Biopsy Techniques for Parotid Neoplasms

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ABSTRACT

Preoperative diagnosis of parotid masses through clinical assessment, imaging, and biopsy is important for optimal management. The use of fine-needle aspiration cytology (FNAC) with or without ultrasound guidance is the biopsy technique of choice. Nonetheless, ultrasound-guided core needle biopsy (USCB) is more accurate and sensitive in diagnosing malignancy, without major complications. USCB should be considered, particularly when FNAC is non-diagnostic.

Key Words: Biopsy, fine-needle; Biopsy, large-core needle; Parotid neoplasms

中文摘要

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通過臨床評估、成像和活檢作出術前診斷對優化管理腮腺腫塊至關重要。使用有或沒有超聲引導的細針抽吸細胞學（FNAC）是活檢技術的最佳選擇。儘管如此，超聲引導的芯針活檢（USCB）在診斷惡性腫瘤方面更準確和靈敏，並無嚴重併發症。當FNAC結果是非診斷性時應考慮使用USCB。

INTRODUCTION

Tumours of the parotid gland are uncommon¹ and usually benign.² An accurate preoperative diagnosis of the tumour is essential for preoperative planning or to exclude surgery for some benign tumours such as Warthin’s tumour, particularly in older or medically unfit patients. A preoperative diagnosis allows for informed consent for more invasive surgery and stratification of risk to surrounding structures, particularly the facial nerve.³ A preoperative diagnosis of malignancy enables better prognostication and consideration of other treatment options such as adjuvant chemotherapy. For tumours in the parotid gland, preoperative diagnosis is particularly important because of the presence of neurovascular structures within the gland and the variety of surgical techniques available.

Clinical examination followed by imaging (usually ultrasonography) and then needle biopsy is widely accepted practice for diagnosis.⁴ Ultrasonography can demarcate lesions in the deep or superficial parotid lobe.
by identifying the plane of the passage of the facial nerve superficial to the main intraparotid vessels. It can characterise parotid lesions with an accuracy of 90%. It is used as both a biopsy guide and an indicator of the need for further imaging (usually magnetic resonance imaging) for large or potentially malignant lesions. There are three main biopsy techniques: fine-needle aspiration cytology (FNAC), ultrasound-guided core needle biopsy (USCB), and intra-operative frozen section.

**FINE-NEEDLE ASPIRATION CYTOLOGY**

FNAC has been used since the late 1980s to replace open biopsy, which requires general anaesthesia and is associated with complications of tumour seeding, infection, bleeding, and fistula formation. FNAC is quick, safe, and well tolerated. It is usually performed ‘blind’ in the clinic, without imaging guidance, by operators with varying degrees of expertise. Blind FNAC has high non-diagnostic rates and high false-negative and false-positive rates. This can be improved by the use of imaging (generally ultrasound) guidance and addition of an on-site cytologist to review and repeat sampling or a cytology technician to assess the sample at the time of the procedure. Ancillary cytology techniques such as flow cytometry or in-situ hybridisation are also used, but they are expensive and not widely available.

In a meta-analysis of 71 studies of blind and ultrasound-guided FNAC with or without optimisation techniques, FNAC had a high specificity (98%) but a lower sensitivity (80%), with a relatively high false-negative rate for malignancy. FNAC also had a high non-diagnostic rate (8.6%), which was likely to be underestimated as not all studies reported their non-diagnostic rates. In addition, the performance of FNAC varied significantly between centres; this may be due to the varying availability of optimisation techniques.

Even when performed with optimisation techniques, FNAC has the diagnostic limitations of a cellular aspirate. The diagnosis of some tumours requires evidence of their interaction with the environment; this cannot be seen with cells alone. FNAC cannot reliably diagnose lymph node hyperplasia, namely to differentiate between reactive lymphoid tissue and low-grade lymphoma. This often results in nodal excision requiring general anaesthesia and a surgical scar, as well as a potential delay in diagnosis. FNAC is unable to differentiate Warthin’s tumours from squamous cell carcinoma (Figure 1) when there is more than one tumour cell type in the same mass, or to differentiate adenoid cystic carcinoma from pleomorphic adenoma.

**ULTRASOUND-GUIDED CORE NEEDLE BIOPSY**

USCB using a spring-loaded automated device is commonly performed in the breast and liver. A smaller bore 18-gauge or 20-gauge needle is generally used for the parotid gland (Figure 2). USCB is slightly more invasive than FNAC and requires local anaesthesia and a small skin incision. In 1999, it was first
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successfully applied to patients with parotid lesions who had non-diagnostic FNAC. USCB has been accurately and safely used to diagnose parotid lesions. In a meta-analysis of 12 studies, USCB had a specificity of 100%, a sensitivity of 96%, and a non-diagnostic rate of 1.2%, with no significant heterogeneity in performance between centres. No major complication, facial nerve injury, or tumour seeding was reported; the rate of subclinical haematoma was 1.6%.

Diagnosis of some parotid tumours requires assessment of their interaction with the surrounding tissues. The core of tissue obtained from USCB can be analysed immunohistochemically for tumour subtyping and grading (Figure 3a). This is especially useful for diagnosing non-Hodgkin lymphoma. Most lymphomas can be accurately diagnosed based on USCB results alone.

Nonetheless, USCB is associated with the risk of damage to the neurovascular structures that run through the parotid gland. Ultrasound guidance enables visualisation of the main intraparotid vessels; no injury to the facial nerve has been reported to date. Advancement in biopsy technique has further reduced the risk of facial nerve injury. USCB has a slightly higher risk of local haematoma formation than FNAC. Nevertheless, there is only one report of haematoma formation requiring surgical intervention and no report of major vascular injury. Colour Doppler ultrasound guidance helps avoid vascular areas during biopsy. The paucity of parotid biopsy complications is attributed to ultrasound guidance, anatomical knowledge, clinical experience, judicious avoidance of vascular areas, a small-calibre biopsy needle, and biopsy of a compressible site so that the clinician can control any bleeding that may occur.

The risk of tumour seeding is associated with needle size and tumour type. In the parotid gland, a seeding can take up to 20 to 30 years to manifest to pleomorphic adenoma. There are two reported cases of parotid tumour seeding following core needle biopsy using a 14-gauge needle. There are also two reported cases of tumour seeding following FNAC of the parotid gland. In a systematic review of tumour seeding in head and neck tissue sampling (salivary glands and lymph nodes but excluding the thyroid gland), only seven cases of tumour seeding (5 in 41,468 FNACs and 2 in 1803 USCBs) have been reported. The risk of tumour seeding is associated with the size of the needle, use of a single or coaxial needle, time of documentation after the procedure, and tumour-related factors. To mitigate
the risk, removal of the biopsy tract during parotid excisional surgery is suggested, although there is no evidence to support its routine practice.

In a subgroup of well-differentiated malignancies (e.g. basal cell carcinoma, oncocytic carcinoma, myoepithelial carcinoma), examination of the entire resected specimen for capsular infiltration is required for diagnosis (Figure 3b). This is similar to follicular thyroid lesions that require examination of the entire resected specimen for capsular infiltration to differentiate follicular carcinoma from adenoma. In a study to determine the optimal number of USCBs and optimal biopsy location (nodule alone; nodule and capsule; or nodule, capsule, and surrounding parenchyma) for diagnosis of thyroid tumours, the diagnostic capability of USCB was significantly higher when biopsy samples included both capsule and surrounding parenchyma.\textsuperscript{23} Similarly, the diagnostic viability and accuracy of USCB in the parotid gland may be increased when the samples include both the lesion and capsule as well as areas of poor capsular definition. This is a technical refinement in USCB that may potentially increase diagnostic yield.

Both ultrasound-guided FNAC and USCB have diagnostic limitations in extensively necrotic tumours, in which a sufficient sample is difficult to obtain to make a definite histopathological diagnosis, particularly for Warthin’s tumour that tends to be cystic/necrotic. In a study comparing 107 patients with ultrasound-guided FNAC and 64 patients with USCB, USCB had a significantly higher sensitivity (94.1\% vs. 55.6\%), specificity (100\% vs. 93.3\%), accuracy (98.4\% vs. 86.9\%) in differentiating benign from malignant lesions, and a higher success rate in diagnosing lymphoma (6/6, 100\% vs. 0/4, 0\%).\textsuperscript{21} Nonetheless, USCB was complicated with haematoma in a patient who required surgical intervention.\textsuperscript{21} In another study comparing 228 patients with USCB and 371 patients with FNAC (472 patients had parotid gland biopsies), USCB had higher sensitivity (88.2\% vs. 58.2\%) and comparable specificity (99.4\% vs. 98.6\%).\textsuperscript{26} In a study comparing 371 patients with ultrasound-guided FNAC and 228 patients with USCB, ultrasound-guided FNAC had lower sensitivity (76\% vs 97\%) and a higher false-negative rate (1.7\% vs. 5.2\%) for malignancy, despite comparable specificity (96\% vs. 99\%).\textsuperscript{27} Despite comparable accuracy in diagnosing benign lesions, USCB was more accurate than FNAC in diagnosing malignancy (80\% vs. 67\%).\textsuperscript{27} The accuracy of FNAC was significantly worse when carried out by trainees; USCB was less operator-dependent once ultrasound guidance skills had been acquired.\textsuperscript{27} FNAC also had a higher rate of inconclusive sampling (19\% vs. 4\%).\textsuperscript{27}

**INTRA-OPERATIVE FROZEN SECTION**

Intra-operative frozen section is used when other biopsy methods are underperforming or not available. In a meta-analysis of 13 studies, intra-operative frozen section had 90\% sensitivity and 99\% specificity.\textsuperscript{28} Although this technique is effective, it is an open surgical biopsy and cannot be considered a first-line biopsy technique.

**CONCLUSION**

An accurate preoperative diagnosis of a parotid tumour is essential for management. Compared with FNAC, USCB is more sensitive for malignancy, with a lower non-diagnostic rate. USCB should be the first-line biopsy technique, particularly when malignancy or lymphoma is suspected. If a parotid lesion is small, deeply placed, or close to neurovascular structures, FNAC may be a safer initial diagnostic modality, and USCB may be the secondary technique for non-diagnostic FNAC samples.

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