Hong Kong J Radiol. 2018;21:94-8 | DOI: 10.12809/hkjr1816819

REVIEW ARTICLE

Biopsy Techniques for Parotid Neoplasms

C Bano[1], K Tekeli[2], J Smith[2], S Hancox[1], J Sinnott[3], S Nachiappan[4], K Ramesar[4], DC Howlett[1]

[1]Department of Radiology, [2]Department of Maxillofacial Surgery, [3]Department of Ear, Nose and Throat Surgery, [4]Department of Pathology, Eastbourne District General Hospital, Eastbourne, United Kingdom

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

腮腺腫瘤活檢技術

C Bano, K Tekeli, J Smith, S Hancox, J Sinnott, S Nachiappan, K Ramesar, DC Howlett

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 uncommon[1] 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

Correspondence: *Dr C Bano, Department of Radiology, Eastbourne District General Hospital, Kings Drive, Eastbourne, United Kingdom.*
Email: chrisbano@gmail.com

Submitted: 20 Oct 2016; Accepted: 7 Mar 2017.

Disclosure of Conflicts of Interest: All authors have no conflicts of interest to disclose.

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%.[4,5] 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.[6,7] FNAC is quick, safe, and well tolerated.[8] 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[9] and high false-negative and false-positive rates.[10] 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.[11] 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.[11] In addition, the performance of FNAC varied significantly between centres; this may be due to the varying availability of optimisation techniques.[11]

Even when performed with optimisation techniques, FNAC has the diagnostic limitations of a cellular aspirate.[9,10] 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.[11,12] 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.[13,14]

ULTRASOUND-GUIDED CORE NEEDLE BIOPSY

USCB using a spring-loaded automated device is commonly performed in the breast[15] and liver.[16] 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

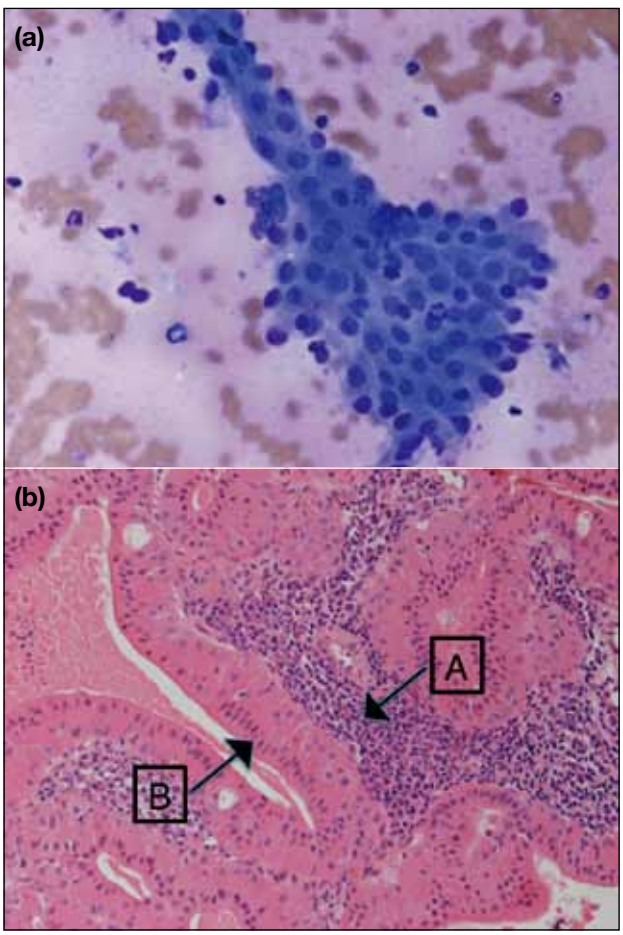

Figure 1. Cytopathology of a lesion located behind the right mandible thought to be parotid in origin. (a) A sample obtained by blind fine-needle aspiration cytology showing a large cluster of coherent epithelial cells and a surrounding cluster of lymphocytes. This is likely to be malignant and possibly squamous in origin (Giemsa, x200). (b) A sample obtained by ultrasound-guided core needle biopsy showing characteristic double layers of lymphocytes (A) and epithelium (B) consistent with Warthin's tumour (H&E, x100).

Figure 2. An 18-gauge core needle with overlying sheath retracted to reveal a tissue sample in biopsy tray.

successfully applied to patients with parotid lesions who had non-diagnostic FNAC.[17] USCB has been accurately and safely used to diagnose parotid lesions.[18,19] 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.[20] No major complication, facial nerve injury, or tumour seeding was reported; the rate of subclinical haematoma was 1.6%.[20]

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[9] (Figure 3a).This is especially useful for diagnosing non-Hodgkin lymphoma.[21] Most lymphomas can be accurately diagnosed based on USCB results alone.[22,23]

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.[12,23] Nevertheless, there is only one report of haematoma formation requiring surgical intervention[21] 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.

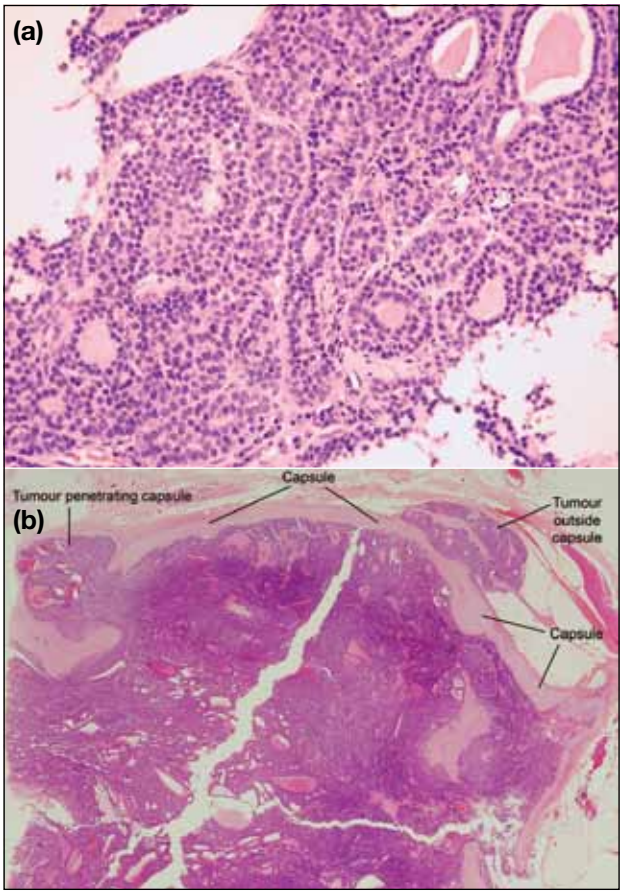

Figure 3. Immunohistochemistry of a clinically and ultrasonographically malignant mass in the right parotid gland. (a) A sample obtained by ultrasound-guided core needle biopsy showing sheets of benign-looking basaloid cells (H&E, x100), and a diagnosis of basal cell adenoma was made. The diagnosis made after fine-needle aspiration cytology was pleomorphic adenoma. (b) The macroscopic histological section showing the tumour penetrating the capsule (H&E, x100), and a diagnosis of well-differentiated basal cell carcinoma was made.

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.[7] There are two reported cases of parotid tumour seeding following core needle biopsy using a 14-gauge needle.[12] There are also two reported cases of tumour seeding following FNAC of the parotid gland.[12] 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.[24] 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.[25] 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%).[21] Nonetheless, USCB was complicated with haematoma in a patient who required surgical intervention.[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%).[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%).[27] Despite comparable accuracy in diagnosing benign lesions, USCB was more accurate than FNAC in diagnosing malignancy (80% vs. 67%).[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.[27] FNAC also had a higher rate of inconclusive sampling (19% vs. 4%).[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.[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.

REFERENCES

1. Speight PM, Barrett AW. Salivary gland tumours. Oral Dis. 2002;8:229-40. cross ref
2. Jones AV, Craig GT, Speight PM, Franklin CD. The range and demographics of salivary gland tumours diagnosed in a UK population. Oral Oncol. 2008;44:407-17. cross ref
3. Mehle ME, Kraus DH, Wood BG, Benninger MS, Eliachar I, Levine HL, et al. Facial nerve morbidity following parotid surgery for benign disease: the Cleveland Clinic Foundation experience. Laryngoscope. 1993;103:386-8. cross ref
4. Lee YY, Wong KT, King AD, Ahuja AT. Imaging of salivary gland tumours. Eur J Radiol. 2008;66:419-36. cross ref
5. Brennan PA, Herd MK, Howlett DC, Gibson D, Oeppen RS. Is ultrasound alone sufficient for imaging superficial lobe benign parotid tumours before surgery? Br J Oral Maxillofac Surg. 2012;50:333-7. cross ref
6. Rimm DL, Stastny JF, Rimm EB, Ayer S, Frable WJ. Comparison of the costs of fine-needle aspiration and open surgical biopsy as methods for obtaining a pathologic diagnosis. Cancer. 1997;81:51-6. cross ref
7. Harris AH, Smith RR. Operative wound seeding with tumor cells: its role in recurrences of head and neck cancer. Ann Surg. 1960;151:330-4. cross ref
8. Batsakis JG, Sneige N, el-Naggar AK. Fine-needle aspiration of salivary glands: its utility and tissue effects. Ann Otol Rhinol Laryngol. 1992;101:185-8. cross ref
9. Layfield LJ, Glasgow BJ. Diagnosis of salivary gland tumors by fine-needle aspiration cytology: a review of clinical utility and pitfalls. Diagn Cytopathol. 1991;7:267-72. cross ref

10. Zbären P, Schär C, Hotz MA, Loosli H. Value of fine-needle aspiration cytology of parotid gland masses. Laryngoscope. 2001;111:1989-92. cross ref
11. Schmidt RL, Hall BJ, Wilson AR, Layfield LJ. A systematic review and meta-analysis of the diagnostic accuracy of fine-needle aspiration cytology for parotid gland lesions. Am J Clin Pathol. 2011;136:45-59. cross ref
12. Douville NJ, Bradford CR. Comparison of ultrasound-guided core biopsy versus fine-needle aspiration biopsy in the evaluation of salivary gland lesions. Head Neck. 2013;35:1657-61. cross ref
13. Lambade PN, Rajkhokar D, Lambade D. Basal cell adenoma of submandibular salivary gland: a case report and literature review. J Maxillofac Oral Surg. 2015;14:999-1003. cross ref
14. Joseph TP, Joseph CP, Jayalakshmy PS, Poothiode U. Diagnostic challenges in cytology of mucoepidermoid carcinoma: report of 6 cases with histopathological correlation. J Cytol. 2015;32:21-4. cross ref
15. Ballo MS, Sneige N. Can core needle biopsy replace fine-needle aspiration cytology in the diagnosis of palpable breast carcinoma. A comparative study of 124 women. Cancer. 1996;78:773-7. cross ref
16. Padia SA, Baker ME, Schaeffer CJ, Remer EM, Obuchowski NA, Winans C, et al. Safety and efficacy of sonographic-guided random real-time core needle biopsy of the liver. J Clin Ultrasound. 2009;37:138-43. cross ref
17. Buckland JR, Manjaly G, Violaris N, Howlett DC. Ultrasound-guided cutting-needle biopsy of the parotid gland. J Laryngol Otol. 1999;113:988-92. cross ref
18. Kesse KW, Manjaly G, Violaris N, Howlett DC. Ultrasound-guided biopsy in the evaluation of focal lesions and diffuse swelling of the parotid gland. Br J Oral Maxillofac Surg. 2002;40:384-8. cross ref
19. Taki S, Yamamoto T, Kawai A, Terahata S, Kinuya K, Tonami H. Sonographically guided core biopsy of the salivary gland masses: safety and efficacy. Clin Imaging. 2005;29:189-94. cross ref
20. Witt BL, Schmidt RL. Ultrasound-guided core needle biopsy of salivary gland lesions: a systematic review and meta-analysis. Laryngoscope. 2014;124:695-700. cross ref
21. Huang YC, Wu CT, Lin G, Chuang WY, Yeow KM, Wan YL. Comparison of ultrasonographically guided fine-needle aspiration and core needle biopsy in the diagnosis of parotid masses. J Clin Ultrasound. 2012;40:189-94. cross ref
22. Ben-Yehuda D, Polliack A, Okon E, Sherman Y, Fields S, Lebenshart P, et al. Image-guided core-needle biopsy in malignant lymphoma: experience with 100 patients that suggests the technique is reliable. J Clin Oncol. 1996;14:2431-4. cross ref
23. Schmidt RL, Hall BJ, Layfield LJ. A systematic review and meta-analysis of the diagnostic accuracy of ultrasound-guided core needle biopsy for salivary gland lesions. Am J Clin Pathol. 2011;136:516-26. cross ref
24. Shah KS, Ethunandan M. Tumour seeding after fine-needle aspiration and core biopsy of the head and neck: a systematic review. Br J Oral Maxillofac Surg. 2016;54:260-5. cross ref
25. Hahn SY, Shin JH, Oh YL. What is the ideal core number for ultrasonography-guided thyroid biopsy of cytologically inconclusive nodules? AJNR Am J Neuroradiol. 2017;38:777-81. cross ref
26. Song IH, Song JS, Sung CO, Roh JL, Choi SH, Nam SY, et al. Accuracy of core needle biopsy versus fine needle aspiration cytology for diagnosing salivary gland tumors. J Pathol Transl Med. 2015;49:136-43. cross ref
27. Eom HJ, Lee JH, Ko MS, Choi YJ, Yoon RG, Cho KJ, et al. Comparison of fine-needle aspiration and core needle biopsy under ultrasonographic guidance for detecting malignancy and for the tissue-specific diagnosis of salivary gland tumors. AJNR Am J Neuroradiol. 2015;36:1188-93. cross ref
28. Schmidt RL, Hunt JP, Hall BJ, Wilson AR, Layfield LJ. A systematic review and meta-analysis of the diagnostic accuracy of frozen section for parotid gland lesions. Am J Clin Pathol. 2011;136:729-38. cross ref