

Accuracy of Fine Needle Aspiration Cytology and Frozen Section Histopathology for Lesions of the Major Salivary Glands

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Abstract

Introduction: Identifying malignancy either preoperatively or intraoperatively can have a significant impact on the management of salivary gland tumours. We review our experience with fine needle aspiration cytology (FNAC) and frozen section (FS) for salivary gland lesions. We analyse the accuracy of both modalities and their influence on management. **Materials and Methods:** Retrospective review of 114 patients who underwent salivary gland surgery, 91 with intraoperative FS and 68 with preoperative FNAC. Both sets of results were compared against each other and the final histopathological diagnosis. **Results:** The accuracy of FS was 92.3%, with a sensitivity and specificity of 62.5% and 100%. Histologic concordance was 92.4% for benign lesions, and 100% for malignant tumours. The accuracy of FNAC was 89.7%, with a sensitivity and specificity of 100%. The non-diagnostic rate was 10.3%. Histologic concordance for FNAC was inferior to that for FS, with only 64.2% of benign lesions and 50% of malignant tumours correctly identified. FNAC did not alter the management of benign disease even when a correct diagnosis was obtained. **Conclusion:** Our results suggest that FNAC and FS are complementary in usefulness for malignant tumours. However, FNAC does not influence the management of benign lesions and routine FNAC for every patient may not be cost-effective.

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Introduction

The histopathology of salivary gland tumours is extremely varied and complex. Amongst the epithelial neoplasms alone, at least 9 different adenomas and 17 different carcinomas are recognised. Furthermore, a host of non-epithelial tumours, lymphomas, secondary tumours and tumour-like lesions may also arise in the salivary glands, contributing to the diagnostic difficulty.¹

Distinguishing neoplastic from non-neoplastic lesions, and benign from malignant tumours of the major salivary glands is extremely important in their management. In particular, since salivary gland tumours are almost always treated surgically, identifying malignancy either preoperatively or intraoperatively is crucial, for this can have a significant impact on the type, extent and radicality of surgery.²

While the history and clinical examination remain important in this respect, and while there are classic symptoms and signs which may suggest malignancy, most

malignant salivary neoplasms have unremarkable features, and are not readily distinguishable from their benign counterparts on clinical criteria alone.³

Preoperative imaging in the form of computed tomographic (CT) or magnetic resonance imaging (MRI) scanning is frequently employed to characterise a lesion prior to surgery. However, while certain radiologic features favour or suggest the diagnosis of malignancy, imaging findings on their own are frequently not sufficiently specific or reliable to make a diagnosis.⁴

Fine needle aspiration cytology (FNAC) has been widely used for many years as a method for assessing salivary gland lesions preoperatively. The reported sensitivity and specificity of FNAC is high for benign salivary neoplasms, but is less good for malignant tumours. In particular, the specific accuracy for distinguishing between the various types of malignant tumours is poor.² This is not surprising, as some salivary gland malignancies cannot be identified by cytological features alone. Several salivary carcinomas

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contain admixtures of similar cell types, and oftentimes it is the relative proportion of different cells, or the architectural arrangement of those cells, that defines the tumour. Furthermore, some carcinomas can only be distinguished from their benign adenoma counterparts by the presence of capsular or peritumoural invasion. This, unfortunately, is not assessable on FNAC.⁵

Frozen section (FS) analysis of salivary gland tumours has traditionally been used to try to identify or exclude malignancy at the time of surgery, and to type the salivary gland lesion. Knowing whether the lesion is malignant, and if possible the exact type of malignancy, can significantly influence the extent of surgery.

The aim of this study was to review our experience with FNAC and FS in salivary gland surgery. We analyse the accuracy of both modalities in our institution and their influence on management.

Materials and Methods

We retrospectively reviewed the medical records of 114 patients who underwent surgery of the major salivary glands at our institution between July 2001 and October 2004. In particular, we noted the clinical diagnosis made before and after surgery, the preoperative FNAC result if any, the intraoperative FS result if any, and the final histopathological report. We also reviewed how the FNAC and FS results influenced the surgical management.

Of the 114 patients, 91 had intraoperative FS assessment of the salivary gland lesion at the time of surgery. Twenty-three patients who did not have FS of the salivary gland itself were excluded from this analysis. This included 4 patients who had salivary gland resection as part of a composite resection for another malignancy [2 squamous cell carcinomas of the ear and 2 nasopharyngeal carcinomas (NPCs)], and 1 patient who had wide excision of a submandibular gland carcinoma together with a radical neck dissection, in whom FS was done only for the assessment of surgical margins. A further 18 patients did not have FS because the surgeon did not think it would alter management (3 pleomorphic adenomas, 1 Warthin's tumour, 9 sialolithiasis, 3 ranulas, 1 intra-parotid node and 1 vascular malformation).

Of the 91 patients with FS, 76 had a parotidectomy, 13 had removal of a submandibular gland, 1 had excision of a sublingual gland, and 1 had the parotid included as part of a composite resection for metastatic NPC. FS results were categorised as benign, malignant or indeterminate (deferred till paraffin section).

Sixty-eight of the 114 patients had preoperative FNAC. FNAC results were categorised as follows:

A. Benign. Cytology suggestive of a benign or non-

neoplastic lesion, or without malignant or atypical cells.

B. Malignant. Cytology suggestive of malignancy.

C. Non-diagnostic. Diagnosis could not be made on basis of material obtained. This included aspirates with an inadequate yield.

The definitions used in the statistical analysis were as follows:

Sensitivity (for malignancy) was defined as the percentage of patients who were correctly diagnosed to have malignancy on FNAC or FS.

Specificity (for the absence of malignancy) was defined as the percentage of patients who were correctly diagnosed to have benign disease on FNAC or FS.

Accuracy (for a given modality) was calculated as the number of true negative plus true positive results for that modality, divided by the sum of the true negative, true positive, false negative and false positive results.

Histologic non-concordance was defined as an FNAC or FS diagnosis which was correctly classified as true positive or true negative for malignancy, but was not completely accurate when compared with the final histological diagnosis.

Deferred diagnosis was one where the pathologist failed to commit to either the presence or absence of malignancy.

Results

Frozen Sections

Of the 91 patients who had FSs performed, 76 had neoplasms, including 62 benign epithelial tumours, 2 benign mesenchymal tumours, 10 malignant epithelial tumours, 1 malignant lymphoma and 1 metastatic carcinoma. The remaining 15 patients had a variety of non-neoplastic conditions.

Of the 79 benign lesions (64 benign neoplasms and 15 non-tumours), all were correctly identified as being non-malignant. Thus, the specificity for the absence of malignancy in our series was 100% (Table 1). The rate of histologic concordance was however lower, with only 73 of the 79 benign lesions correctly identified (92.4%) (Table 2).

Of the 12 malignant lesions, only 5 were correctly identified as being malignant. Thus the sensitivity for identifying malignancy in our series was only 41.7% (Table 3). However, the histologic concordance in this group was 100% and all patients had their cancers correctly identified. Of the remaining 7 patients, 3 had a false negative result and 4 had a deferred diagnosis (Table 2).

One of the 3 false negative reports resulted in a negative clinical impact as the patient had to undergo further surgery. The remaining 2 patients with false negative reports had

Table 1. Results of Frozen Sections and FNAC

Final diagnosis	Frozen section (n = 91)			Total
	Benign	Malignant	Deferred	
Benign	79	0	0	79
Malignant	3	5	4	12
Total	82	5	4	91

Final diagnosis	FNAC (n = 68)			Total
	Benign	Malignant	Inadequate yield	
Benign	53	0	5	58
Malignant	0	8	2	10
Total	53	8	7	68

FNAC: fine needle aspiration cytology

lymphoepithelial carcinomas and were sent for adjuvant radiotherapy.

The overall accuracy of FS in our series was 92.3%. When deferred diagnoses were excluded, the accuracy was

96.6%. When benign and malignant lesions were separately assessed, the accuracy for benign lesions was 100%, but the accuracy for malignant lesions was only 62.5%.

FNAC

Of the 68 patients who had a preoperative FNAC, there were 10 malignancies and 58 non-malignant diagnoses. Sixty-one of the 68 FNACs (89.7%) had an adequate cell yield for diagnosis. When adequate, the sensitivity and specificity of FNAC for identifying or excluding malignancy was 100% (Table 1). All 8 malignant neoplasms were identified as malignant, and all 53 benign or non-neoplastic lesions were correctly identified as being benign. However, when inadequate aspirations are included, the overall accuracy of FNAC dropped to 89.7%.

Furthermore, the histologic concordance was even lower, with only 38 of 61 lesions (62.3%) correctly identified. The histologic concordance for benign lesions was 64.2% (34 of 53), and the histologic concordance for malignant lesions was 50% (4 of 8) (Table 4).

Table 2. Correlation between Frozen Section Diagnoses and Permanent Section Diagnoses

Permanent section	No of cases	Frozen section	No of cases
Benign tumours	64		
Pleomorphic adenoma	34	Pleomorphic adenoma	34
Warthin's tumour	26	Warthin's tumour	25
		Oncocytic tumour, papillary intracystic*	1
Basal cell adenoma	2	Basal cell neoplasm	1
		Reactive lymph node*	1
Schwannoma	1	Schwannoma	1
Dendritic cell tumour	1	Spindle cell tumour – no malignancy	1
Non-neoplastic	15		
Lymphoepithelial cyst	3	Cyst with ductal lining	2
		Warthin's tumour	1
Chronic sialadenitis	2	Chronic sialadenitis	2
Abscess	2	Abscess	2
Radiation effect	1	Adipose tissue, fibrous tissue, small lymphoid aggregate – no malignancy*	1
Oncocytosis	1	Benign oncocytic tumour	1
Lymphangioma	1	Fibrovascular tissue – benign, parotidnormal, no malignancy	1
Kimura's disease	1	Kimura's disease	1
Infarcted lymph node, normal salivary gland	1	Necrotic material*	1
Castleman's disease	1	Benign lymphadenopathy*	1
Intraparotid lymph node	1	Atypical lymphoid hyperplasia	1
Inflamed salivary duct cyst oncocytic ductal and acinar metaplasia	1	Benign epithelial lesion*	1

* Does not show histological concordance

Table 3. Frozen Section and Final Histological Diagnoses of Malignant Tumours

Frozen section diagnosis	Final diagnosis
Correct diagnoses	
Low-grade adenocarcinoma	Basal cell adenocarcinoma
Acinic cell carcinoma	Acinic cell carcinoma
Invasive oncocytic neoplasm	Oncocytic carcinoma
Mucoepidermoid carcinoma	Mucoepidermoid carcinoma
Poorly differentiated carcinoma	Poorly differentiated carcinoma
Incorrect diagnoses	
Chronic sialadenitis with metaplasia	Lymphoepithelioma-like carcinoma
Pleomorphic adenoma variant	Epithelial-myoepithelial carcinoma
Warthin's tumour	Undifferentiated lymphoepithelial carcinoma
Deferred diagnoses	
Atypical epithelial tumour	Adenoid cystic carcinoma
Salivary gland tumour query mimic adenoma vs low-grade adenocarcinoma	Basal cell adenocarcinoma – low-grade
Epithelial tumour	Acinic cell carcinoma
Atypical lymphoid infiltrate	Extranodal marginal zone lymphoma of MALT type

MALT: mucosa-associated lymphoid tissue

Discussion

Frozen Section

In our series, the overall accuracy of FS for identifying lesions as benign or malignant was 92.3%. When deferred diagnoses were excluded, the accuracy improved to 96.6%. This is in agreement with several reports in the literature.^{6,7}

However, it is well recognised that FS analysis for malignant salivary gland tumours is more difficult and less accurate than for benign tumours,⁸ and when we analysed benign and malignant tumours separately, a significant difference was noted. The accuracy of FS for identifying lesions as benign was excellent (100%), but the accuracy for identifying lesions as malignant was significantly lower (62.5%). In particular, the inaccuracy appears to lie with false negative diagnoses.

This fall-off in accuracy for malignant tumours is consistent with what is reported in the literature,⁷⁻⁹ but is nonetheless disturbing. For benign tumours of the major salivary glands, the nature and extent of surgery is fairly standard, and the surgeon is less dependent on the FS report when deciding what to do. However, when dealing with malignant tumours, the surgeon frequently relies on the FS result to make certain decisions, including whether to perform a partial or total parotidectomy, whether to include

an elective neck dissection, or whether to sacrifice adjacent structures such as skin, ear canal and facial nerve.

While there were no false positive FS diagnoses in our series, meaning no patient ran the risk of having more extensive surgery than was necessary, the 3 false negative diagnoses could have resulted in patients receiving less than adequate surgery. As it turned out, only 1 patient required repeat surgery. The other 2 patients had lymphoepithelial carcinomas, and their treatment was completed with adjuvant radiotherapy.

In our series, 5.1% of the FS diagnoses were deferred. This is again similar to what is reported in the literature.⁸ While every effort is made to keep the deferral rate low, it is sometimes not possible to obtain a definite diagnosis on FS. In such situations, we recognise that a deferred diagnosis is preferable to either a false positive or false negative diagnosis.

FNAC

When an adequate yield was obtained on FNAC, the specificity and sensitivity in our series was excellent (100%), and this compares favourably with other reports in the literature.¹⁰⁻¹² However, the percentage of non-diagnostic yields in our series was much higher than expected (10.3%).^{11,13} It has been shown that the diagnostic yield of FNAC is improved if it is done in the presence of a cytotechnologist.⁸ We have recently started performing all FNACs with a cytotechnologist in attendance who prepares the slides and checks the adequacy of yield. This allows immediate re-aspiration if the first FNAC is deemed inadequate. It is hoped that with this approach we will be able to reduce the percentage of non-informative FNACs in our practice.

Another point to note about our results is that while the accuracy of FNAC for identifying or excluding malignancy was good, the histologic concordance was significantly poorer (62.3%). This is at the low end of the 60% to 75% usually reported in the literature.¹⁴ As pointed out before,¹⁵ it is probable that centres with dedicated head and neck pathologists, who are especially proficient at interpreting salivary gland FNACs, will report superior results.

Comparison Between FNAC and FS

Several authors have compared the diagnostic accuracy of FS and FNAC in the assessment of salivary gland lesions. In most reports, both modalities have been found to be equally reliable, with accuracies ranging from 89% to 95%.^{12,16} Likewise in our series, the overall accuracy for FS and FNAC was similar at 92.3% and 89.7%, respectively. When deferred diagnoses on FS and inadequate aspirates on FNAC were excluded, the accuracy improved to 95.8% and 100%.

Table 4. Correlation between FNAC Diagnoses and Permanent Section Diagnoses

Histodiagnosis	No of cases	Cytodiagnosis	No of cases
Benign tumours	41		
Pleomorphic adenoma	23	Pleomorphic adenoma*	19
		No malignant cells	1
		Oncocytic cells	1
		Epithelial tumour	1
		Normal tissue	1
Warthin's tumour	15	Warthin's tumour*	10
		Oncocytic cells with chronic inflammation	2
		Inadequate yield†	1
		Chronic sialadenitis	1
		Inflamed cyst contents	1
Basal cell adenoma	2	Pleomorphic adenoma	1
		No malignant cells	1
Schwannoma	1	Schwannoma*	1
Non-neoplastic lesions	17		
Sialolithiasis/Sialadenitis	4	Low/no yield†	4
Inflamed salivary duct cyst	1	Lymphocytic yield	1
Radiation effect	1	No malignant cells	1
Oncocytosis	1	Oncocytic cells*	1
Lymphoid hyperplasia in lymph node	1	Reactive lymph node*	1
Lymph node	2	Lymphocytic yield	2
Lymphoepithelial cyst	3	Salivary cystic lesion with chronic inflammatory yield*	1
		Cyst – no malignant cells	1
		Reactive lymph node – no malignant cells	1
Castleman's disease	1	Lymphocytic yield	1
Kimura's disease	1	Inflammatory yield	1
Abscess	2	Infected cyst*	1
		Lymphoepithelial cyst	1
Malignant tumours	10		
Acinic cell carcinoma	2	Acinic cell tumour*	1
		Cyst contents – no epithelial content†	1
Oncocytic carcinoma	1	Atypical cells suspicious of malignancy	1
Adenoid cystic carcinoma	1	Salivary gland tumour – pleomorphic adenoma vs adenoid cystic carcinoma*	1
Basal cell carcinoma	1	Atypical cells	1
Extranodal marginal zone lymphoma of MALT type	1	Atypical cells with necrosis	1
Lymphoepithelioma-like carcinoma	1	Degenerate cells†	1
Mucoepidermoid carcinoma	2	Mucoepidermoid carcinoma*	1
		Malignant cells	1
Recurrent nasopharyngeal carcinoma (poorly differentiated carcinoma)	1	Poorly differentiated carcinoma*	1
Total	68	Total	68

FNAC: fine needle aspiration cytology; MALT: mucosa-associated lymphoid tissue

* Shows histological concordance

† Non-diagnostic

However, on closer examination, each modality appears to have a different strength. In the small number of malignant tumours we had, FNAC was much more sensitive in identifying malignancy (8 out of 8, or 100%) than FS (5 out of 12, or 41.7%). Conversely, FS was better at correctly identifying the type of malignancy than FNAC. Histologic concordance was 100% (5 of 5) for FS, compared to just 50% (4 of 8) for FNAC.

The difference in histologic concordance between the 2 modalities is not unexpected. As mentioned above, several types of salivary gland malignancy can only be identified based on architectural or invasive features.⁵ It is therefore no wonder that FNAC is less successful in this respect. A recent report by Zbaren et al¹⁷ on primary parotid carcinomas has shown that FNAC cannot be relied upon to type or grade malignant salivary tumours, and in this respect, FS is superior. The authors concluded that FNAC should not be used as the sole determinant of surgical management for primary parotid carcinomas.

The difference in sensitivity for identifying malignancy between the 2 modalities is however more difficult to explain. One would normally assume that being able to see the architectural pattern of the tumour on FS would give this modality the edge over FNAC in diagnosing malignancy. However, it is possible that because of better fixation, a well prepared FNAC may be better able to diagnose malignancy than FS. Another possibility is that pathologists may be more willing to call malignancy on FNAC, knowing that the patient is going for surgery anyway, and that a confirmatory FS will be performed. However, when faced with a possible malignancy on FS, unless absolutely certain, they may be less willing to commit to a diagnosis of malignancy, fearing that this would immediately influence the extent and radicality of surgery. A higher false negative rate on FS has been reported by others as well.¹³

Whatever the explanation, it appears that FNAC and FS have complementary uses in the management of salivary gland lesions. The clear advantages of FNAC include the ability to distinguish between salivary and non-salivary gland lesions, and between neoplastic and non-neoplastic pathology preoperatively. FNAC also appears to be more sensitive at picking up malignancy, thus allowing for the appropriate counselling of patients prior to surgery.

The clear advantages of FS on the other hand include the ability to assess margins and lymph nodes at the time of surgery. This obviously has a direct impact on the extent of surgery. It also appears that in obviously malignant lesions, FS is better able to type the malignancy.¹⁷ This is important as the extent of surgical treatment differs for different salivary gland malignancies.

Impact

What then is the impact of this? Given that FNAC and FS have complementary strengths, should all patients have both FNAC and FS performed routinely? It has been the practice in our department to do FS for most salivary gland lesions at the time of surgery for the reasons given above. However, we have not routinely performed preoperative FNACs for all patients. We share Spiro's view that for benign tumours which constitute the majority of salivary gland lesions, the results of FNAC do not significantly influence the treatment decisions even when a correct diagnosis is obtained.¹⁸ Therefore, we perform FNACs for 3 main reasons. Firstly, when there is diagnostic doubt as to whether we are dealing with a salivary or non-salivary lesion, or whether the lesion is neoplastic or inflammatory; secondly, when malignancy in a salivary lesion is suspected on clinical grounds; and finally, when we wish to avoid surgery. The last scenario usually arises when confronted with an elderly patient with a suspected Warthin's tumour.

Given the increased sensitivity of FNACs for diagnosing malignancy, should we start performing FNACs for all salivary gland neoplasms just in case a seemingly benign tumour proves malignant? In our series, FNAC picked up 2 malignancies in patients who were not suspected to have cancer clinically, and in whom FS was unable to determine malignancy at the time of surgery. Yet this did not affect either the surgical management or the outcome. Firstly, surgeons still tend to trust a FS result over an FNAC result, and it is unlikely that one would ever extend the scope of surgery based purely on an FNAC result, unless the corresponding FS result corroborated the diagnosis. Secondly, both the FNACs in question showed "malignant cells", but were unable to type the malignancy. Even if one were willing to plan surgery based solely on an FNAC result, one would need a definite typing of the tumour. For instance, malignant cells from an adenoid cystic carcinoma would not justify an elective neck dissection. Similarly, malignant cells from a lymphoepithelial tumour would not justify any additional surgery. Therefore, we feel that the usefulness of doing routine FNACs for all tumours is far from clear, and may do no more than increase the cost of healthcare. This view is not ours alone and is shared by several other authors.^{15,18,19}

Conclusion

In conclusion, FNAC and FS are useful modalities for assessing salivary gland lesions preoperatively and intraoperatively. The results from our institution suggest that FNAC and FS have overall accuracies of 90%, and are complementary in usefulness. We feel that when a salivary gland lesion is suspected to be malignant on clinical or radiological grounds, there is merit in performing both

investigations. This provides maximum information for preoperative patient counselling and intraoperative surgical planning.

However, we feel that the usefulness of performing routine FNACs for every salivary gland lesion remains unclear. The vast majority of salivary gland tumours are benign, and preoperative FNAC adds nothing to the management of these patients. In our experience, even in the uncommon scenario where an FNAC picks up an unsuspected malignancy, unless the FNAC result is corroborated by a FS result, the FNAC alone has not affected the surgical management of the patient. Performing routine FNACs for every single patient may therefore not be cost-effective. On the other hand, we believe that FS should be performed for all tumours at the time of surgery for an unexpected FS result can and does influence the surgical management of the patient.

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