Over the years, needle biopsy has dramatically changed the evaluation of head and neck lesions. Prior to routine use of needle biopsies, surgical biopsy was a primary technique for tissue diagnosis in the head and neck. However, with the improvement of image quality and development of different needle systems, fine-needle aspiration (FNA) and core-needle biopsy (CNB) have become the primary methods for making a tissue diagnosis in the thyroid and salivary glands, as well as in lymph nodes. While FNA of head and neck lesions is a well-established technique, CNB is increasingly recognized as a preferred diagnostic technique, particularly with lymph nodes and salivary gland lesions. The goal of this article is to review the role of CNB in evaluating head and neck lesions.

Overview of Biopsy Techniques
Palpation-guided FNA of neck lesions is commonly performed in a clinic setting and is a reasonable initial diagnostic procedure. Image-guided FNA, however, has been shown to produce higher diagnostic yield. US is the preferred method of imaging guidance, although CT guidance can be helpful for deeper lesions, particularly near the skull base. FNA is performed using narrow-gauge needles (20 to 25 gauge) with the goal of removing sufficient cells for cytologic analysis. FNA biopsies can be performed with or without suction (capillary action). We generally begin with an FNA biopsy using a 25-gauge needle with capillary action and add suction or use a larger needle if the initial passes yield an insufficient sample. One benefit of US-guided FNA is its safety, with a very low incidence of significant complications. The main disadvantage of FNA is the small sample acquired, which can lead to cases of an insufficient sample or non-diagnostic results.

CNBs are performed with larger gauge cutting needles (16 to 20 gauge) to harvest tissue fragments, allowing histologic assessment and identification of the architectural features of the specimen. There are many core biopsy devices, including semi-automated and fully automated side-cut needles as well as fully automated end-cut needles. CNB has been shown to increase diagnostic yield compared with FNA biopsy of salivary lesions and cervical lymph nodes. The principal disadvantage of CNB is the concern for a greater incidence of significant complications, including tumor implantation along the biopsy tract, hemorrhage, and damage to adjacent structures, although the actual risk is low.

There are multiple differences between the FNA and CNB techniques. Preliminary cytologic assessment of fine-needle aspirates may be performed by an onsite pathologist, allowing real-time feedback to assess the adequacy of a sample. Although immediate assessment of core specimens is feasible with touch prep technique, core specimens are generally placed in solution to be examined after the procedure. Core specimens generally provide larger specimens for subsequent immunohistochemical analysis, although such analysis can be successful with FNA if sufficient sample is available for creation of a cell block. With CNB there is the risk of sample bias, as often only 1 or 2 samples are obtained, whereas with FNA a larger portion of the lesion can be sampled by directing the needle throughout all portions of the lesion with real-time US guidance.
Core-Needle Biopsy in the Evaluation of Head and Neck Lesions

Image-guided head and neck needle biopsies are commonly performed using single needle technique. Coaxial technique using an introducer needle allows multiple needle samples with a single puncture and can be performed particularly with deeper lesions. Disadvantages of coaxial technique include larger needle size and the potential for introducing gas into the tissues surrounding a targeted lesion, which can impair US visualization.

The indications for, results of, and potential complications of CNB vary between different tissues of the head and neck. Highlighted below are the specific issues regarding CNB in the thyroid, salivary glands, and cervical lymph nodes.

Thyroid Gland

The thyroid gland is in the anterior cervical neck, just inferior to the larynx, in the visceral space. It is anterior to the trachea and esophagus, and medial to the carotid sheaths. The arterial supply to the thyroid is from the superior and inferior thyroid arteries. The superior thyroid artery is the first anterior branch of the external carotid artery and runs superficially along the anterolateral surface of the thyroid. The superior thyroid artery is the landmark for identifying the superior laryngeal nerve, which courses with the artery until approximately 1 cm from the superior thyroid pole. The inferior thyroid artery arises from the subclavian artery in the thyrocervical trunk. It ascends vertically, then curves medially to enter the tracheoesophageal groove in a plane posterior to the carotid space. Most of its branches penetrate the posterolateral aspect of the thyroid. Posterioromedial to the thyroid is the tracheoesophageal groove where the paratracheal nodes, recurrent laryngeal nerve, and parathyroid glands are located. The recurrent laryngeal nerve is associated with the inferior thyroid artery at approximately the junction of the lower and middle thirds of the thyroid gland.

In 2015, the American Thyroid Association updated guidelines for the work-up of adult patients with thyroid nodules. These recommendations combine nodule size, sonographic appearance, and clinical risk factors to determine the need for FNA, with FNA rarely indicated for nodules < 1 cm. Nodules highly suspicious for malignancy based on sonographic appearance include those that are solid and hypoechoic, or have a solid hypoechoic component in a partially cystic nodule with one or more of the following characteristics: irregular margins, microcalcifications, greater height than width, rim calcification with small extrusive soft-tissue components, or evidence of extrathyroidal extension. Prior to FNA, patients should have a thorough diagnostic US examination, as findings on diagnostic US change management in more than half of patients. Specifically, if suspicious lymph nodes are discovered, then FNA of at least one node is generally indicated.

When biopsy of a thyroid nodule is indicated, FNA is the procedure of choice. FNA provides samples that are satisfactory for interpretation in 89% to 95% of cases; 55% to 74% of samples are definitively benign and 2% to 5% are definitively malignant. In the case of a thyroid nodule, FNA yielded suspicious lymphocytes. Subsequent US-guided core biopsy using a semi-automated side-cut needle (thin arrows) with the specimen trough (thick arrows) was deployed within the lesion. Core biopsy confirmed thyroid lymphoma.

FIGURE 1. An 80-year-old woman with a rapidly enlarging right paramedian low neck mass. She has a history of radioactive iodine ablation for Graves’ disease 40 years earlier. Transverse US of the neck (A) demonstrates a hypoechoic ill-defined mass in the right lobe of the thyroid, which corresponds to an area of marked hypermetabolism on PET-CT (B). FNA yielded suspicious lymphocytes. Subsequent US-guided core biopsy (C) using a semi-automated side-cut needle (thin arrows) with the specimen trough (thick arrows) was deployed within the lesion. Core biopsy confirmed thyroid lymphoma.
setting of nondiagnostic cytology, repeat FNA with US guidance and onsite cytology review for adequacy is suggested and may yield a diagnostic result in 60% to 80% of nodules. If the second US-guided FNA is also nondiagnostic, it has been shown that a third FNA is less likely to be diagnostic. At this point, further evaluation of the US characteristics can help determine the next step. If the lesion has suspicious imaging characteristics, then further workup with either CNB, molecular testing, or surgical excision should be considered.

The role of CNB of thyroid nodules remains controversial. In the setting of a nondiagnostic FNA, CNB has been reported to have a higher diagnostic rate than repeat FNA, with diagnostic rates of >95%. CNB has also been shown to have highly diagnostic results in the setting of a calcified thyroid nodule where FNA adequacy may be difficult. One study, however, suggested that CNB may be less sensitive than FNA for the diagnosis of malignancy. Subsequent studies have found a higher sensitivity for detecting malignancy with CNB as compared with FNA, although CNB may be limited in the setting of a follicular lesion. The limitation of CNB in the setting of follicular lesions is not surprising, as the histologic differentiation between follicular adenoma and low-grade follicular carcinoma requires evaluation of the entire specimen to detect capsular invasion. One meta-analysis concluded that CNB had suboptimal sensitivity for malignancy (68%); however, this meta-analysis did not include the most recent reported studies. CNB of the thyroid is considered safe by most recent reports with occasional hematomas and self-limited hemoptysis, but no major complications requiring intervention.

In the setting of a nondiagnostic thyroid nodule FNA, molecular testing of FNA samples is an option. Like CNB, the role of molecular testing has not been definitively established, particularly given the rapid advancement of molecular testing techniques. For instance, one molecular testing technique has been reported to have sensitivity and specificity of >90% for both follicular lesions and atypia of undetermined significance.

Molecular testing is generally performed with FNA aspirates and, therefore, has the theoretical advantage of decreased risk of complications as compared with CNB. Additionally, it is possible (and our practice) to collect specimens for molecular testing at the time of the initial FNA, although this requires an additional 1 to 3 needle sticks per nodule. The molecular testing specimens can be retained in the laboratory for several months, allowing a
decision on whether to send the specimen for molecular testing to be made after final cytopathology results. The major advantage of this approach is that the patient does not have to return for a second biopsy procedure.

In addition to primary thyroid malignancies, primary thyroid lymphoma is another important pathology to consider. Thyroid lymphoma comprises 1% to 5% of all thyroid malignancies and most commonly consists of either marginal zone (mucosa-associated lymphoid tissue) lymphoma, which has a good prognosis, or diffuse large B-cell lymphoma, which has a poor prognosis.\(^{32}\) When the FNA results suggest lymphoma or when the clinical suspicion for lymphoma is high in the presence of a nondiagnostic FNA, subsequent collection of material for flow cytometry and CNB can be obtained (Figure 1). CNB has been reported to have a 90% diagnostic rate for thyroid lymphoma.\(^{28}\)

**Salivary Glands**

The parotid gland is the largest of the salivary glands and lies in the parotid space, which is the most lateral major suprahyoid neck space. The parotid gland is bound superiorly by the external auditory canal, inferiorly by the mandible, anteriorly by the masticator space, and posteriorly by the sternocleidomastoid and posterior belly of the digastric muscles. The parotid gland is divided into superficial and deep lobes, which are anatomically delineated by the facial nerve. While the facial nerve cannot be directly visualized sonographically, its position can be inferred by the retromandibular vein, which commonly runs just deep to the facial nerve. The external carotid artery runs deep to the retromandibular vein and ascends through the gland to give rise to the posterior auricular, maxillary, and superficial temporal arteries. The accessory lobe of the parotid is positioned anteriorly along the parotid duct and lies superficial to the masseter muscle.\(^{33}\)

The submandibular glands are in the anterior portion of the submandibular triangle, below the floor of the mouth. The submandibular duct connects the gland to the floor of the mouth. Similar to the parotid gland, the submandibular gland is made up of superficial and deep lobes delineated by the mylohyoid muscle. Three nerves are closely associated with the submandibular glands: lingual, hypoglossal, and the marginal mandibular branch of the facial nerve. The lingual nerve begins lateral to the submandibular duct and courses anteromedially. The hypoglossal nerve is deep to the gland and runs superficial to the hyoglossus muscle but deep to the digastric muscle. The marginal mandibular branch of the facial nerve runs inferior to the submandibular gland. The submental arteries and veins provide blood supply to the gland.

US is the initial modality of choice for investigating a salivary gland lesion. MRI is a useful second-line imaging test, particularly for deep parotid lobe lesions that may be difficult to fully visualize with US due to limited deep sound penetration or when perineural spread of tumor is suspected. US guidance during needle biopsy allows for direct visualization of the needle within the mass, facilitating targeting of solid portions of the mass and avoidance of adjacent vascular structures.

Approximately 70% of parotid masses are neoplasms.\(^{34}\) The differential diagnosis of parotid neoplasms is complex, as the World Health Organization (WHO) classifies 28 types of salivary malignancies, many of which have low-, intermediate-, and high-grade varieties.\(^{35}\) Additionally, more than a dozen benign neoplasms may occur in the salivary glands.\(^{36}\) The likelihood of malignancy for a salivary neoplasm is inversely proportional to the
gland size, with 15% to 32% of parotid tumors, 41% to 45% of submandibular tumors, and 70% to 90% of sublingual tumors found to be malignant. 36

Needle biopsy of a salivary lesion is generally requested to determine whether a lesion requires surgical excision, as many salivary lesions are treated nonoperatively. Additionally, even if surgical excision is planned, preoperative diagnosis allows optimal patient counseling regarding prognosis and, in the setting of parotid tumors, the likelihood of facial nerve injury or sacrifice during surgery. 35,37 Although previously common, surgical incisional biopsy is now generally contraindicated because of the risks of infection, tumor seeding, facial nerve injury within the parotid gland, as well as sialocele and fistula formation. 34

Surgical biopsy has been replaced by FNA. While FNA is safe, quick and readily performed in the outpatient setting, it is not without limitations, specifically a fairly high rate of nondiagnostic samples and a limited sensitivity for malignancy. Nondiagnostic rates for salivary FNA have been reported to vary between 12% and 50%, with sensitivities varying between 64% and 88%, with considerable heterogeneity between studies. 4,5,38

CNB of salivary gland lesions has emerged as the preferred method to overcome the limitations of FNA. In three studies directly comparing FNA and CNB of salivary lesions, the nondiagnostic rate was 19% to 56% for FNA and 4% to 5% for CNB, while the sensitivity for malignancy was 60% to 76% for FNA and 89% to 93% for CNB. 15-17 Typically, core biopsies are sufficient for formal histologic and immunohistochemical analysis, thus allowing for

**FIGURE 4.** A 38-year-old man with a history of papillary thyroid carcinoma (PTC). Longitudinal and transverse gray-scale images (A) demonstrate an enlarged lymph node (arrows) with calcifications, hyperechoic foci, and cystic changes. Longitudinal and transverse color Doppler imaging (B) demonstrates disordered blood flow. US image during FNA (C) demonstrates a 25-gauge needle (black arrows) within the abnormal lymph node (white arrows). The FNA confirmed metastatic papillary thyroid carcinoma (PTC).
grading and typing of malignancies to include lymphoma. Also, CNB can help determine salivary gland involvement in systemic diseases such as Sjögren disease and sarcoidosis.

The major concern regarding CNB of salivary lesions has been an increased risk of significant complications, such as facial nerve injury during parotid biopsies. While facial nerve injury remains a theoretical possibility, the recent literature regarding CNB of salivary masses reports only occasional minor complications such as hematoma, but no nerve injuries or other major complications. A key step in avoiding nerve injury is thought to be use of careful technique that limits deployment of the cutting notch of the CNB entirely within the targeting lesion (Figure 2). Another potential complication is needle tract seeding with subsequent tumor recurrence; however, the exact incidence of this is unknown as tumor recurrence may be 10 or more years after the biopsy. Tumor seeding has been rarely reported with both FNA and CNB; the risk of tumor seeding is likely less with needle biopsy than with surgical biopsy.

The safety and efficacy of CNB of salivary lesions has led some authors to recommend CNB as the initial biopsy technique, although others leave open the possibility of starting with FNA in institutions where FNA has been successful. In our practice, we most commonly begin with FNA, but have a low threshold to add CNB for lesions with a solid component if the preliminary FNA results suggest nondiagnostic cytology.

Lymph Nodes

Cervical lymph nodes are composed of lymphoid tissue and are located along the lymphatic vessels in the neck. Each lymph node is encapsulated by fibrous tissue and contains a cortex and medulla. The cortex is composed of densely packed lymphocytes, while the medulla consists of medullary trabeculae, medullary cords and sinuses. Normal lymph nodes are ovoid or reniform in shape, with sharp distinct margins. Pathologic lymph nodes commonly exhibit alterations of shape, morphology and vascularity. Lymph nodes suspicious for malignancy are typically more round, with irregular or ill-defined margins, and may contain a central area of calcification or necrosis. On US, this is demonstrated by a loss of the normal echogenic fatty hilum and internal heterogeneity. Normal lymph nodes show central hilar vascularity, whereas malignant nodes show eccentric or absent vascularity, peripheral perfusion, focal perfusion, or multifocal aberrant vascularity. Although larger nodes tend to have a greater likelihood of malignancy, lymph node size is a poor predictor of malignancy. The anatomic location of cervical lymph nodes is based on 7 nodal stations, levels I-VII. Level Ia nodes are submental and medial to the anterior bellies of the digastric muscles. Level Ib nodes are submandibular and posterolateral to the anterior belly of the digastric muscles. Level II nodes are the upper jugular nodes and are anterior to the posterior border of the sternocleidomastoid muscle (SCM) and lateral to the submandibular gland. Both level I and level II nodes are bounded inferiorly by the inferior margin of the hyoid bone. Level III nodes are the middle jugular nodes between the inferior border of the hyoid bone and cricoid cartilage. Level IV are the inferior jugular nodes, located from the inferior border of the cricoid cartilage to the superior margin of the clavicle. Both level III and level IV are anterior to the posterior border of the SCM and lateral to the medial margin of the common and internal carotid arteries. Level V are posterior to the posterior border of the SCM, with Va being posterior to level II and III. Level Vb nodes are posterior to level IV and extend inferiorly to the superior clavicle. Level VI nodes are anterior to the visceral spaces from the inferior margin of the hyoid bone to the manubrium, medial to the common and internal carotid arteries. Level VII are the superior mediastinal nodes between the common carotid arteries, below the superior margin of the manubrium to the level of the brachiocephalic vein.

Metastatic carcinoma to neck lymph nodes tends to follow predictable patterns in an untreated neck. Oropharyngeal squamous cell carcinoma, which is often associated with the human papilloma virus (HPV), tends to spread to bilateral level II and level III lymph nodes. Oral cavity cancer, including anterior tongue, lips, and floor of mouth tumors, typically involves level I or level II lymph nodes. Cutaneous primary squamous cell carcinoma of the midface and scalp most commonly spreads to intraparotid lymph nodes, followed by level II and level V nodes. Papillary thyroid cancers tend to metastasize to levels III, IV and VI. In papillary thyroid cancer, level II involvement is less common and level I involvement is rare, although any lymph node level may be involved with widespread disease. Metastatic disease to neck lymph nodes from an infraclavicular primary tends to most prominently involve the suprACLavicular lymph nodes (at the inferior aspect of level IV and Vb). Lymph node involvement of lymphoma can include any nodal basin in the neck, including the intraparotid nodes.

US-guided needle biopsy is well established in the evaluation of neck lymph nodes, although the procedural approach should be customized for each patient based on the clinical scenario. In a patient with a suspicious cervical node, or cluster of nodes, and no history of malignancy, the most likely diagnoses are reactive/infectious adenopathy, lymphoma, and metastasis from an unknown primary malignancy. In this situation, we begin with US-guided FNA. If the preliminary cytopathology yields a polymorphous population of lymphocytes with no suspicious cells and our clinical suspicion based on the patient presentation and sonographic appearance of the nodes is low, then we stop with FNA.

If there is a greater suspicion for malignancy, then we will add FNA passes
for flow cytometry. Flow cytometry can be performed with both FNA and core samples, as long as the samples are placed in the appropriate medium, such as the Roswell Park Memorial Institute (RPMI) solution. Whether FNA or core specimens are preferred for flow cytometry is a matter of institutional preference. With a high level of suspicion based on clinical presentation or preliminary cytopathology, then we will add a core biopsy (Figure 3). As compared with FNA alone, CNB has been shown to increase the diagnostic yield for lymphoma and decrease the need for excision biopsy. A recent meta-analysis found CNB to have a sensitivity of 92%, specificity of 93%, and accuracy of 92% in distinguishing lymphoma from reactive adenopathy.

In a patient with a recently diagnosed primary malignancy and neck lymph nodes suspicious for metastasis, we find that FNA is frequently sufficient to confirm metastasis, provided that the primary malignancy has been sufficiently sampled and there is no need for further pathologic evaluation or molecular testing. In a patient with suspected intraclavicular primary malignancy without a pathologic diagnosis and suspected neck node metastasis, the neck nodes are an excellent location to sample the disease, due to the ease of sampling the neck and the very low rate of significant complications. In this setting, CNB is frequently indicated to allow for complete pathologic and molecular tissue evaluation.

Suspicious cervical lymph nodes in a patient previously treated for papillary thyroid carcinoma (PTC) is a unique but commonly encountered situation. Lymph nodes containing metastatic PTC commonly have cystic changes, calcification or hyperechoic foci, and disordered vascularity (Figure 4). Although CNB may have a role in highly selected cases of metastatic thyroid cancer, tissue thyroglobulin assay is the test of choice for suspicious lymph nodes with negative cytology in a patient with a history of PTC.

When we perform FNA of a suspicious lymph node in a patient with a history of PTC, we essentially always collect material (one FNA pass washed in 1cc of saline) for tissue thyroglobulin assay, unless the preliminary cytopathology is unequivocally positive.

**Conclusion**

Fine-needle aspirations and core-needle biopsies have supplanted surgical biopsies for most head and neck lesions. Although these procedures are not immune to the risk of complications, the use of image guidance has increased their safety and efficacy. CNB in particular has well-established indications for head and neck masses involving salivary glands, particularly the parotid gland, and cervical lymph nodes. Its use in the assessment of thyroid lesions remains controversial with the rapid advancement of molecular testing techniques that can be used with thyroid FNA samples. In the end, the decision to use FNA vs CNB needs to be based on the specific and sometimes unique presentation of each case.

**References**

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