European Annals of Otorhinolaryngology, Head and Neck diseases 138 (2021) 269–274

Available online at ScienceDirect www.sciencedirect.com

Elsevier Masson France EM|consulte www.em-consulte.com/en

SFORL Guidelines

Guidelines of the French Society of Otorhinolaryngology–Head and Neck Surgery (SFORL), part I: Primary treatment of pleomorphic adenoma

S. Vergez [a,*,1], N. Fakhry [b,1], C. Cartier [c], T. Kennel [c], M. Courtade-Saidi [d], E. Uro-Coste [d], A. Varoquaux [e], C.-A. Righini [f], O. Malard [g], P. Mogultay [c], J. Thariat [h], S. Tronche [i], R. Garrel [c,1], D. Chevalier [j,1]

[a] *Service d'ORL et de chirurgie de la face et du cou, hôpital Larrey, institut universitaire du cancer de Toulouse Oncopole, CHU de Toulouse, Toulouse, France*
[b] *Service d'ORL et chirurgie de la face et du cou, hôpital de la conception, AP–HM, Aix-Marseille Université, Marseille, France*
[c] *Service d'ORL et de chirurgie de la face et du cou, CHU de Montpellier, Montpellier, France*
[d] *Service d'anatomie et cytologie pathologiques, institut universitaire du cancer de Toulouse Oncopole, INSERM CRCT–Équipe 11, Toulouse, France*
[e] *Service de radiologie, hôpital de la conception, AP–HM, Marseille; AMU, Faculté de Médecine Timone CNRS–Centre for Magnetic Resonance in Biology and Medicine, Marseille, France*
[f] *Service d'ORL et de chirurgie de la face et du cou, CHU de Grenoble Alpes (CHUGA), Grenoble, France*
[g] *Service d'ORL et de chirurgie de la face et du cou, CHU Hôtel Dieu, Nantes, France*
[h] *Département de radiothérapie, centre François-Baclesse, Caen; Laboratoire de Physique Corpusculaire IN2P3/ENSICAEN–UMR6534–Unicaen–Normandie Université, Caen, France*
[i] *Société française d'ORL et chirurgie cervico-faciale, Strasbourg, France*
[j] *Service d'ORL et de chirurgie de la face et du cou, CHU de Lille, Lille, France*

ARTICLE INFO

Keywords:
Pleomorphic adenoma
Salivary glands
Parotid
Submandibular gland

ABSTRACT

Introduction: The authors present the guidelines of the French Society of Otorhinolaryngology–Head and Neck Surgery (SFORL) for the diagnosis and treatment of pleomorphic adenoma (PA) of the salivary glands.
Method: A review of the literature was performed by a multidisciplinary task force. Guidelines were drafted based on the articles retrieved and the workgroup members' individual experience. Guidelines were graded A, B, C or expert opinion by decreasing level of evidence.
Results: In clinically suspected salivary gland PA, MRI should be performed, including head and neck lymph node levels. Fine needle aspiration cytology is particularly recommended for tumours difficult to characterise by MRI. Frozen section biopsy should be performed to confirm diagnosis and adapt the surgical procedure in case of intraoperative findings of malignancy. Complete resection of the parotid PA should be performed en bloc, including margins, when feasible according to tumour location, while respecting the facial nerve. Enucleation (resection only in contact with the tumour) is not recommended. For the accessory salivary and submandibular glands, complete en bloc resection should be performed.

1. Introduction

Pleomorphic adenoma (PA) is the most frequent benign tumour of the parotid gland, at around 4.5/100,000 in Europe [1] (level of evidence, 4). Its benign nature is reassuring for the patient but should not lower the therapeutic stakes incurred by proximity to the facial nerve, risk of recurrence [2] (level of evidence, 4) and rare but possible malignant transformation [3] (level of evidence, 4). The main aim of the present study was to draw up guidelines for primary diagnostic and therapeutic strategy in PA. Secondary objectives comprised description of diagnostic imaging with clinical suspicion of parotid PA, determination of the role of cytology in PA work-up, and of frozen section biopsy during resection of suspected PA, and description of surgical strategies in parotid and non-parotid PA.

2. Material and method

A multidisciplinary workgroup was tasked with defining therapeutic strategy for PA, from initial radiological and cytological

* Corresponding author at: Service ORL et chirurgie cervico-faciale, CHU Toulouse-Larrey, 24, chemin de Pouvourville, Toulouse, France.
E-mail address: vergez.s@chu-toulouse.fr (S. Vergez).
[1] Equal contributions.

https://doi.org/10.1016/j.anorl.2020.09.002
1879-7296/

work-up for clinically suspected PA to surgical treatment strategy. Guidelines were based on a literature review by Medline search combining the search-terms "pleomorphic adenoma", "salivary tumour", "parotid", "submandibular", "accessory salivary glands", "diagnosis", "MRI", "ultrasound", "CT scan", "PET-CT", "fine needle aspiration cytology", "pathology", "frozen section", "surgery", "parotidectomy" and "extra-capsular dissection". The review was drawn up in the light of the workgroup member's experience and guidelines were graded A, B, C or expert opinion according to decreasing level of evidence.

3. Diagnostic imaging and characterisation of clinically suspected parotid PA

The objectives of imaging in clinically suspected PA are multiple: to assess the clinical suspicion, establish tumour size and extension, rule out metastatic lymph-nodes, rule out perineural invasion, guide any needle biopsy, and distinguish between recurrence and post-treatment remodelling.

3.1. Screening and characterisation of subcentimetric parotid formations

The scope of imaging, whether MRI, CT or ultrasound, being around 1 cm, none of the methods have the requisite sensitivity and specificity to screen and characterise subcentimetric salivary gland lesions. If the lesion is in an accessible location, ultrasound is the examination of choice for ruling out non-tumoral lesions, such as normal lymph nodes, inflammatory adenitis or chronic sialadenitis nodules [4] (level of evidence, 3). When the lesion is accessible, ultrasound is the first-line technique for assessing non-progression at 4–6 weeks (expert opinion).

3.2. Screening and characterisation of supracentimetric parotid formations

MRI is the examination of choice for determining local extension and characterising parotid tumour, ideally with a coronal sequence to screen for concomitant cervical lymphadenopathies and diffusion- and perfusion-weighted sequences to enhance the specificity of characterisation.

PA presents as an intraparotid lesion in T2 hypersignal without satellite lymphadenopathy [5] (level of evidence, 4).

There is usually a thin capsule showing T2 hyposignal, with heterogeneous enhancement on contrast medium injection. Lesions in T2 iso- or hypo-signal with respect to the gland are probably not PAs. Signs of perineural involvement around the facial nerve (thickening and gadolinium uptake on T1) are not compatible with PA. Restriction on diffusion weighting, with apparent diffusion coefficient (ADC) $< 1 \times 10^{-3}$ mm^2/s, is likewise not compatible with PA [6] (level of evidence, 3). In dynamic contrast-enhanced perfusion MRI, progressive enhancement is more usual [7] (level of evidence, 3), rapid enhancement (< 110 s) with weak lesion wash-out (< 30 %) is more rare [8] (level of evidence, 4). Wash-out > 30 % seems incompatible with PA [8] (level of evidence, 4).

CT is not recommended in first line. Less specifically than MRI, it reveals a well-delineated intraparotid lesion with heterogeneous enhancement [9] (level of evidence, 4). Enlarged stylomastoid foramen (suggesting facial nerve invasion) or lymphadenopathies are basically incompatible with PA. 18-FDG PET-CT is not recommended. Hyperfixation is basically incompatible with PA [10] (level of evidence, 4).

Guideline

- Morphologic MRI should be performed, including the head and neck lymph-node areas, ideally with diffusion and perfusion sequences, for characterisation and extension assessment of supracentimetric parotid lesions (Grade B).
- Contrast-enhanced CT is an alternative to MRI in case of contraindications (expert opinion).
- For subcentimetric lesions, ultrasound is recommended in first line (expert opinion).
- 18-FDG PET-CT is not recommended in first line for suspected PA (Grade C).

3.3. Postoperative radiologic PA surveillance strategy

PA recurrence may be single or multiple, with up to 100 nodular elements, usually within the parotid space or sometimes all along the surgical scar [11] (level of evidence, 3).

MRI is the examination of choice for screening PA recurrence and analysing extension. Recurrences usually present an aspect similar to that of the primary, in T2 hypersignal. A T2 fat-sat sequence can facilitate screening [10] (level of evidence, 3).

Guideline

- MRI is the gold-standard examination for surveillance of patients at high risk of recurrence (Grade C).
- MRI should not be performed within 6 months of surgery (Expert opinion).

4. Role of cytology in PA work-up

Fine-needle aspiration cytology (FNAC) is frequently practiced as part of the preoperative work-up for salivary gland lesions. It is easy to perform, with very few complications: 0.1% hematoma, 0.16% infection or inflammation, 0.1% pain, and almost no risk of facial nerve lesion [12] (level of evidence, 2). Recently, the Milan system provided a classification of salivary gland cytopathology (Table 1) [13].

4.1. Sampling technique

FNAC should be performed by an experienced clinician, radiologist or cytopathologist. A 23–27 G needle is used, preferably without aspiration. The sample is either spread on slides and quickly air-dried, or collected in liquid (of various types depending on the supplier).

In a meta-analysis, Liu [12] (level of evidence, 2) showed that ultrasound-guided FNAC had greater sensitivity (0.85; 95% confidence interval (95% CI), 0.76–0.91) and specificity (0.98; 95% CI, 0.95–0.99) than without ultrasound guidance [respectively, 0.78 (0.74–0.82) and 0.97 (0.96–0.98)]. In head and neck lesions in general (salivary glands, cervical lymph nodes, thyroid), ultrasound guidance gives significantly fewer non-contributive FNAC samples than palpation guidance (17.1% versus 6.2%), especially in subcentimetric lesions (38.6% versus 2.9%), with significantly lower discordance with postoperative histology (5.4% versus 12.8%) [14] (level of evidence, 4).

Table 1
Milan classification of salivary gland cytology (adapted from Faquin et al. [13]).

Diagnostic category	Malignancy risk	Treatment recommendations	Examples
I. Non-diagnostic	25%	– Clinical and radiological correlation – Repeat FNAC	Normal salivary parenchyma, non-mucinous sample
II. Non-neoplastic	10%	–Clinical follow-up and radiological correlation	– Chronic sialadenitis – Intraparotid reactional lymph-node
III. Atypia of uncertain significance (AUS)	20%	Repeat FNAC or surgery	Mucinous cystic material, predominantly oncocytic, benign metaplasia versus neoplasm
IV. Neoplasm			
a. Benign	< 5%	Surgery or clinical follow-up	Pleomorphic adenoma, Warthin tumour
b. Salivary tumour of uncertain malignant potential (SUMP)	35%	Surgery	Basaloid cell neoplasm, pleomorphic adenoma with atypia
V. Suspicion for malignancy (SM)	60%	Surgery	
VI. Malignant	90%	Surgery	Salivary duct carcinoma, cystic adenoid carcinoma

FNAC: fine-needle aspiration cytology.

4.2. FNAC in PA work-up

Cytology/histology concordance was reported to be 97% in PA [15] (level of evidence, 4), in agreement with Klijanienko et al. [16] (level of evidence, 3). On the Milan system [16], malignancy risk in FNAC for benign tumour was 3.4 ± 1.3%, sensitivity 95% and specificity 93 % [17] (level of evidence, 2). Similar results were reported by Farahani and Baloch [18] (level of evidence, 2), with 4% malignancy in the benign tumour group. Diagnostic performance in PA was 97.5 % for Choy et al. [19] (level of evidence, 4), with 2.7% malignancy in benign tumour. Stanek and Khariwala [20] (level of evidence, 4) considered needle biopsy to make an important contribution to diagnosis and that performance was enhanced by ultrasound guidance. The pitfalls for cytologic diagnosis of PA consist in cystic adenoid carcinoma, carcinoma ex-PA, mucoepidermoid carcinoma and myoepithelial cell tumour [21] (level of evidence, 4), [22] (level of evidence, 2). The Milan system classifies PA with non-classical aspect as salivary tumours of uncertain malignant potential [SUMP], which should limit the risk of misdiagnosis [13].

4.3. Comparison of diagnostic performance between cytology and MRI

To differentiate benign from malignant tumours, a retrospective study of 543 patients by Tryggvason et al. [23] (level of evidence, 3) reported 85.7% and 99.5% sensitivity and specificity for cytology, compared to 81.8% and 67.3% for MRI. More specifically in AP, there were no false positives among the 186 cases analysed on cytology, whereas 7 of the 71 benign tumours were diagnosed as malignant on MRI. Heaton et al. [21] (level of evidence, 4) compared cytology and MRI in PA; positive predictive value (PPV) was 97.8% for cytology and 96.2% for MRI: i.e., no significant difference. The authors recommended associating the two to enhance performance. Zaghi et al. [24] (level of evidence, 4) drew up a decision-tree for diagnosis of PA on MRI, reporting 44% sensitivity (95% CI: 0.29–0.60), 95.1% specificity (95% CI: 0.86–0.99); 85.7% PPV (95% CI: 0.70–1) and 71.9% negative predictive value (NPV) (95% CI: 0.62–0.82); diagnostic performance was 74.8% (95% CI: 0.66–0.83).

Associating MRI and cytology enhances preoperative diagnostic performance in PA.

4.4. Role of ultrasound-guided core needle biopsy in PA work-up

Ultrasound-guided core needle biopsy (CNB) has emerged as an alternative to surgical biopsy. It uses a 16–19 G needle, usually under local anesthesia. Diagnostic performance was reviewed in a meta-analysis by Kim and Kim [25] (level of evidence, 3), showing excellent sensitivity (94%; 95% CI: 0.92–0.96) and specificity (98%; 95% CI: 0.97–0.99). The rate of non-diagnostic CNB was low, at 3.26 %. Complications mainly comprised hematoma (0.5%). No tumoral spread was reported (although follow-up was insufficient), and no facial palsy. Performance was unrelated to the operator's experience, unlike in fine-needle aspiration cytology. In a meta-analysis by Witt and Schmidt [26] (level of evidence, 3), sensitivity and specificity for salivary gland CNB were respectively 96% (95% CI: 87–99) and 100 % (95% CI: 84–100). Hematoma risk was 1.6%. Diagnostic performance was homogeneous across studies, unlike in FNAC. Novoa et al. [27] (level of evidence, 2) did not recommend CNB as an alternative to FNAC, but advocated its use in case of repeated failure of needle aspiration cytology or when non-operative treatment is foreseen or the patient refuses surgery.

Guideline

- Fine-needle aspiration cytology (FNAC) shows very good diagnostic performance for benign tumours in general and for PA in particular (Grade B).
- FNAC is particularly recommended for tumours difficult to characterise on MRI (subcentimetric, or with atypic signal) or if the patient refuses surgery (Grade B).
- FNAC is recommended immediately after MRI or later to circumvent interpretation artifacts (Expert opinion).

Guideline

- Core needle biopsy is not recommended as a first-line replacement for fine-needle aspiration cytology (Grade C).
- It may be useful in case of non-contributive needle biopsy, or if surgery is delayed or is refused by the patient (Grade C).

5. Role of frozen section biopsy in resection of suspected PA

Five single-centre retrospective studies reported the performance of frozen-section biopsy in salivary gland tumour, mainly comprising PA [28–30] (level of evidence, 4) (Table 2). Sensitivity for diagnosis of PA was 88.8–100%, and 99.4% in a series of more than 1000 patents, including 551 cases of PA [28] (level of evidence, 4). Specificity for PA was systematically > 95%. Histology

Table 2
Performance of frozen-section histology in salivary gland tumour treatment [28–30].

	Sensitivity for all tumours	Sensitivity for pleomorphic adenoma	Sensitivity for malignant tumour
Wang et al. [28]	86.9% (1019 cases)	99.4% (551 cases)	79.7% (148 cases)
Tew et al. [29]	87.4% (159 cases)	96.3% (82 cases)	70% (34 cases)
Ogawa et al. [30]	91.7% (48 cases)	100% (27cases)	77.7 (18 cases)

sought to diagnose malignant or benign status and if possible grade in case of malignancy. This information, obtained before the patient comes around from anesthesia, allows surgery to be extended, avoiding revision procedures so far as possible. However, definitive histology of the specimen is needed to guide subsequent treatment, as frozen sections are of poorer quality than paraffin-fixed sections, and do not allow immunohistochemical or molecular analysis. Expert opinion suggests that error in frozen section examination is minimised if the pathologist has the whole, unfragmented specimen: one of the most reliable signs of malignancy is poor tumour delineation with peritumoral invasion, which can only be assessed if the pathologist has the interface available. Enucleation and fragmentation preclude this and are to be avoided, risking unclear diagnosis even on definitive examination and also hindering resection quality assessment (margins not visible, specimen not locatable).

Guideline

- In case of preoperative suspicion of PA, frozen section histology should be performed on the entire tumour, including adjacent tissue, to determine diagnosis and if necessary adapt surgery to malignancy (Expert opinion).

6. Treatment strategy

6.1. Surgical strategy for suspected parotid PA

Treatment is exclusively surgical. The previous debate between total versus superficial parotidectomy is now between parotidectomy and tumour resection beyond the capsule, including healthy gland tissue (i.e., extracapsular dissection), in contrast to enucleation or total parotidectomy [31–33] (level of evidence, 4). Extracapsular dissection involves a very limited approach to the parotid area, with or without facial nerve dissection, aiming to remove the tumour while sparing the capsule and, if possible, resecting in healthy tissue. Exceptionally, in expert hands, it may be a useful attitude, but cannot be recommended as standard practice due to the surgical risks involved (facial nerve and/or salivary duct lesion) and risk of recurrence [34] (level of evidence, 4).

Surgery should remove the tumour and the whole capsule with a margin of adjacent parotid tissue, avoiding capsule breach. Risk of recurrence is greater with positive margins or capsule opening and in hypocellular myxoid forms, but this information is available only on definitive examination [35] (level of evidence, 4). Kadletz et al., in a series of 894 tumours, advised against extracapsular dissection due to the significantly higher rates of recurrence and facial palsy [36] (level of evidence, 4). This was not confirmed in the series of 2465 patients reported by Mantsopoulos et al. [37] (level of evidence, 4). Grosheva et al. [38] (level of evidence, 2), in a prospective study, demonstrated a link between severity of postoperative facial palsy and the number of dissected facial nerve branches.

When preoperative suspicion of PA is not confirmed on frozen-section biopsy and cancer is confirmed or suspected, one-stage total parotidectomy is recommended, as insufficient resection impairs prognosis [39] (level of evidence, 4). When frozen-section biopsy suggests carcinoma, level IIA, IIB, III and IV neck dissection can be performed [40,41] (level of evidence, 4), in the same or a second step, without increasing morbidity, awaiting definitive pathology and confirmation of the indication. When frozen-section biopsy results are doubtful as to grade and/or type, totalisation may be indicated, but neck dissection need not be associated.

There is no consensus regarding neuromonitoring in primary parotid AP surgery, whereas it is recommended by the workgroup in revision surgery (see article on treatment of recurrent AP).

Postoperatively, surveillance is essentially clinical, although modalities cannot be specified due to lack of evidence in the literature (expert opinion). MRI is reserved for suspected recurrence and at-risk situations.

Guideline

- In case of preoperative suspicion of parotid PA, complete en bloc tumour resection is recommended, including healthy margins if the tumour site allows, sparing the facial nerve (Grade C).
- Resection should not be limited to tumour contact (simple enucleation) (Grade C).
- In case of PA confirmed on frozen section, total parotidectomy should not be systematic, although it may be necessary in order to secure adequate margins (Grade C).
- If there is a doubt as to possible carcinoma on frozen section histology, parotidectomy should be totalised in the same step (Expert opinion).
- If frozen section histology confirms carcinoma, total parotidectomy should be performed, possibly associating neck dissection. The patient should be informed as to this possibility in advance (Grade C).

6.2. Management of non-parotid PA

6.2.1. Submandibular gland (SMG) PA

The frequency of benign tumours in the SMG is the same as in the parotid: around 80% [42] (level of evidence, 4). PA is the most frequent [42] (level of evidence, 4). Diagnosis is suggested by MRI and FNAC [43] (level of evidence, 4). The treatment of choice is en bloc resection of tumour and gland, avoiding capsule breach [44] (level of evidence, 4). Possible preoperative misdiagnosis and association with malignant pathologies justify frozen-section biopsy. In case of malignancy, neck dissection is recommended in at least level I [45] (level of evidence, 4).

6.2.2. Adnexal or minor salivary gland PA or PA with salivary heterotopia

Distinguishing between adnexal, minor and heterotopic salivary tissue is clinically important. Adnexal salivary glands are glandular structures detached from a major salivary gland, developing along lateral duct systems. Minor salivary glands are, by definition, normal oral-cavity submucosal salivary glands, in the mucosa of the lips, internal cheeks, hard or soft palate or tongue. Heterotopic salivary tissue is found outside of the above locations, resulting

Guideline

- In suspected SMG PA, dedicated preoperative MRI is recommended, on the same protocol as for the parotid, possibly with ultrasound-guided fine-needle aspiration cytology (Grade C).
- In preoperatively suspected SMG PA, total submandibulectomy is recommended (Grade C).
- In preoperatively suspected SMG PA, frozen-section biopsy is recommended, with, as necessary, neck dissection of at least level I, after informing the patient (Grade C).

from embryonic malpositioning [46] (level of evidence, 4). Heterotopic salivary tumours are found in the larynx, nasal cavities or paranasal sinuses; reports were mainly of single cases except for Kuo et al.'s series of 38 cases [47] (level of evidence, 4). PA is the most common neoplasm in non-major salivary glands, with a frequency of 56 % according to Yih et al. [48] (level of evidence, 4). Locations mainly comprise the palate, followed by the upper lip [49] (level of evidence, 4). CT-MRI is useful for local extension assessment and differential diagnosis: signs of malignancy such as infiltration, T2 iso- or hypo-signal T2, adenopathy and perineural invasion and bone invasion [50] (level of evidence, 4). Preoperative diagnosis should be based on FNAC, to guide surgery [47] (level of evidence, 4). Surgical biopsy should be limited and positioned so that the approach is removed in resection, to limit the risk of local recurrence by spillage. Treatment is exclusively surgical by complete en bloc resection [47] (level of evidence, 4). In the oral cavity, reconstruction of the lip or palate is frequently performed, using a locoregional flap for small defects; for larger defects, a pediculated or free flap may be needed [47] (level of evidence, 4). Recurrence mainly concerns minor glands or heterotopic tissue due in 10% of cases to insufficient primary resection [47] (level of evidence, 4). Surveillance needs to be prolonged [47] (level of evidence, 4).

Guideline

- In case of suspected adnexal or minor salivary gland PA or PA in heterotopic tissue, MRI should be associated to CT for extension assessment and screening for differential diagnoses of malignancy (Grade C).
- In case of suspected adnexal or minor salivary gland PA or PA in heterotopic tissue, preoperative histologic diagnosis should be performed for large tumours to ensure quality of resection and possible reconstruction (Grade C).
- For small superficial tumours, en bloc resection should be performed in first line, with pathologic analysis (Grade C).
- In adnexal or minor salivary gland PA or PA in heterotopic tissue, complete en bloc resection is recommended (Grade C).
- In extensive resection of minor salivary gland PA or PA in heterotopic tissue, surgical reconstruction is recommended (Grade C).

Disclosure of interest

The authors declare that they have no competing interest.

Acknowledgments

The authors thank the members of the reading group: Cécile Badoual, Claude Bigorgne, Alexandre Bozec, Philippe Céruse, Jean-Paul Cuttoli, Erwan de Mones del Pujol, Florent Espitalier, Bruno Guelfucci, Florian Jalbert, Franck Jegoux, Muriel Kany, Jerzy Klijanienko, Jérôme Le Bourdon, Marc Makeieff, Dominique Notte, Arnaud Paganelli, Gaël Potard, Nicolas Saroul and Philippe Schultz.

References

[1] Valstar MH, de Ridder M, van den Broek EC, et al. Salivary gland pleomorphic adenoma in the Netherlands: a nationwide observational study of primary tumour incidence, malignant transformation, recurrence, and risk factors for recurrence. Oral Oncol 2017;66:93–9.
[2] Wittekindt C, Streubel K, Arnold G, et al. Recurrent pleomorphic adenoma of the parotid gland: analysis of 108 consecutive patients. Head Neck 2007;29(9):822–8.
[3] Chen CP, Wang SJ, van Zante A, Yom SS. Stepwise regional and distant progression of recurrent pleomorphic adenoma. J Otolaryngol Head Neck Surg 2011;40(1):E5–10.
[4] Desmots F, Fakhry N, Mancini J, et al. Shear wave elastography in head and neck lymph node assessment: image quality and diagnostic impact compared with B-mode and Doppler ultrasonography. Ultrasound Med Biol 2016;42:387–98.
[5] Ikeda K, Katoh T, Ha-Kawa SK, et al. The usefulness of MR in establishing the diagnosis of parotid pleomorphic adenoma. Am J Neuroradiol 1996;17:555–9.
[6] Habermann CR, Arndt C, Graessner J, et al. Diffusion-weighted echo-planar MR imaging of primary parotid gland tumours: is a prediction of different histologic subtypes possible? Am J Neuroradiol 2009;30:591–6.
[7] Hisatomi M, Asaumi JI, Yanagi Y, et al. Assessment of pleomorphic adenomas using MRI and dynamic contrast enhanced MRI. Oral Oncol 2003;39:574–9.
[8] Yabuuchi H, Matsuo Y, Kamitani T, et al. Parotid gland tumours: can addition of diffusion-weighted MR imaging to dynamic contrast-enhanced MR imaging improve diagnostic accuracy in characterisation? Radiology 2008;249:909–16.
[9] Kakimoto N, Gamoh S, Tamaki J, et al. CT and MR images of pleomorphic adenoma in major and minor salivary glands. Eur J Radiol 2009;69:464–72.
[10] Moonis G, Patel P, Koshkareva Y, et al. Imaging characteristics of recurrent pleomorphic adenoma of the parotid gland. Am J Neuroradiol 2007;28:1532–6.
[11] Seo YL, Yoon DY, Baek S, et al. Incidental focal FDG uptake in the parotid glands on PET/CT in patients with head and neck malignancy. Eur Radiol 2015;25:171–7.
[12] Liu CC, Jethwa AR, Khariwala SS, et al. Sensitivity, specificity, and post-test probability of parotid fine-needle aspiration: a systematic review and meta-analysis. Otolaryngol Head Neck Surg 2016;154:9–23.
[13] Faquin WC, Rossi ED. The Milan System for reporting salivary gland cytopathology. New York: Springer; 2018.
[14] Conrad R, Yang SE, Chang S, et al. Comparison of cytopathologist-performed ultrasound-guided fine-needle aspiration with cytopathologist-performed palpation-guided fine-needle aspiration. A single institutional experience. Arch Pathol Lab Med 2018;142:1260–7.
[15] Consamus EN, Smith D, Pina Oviedo S, et al. Diagnostic accuracy of fine-needle aspiration cytology of salivary gland lesions: a 6-year retrospective review. J Am Soc Cytopathol 2015;4:63–73.
[16] Klijanienko J, Vielh P. Fine-needle sampling of salivary gland lesions. I. Cytology and histology correlation of 412 cases of pleomorphic adenoma. Diagn Cytopathol 1996;14:195–200.
[17] Wei S, Layfield LJ, LiVolsi VA, et al. Reporting of fine needle aspiration (FNA) specimens of salivary gland lesions: a comprehensive review. Diagn Cytopathol 2017;45:820–7.
[18] Farahani SJ, Baloch Z. Retrospective assessment of the effectiveness of the Milan system for reporting salivary gland cytology: a systematic review and meta-analysis of published literature. Diagn Cytopathol 2019;47:67–87.
[19] Choy KCC, Bundele MM, Li H, et al. Risk stratification of fine-needle aspiration cytology of parotid neoplasms based on the Milan system – Experience from a tertiary centre in Asia. Head Neck 2019;41:3125–32.
[20] Stanek JJ, Khariwala SS. What is the utility of fine-needle aspiration in parotid gland neoplasms? Laryngoscope 2019;129:1255–6.
[21] Heaton CM, Chazen JL, van Zante A, et al. Pleomorphic adenoma of the major salivary glands: diagnostic utility of FNAB and MRI. Laryngoscope 2013;123:3056–60.
[22] Ahn S, Kim Y, Oh YL. Fine needle aspiration cytology of benign salivary gland tumours with myoepithelial cell participation: an institutional experience of 575 cases. Acta Cytol 2013;57:567–74.
[23] Tryggvason G, Gailey MP, Hulstein SL, et al. Accuracy of fine-needle aspiration and imaging in the preoperative workup of salivary gland mass lesions treated surgically. Laryngoscope 2013;123:158–63.
[24] Zaghi S, Hendizadeh L, Hung T, et al. MRI criteria for the diagnosis of pleomorphic adenoma: a validation study. Am J Otolaryngol 2014;35:713–8.
[25] Kim HJ, Kim JS. Ultrasound-guided core needle biopsy in salivary glands: a meta-analysis. Laryngoscope 2018;128:118–25.
[26] Witt BL, Schmidt RL. Ultrasound-guided core needle biopsy of salivary gland lesions: a systematic review and meta-analysis. Laryngoscope 2014;124:695–700.
[27] Novoa E, Gürtler N, Arnoux A, Kraft M. Role of ultrasound-guided core-needle biopsy in the assessment of head and neck lesions: a meta-analysis and systematic review of the literature. Head Neck 2012;34:1497–503.
[28] Wang YL, Zhu YX, Chen TZ, et al. Clinicopathologic study of 1176 salivary gland tumours in a Chinese population: experience of one cancer centre 1997–2007. Acta Otolaryngol 2012;132(8):879–86.

[29] Tew S, Poole AG, Philips J. Fine-needle aspiration biopsy of parotid lesions: comparison with frozen section. Aust N Z J Surg 1997;67(7):438–41.
[30] Ogawa T, Kojima I, Ishii R, et al. Clinical utility of dynamic-enhanced MRI in salivary gland tumours: retrospective study and literature review. Eur Arch Otorhinolaryngol 2018;275(6):1613–21.
[31] Quer M, Guntinas-Lichius O, Marchal F, et al. Classification of parotidectomies: a proposal of the European Salivary Gland Society. Eur Arch Otorhinolaryngol 2016;273(10):3307–12.
[32] McGurk M, Thomas BL, Renehan AG. Extracapsular dissection for clinically benign parotid lumps: reduced morbidity without oncological compromise. Br J Cancer 2003;89:1610–3.
[33] Zbaren P, Vander Poorten V, Witt RL, et al. Pleomorphic adenoma of the parotid: formal parotidectomy or limited surgery? Am J Surg 2013:109–18.
[34] Xie S, Wang K, Xu H, et al. PRISMA-extracapsular dissection versus superficial parotidectomy in treatment of benign parotid tumours: evidence from 3194 patients. Medicine 2015;94(34):e1237.
[35] Dulguerov P, Todic J, Pusztaszeri M, Alotaibi NH. Why do parotid pleomorphic adenomas recur? A systematic review of pathological and surgical variables. Front Surg 2017;4(26):1–8.
[36] Kadletz L, Grasi S, Grasi MC, et al. Extracapsular dissection versus superficial parotidectomy in benign parotid gland tumours: the Vienna medical school experience. Head Neck 2017;39:356–60.
[37] Mantsopoulos K, Mueller SK, Goncalves M, et al. Does increasing the incidence of extracapsular dissection for benign tumours of the parotid correlate with an increased need for revision surgery? Oral Oncol 2019;94:111–4.
[38] Grosheva M, Pick C, Granitzka T, et al. Impact of extent of parotidectomy on early and long term complications: a prospective multicentre cohort study. Head Neck 2019;41:1943–51.
[39] Tam S, Sandulache VC, Metwalli KA, et al. Incompletely treated malignancies of the major salivary gland: towards evidence based care. Head Neck 2018;40:1630–8.
[40] Zbaren P, Schupbach J, Nuyens M, Stauffer E. Elective neck dissection versus observation in primary parotid carcinoma. Otolaryngol Head Neck Surg 2005;132:387–91.
[41] Stennert E, Jungehuelsing M, Guntinas-Lichius O, et al. High incidence of lymph node metastasis in major salivary gland cancer. Arch Otolaryngol Head Neck Surg 2003;129:720–3.
[42] Spiro RH. Salivary neoplasms: overview of a 35-year experience with 2807 patients. Head Neck Surg 1986;8:177–84.
[43] Covinsky M, Cai Z, Ambelil M, et al. Low grade carcinoma ex-pleomorphic adenoma: diagnosis and diagnostic challenges caused by fine needle aspiration: report of three cases and review of literature. Head Neck Pathol 2018;12:82–8.
[44] Molina EJ, Mayer K, Khurana J, Grewal H. Pleomorphic adenoma of the submandibular gland. J Pediatr Surg 2008;43:1224–6.
[45] Lombardi D, Accorona R, Lambert A, et al. Long-term outcomes and prognosis in submandibular gland malignant tumours: a multicentre study. Laryngoscope 2018;128:2745–50.
[46] Ghannam MG, Singh P. Anatomy, head and neck, salivary glands. StatPearls, Treasure Island (FL): StatPearls Publishing; 2019.
[47] Kuo YL, Tu TY, Chang CF, et al. Extra-major salivary gland pleomorphic adenoma of the head and neck: a 10-year experience and review of the literature. Eur Arch Otorhinolaryngol 2011;268:1035–40.
[48] Yih WY, Kratochvil FJ, Stewart JCB. Intra-oral minor salivary gland neoplasms: review of 213 cases. J Oral Maxillofac Surg 2005;63:805–10.
[49] Bergman F. Tumours of the minor salivary glands. A report of 46 cases. Cancer 1969;23:538–43.
[50] Abdel Razek AAK, Mukherji SK. Imaging of minor salivary glands. Neuroimaging Clin N Am 2018;28:295–302.