

# Retrospective Analysis of Diagnosis by Intraoperative Frozen Section and Routine Paraffin Embedded Tissue in 638 Thyroid Disease Patients

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**OBJECTIVE** To summarize a common pathogenetic condition, the pathologic characteristics shown in frozen section and our experience utilizing 2 different diagnostic methods in cases of common thyroid diseases (TD).

**METHODS** Data from 638 cases with frozen sections from thyroid tissue were retrospectively analyzed. The intraoperative frozen sections of the patients and postoperative diagnostic results of routine paraffin sections were compared.

**RESULTS** In the 683 patients, the gender ratio of females to males was 2.64 : 1, and the ratio between the patients with nodular goiter (NG) and the patients with thyroid adenoma was 1.5 : 1. The oldest age group of patients with thyroid cancer (TC) ranged from 40 to 49 years. Frozen section pathologic examination has been employed more and more in the diagnosis of thyroid diseases, and the detection rate of TC has increased year by year, i.e., the rate increased to 6.45%, 7.58%, 14.55% and 16.57%, respectively, in 2005, 2006, 2007 and 2008. Thyroid papillary carcinoma (TPC) was the most commonly seen malignant tumor of the thyroid (MTT), which accounted for approximately 94.8% of MTTs and 11.44% of the total TDs. Micropapillary carcinoma accounted for 27.4% of TPC, and multifocal carcinomas accounted for 15.58% of TCs. Many of the TCs (19.48%) were complicated by benign diseases such as adenoma, NG and thyroiditis. The coincidence rate of diagnoses made by frozen section and paraffin embedding for thyroid disease was 98.59%. Calcification was rather common in NG and TPC, and there were significant differences in psammoma bodies (PMB) between the calcifications of TPC and NG ( $P < 0.01$ ).

**CONCLUSION** TPC ranks first in the incidence of MTTs and accounts for 94.8% of all MTTs. About 1/4 of TPCs are micropapillary carcinoma, while 1/5 are accompanied by benign disease, such as adenoma, NG and thyroiditis. PMB are of importance and of significance in the diagnosis of TPC.

**KEY WORDS:** thyroid disease, intra-operative frozen section, paraffin imbedding, pathologic analysis.

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## Introduction

Thyroid disease (TD) is one of the most commonly seen diseases in the Daqing district, Heilongjiang Province, China. Over the past 3 years, frozen section diagnosis for patients with thyroid diseases has increased each year in the Department of Pathology, Long Nan Hospital, Daqing, Heilongjiang, China. Conferring the correct diagnosis and devising individualized treatment for TD patients are of significance. In this paper, the experiences we have gained from compre-

hensive methods for the pathologic diagnosis of thyroid diseases in our hospital during a period from 2005 to 2008 were summarized, with the goal to further improve the accuracy of diagnosis and the differentiation of TD from other related diseases.

## Materials and Methods

Data from 638 patients undergoing intraoperative frozen section diagnosis of thyroid diseases in our hospital, during the period from January 2005 to October 2008 were collected. The age of the patients ranged from 15 to 76 years. The results of all frozen sections were confirmed and analyzed by 2 or more experienced pathologists. The cancer cases with 2 or more malignant foci were considered multiple malignant foci, and the cases with solitary foci at 1.0 cm or less were regarded as microcarcinoma. SPSS 12.0 was used for data processing, and the  $\chi^2$  test was utilized. The value of  $P < 0.05$  was considered statistically significant in the hypothesis test.

## Results

In the 638 TD cases, the female-male ratio was 2.64:1. Since the number of cases receiving surgery for removal of inflammatory diseases of the thyroid decreased year to year, the detection ratio of nodular goiter (NG) and thyroid adenoma (TA) increased year to year, with an average ratio of 1.5:1. The detection rate of thyroid cancer (TC) by frozen section increased year to year, with 6.45%, 7.58%, 14.55% and 16.57%, respectively, in each year from 2005 to 2008 (Table 1). In the 77 TC patients, 50 were female (64.94%), and 27 male (35.06%) with the ages ranging from 20 to 76 years. The oldest age group of patients was 40 to 49 years. Of these TC

cases, 73 were papillary carcinomas, 2 follicular carcinomas (FCC), 1 SqCa and 1 a malignant small cell tumor. Based on our study, thyroid papillary carcinoma (TPC) is a common disease, accounting for 11.44% of the total TDs. Among the TPC cases in this study, 20 were micropapillary carcinomas, accounting for 27.4% of the total TPC, with a minimum diameter of 1 mm. Twelve were multifocal carcinomas, in which 8 were bilateral carcinomas, accounting for 15.58% of total TC cases. In the TC cases, 15 (19.48%) were accompanied by benign diseases: 4 were complicated by adenoma, 5 by NG and 6 by thyroiditis. Diagnosis by frozen section examination in 7 cases was confirmed malignant by the subsequent examination of paraffin embedded tissue. Two patients were diagnosed with occult carcinomas after frozen section. The results from examination of frozen section and paraffin embedded tissue of the thyroid were in accordance, with a coincidence rate of 98.59%.

Calcification was very common among the NG and TPC cases. In a review of the 638 cases, 74 were calcific diseases. Psammoma bodies (PMB) accounted for 86.96% of the TPC and 8.7% of the NG cases. Plaquelike calcifications accounted for 78.43% of the NG and 19.61% of the TPC cases. There were significant differences in PMB between the TPC and NG groups ( $P < 0.01$ ).

## Discussion

In recent 20 years, the incidence of TC has clearly increased<sup>[1]</sup>. It was shown in the surgical pathologic diagnosis of NG and TA cases that NG was more commonly seen compared to TA, and that the incidence ratio between NG and TA was approximately 2-3:1<sup>[2]</sup>. In our hospital, the incidence ratio between the 2 groups of the

**Table 1. Frozen section pathologic diagnosis of 638 thyroid cases during the period from 2005 to 2008 (n, %).**

	2005	2006	2007	2008	Total
TC (Female)	7 (87.5)	9 (90)	18 (58.06)	16 (57.14)	50 (64.94)
TC (Male)	1 (12.5)	1 (10)	13 (41.94)	12 (42.86)	27 (35.06)
TC	8 (6.45)	10 (7.58)	31 (14.55)	28 (16.57)	77 (12.07)
Thyroiditis	9 (7.26)	7 (5.30)	9 (4.23)	6 (3.55)	31 (4.86)
TA	54 (43.55)	64 (48.48)	55 (25.82)	42 (24.85)	215 (33.70)
NG	45 (0.83)	59 (0.92)	120 (2.18)	99 (2.36)	323 (1.50)
Total thyroid cases with frozen section	124 (26.72)	132 (30.99)	213 (33.39)	169 (45.31)	638 (33.56)
Total cases with frozen sections	464	426	638	373	1901

Numbers in the brackets of NG refers to the ratio of the incidence between NG/TA.

**Table 2. Distribution of different types of calcifications in benign and malignant thyroid tumors.**

	NG	Papillary carcinoma	Atypical adenoma	Total
Lamellar calcification (PMB)	2	20	1	23
Plaquelike calcification	40	10	1	51

patients was less than 1 in the year from 2005 to 2006, and the ratio normalized during 2007 to 2008. Loose diagnostic criteria applied to some of the adenoma cases resulted primarily from the mono-nodular goiters which had been misdiagnosed as adenomas. This is because the adenomas are usually represented as the singular nodus, and the nodular goiters are often reflected as multiple nudi. Most of the mono-nodular goiters were subjectively diagnosed as adenoma, thus resulting in an inversion of the proportion between the two diseases.

TPC was the most commonly seen malignant tumor of the thyroid (MTT), accounting for approximately 94.8% of the total MTTs. FCC was proportionately less, accounting for 2.6% of MTTs. About 1/5 of the TPC cases were complicated by benign diseases, such as adenoma, NG and thyroiditis, of which 5.19% were complicated by TA, 6.49% by NG, and 7.79% by thyroiditis. Research on the pathogenesis of TC complicated by thyroiditis was seldom reported; however, the prognosis of the disease was favorable, which might correlate to a great number of well differentiated papillary carcinomas, as well as microcarcinomas and occult cancer in the concomitant cancers<sup>[3]</sup>.

The detection rate of micropapillary carcinoma was high, accounting for approximately 1/4 of total TPCs. Li et al.<sup>[4]</sup> reported that examination by ultrasonic B scanning, in combination with fine needle aspiration (FNA) and intraoperative frozen section, could increase the accuracy rate in the clinical diagnosis of thyroid microcarcinoma, thus imparting clinical value to this approach.

In 9 of the 638 cases, the frozen section failed to show malignant features, but through examination of paraffin embedded tissue, a final diagnosis of malignancy could be conferred. Of the 9 cases, 2 were occult cancer, with diameters < 2 mm, 1 failed to be detected during frozen section sampling as the specimen was very large and the malignant focus was 3 mm in diameter. In addition, 2 required decalcification and were confirmed as malignant after this was performed, and 2 failed conclusive diagnosis because the tumor was small and localized inside the cell envelopes, with edema, slight cellular heteromorphism and without the usual stromal reaction to malignancy. Further, 1 failed the conclusive diagnosis of FCC at frozen section, and 1 with lymphatic metastasis missed detection owing to extensive cystic degeneration of the thyroid tissue, which was similar in appearance to a branchial cleft cyst. Intraoperative frozen section can be an excellent method in determining the diagnosis of thyroid-occupying lesions; however, limitations due to sampling, tumor heterogeneity and insidious forms of the affection, as well as the quality of the frozen sections are the main factors that lead to incorrect and delayed diagnoses<sup>[5]</sup>.

This study on thyroid nodules in 638 patients has shown that the overall rate of calcification of nodules was 11% (74/638). In the 74 calcified nodules, 30 were

diagnosed as cancer, accounting for 40.54% (30/74) of the calcified nodules. The calcification rate of the malignant thyroid nodules was 38.96% (30/77). In China, Lai et al.<sup>[6]</sup> reported that the calcification rate of malignant thyroid nodules was 52.9%. PMB is an important reminder of the presence of malignancy and its proportion was much higher in TC than in the benign thyroid tumors. The differences between the 2 groups of patients were significant ( $P < 0.01$ ), which was in accordance with the recent report of Wang et al.<sup>[7]</sup> Hao et al.<sup>[8]</sup> analyzed the differences in the incidence of benign and malignant tumors among the calcified nodules in different age groups, indicating that increased vigilance for the potential for malignancy is needed for patients of over 45 years and with calcified thyroid nodules. It is well-known that the formation of PMB results from focal and progressive infarction at the pointed end of the thyroid nodule, causing calcium salt deposition. The osteopontin produced by the macrophage at the site of involvement plays an important role in the formation and development of PMB<sup>[9,10]</sup>. Further, plaque-like calcifications are usually located within the spaces of fibrous tissue, which results in local degeneration and this is frequently seen in the benign thyroid diseases.

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