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# The Role of Aspiration Cytology in the Management of Thyroid Nodules

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**Abstract**—*In the hands of an experienced cytologist aspiration cytology is a safe and hitherto the best diagnostic tool in the evaluation of nodular thyroid lesions. In histologically verified case series 50–90% of confirmed thyroid cancers can be detected by aspiration biopsy, the sensitivity being dependent on sampling errors, microscopic misinterpretation and the variation in attitude towards indeterminate diagnoses in the decision for diagnostic surgery. The number of proven benign cases that are correctly identified as such by biopsy varies accordingly and approx. 75% (specificity). In comparison with imaging procedures, including those giving information of functional activity, the combined sensitivity and specificity rates of aspiration cytology come closest to the ideal discriminatory situation. In combination with case history and careful clinical examination, fine needle aspiration cytology is the best guidance for an optimal selection of patients for therapeutic or diagnostic surgery. Future development of sensitive markers for malignant degeneration will probably increase the selective power of this diagnostic technique.*

## INTRODUCTION

ALTHOUGH known for more than 50 years [1] and routinely used for diagnosis of thyroid lesions since the '50s [2–4], it is not until the last 15 years that fine needle aspiration biopsy (FNA) has gained a wide acceptance. The strategy in diagnosis of structural thyroid lesions is two-fold: (1) with the highest possible sensitivity select patients for therapeutic surgery and (2) with the highest possible specificity exclude patients from pure diagnostic surgery. Accumulating experience from comparison of different techniques in histologically verified case series indicates that needle aspiration cytology, although not ideal, comes closest to the goal in this respect [5–9]. The aim of the present review is to give some information on the limitations and possibilities with biopsy cytology in the management of thyroid nodules.

## BIOPSY TECHNIQUE

In core biopsy, as initially obtained with a Silverman needle and later with the invention and use of the Tru-cut Travenol needle (TNB), the sampled thyroid tissue mainly retains its spatial arrangement including the important borderlines towards vessels and connective tissues. The histopathological interpretation is based on criteria familiar to the pathologist. The drawbacks of TNB are, although rare, the risk of local discomfort, reactive fibrosis along the biopsy track and of bleeding. Further, a smaller number of biopsies can be collected as compared to FNA sampling.

In needle aspiration biopsy the two- and three-dimensional arrangements in cellular clusters, the appearance of individual cells and background material such as the colloid, are used in the interpretation of the aspirate [8, 10, 11]. The spatial relation to vessels and connective tissue is, however, lost which is a significant drawback in the diagnostic differentiation between benign and some well differentiated malignant lesions [12]. The fine-needle aspiration biopsy (FNA) with a 22- to 25(27-) gauge needle is simple, economic and relatively more comfortable for the patient [13]. The FNA technique, however, requires a long period of practice before an acceptable level of diagnostic accuracy is reached [13, 14]. Reasons for reduction of FNA sensitivity (false-negatives) are miss at aspiration, intraglandular geographical errors, microscopical misinterpretation, diagnosis of cellular atypias and indeterminate diagnosis [14, 15]. Variation in sensitivity and specificity rates are also dependent on the varying attitude towards indeterminate cases as recently discussed [16].

The diagnostic yield is approx. 95% [9, 17] and slightly higher for FNA (96%) than TNB (91%) in

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lesions bigger than 10 mm [18, 19]. In smaller nodules the diagnostic yields are reduced to approx. 80%. In the case of an inadequate specimen immediate reaspiration is mandatory [20].

In follicular neoplasms the malignant diagnosis is based on local invasion into vessels and the capsule [11, 21,22]. Theoretically it might be possible to observe this sign of malignancy in core biopsies only and consequently TNB has been advocated to distinguish between benign and malignant follicular tumours [22–24]. In controlled case series in which both types of biopsy technique have been compared on the same thyroid lesion [18, 25], however, TNB gave the most accurate diagnosis of non-follicular diagnoses. For follicular diagnoses the false-negative errors for FNA and TNB were relatively high, 6.8% and 12.8% respectively [18] which indicate the notoriously reported difficulty of distinguishing between benign and malignant follicular lesions [14, 26–28].

The overall diagnostic accuracy (the combined true-positive and true-negative diagnosis) was very high for both techniques (96–98%). The combined use of both techniques has been advocated [18] and is currently reported to increase the diagnostic accuracy [9], but most of the recent reports reflect the dominant use of FNA only [17, 19, 20, 29, 30].

## THE INSIDIOUS THYROID LESIONS

The various types of possible benign and malignant structural disturbances in the thyroid are numerous and their cytological features have recently been reviewed [6, 10, 11, 31]. In most cases it is easy for the cytologist to palpate the target for the biopsy but the variation in anatomy of the neck structure may occasionally make it impossible to correctly identify lesions of considerable size in upper, rear and lower parts of the gland, the intrathoracic extensions not being encountered. There may further be a varying number of various lesions present in the same gland. Both malignant and benign synchronous neoplasias may be present in otherwise normal thyroid tissue as well as in thyroids with hyperplastic regions [14, 32, 33]. Unilateral multicentric cancers have been reported in 20% of cases [34] and bilaterally in 10–25% [32, 34]. Whole-organ sectioning has further demonstrated intrathyroidal metastases and that 70/80 cancers extend from one side into the isthmus, the opposite lobe or into the pericapsular lymph nodes of the opposite lobe [35]. This situation in which single or multiple malignant neoplasias may thrive in the neighbourhood of more prominent benign lesions of different types creates a sampling problem, which is generally solved by sampling from multiple regions as indicated by palpation or preoperative scintigraphy [15, 36]. Geographical sampling errors have been reported [18] and in our experience [32] as well as in that of others [14] missed cancers of significant size (10–15 mm) have later been histologically verified despite the aid of very experienced cytologists.

## CYTOLOGY AND THERAPEUTIC SURGERY

False-positive aspiration cytology is rare. Apart from three studies indicating false malignancies in about 10% [5, 37, 38] the majority of case series demonstrate figures from 0% [3, 7, 39–44] to 4% [14, 22, 30]. Nearly all patients with biopsies indicating malignant lesions are referred to surgery which gives a histological confirmation of the lesion. Consequently the error rates are quite reliable. Thus, if aspiration cytology reveals a carcinoma, surgery is strongly recommended and performed as therapeutic surgery with removal of all thyroid tissue [45].

## CYTOLOGY AND DIAGNOSTIC SURGERY

The real value in aspiration biopsy lies in the selection of patients for diagnostic surgery. In the case of benign cytological diagnoses it is therefore important for the clinician to know the risk for a false-negative diagnosis, which may lead to a less good advice regarding to treatment of a nodule.

The inherent problem in the evaluation of the accuracy of cytological diagnosis is the lack of histological verification in the majority of cases. In histologically verified case series with a low percentage of malignancies the accuracy is high regarding the rate of false-negatives. In case series where patients are selected for surgery on strong indications for malignancy only, a high percentage of the patients will prove to have a thyroid malignancy [25]—the false-negative rate, however, will probably be too low. In the light of a recently published study on the frequency of small carcinomas (< 10 mm) in autopsy cases in which 6% were proven to have malignant papillary lesions [46], low figures of false-negative biopsy diagnoses must further be questioned.

The cytologist generally summarizes the results by referring the diagnoses to any of five groups (Fig. 1). Group I, normal tissue, is rarely used in the diagnosis of thyroid nodules. In group II are encountered both hyperplastic lesions (colloid goitre, multinodular goitre) and benign neoplasias (follicular adenoma). The false-negative rate for the former diagnoses (referred to as IIb) is reported to be 2–4% [32, 47], but 9.8% malignancy in multinodular goitre has been found [48]. In the case of follicular adenomas (group IIk) the false-negative error rate is higher, approx. 7–15% [18, 32, 49]. Biopsies with cellular atypias are referred to group III. In this group the frequence of malignancy varies between 15 and 25% [7, 17, 30, 32, 38, 39, 50, 51].

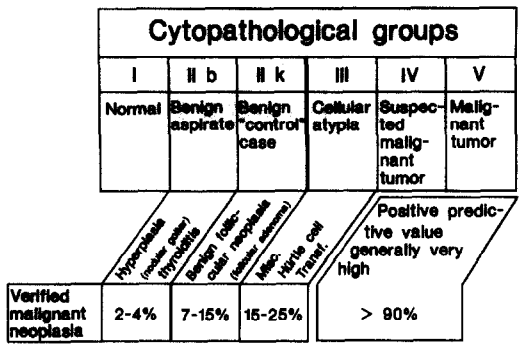


*Fig. 1. In histopathologically verified case series the incidence of cancer observed after diagnostic lobectomy varies between the different cytological groups. Knowledge of these figures is important for the strategy of management of thyroid nodules.*

The knowledge of these figures is important for the strategy of management. Thus, if all patients with group III diagnoses are operated with a diagnostic lobectomy approx. 20% will prove to have a malignant lesion—if all patients with follicular adenomas (group IIk) are referred to surgery a malignant lesion will be found in approx. 10% of cases.

The majority of patients with thyroid nodules have hyperplastic structural lesions (group IIb). In these cases with low risk for cancer, case history including local discomfort and vocal cord dysfunction, clinical examination and thyroid imaging techniques are of relatively greater importance for the decision of strategy [32] (Fig. 2).

In a decision analysis of the non-functioning thyroid nodule Molitch *et al.* [52] did not find any real difference between quality-adjusted life expectancy if patients were initially diagnosed/treated with any of (1) direct surgery, (2) initial therapy with thyroxine and (3) aspiration cytology. A slight superiority for aspiration cytology was, however, found. They stated that 'the controversy concerning the *best* management of the *cold* nodule is an illusion'. In our experience cancer was found in higher frequency in cases with normal scintiscans [32] and in this respect we agree since it seems irrelevant whether a nodule is *cold* or not. The strategy of management of thyroid lesions must be based on other information and among available methods, aspiration cytology so far appears to be the best. Scintigraphy is, however, recommended to differentiate between functioning and non-functioning lesions in case of single nodules with benign cytology (Fig. 2). The latter cases should be recommended a diagnostic lobectomy. Future addition of information from DNA-measurements in aspirated samples may further strengthen the diagnostic accuracy.

Finally, it must be emphasized that the best decision for the choice of diagnostic surgery is probably made when the clinician has a keen interest in the diagnostic accuracy of the cytological diagnosis in his/her hospital and actively follows up their histopathological verification.

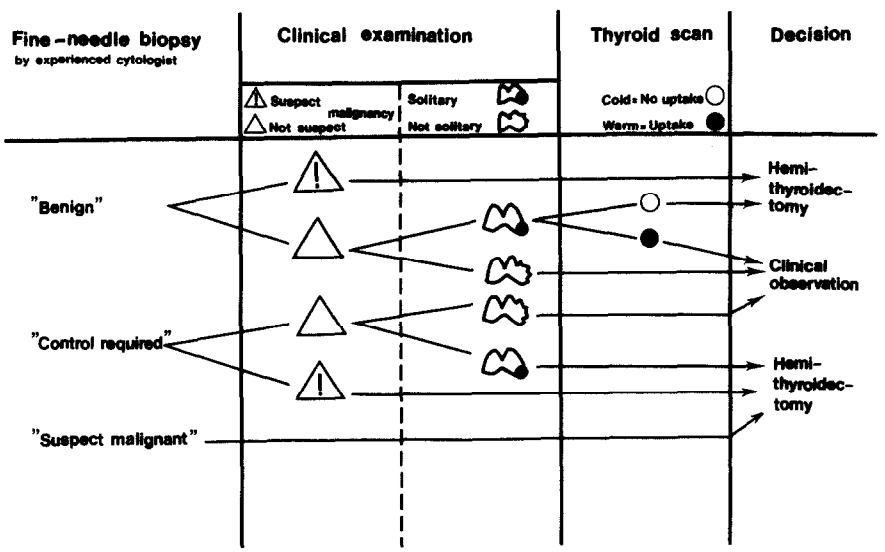


*Fig. 2. Schedule used as a basis for choice of treatment for thyroid nodules (from Lennquist S.* Svensk Kirurgi **41**, 2, 49, 1983). *In regard to fine-needle biopsy, all reported as 'follicular adenoma' are included in the group 'control required', since in these cases cytologic distinction between a malignant and a benign lesion is scarcely feasible. In the work up, thyroid scan is used only to separate patients with clinically and cytologically 'benign'* solitary *nodules. Those* without *radio-iodine uptake in the nodule are recommended hemithyroidectomy. Clinical observations is recommended to those patients with clinically not suspect multinodular goitres even if FNA indicates that control is required. All patients with 'suspected malignant' lesions are recommended surgery knowing that* 25% *of the cases in this group carry a carcinoma (Fig.* 1).

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