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The Role of Fine Needle Aspiration Cytology and Frozen Section Histopathology in the Management of Parotid Gland Tumours: A 5- Year Experience in a UK Teaching Hospital

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Abstract

Multiple studies exist outside the UK evaluating both fine needle aspiration cytology (FNAC) and frozen section histopathology (FS) in the management of parotid tumours. There is contention regarding use of FS to base treatment decisions. Our objective was to clarify whether the findings from our UK study are in agreement with the world literature.

We conducted a retrospective review of all patients undergoing parotid surgery by the same ENT surgeon at our institution over a 5 year period. We collected data on age, gender, FNAC, FS and final histological diagnosis.

75 patients were identified. 55 had diagnostic pre-operative FNAC and 17 had intra-operative FS. The accuracy of pre-operative FNAC was 80% and concordance with final histology was 80.5% for benign lesions and 75% for malignant. Equivalent results for FS were 94%, 92% and 100% respectively.

FS was more accurate than *FNAC*, particularly in detecting malignant lesions. Where pre-operative *FNAC* remains non-diagnostic, *FS* may facilitate detection of malignancy and guide intra-operative decision-making.

Keywords: Cytology, frozen section, histopathology, parotid, salivary, tumour, neoplasm

INTRODUCTION

Cancer of the major salivary glands is relatively uncommon. According to data from the UK Office for National Statistics, it accounted for 0.2% of all malignant neoplasms and 9% of head and neck cancers registered in England from 2009 to 2013.¹ Most tumours are benign with pleomorphic adenoma being the most common histological type accounting for 60-70% of benign tumours.^{2,3}

As with all other areas of head and neck surgery, distinguishing neoplastic from non-neoplastic lesions and benign from malignant tumours is extremely important. This particularly applies to the management of salivary gland tumours as they are almost always treated surgically. Hence, identifying malignancy either preoperatively or intraoperatively is crucial as this can have significant impact on the type, extent and radicality of surgery, i.e. superficial parotidectomy for benign lesions and total conservative parotidectomy plus or minus neck dissection for malignant lesions.⁴

There are multiple studies outside the United Kingdom evaluating the utility of both fine needle aspiration cytology (FNAC) and frozen section histopathology (FS) in the management of parotid gland tumours.⁵⁻⁸ The overwhelming consensus from most studies is that FS may be slightly more accurate than FNAC but the two investigations play a complementary role in operative decision-making.

There is some contention regarding the use of FS to base treatment decisions but it is generally agreed that the expertise of the reporting histopathologist is a vital factor. The aim of this study was to compare

the accuracy of FNAC with FS in the management of parotid gland tumours and to explore the subsequent impact on operative decision-making. We sought to clarify whether the findings from our UK study are in agreement with the world literature.

PATIENTS AND METHODS

The current policy at our institution is to request intra-operative FS only when anticipated that this information may lead to a change in intra-operative decision-making. For example, FS would be requested if FNA was non-diagnostic or inconclusive on 2 or more specimens. The decision to perform FS is usually made after discussion of the case and review of the FNA results at the head and neck multi-disciplinary meeting. To clarify, FS was only performed following complete tumour resection with appropriate margins. This is necessary to avoid spillage of tumour cells which could occur during an incisional biopsy.

We conducted a retrospective review of all patients undergoing parotid surgery by the same consultant ENT surgeon at our institution over a 5 year period from September 2012 to September 2017. We collected data on age, gender, initial radiological imaging, FNAC (including method for obtaining i.e. freehand or ultrasound-guided), FS if performed and final histological diagnosis. Both FNAC and FS findings were compared with final histology to determine accuracy.

RESULTS AND ANALYSIS

Age and Gender Distribution



Fig 1. Gender Distribution

75 patients were identified over the 5 year period. The age range was 12 to 82 with a mean age of 55. **Initial Imaging** The male: female gender distribution was 45:55 (see Figure 1)

Initial Baseline Imaging



Fig 2. Initial Baseline Imaging

Initial baseline imaging modalities are demonstrated in Figure 2. 98.7% (74/75) of patients underwent ultrasound (US) imaging as part of their initial assessment. The one patient who did not have an ultrasound scan had primary ear canal squamous cell carcinoma (SCC) involving intraparotid lymph nodes, for which CT (computerised tomography) and MRI (magnetic resonance imaging) scans were deemed more appropriate. 50 patients had baseline MRI imaging, 7 patients had a CT scan. At our unit, the current practice of the senior author is to investigate parotid lumps with an ultrasound-guided FNA and if surgery is planned as definitive treatment, then an MRI scan is also requested.

Frequency of FNAC and FS tests

55 (73%) patients had diagnostic pre-operative FNAC and 17 (23%) had intra-operative FS. 5 patients had non-diagnostic FNAC results.

60 (80%) patients had pre-operative FNAC results available on our IT systems.

The remaining 15 patients who did not have FNAC are accounted for as follows:

- In 5 cases, completion parotidectomy was being undertaken for known malignancy hence FNAC was not repeated.
- In a further 5 cases, there was a clear history and radiological evidence of recurrent sialadenitis with no suspicious features; hence FNAC was deemed unnecessary.
- In one case, there was a deep lobe parapharyngeal tumour and intra-oral biopsies were taken rather than external FNAC as this was felt to provide the best route for accessing the tumour.
- Another patient had biopsy-proven primary ear canal skin SCC with intraparotid nodal involvement.

- One patient had a core biopsy done rather than FNAC.
- In one case, there was clear sonographic evidence of a benign epidermoid cyst and it was felt that FNAC was not required.
- In the final case, there was clear radiological evidence of multifocal recurrence of known previous pleiomorphic salivary adenoma. FNAC to further prove this was felt to be superfluous.

Diagnostic Yield for FNAC

15.4% (10/65) of FNAC tests performed were nondiagnostic. Some patients had repeat FNAC attempts; hence 65 tests were performed on 60 patients, of which 55 were diagnostic.

Interestingly, the diagnostic yield for FNAC did not appear to be significantly affected by the technique used and was 83.3% (30/36) for a freehand technique and slightly higher at 86.2% (25/29) for an ultrasound-guided technique.

Analysis of FNAC Findings

FNAC results were analysed and compared with the final histology. The results are summarised in table 1.

FNAC Analysis	95% CI	
Sensitivity	42.9%	17.7 - 71.1
Specificity	94.3%	80.8 - 99.3
Positive Predictive Value	75%	40.7 - 92.9
Negative Predictive Value	80.5%	72.2 - 86.7
Accuracy	79.6%	65.7 - 89.8
Concordance with final histology for benign lesions	80.5%	-
Concordance with final histology for malignant lesions	75%	-

Analysis of FS findings

FS results were analysed and compared with the final histology. The results are summarised in table 2.

Table 2. FS analysis

FS Analysis	95% CI	
Sensitivity	83.3%	35.9 - 99.6
Specificity	100%	71.5 - 100
Positive Predictive Value	100%	-
Negative Predictive Value	91.7%	64.8 - 98.5
Accuracy	94.1%	71.3 - 99.9
Concordance with final histology for benign lesions	91.7%	-
Concordance with final histology for malignant lesions	100%	-

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Table 1. FNAC analysis

Impact on Surgical Management

17 cases in which frozen section was performed and

All key data is summarised in Table 3 which shows all also shows cases of particular interest described below.

Table 3. Key Data

DATE	Age	Gende	PROCEDURE	Pre-operative imaging findings	Pre-operative FNAC findings	FNAC -freehand vs US-guided	Intra-op frozen section findings	Final histology	Does FNAC correlate with final histo?	does frozen correlate with final histo?
05/11/2012	35	* M	EXCISION OF PAROTID GLAND NEC	would be consistent with a pleomorphic adenoma	right parotid giand pieomorphic salivary adenoma	us- gui dea	not done	pT2 at least, deep margin postive	No- benign to manghant	N/A- trozen not done
25/02/2013	34	F	PARTIAL EXCISION OF PAROTID GLAND	Right parotid mass. ultrasound appearances suggestive of a pleomorphic adenoma	in keeping with origin from a cyst. No epithelium or parotid tissue is present and therefore the nature of the cyst cannot be determined. No malignant cells are seen.	freehand	not done	Right superficial parotid gland pleomorphic salivary adenoma.	No- fnac -cyst contents only to pleiomorphic but benign to benign	N/A- frozen not done
18/03/2013	39	M	TOTALEXCISION OF PAROTID GLAND- Completion right parotidectomy with right level I-III neck lymph node dissection	US+MRI-Appearances suggest a small collection (seroma or abscess) at the right superficial parotidectomy bed rather than recurrent disease.	not done -re-operation as mucoepidermoid ca with close margin	n/a	Sections show chronically inflamed and scarred salivary gland tissue with acinar atrophy consistent with the defacts of previous surgery. No residual/recurrent muccepidermoid carcinoma is identified	Right parotid gland fibrosis and chronic inflammation consistent with previous surgery, no residual/recurrent mucoepidermoid carcinoma identified. Single microscopic metastatic deposit of mucoepidermoid carcinoma in 1 intraparotid lymph node	n/a- fnac not repeated	yes
17/06/2013	78	S F	PARTIAL EXCISION OF PAROTID GLAND	US- couple of lesions in the subcutaneous fat at or below the level of the left parotid tail. These could represent recurrent pleomorphic adenoma	cytologically low grade salivary gland tumour. The differential diagnosis includes pleomorphic salivary adenoma however other cytologically low grade tumours including malignant tumours are not excluded	freehand	low grade salivary gland tumour but this does not appear to be a pleomorphic adenoma and does not appear to be overtly malignant	morphology would be compatible with a monomorphic adenoma but this is recognised to be part of the pleomorphic salivary adenoma spectrum. Probable recurrent pleomorphic salivary adenoma	Yes	Yes-
23/09/2013	48	8 F	PARTIAL EXCISION OF PAROTID GLAND	US + MRI-3.5 cm right deep lobe of parotid mass. Imaging characteristics not typical of a pleomorphic adenoma and cytohistological correlation is a dvised	Warthin's tumour	US- gui ded	not done	PpT2 PpT3, NO, MX High grade sallvary duct carcinoma of deep lobe of parotid gland	No-benign to malignant	N/A- frozen not done
03/02/2014	82	F	PARTIAL EXCISION OF PARD'TID GLAND. Unknown primary TO NJ SCC R neck- right parotidectomy + neck dissection	US+ MRI - Poorly differentiated carcinoma of right level 11/parotid tail region. Overlying subcutaneous metastasis + PET CT - chest clear	not done- biopsy of parotid under GA at Yorkshre clinic- poorly differentiated ca possible salivary gland origin- probably in R parotid	n/s	Frozen section of the two samples taken for examination showed the presence of normal partol gand with a minor degree of fibrosis. No malignancy was identified.	Right selective neck lymph node dissection with biopsy of necrotic cavity at level II biphasic poorly differentiated carcinoma with squamous and salivary gland features assumed metastatic to single level IIa lymph node (1/31 nodes positive)	n/a- initial fna not done- has parotid biopsy under GA	n/a-frazen WAS FOR RESECTION MARGINS ONLY
03/03/2014	55	i M	PARTIAL EXCISION OF PAROTID GLAND	US-MMR- Well defined right parapharyngsal mass with no local aggressive features. This is likely arising from the deep icher acteristics characteristics are not completely typical of a pleomorphic admons this would seem the most likely diagnosis	Deep lobe right parapharyngeal tumour- intraoral biopsies done- no neoplasia	n/a	Section examined for frozen section shows Pleomorphic sall vary adenoma	Right parapharyngeal tumour PSA.	yes	yes
18/08/2014	55	м	PARTIAL EXCISION OF PARDTID GLAND	US ? PSA, MRI-large mass superficial lobe of right parotid bulging into deep lobe ? PSA but ont twicel appearance	non-diagnostic FNAC x 2	freehand	reactive lymph nodes	Right parotid gland pleomorphic salivary adenoma.	n/a- initial fna inconclusive	No but reactive lymph nodes to PSA i.e. Benign to benign
29/09/2014	76	F	PARTIAL EXCISION OF PAROTID GLAND	US-3 cm right level II morphological abnormal lymph node with abundant flow is concerning for metastatic disease it lies adjacent to parotid tail, but is separate from it. No other cervical lymphadenopathy. Normal parotids and submandhular glands	FNA from right neck lump Findings in keeping with papillary cystadenoma lymphomatosum (Warthin's tumour)	freehand	frozen section confirms a Warthin's tumour with the characteristic cycologically bland double layered oncocytic epithelium and a prominent intervening lymphoid stroma.	Tail right parotid gland Warthin's tumour	yes	yes
29/09/2014	69	9 F	TOTAL EXCISION OF PAROTID GLAND	US + MB: 22mm lecion R paroto 4 spans both superficial and depilobe: No typical features for PSA Molignancy cannot be excluded	FRA Inconclusive.	freehand	Prozen section. Mucoepidermoid carcinoma	DIAGNOSS: A Night parallé des lobe No malignarry seen. B Night parallé des lobe Focus of salivary duct carcinoma. C Night paraditednom Salivary duct carcinoma, DT NO, pleas se ed data. D Night level Incodes and Dight level Incodes and Dight level Incodes and salivary duct 2 lymph nodes and salivary gaind free from lesion. P Night level Incodes and salivary Sand free from lesion. P Night level Incodes and nodes free from lesion.	n/s- fina inadequate	ye ba mucooplørmold cardnoma to sallvary duct cardnoma Le. malignant to malignant
06/10/2014	45	F	PARTIAL EXCISION OF PAROTID GLAND	US- Well-defined left parotid mass, which given the long history is likely a pleomorphic adecompa	FNA, left parotid lump Possibility of pleomorphic salivary adenoma	freehand	not done	Left parotid gland Basal cell adenoma	no but psa to basal adenoma i.e. benign to benign	n/a-frozen not done
09/10/2014	45	F	PARTIAL EXCISION OF PARDTID GLAND	US+MRI:consistent with a pleomorphic salivary adenoma	Benign SPINDLE CELLS	freehand	not done	Benign PSA	NO BUT BENIGN SPINDLE CELL TO PSA - benign	n/a frozen not done
15/12/2014	66	F	TOTAL EXCISION OF PAROTID GLAND	US+MRI- Concerning right parotid mass given the history of facial nerve paisy. It is not possible to exclude malignancy such as adenoid cystic carcinoma	FNA from right parotid and right level II lymph node Positive for mallgnant cells, (muccepidermoid carcinoma or sallvary duct carcinoma could be considered as well).	US- gui ded	facial nerve deep to turnour- positive for malignant cell and proximal stump negative for malignant cells.	Facial nerve deep to tumour involved by metastatic salivary duct carcinoma. B) Proximal stump facial nerve involved by metastatic salivary duct carcinoma	yes	yes
11/05/2015	62	M	PARTIAL EXCISION OF PAROTID GLAND	US- R parotid benign salivary neoplasm ? PSA ? Warthin's	FNA cystic tumour ? Warthin's ? Mucoepidermoid ca- not typical for PSA	freehand	Warthin's tumour with no malignancy identified	Right parotid gland Warthin's tumour	liez	yes
11/05/2015	47	F	PARTIAL EXCISION OF PAROTID GLAND	US- ? PSA, MRI- indeterminate left parotid lesion- not typical of PSA	Fine needle aspect left parotid gland - cytologically low grade salivary gland tumour	US- gui ded	Pleomorphic salivary adenoma. No evidence of malignancy	Pleomorphic salivary adenoma	hez	yes
07/09/2015	69	F	TOTAL EXCISION OF PAROTID GLAND- NB prev. R PSA 1994	MRI- imaging appearances are non-specific and may represent benign or malignant pathology or a combination. US- recurrent PSA disease recurrence R parotid bed.	FNA- right parotid Consistent with mycepithelioma - Mycepithelioma and basal cell a denoma are in the same spectrum as Pleomorphic adenoma. consistent with recurrent PSA	freehand	right level 2 node-Reactive lymph node. No evidence of pleomorphic adenoma/malignancy	Pleomorphic salivary adenoma (multifocal, margin positive with reactive lymph node	yes- frozen section from lymph nodes only	Yes
05/10/2015	75	5 M	PARTIAL EXCISION OF PAROTID GLAND	US + MRI- Mass in superficial aspect of left parotid not typical of PSA	fna - possibility of squamous cell carcinoma, Warthin's tumour with squamous metaplasia is in the differential diamonin	freehand	The salivary gland lesion is a Warthin's tumour	Left superficial parotid Warthin's tumour	no- scc to warthin's-i.e. malignant to benign	yes
07/10/2015	52	M	TOTAL EXCISION OF PAROTID GLAND	US- likely PSA	fna inadequate, core biopsy- cores of connective tissue focally infiltrated by a malignant epithelioid tumour	US- gui ded	frozen section appearances raise the possibility of a high grade salivary duct carcinoma.	Left parotid gland high grade salivary duct carcinoma	n/a- fnac inadequate	yes
23/11/2015	26	5 M	EXCISION OF PAROTID GLAND NEC	US- left parotid nodule ? Warthin's	? Warthin's left parotid	? Nil on system	not done	Left parotid gland (superficial lobe) Multiple benign lymphoepithelial	no but benign to benign	N/A- frozen not done
22/02/2016	57	M	PARTIAL EXCISION OF PAROTID GLAND	US-appearances of an abnormal lymph node, parolid gland does not appear to be invaded. CT - Weil-defined, heterogenous enhancing mass within the superficial aspect of the left parotid tail. No evidence of local or distant metastatic disease. Radiological staging T2 N0 M0.	FNA not done- core blopsy showed low grade salivary tumour	US- gui ded	frozen section appearances are not entirely characteristic of a pleomorphic salvary ademose but also do not show unequivocal evidence of malignancy	restors yr meiodegoloef a cyss Left parotid gland pleomorphic sallvary adenoma	n/a- fna not done	yes
03/10/2016	82	E M	TOTAL EXCISION OF P ARADTD GLANO- EXCISION OF SKIN LEFT NECK + LOWER ASPECT OF PINNA- Left parotid SCC involving pinna	US-MBI: Diffusely abnormal I eft parotid, with lobulated mass. No nodes. US- multiple intraparotid lesions- diffuse inflammatory change. PETCT- uptake in parotid + EAC	fna-suspicious	? Done externally	Yes- LEAC + deep parotid margin- poorly differenti ated scc	Invasive poorly differentiated squamous cell carcinoma of skin of left side neck (pt2). Metastatic squamous cell carcinoma with extra capular spread to one intra/peri parotid i ymph and one lymph node at level	hez	yes
28/11/2016	79	F	TOTAL EXCISION OF PAROTID GLAND	US+ MRI- Right parotid mass gradually increasing in size.	FNA at CRH ? Malignancy	unknown - done externally	tumour is most likely an adenoid cystic carcinoma although infiltrating basal cell adenocarcinoma remains in the differential diagnosis	Right partial parotidectomy malignant parotid tumour, probable adenoid cystic carcinoma.	yes	yes
05/12/2016	71	М	PARTIAL EXCISION OF PARDTID GLAND	US+MRI- Sizable hypoechoic mass adjacent to the right parotid gland. This may represent an exophytic parotid mass or an abnormal right level II lymph node	FNA- Necrotic epithelial cells present suspicious of malignancy, Core biopsy oncocytoma/multifocal nodular oncocytic hyperplasia	freehand	frozen section shows a tumour comprising cytologically bland bilayered oncocytic optibelium with lymphoid tissue in the intervening stroma. There is no evidence of malignancy. The appearances are of a Warthin's tumour	Right parotid gland Warthin's tumour	no- malignant to benign	yes
22/05/2017	50) F	PARTIAL EXCISION OF PARDTID GLAND	USGSmall well-defined lesion within the left parotid tail. Imaging appearances are non-specific:MRISmall, non-specific, well defined lesion within the left parotid tail. No suspicious features or enlarged ymph nodes (TI NO).	low grade salivary gland neoplasm	USG guided	This is a reactive lymph node embedded in fibrocollagenous tissue. No exidence of malignary is seen. B) The salivary gland tissue shows chronic atrophy and Bhorois. There is no evidence of neoplasia.	Left parotid lymph node - Reactive node B) Parotid lump - Atrophy and fibrosis No evidence of malignancy	NO-low grade salivary neoplasm to reactive node-benign to benign	165

Suspected Benign Diagnosis Later Confirmed as Malignancy

In 2 cases, benign FNA cytological diagnoses were later confirmed to be malignant on final histology, thereby requiring further surgery in the form of completion parotidectomy and selective ipsilateral neck dissection.

Suspected Malignant Diagnosis Later Confirmed as Benign (Malignancy Refuted)

In a further 2 cases, a suspected malignant FNAC diagnosis was confirmed to be benign with FS, avoiding unnecessary radical surgery.

In the remaining 5 cases where there were disconcordant FNAC diagnoses, management was unchanged.

All FS analyses were performed on intraparotid tissue. The one case in which FS was used to assess clearance margins only was excluded from the data analysis. In the only other disconcordant case, intra-operative management was unchanged with suspected reactive intraparotid lymph nodes later being confirmed to represent benign pleiomorphic salivary adenoma. To reiterate, FS was only performed following complete resection with appropriate margins.

DISCUSSION

Salivary gland tumours present mainly in two ways; as a simple palpable lump (well defined, discrete and mobile) or a lump with associated pain, rapid growth, fixity to surrounding structures, nerve involvement or neck metastasis. The second category may suggest possible malignancy. Open biopsy may be associated with tumour seeding or spillage and is therefore not recommended. Indications for FS can be broadly divided into four main categories:

- Clarification of the diagnosis.
- Checking resection margins.
- Assessing facial nerve involvement.
- Checking for cervical nodal involvement i.e. is neck dissection required at the same time?

Salivary gland neoplasms can be diagnostically challenging. Most of them have cytologically low-grade nuclear morphologic features. Thus interpretation of FNA cytology relies on the tumour fragments with retained architectural features and cellular materials (mucin and myxoid matrix). Certain neoplasms demonstrate considerable morphologic overlap, making cytological distinction difficult. In addition, some aspirate specimens may have insufficient architectural clues for making a definitive diagnosis. Properly performed FS has an advantage over FNAC in that the architectural features such as capsular and perineural invasion are retained and when present may help favour diagnosis of malignancy. This improves the sensitivity and specificity of FS in comparison to FNAC.

However, FS can have high false positive rates; therefore it is essential that if FS is considered, it is performed by an expert, highly experienced histopathologist. Both FNAC and FS play a complementary role in the operative management of parotid gland tumours.

In our study, FS was more accurate than FNAC (94.1% vs 79.6%); particularly in detecting malignant lesions (PPV- 100% vs 75%). This is in agreement with the findings from other studies.⁵⁻⁸ UK National Multidisciplinary Guidelines suggest ultrasound-guided FNAC for all salivary tumours⁹. It is noteworthy that in our series, freehand FNA was almost as accurate as ultrasound-guided FNAC (83.3% vs 86.2%). However, this cannot be assumed to be universally applicable and will depend on the experience of clinicians performing FNAC tests.

In cases where pre-operative FNAC remains nondiagnostic, FS may help to detect the presence of malignancy and guide decision-making with regard to the extent of surgery; specifically, superficial parotidectomy for benign lesions and total conservative parotidectomy plus or minus neck dissection for malignant lesions. At our unit, we do not use FS to assess cervical node involvement as it is our policy in general to perform a selective neck dissection for malignant parotid tumours in the N0 neck.

CONCLUSION

FS assesses cell architecture whereas FNA looks at cell details. The two investigations should complement each other. FS has an important role in cases where clinical assessment and FNAC results have not proven the diagnosis of malignancy. Thus we have shown that FS is a very useful investigative tool in the management of parotid tumours. At our institution, all cases have up to 2 attempts at FNAC and if these remain inconclusive, then FS is used to guide the extent of surgery. This is useful to tailor the extent of surgery according to whether or not the tumour is

malignant. FS will not necessarily provide the exact diagnosis in terms of the precise histopathological type of tumour but is helpful in indicating if the lesion is benign or malignant. Therefore in cases where the tumour is malignant, appropriate radical surgery e.g. total parotidectomy and selective neck dissection is done at the time; thereby preventing the potential need for further surgery at a later stage by way of a completion parotidectomy with its inherent increased surgical risks including facial palsy.

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SUMMARY

- Multiple studies exist outside the UK evaluating the utility of both fine needle aspiration cytology (FNAC) and frozen section histopathology (FS) in the management of parotid gland tumours.
- FS assesses cell architecture whereas FNAC looks at cell details. The two should complement each other.
- In our study, FS was more accurate than FNAC, particularly in detecting malignant lesions. This is in agreement with the world literature.
- FS plays a role in cases where clinical assessment and FNAC results have not proven malignancy, but its use is contentious.
- In such cases, FS can be used to guide the extent of surgery.
- For malignant tumours, appropriate radical surgery is performed at the time; precluding the need for further surgery at a later stage with increased inherent surgical risks such as facial palsy.

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