracy of between 69% and 95% and a specificity of between 58% and 90% [4], has become a first-line tool in the investigation of nodular thyroid disease [5,6].

We conducted a retrospective study, evaluating 170 patients with a solitary thyroid nodule, and compared the preoperative FNAB cytology with the final histologic evaluation.

Patients and Methods
A retrospective cohort review was performed on 170 cases of solitary thyroid nodules between the years 1994 and 1997. Fine-needle aspiration cytology was performed preoperatively and the results were compared with the final postoperative histologic evaluation. The patients included 129 females and 49 males aged between 12 and 86 years (mean age 47.5 years).

The FNAB was performed without anesthesia, using a 23-gauge needle mounted on a syringe. The nodule was grasped by the fingers and four to eight passes were made into the nodule while applying suction. Most of the specimens were embedded in hematoxylin-eosin, and the Giemsa staining method was used when needed. Nodules less than 1 cm in diameter were aspirated under ultrasound guidance.

The cytology results were divided into four groups as follows: benign, malignant, suspicious, and unsatisfactory. Benign findings included thyroid cysts, colloid nodules, adenoma (except for follicular carcinoma and Hurthle cell carcinoma), normal thyroid tissue, and benign hyperplasia. Malignant findings comprised papillary carcinoma, medullary carcinoma and Hurthle cell carcinoma. Suspicious findings included atypical follicular cells or Hurthle cells. Unsatisfactory results were obtained in cases where there was insufficient tissue for histologic evaluation. In addition, the results were classified into one of four categories: a) positive: preoperative malignancies confirmed by subsequent histologic examination, b) negative: benign preoperative results with a matching final histologic workup, c) false-positive: preoperative FNAB results demonstrating malignancy or suspected malignancy with benign postoperative histology, and d) false-negative: benign preoperative FNAB results with malignant postoperative histology. Five factors were analyzed when comparing the preoperative FNAB results with the final histologic findings: sensitivity, specificity, accuracy, positive and negative predictive values.

Statistical evaluation of the sensitivity, specificity, accuracy, and positive and negative predictive values is shown in Table 1.

Results
Benign preoperative lesions were diagnosed in 82 cases (48%), while malignancy was suspected in 51 specimens (30%). The

Table 1. Statistical evaluation
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<td>Sensitivity</td>
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<td>Specificity</td>
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<td>Accuracy</td>
<td>(TP+TN)/All</td>
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TP = true positive, TN = true negative, FP = false positive, FN = false negative
Although 76% of the adult population [2,7–9], the overall incidence of Solitary thyroid nodules are common, occurring in approximately 4–7% of the adult population [2,7–9], the overall incidence of malignancy in solitary thyroid nodules being 10%. In about 6% of postmortem specimens, carcinoma of the thyroid is diagnosed mainly as a multifocal form within the thyroid gland, and in some cases neck metastases are also present. Most of these tumors are small, with a diameter of 4–10 mm [10]. The preoperative histologic evaluation is crucial in selecting patients for surgery and establishing the extent of the surgery. In the past these decisions were made according to thyroid scanning, but the specificity of this method is low [11], leading to a high rate of false-positive results, many cases of unnecessary surgical procedures, and a low incidence of malignancies found on final histologic evaluation [7].

Studies from the Mayo Clinic have shown the benefits of FNAB as a routine diagnostic method in the treatment of thyroid malignancy. This has resulted in a reduction in the rate of resections of the thyroid gland in suspected cases, from 67% to 43%. The percentage of malignancy on final histologic evaluation rose from 14% to 25%; therefore, unnecessary operations were avoided and costs were reduced by 25% [12]. Garcia Mayor et al. [13] reported having reduced by half the rate of surgical interventions in suspected cases of thyroid nodules between the years 1980 and 1993, and increased the rate of confirmed cancer on final histologic evaluation from 14.7% to 32.9%.

The reported sensitivity of FNAB is between 80% and 95% according to most authors [5,10,14–16], and specificity ranges from 70% to 100% [4], with false-positive and negative results in 5–25% of cases [17,18]. Accuracy is estimated to be between 92% and 95% [19,20] and varies according to the histologic evaluation. In cases of papillary carcinoma the accuracy is about 80% [21], due to the pathognomonic features on histologic specimen examination. The accuracy of FNAB in cases of follicular cancer is lower and estimated to be between 10% and 40%, mainly because structural features of cell groups and the capsule of the nodule are essential to the diagnosis, and are not seen on FNAB cytology [21,22]. However, a few pathologists have been able to identify cytologic features corresponding to follicular malignancy [23].

In addition, two main factors that result in lowering the accuracy of the test in cases of follicular cancer are insufficient tissue for diagnosis, and cases of Hurthle cell carcinoma and follicular tumors. In 10% of the cases there is insufficient tissue for diagnosis, usually due to a cystic lesion containing blood or fluids. The solution in most of these cases is to repeat the FNAB. In cases of follicular or Hurthle cell tumor, tissue block is needed to differentiate between benign and malignant cases since FNAB cannot evaluate penetration to blood vessels or the capsule [24].

Gharib and colleague [25] reported 17% suspicious results on their FNAB evaluation, 20–25% of which proved to be malignant on final histologic evaluation. In our report, 37 cases (22%) were found to be suspicious and 11 of them (29.7%) were malignant on final histologic evaluation.

Reducing the needle gauge and performing the FNAB under ultrasound guidance have been proposed for better FNAB results but have not proved to be beneficial [25].

Regarding the use of ultrasound, in our study 12 FNABs (7%)...
were performed under ultrasound guidance. In these cases, specificity was 100% and sensitivity 50%, but accuracy was only 58.3%. This low accuracy was probably due to the fact that the nodules requiring ultrasound assessment are the smallest and deepest of all – making the diagnosis harder.

**Conclusion**

FNAB is now the gold standard in the evaluation of thyroid nodules. Our findings show this technique to be accurate, efficient and reliable in the diagnosis and evaluation of thyroid nodules.

**References**


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**Capsule**

**Manufacturing tetracyclines**

Pharmaceutical chemists try constantly to modify the structures of antibiotic compounds as bacteria develop resistance to the drugs currently in use. In the case of tetracycline, which treats a broad range of infections including pneumonia, efficient synthetic routes to derivatives have proven hard to develop. Charest and associates have found a strategy to access a broad range of structural variants (all of them 6-deoxytetracyclines) in sufficient quantity for bacterial testing in culture. Tetracyclines consist of four consecutively fused carbon rings, labeled A through D, and D-ring variations have shown particular promise against resistant bacteria. The authors prepared the AB fragment first, and then used the same reaction sequence to attach any of six distinctly modified D rings, forming the C ring in the process. The overall routes proceed in 5 to 7% net yield in 14 steps from benzoic acid.