VM100 Thyroid FNA: Diagnoses and Differentials
Michael R. Henry, MD, FCAP
Mayo Clinic, Rochester MN
September 30, 2007 8:30 – 10:00 AM

Fine Needle Aspiration Cytology of the Thyroid

Purpose

Palpable nodules of the thyroid are quite common, occurring in approximately 4-7% of the adult population. The incidence of neoplasia in these nodules is, however, quite low. Over 90% of nodules are benign lesions, which can be followed or treated medically. Fine needle aspiration (FNA) of the thyroid enables the clinician to select those patients who would most benefit from surgery. Using thyroid FNA along with other radiologic techniques, the number of thyroidectomies in the U.S. has been decreased by about half, while at the same time doubling the incidence of cancers found in the surgical specimens which are obtained. FNA can and should be used as the initial diagnostic procedure for most euthyroid patients with palpable nodules.

While aspiration cytology is a very good way to distinguish between most benign and malignant lesions of the thyroid, it has its limitations, especially when trying to differentiate between cellular adenomatoid nodules in nodular goiters and follicular neoplasms. Also, as will be covered below, follicular and Hürthle cell carcinomas cannot be distinguished accurately from follicular or Hürthle cell adenomas.

Technique

FNA of the thyroid can be performed by either the pathologist or any other appropriately trained clinician. Learning the proper techniques and then developing these skills through practice is the key to consistently obtaining diagnostic material. Thyroid aspiration is not an easy skill to master and even skilled practitioners can fail to get an adequate specimen in up to 20% of the time. It is becoming quite common to perform thyroid FNA under ultrasound guidance. If possible, a pathologist or cytotechnologist should be present when these are done to make immediate assessments of adequacy. As thyroid nodules can be very vascular, both aspiration and non-aspiration techniques using 23 or 25 gauge needles are recommended. The patient should be placed in the supine position with the neck hyperextended. As the area can be quite sensitive, local anesthesia is recommended. At least three or four passes should be made to assure adequate sampling. If cyst fluid is obtained, aspirate as much of the fluid as possible and repalpate to detect any residual mass, then reaspirate if indicated. Both alcohol fixed and air-dried direct smears should be prepared and excess material should be flushed into a fixative or balanced salt solution and prepared as either cytospins or cell blocks.

Diagnostic Considerations

To simplify the sometimes difficult and confusing area of differential diagnosis in thyroid FNA the following diagnostic schema is offered:

UNSATISFACTORY or **NONDIAGNOSTIC**: The adequacy of an aspiration should always be judged in a clinical context. In the absence of mitigating clinical considerations an adequate a thyroid aspirate must contain fragments of well-preserved thyroid epithelium in otherwise interpretable smears. We recommend a minimum of 6 fragments of well-preserved follicular epithelium. Occasionally specimens may contain abundant colloid and numerous macrophages with only rare follicular cells or a cystic lesion may yield only histiocytes. In these cases while the overall interpretation is Non-diagnostic, an additional descriptive diagnosis with a qualifying statement about the scant amount of epithelium is appropriate. Clinical correlation and judgment is then needed to determine the course of therapy. In many nondiagnostic smears repeat aspiration may be indicated.

NEGATIVE or BENIGN: This category includes the cytologic diagnosis of benign cysts and benign nodules such as a colloid nodule or nodular goiter. At the Mayo Clinic we use the term Benign Thyroid Nodule to encompass these benign hyperplastic lesions. This category also includes

© 2007 College of American Pathologists. Materials are used with the permission of the faculty.

inflammatory lesions such as Hashimoto's thyroiditis. These lesions have a very low probability of malignancy and may be clinically followed. Repeat aspiration may be indicated if the nodules fail to respond to TSH suppression or continue to enlarge.

SUSPICIOUS or INDETERMINATE: This includes most of the hyper-cellular follicular lesions, which represent either follicular neoplasia or at times hyperplastic nodules in an adenomatoid goiter. This category also includes most Hürthle cell lesions. Occasionally there are smears, which may be suggestive, but not diagnostic of other specific malignancies such as papillary carcinoma or medullary carcinoma. Lesions in this category generally require surgery for a definitive diagnosis, most often hemithyroidectomy, but may be followed if there is significant surgical risk. If carcinoma is suspected and the aspirate is less than optimal, a repeat aspiration may be indicated. In our experience of over 1,200 thyroid aspirates in a 5-year period with surgical follow-up, a diagnosis of suspicious or positive has a PPV of 90% with a NPV of 65% for neoplasia.

MALIGNANT: This includes any aspiration on which an unequivocal diagnosis of malignancy can be made. This diagnosis should be as specific as possible as the type of operation or other therapy may be based on this information. For instance a diagnosis of papillary carcinoma now leads to a total thyroidectomy without frozen section confirmation in most surgical practices. Again in our experience the specificity of a diagnosis of PTC is about 99%.

This diagnostic scheme closely matches the flowchart recommended by the American Association of Clinical Endocrinologists in their guidelines for clinical practice for the diagnosis and management of thyroid nodules. While more complex schemes have been proposed, including the separation of cellular follicular lesions into a separate category, the limited clinical options available make a more simplified scheme more clinically useful. It must be remembered that for the most part, except in those cases when a definitive diagnosis can be rendered, thyroid FNA is not so much diagnostic but used in the triage of nodules to follow-up or surgery.

Cytology of the Normal Thyroid

The normal thyroid is composed of follicles where follicular epithelial cells surround a variable amount of colloid. The interfollicular stroma is highly vascularized. It has been reported that normal thyroid does not aspirate very well yielding only scantly cellular, bloody smears. Normal follicular cell nuclei vary only slightly in size but have a variable amount of cytoplasm. The nuclei are round and regular with smooth nuclear membranes and fine chromatin. Nucleoli are not normally prominent but may be present especially in hyperplasia. Single follicular cells resemble small lymphocytes in both size and shape and it is often difficult to differentiate between them.

The identification of colloid is important in thyroid aspirates. The appearance of colloid varies considerably and it may be difficult to differentiate colloid from the normal serum background. Colloid may appear as thick, amorphous material with sharply circumscribed edges or as a thin, translucent material in the background. In pap smears the color varies from pink-orange in thick smears to pale green in thin smears with scant blood. On air-dried smears the colloid is violet-blue with a tendency to crack in a linear fashion. Blood elements are common in thyroid aspirates due to the high vascularity of the organ. Be aware that while lymphocytes and neutrophils are a normal constituent of blood increased numbers may indicate thyroiditis.

CYSTIC LESIONS

Nodular Goiter

The majority of thyroid cysts arise as the result of degenerative changes in a nodular goiter. These cysts normally contain large numbers of histiocytes with or without hemosiderin. Colloid may or may not be present. The number of follicular cells varies and if none are seen, the possibility of cystic papillary carcinoma cannot be excluded. Of interest, approximately 15% of surgically removed cystic lesions are malignant, the majority consisting of papillary carcinoma. Large follicular neoplasms, generally greater than 4 cm, can become cystic due to central degeneration as well. It is important to sample solid areas of these lesions to ensure a proper diagnosis.

Thyroglossal Duct Cyst

These cysts are congenital in nature and are usually found in the midline and superior to the thyroid. When present inferior to the hyoid, they may be clinically confused with a thyroid nodule. Thyroglossal duct cysts are lined by either a stratified squamous epithelium or respiratory type columnar epithelium. The aspirates typically contain these epithelial cells with a variable amount of chronic inflammation. Thyroid tissue may be present within the cyst wall and may also be seen in the aspirate. Papillary carcinoma of the thyroid has also been described as arising from a thyroglossal duct cyst.

Parathyroid Cysts

Occasionally parathyroid adenomas can be cystic. Most of these are hormonally inactive and thus easily mistaken for solitary thyroid nodules. The fluid from a parathyroid cyst tends to be clear rather than the brown hemorrhagic fluid most commonly associated with cystic goiters. Parathyroid cyst fluid may contain either papillary clusters of cells similar to those seen in papillary carcinoma or microfollicles suggestive of a follicular thyroid lesion. The papillary clusters from a parathyroid adenoma contain cells, which are smaller, more tightly cohesive and lack the nuclear features of papillary carcinoma of the thyroid. In cysts containing only microfollicles it may be impossible to distinguish between thyroid and parathyroid origin. In cases where a parathyroid cyst is suspected, hormonal analysis of the fluid for PTH (specifically the C-terminal end) may be useful.

Malignant Cysts

Complex solid-cystic lesions may represent a neoplasm with central degeneration or necrosis. As mentioned earlier, the frequency of malignancy in cystic lesions of the thyroid, which are surgically removed, is approximately 15%. While papillary carcinoma most frequently undergoes cystic degeneration follicular and Hürthle cell neoplasms can also become cystic. Either bloody or clear fluid can be seen in neoplastic cysts and all cystic fluid obtained from a thyroid aspiration should be sent for examination. While the cellularity may be scant, the cells that are present in the fluid should retain the nuclear features needed to differentiate a papillary lesion from a follicular one. Completely acellular aspirates of fluid should be considered nondiagnostic and repeat aspiration of any remaining nodule must be performed.

THYROIDITIS

Chronic Nonspecific Thyroiditis

Increased numbers of lymphocytes may be seen in a variety of disorders including Hashimoto's thyroiditis, goiter and Grave’s disease. Look for epithelial changes for a more specific diagnosis.

Granulomatous Thyroiditis (DeQuevaine's Thyroiditis or Subacute Thyroiditis)

DeQuevaine's thyroiditis is probably viral in origin and presents as a painful generalized swelling of the thyroid and is thus generally not a diagnostic problem. Occasionally, it may be painless with only focal involvement and thus present as a solitary nodule at which point it may be aspirated. The aspirates in the acute phase of the disease are characterized by inflammation, both acute and chronic, with multinucleated giant cells and epithelioid granulomas. Later the thyroid may undergo fibrosis and yield scantly cellular smears with fragments of connective tissue.

Hashimoto's Thyroiditis

This autoimmune thyroiditis characterized by a marked lymphocytic infiltrate with prominent germinal centers and plasma cells. Antithyroid and antimicrosomal antibodies are found in 70% of the cases. The process induces degenerative changes in the follicular epithelium including oxyphilic change and Hürthle cell metaplasia sometimes with significant cytologic atypia. The epithelium may become hyperplastic and papillary.

The aspirates are variably cellular depending on the amount of fibrosis present. Lymphoid cells are numerous and polymorphous in nature. Plasma cells and transformed lymphocytes are found in almost every case. Follicular cells demonstrating Hürthle cell change along with the lymphocytes are necessary to make the diagnosis of Hashimoto's thyroiditis. Remember that these cells can demonstrate a high degree of atypia and be cautious of making a call of Hürthle cell neoplasm in the face of clinical or cytologic evidence of thyroiditis. Features useful in distinguishing Hürthle Cell neoplasms are discussed below.

Papillary carcinoma, follicular neoplasia or lymphoma may all occur in association with Hashimoto's thyroiditis. Papillary carcinoma will show the characteristic nuclear features and papillary fragments with vascular cores. The papillary follicular fragments seen in the hyperplasia associated with Hashimoto's don't contain a vascular core. Primary lymphoma of the thyroid is typically of the large cell type and is not normally a diagnostic problem. However, low-grade lymphomas may occur in association with thyroiditis. If the lymphoid population appears to be monomorphic with atypical cleaved nuclei, then immunohistochemistry or flow cytometry may be helpful in defining a monoclonal population. The bottom line is that if lymphoma is suspected, then surgical excision is indicated.

LESIONS WITH FOLLICULAR CELLS

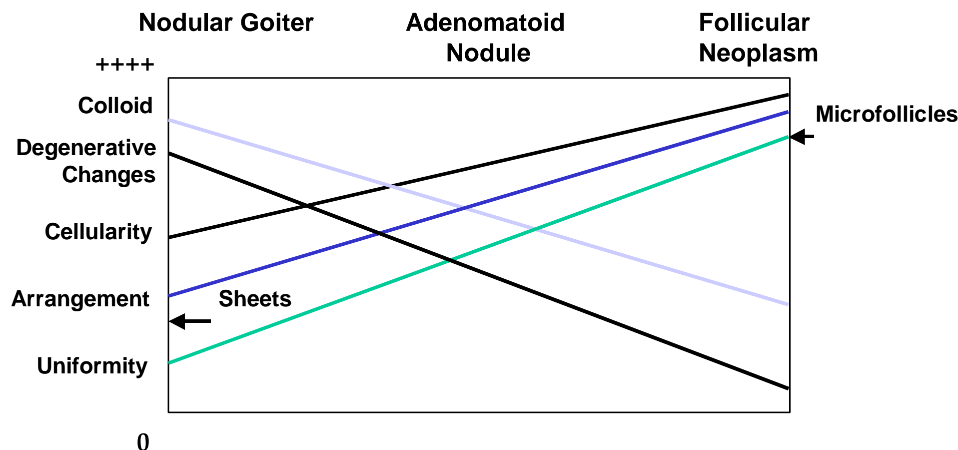
BENIGN THYROID NODULE (Goiter, Adenomatoid Nodule, Multinodular Goiter)

Nodular goiters are very common disorders and represent by far the most common reason for thyroid aspiration. The cellular composition of the aspirate depends on the nature of the goiter. Nodular goiters typically have a multinodular pattern with follicles of varying sizes. Some follicles are large, distended with colloid and lined by atrophic epithelium. Smaller follicles also contain colloid but may show epithelial hyperplasia with papillary tufts extending into the follicles. Degenerative changes including hemorrhage, fibrosis and calcification are common. Some nodules may be composed of hyperplastic follicular epithelium with scant colloid and may be difficult to differentiate from follicular adenoma. These nodules are sometimes referred to as cellular or adenomatoid nodules.

Typical aspirates contain abundant colloid with variable numbers of follicular cells. The follicular cells show uniform, round, regular nuclei and may be present in honeycomb sheets, papillary fragments, small follicles or single cells. In most cases a mixture of these features are seen with variability in the size and shapes of the follicular groups. Hürthle cell metaplasia may be seen in occasional groups but should not be present in the majority of the cells. A predominance of Hürthle cells may suggest a Hürthle cell neoplasm or Hashimoto's thyroiditis, but the presence of the other features associated with goiter should point the diagnosis towards nodular goiter. Degenerative features are common including histiocytes with hemosiderin, lymphocytes, calcific debris, cholesterol crystals and stromal cells. Most goiters will show a mixture of the above features.

Highly cellular smears with large numbers of follicular cells present a difficult differential between a hyperplastic adenomatoid nodule and a follicular neoplasm. In a hyperplastic nodule the cells tend to retain the honeycomb configuration with evenly spaced, round regular nuclei. Larger follicles are common with an occasional microfollicle. The amount of colloid aspirated may be scant. If the possibility of follicular neoplasm cannot be excluded these aspirates should be signed out as indeterminate with a differential including hyperplastic nodule and follicular neoplasm.

When the FNA contains follicular cells the features charted below can be used to help differentiate between nodular goiter and follicular neoplasia. These changes are a spectrum and often cellular adenomatoid nodules cannot be distinguished from neoplasia.



FOLLICULAR NEOPLASIA

Follicular neoplasms are the most common thyroid tumor and typically present as solitary cold nodules. These lesions are true neoplasms characterized by a predominantly follicular pattern and include both follicular adenoma and follicular carcinoma. The diagnosis of follicular carcinoma is generally made by demonstrating invasion of the capsule surrounding the nodule or invasion of blood vessels within the capsule. The morphology of the cells in both follicular adenoma and follicular carcinoma tends to be very similar making it difficult if not impossible to cytologically distinguish between benign and malignant neoplasms. However this distinction is not necessary as the treatment for both is lobectomy.

Aspirations of follicular neoplasms are hypercellular with little background colloid. The cells are present in syncytial fragments often in a microfollicular or trabecular arrangement. The nuclei are enlarged but round and uniform and may show crowding and overlapping. Nucleoli are not generally prominent. The cellular population demonstrates a monomorphism with few larger follicles or sheets of cells. While cystic changes can be seen in follicular neoplasia it is not common and few of the degenerative changes seen in goiter such as histiocytes, stromal fragments or cholesterol crystals should be seen.

Follicular carcinomas occur in two varieties: widely invasive and aggressive or minimally invasive and encapsulated. Widely invasive carcinomas are readily recognized as carcinoma clinically and the role of aspiration is generally limited to confirming the primary site as thyroid. As mentioned above minimally invasive carcinoma must be diagnosed histologically following thyroid lobectomy. Aspirates from follicular adenomas and follicular carcinoma demonstrate very similar findings. Cytologic features that are worrisome for carcinoma include; mitotic figures, marked nuclear crowding, marked cellular atypia and pleomorphism, hyperchromatic nuclei and prominent, variable nucleoli.

HURTHLE CELL NEOPLASIA

This is a variant of a follicular neoplasm composed predominantly of Hürthle cells. As in follicular neoplasia Hürthle cell lesions can be benign adenomas or malignant carcinomas. Again, the distinction is made by demonstrating invasive features on histology. The cytologic pattern in a Hürthle cell neoplasia is cellular with a microfollicular or trabecular pattern or numerous single cells. The cells are polygonal with abundant granular cytoplasm and large nuclei with prominent nucleoli. Eccentric nuclei, binucleation and nuclear atypia may be present and are not necessarily malignant features.

The differential diagnosis of Hürthle cell change includes Hashimoto's Thyroiditis, nodular goiter and Grave's Disease. Hürthle cell neoplasms have a predominantly Hürthle cell population, generally over 90%, with increased numbers of single Hürthle cells. Few lymphocytes or plasma cells should be seen. The Hürthle cell changes seen in nodular goiter tend to have less prominent nucleoli and occur in the background of the other cellular findings found in goiters.

PAPILLARY CARCINOMA

This is the most common malignant tumor of the thyroid. Histologically, papillary carcinoma presents varied patterns. The typical lesion is composed of neoplastic papillary structures with fibrovascular cores. The epithelial cells may be cuboidal, columnar or squamoid with variable cytoplasm surrounding a central ovoid nucleus. The nuclei have a ground glass appearance when poorly fixed, the so-called Orphan Annie nuclei. Papillary carcinomas are often mixed with a follicular pattern, however the nuclei seen are the typical papillary nuclei. Stromal fibrosis is common as is the presence of psammoma bodies. Cystic degeneration is very common and a lymphocytic infiltrate may be prominent.

Aspirates from papillary carcinoma tend to be very cellular and contain both papillary fragments with vascular cores and monolayered sheets. Single cells and follicular groups may also be present. The nuclear characteristics are the most important diagnostic feature, consisting of large (18-50µm) nuclei, finely granular chromatin, nuclear grooves or "popcorn" nuclear membranes and intranuclear inclusions. The cytoplasm is dense and cyanophilic. Other helpful features include psammoma bodies, multinucleated giant cells and bubble gum colloid. As any one of the above features may be seen in benign processes an unequivocal diagnosis should be made only if several are present. Papillary carcinoma with cystic degeneration may be difficult to diagnose by FNA as aspirates from these lesions may contain histiocytes and foam cells with few or no diagnostic cells. The epithelial fragments from cystic lesions should be examined closely for the nuclear features of papillary carcinoma.

Several variants of papillary carcinoma have been described. Three of these, tall cell, sclerosing diffuse and trabecular, may act more aggressive clinically. The tall cell variant has been described as having the nuclear features of a typical papillary carcinoma along with columnar cells with eccentric nuclei

and abundant granular cytoplasm. Other features described for the aggressive variants of papillary carcinoma include increased cell size, increased number of nuclear inclusions and increased nuclear pleomorphism. Papillary Hürthle cell tumors also occur and appear to behave as typical papillary carcinoma. The cytologic features of these lesions are for the most part indistinguishable from other Hürthle cell neoplasms. The presence of nuclear grooves may suggest a papillary lesion but intranuclear inclusion are not helpful as they can be seen in up to 30% of non-papillary Hürthle cell lesions.

The diagnosis of papillary carcinoma should be made only when definitive features are present as the most common recommended follow up procedure will be a total thyroidectomy. The reason for this clinical decision relates to the extremely high specificity for a cytologic diagnosis of papillary carcinoma (99%) versus the lower specificity of frozen section and the morbidity involved in performing a second completion surgery.

MEDULLARY CARCINOMA

Medullary carcinomas are derived from calcitonin producing parafollicular ("C") cells. They account for about 5-10% of thyroid malignancies. Most medullary carcinomas occur as sporadic tumors but 10-20% occur as part of one of the MEN syndromes. The microscopic appearance of medullary carcinoma is quite variable. The tumor cells tend to be arranged in nest like solid patterns. The cells vary from round to spindle shaped with bland nuclei. Interspersed among the nests of cells is a variable amount of homogenous eosinophilic material which stains as amyloid.

FNA specimens are usually cellular with numerous single cells and loosely cohesive groups. The cells are typically round to oval with eccentric nuclei (plasmacytoid), but may be spindle shaped or epithelioid. Binucleation is common and intranuclear cytoplasmic inclusions may be seen. The cytoplasm may be granular and when stained with Giemsa will demonstrate small red granules. Amyloid appears as dense amorphous globules or fragments and can be stained with Congo Red then observed under polarization for the distinctive apple green birefringence. Immunohistochemistry for calcitonin can also be very helpful.

Depending on the cytologic presentation, the differential diagnosis of medullary carcinoma includes either oxyphilic (Hürthle cell) neoplasms or anaplastic carcinoma. Anaplastic carcinoma will be aggressive clinically and demonstrate much more nuclear pleomorphism. The eccentrically placed and larger nuclei and red granules seen in the cytoplasm of medullary carcinoma help differentiate these lesions from Hürthle cells.

ANAPLASTIC CARCINOMA

These very aggressive tumors of the elderly are usually present with a rapid increase in size with extension of the tumor into the surrounding soft tissue. The tumors are characterized by marked cellular pleomorphism with either giant cells or spindle shaped cells. There may be considerable necrosis. The diagnosis of malignancy is not a problem with these lesions if an adequate sample is obtained. Some anaplastic carcinomas may be very sclerotic and yield only scantly cellular specimens so that careful attention to nuclear detail may be important. Anaplastic carcinoma may arise in a papillary or follicular carcinoma and may be admixed with papillary or follicular elements on the aspirate. The differential diagnosis of anaplastic carcinoma would include metastatic poorly differentiated tumors so a good clinical history is important, as may be special stains. Anaplastic carcinomas are typically keratin positive but thyroglobulin negative.

LYMPHOMA

Malignant lymphoma may involve the thyroid either as a primary or secondary lesion. Usually primary thyroid lymphoma arises in a thyroid with chronic lymphocytic thyroiditis. Women are affected more than men and most patients are elderly. The most common type is a large cell lymphoma with areas of necrosis and large pleomorphic cells in a cellular aspirate. The differential diagnosis would include an anaplastic carcinoma or possibly a florid thyroiditis. Immunohistochemistry or a separate aspirate for flow cytometry may be very helpful.

METASTATIC TUMORS

Metastatic tumors to the thyroid are unusual but can occur. The most common primary sites are kidney, breast and lung but other tumors may be seen. In our series from Mayo other tumors included renal cell carcinoma, squamous cell carcinoma, adenocarcinoma, melanoma, neuroendocrine carcinoma, synovial sarcoma, mucoepidermoid carcinoma, neurofibrosarcoma, chordoma and thymoma A clinical history of malignancy is helpful but thyroid metastasis may be the first indication of tumor. Renal cell

carcinoma and ductal carcinoma of the breast may be especially difficult to diagnose as a metastasis in the absence of a known primary. Renal cell carcinoma may closely resemble Hürthle cell change and well-differentiated ductal carcinoma may appear similar to either medullary carcinoma or follicular neoplasia.

RARE PRIMARY TUMORS

Other benign neoplasm and malignancies may rarely arise in the thyroid. Epidermal inclusion cysts cytologically and histologically similar to those seen in the subcutaneous tissue may be seen. Mucoepidermoid carcinoma has also been reported. The cytologic features are similar to those seen in primary lesions of the salivary gland. Squamous cell carcinoma can also rarely arise in the thyroid. Primary angiosarcoma occurs in the thyroid, especially in patients from the alpine regions of Europe.

MAYO CLINIC EXPERIENCE

Searching the Mayo Clinic Cytology and Surgical Pathology records, a total of 5,722 patients with thyroid FNA specimens between January 2001 and the end of June 2005 were identified. Of these, 1,277 (22%) had biopsy follow up and are included in the following table.

Thyroid Diagnosis By Cytology and Histology

Cytology Diagnosis	N (%)	Histology Diagnosis N (%)						
		Follicular/ Hürthle Cell Adenoma	Benign *	Follicular/ Hürthle Cell Carcinoma	Papillary Carcinoma (PTC)	Lymphoma	Other Thyroid Cancer †	Non-Thyroid Cancer ‡
Nondiagnostic	123 (10)	41 (33)	68 (55)	3 (2)	9 (7)	1 (1)	0 (0)	1 (1)
Negative (Benign Thyroid Nodule)	310 (25)	68 (22)	215 (69)	5 (2)	16 (5)	3 (1)	1 (0)	2 (1)
Follicular/ Hürthle Neoplasm (FN)	336 (28)	240 (71)	55 (16)	18 (5)	22 (7)	0 (0)	0 (0)	1 (0)
Suspicious for Papillary Cancer	111 (9)	16 (14)	16 (15)	2 (2)	75 (68)	0 (0)	2 (2)	0 (0)
Suspicious for Malignancy, NOS	30 (2)	5 (17)	8 (27)	1 (3)	0 (0)	7 (23)	6 (20)	3 (10)
Positive	309 (25)	4 (1)	3 (1)+	3 (1)	262 (85)	5 (2)	15 (5)	17 (6)

* Includes goiter, adenomatous nodule, Hashimoto thyroiditis, and other benign diagnoses
\+ Includes hyalinizing trabecular adenoma (1) adenomatous nodule (2)
† Includes anaplastic, medullary and insular carcinoma
‡ Includes metastatic or locally invasive renal cell carcinoma, squamous cell carcinoma, adenocarcinoma, melanoma, neuroendocrine carcinoma, synovial sarcoma, mucoepidermoid carcinoma, neurofibrosarcoma, chordoma and thymoma

The PPV for malignancy with a diagnosis of positive for PTC by cytology was 98.9%. Of the three benign cases, one was a hyalinizing trabecular adenoma, which is notoriously difficult to distinguish from PTC. When including suspicious for PTC cytology results, the sensitivity for detecting PTC was 87.5% with a specificity of 94.8%. When using cases called suspicious or positive by cytology, the sensitivity and specificity for detecting malignancy was 82.9% and 93.0%, respectively. When evaluating cases called FN, suspicious and positive, the sensitivity and specificity for neoplasia was 82.4% and 77.5%, respectively.