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The Usefulness of Fine-Needle Aspiration Cytology in the Management of Parotid gland masses at Chris Hani Baragwanath Academic Hospital

Research Report

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DECLARATION

I, Fanelesibonge Brightness Mdletshe, declare that this dissertation is my own work. It is being submitted in partial fulfilment of the requirements for the degree of Master of Medicine in the branch of Otolaryngology, division of Neurosciences at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

Dr F.B Mdletshe

Signed……..

Date……day of ……2019

DEDICATIONS

I would like to dedicate this work to my late grandparents Thuthukile and Joseph Mdletshe who taught me love and worked tirelessly to ensure that we had opportunities to succeed in life.

ACKNOWLEDGEMENTS

I would like to express my appreciation and gratitude to:

- Professor T. Luvhengo my supervisor for his unwavering support and guidance throughout this project.
- Dr S.D Masege my co-supervisor for all his dedication to teaching and registrar development.
- The ENT Department at the University of Witwatersrand for offering me a post to train as a specialist at this institution.
- My family and friends who have supported me endlessly throughout this journey.

ABSTRACT

BACKGROUND: Salivary gland tumours account for 3% of all head and neck tumours and 85% salivary gland tumours arise from the parotid gland. 80% of the parotid gland tumours are benign while 20% are malignant. The gland is also the site of various non-neoplastic conditions that can present a diagnostic challenge clinically and on investigations. Fine needle aspiration cytology (FNAC) is relied upon for preoperative workup but the vast number of histological subtypes including heterogeneity of tumours compounds cytological analysis. However, FNAC still forms an integral part of preoperative decision-making. It can assist in distinguishing between neoplastic and non-neoplastic conditions and often forms the basis of a decision to not proceed to surgical management in some patients with parotid gland masses.

AIM: To determine the diagnostic value of fine-needle aspiration cytology in patients presenting with parotid gland masses and CHBAH.

METHODS: A retrospective review of records of patients that had preoperative fine-needle aspiration cytology (FNAC) for parotid gland mass followed by parotidectomy over a 5 year period, between January 2013 and December 2017. Information was retrieved from patient discharge summaries kept in the ENT Department, the operating theatre record and histopathology reports from the National Health Laboratory Services (NHLS) database. The data collected included age, sex, preoperative FNAC results, post-operative histology results, presenting symptoms and clinical signs.

RESULTS: A total of 77 patient records were retrieved and reviewed. 63 patients met the inclusion criteria. 52% of the patients were male and 48% were female. Their average age was 43.3 years (range: 23-74 years). 71% (45/63) of the tumours were benign, and 21% (13/63) were malignant while 8% (5/63) showed inflammatory lesions

on FNAC. (41/45) 91.1% of the benign tumours on FNAC had a corresponding benign tumour result on histology. 30.8% (4/13) cases identified as malignant on FNAC showed a corresponding malignant result on histology. The sensitivity and specificity of FNAC to detect malignant tumours was 33.3% and 97.6% respectively. The negative and positive predictive values were 83% and 80% whilst the accuracy was calculated at 83%.

CONCLUSION: FNAC for parotid gland masses is more reliable in the diagnosis of benign than malignant tumours. Lymphoid lesions and non-neoplastic diseases often result in false positive and negative diagnoses on FNAC. The accuracy of FNAC in correctly identifying malignant tumours is low and surgical decision should rely on combination of findings from clinical and imaging investigations.

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ABBREVIATIONS

FNAC: Fine-needle aspiration cytology

WHO: World Health Organisation

CHBAH: Chris Hani Baragwanath Academic Hospital

ENT: Ear, Nose and throat

NHLS: National Health Laboratory Services

CEO: Chief Executive Officer

Ca: Carcinoma

ZN stain: Ziehl-Nielsen stain

TB: Tuberculosis

LEP cyst: Lymphoepithelial cyst

HIV: Human Immunodeficiency Virus

NPV: Negative predictive value

PPV: Positive predictive value

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CHAPTER 1: INTRODUCTION

The human body has three pairs of major salivary glands and up to a thousand minor salivary glands in the aero-digestive tract. The major salivary glands are parotid, submandibular and sublingual glands. The parotid gland is the largest of the major salivary glands which is found anterior to the external auditory canal; overlying the level of the zygoma superiorly and the ramus of the mandible laterally.

Anteriorly, the parotid gland extends to overlie the masseter muscle and the sternocleidomastoid posteriorly. The outer aspect of the gland is covered by an extension of the deep cervical fascia which is continuous posteriorly with the fascial envelope of the sternocleidomastoid and anteriorly with the fascia covering the masseter muscle. The blood supply to the gland is from the external carotid artery which gives off branches in the gland. Venous drainage is by means of the retromandibular and facial veins. There are two groups of lymph nodes closely associated with the parotid gland; a series of superficial lymph nodes under the external parotid fascia and another group of lymph follicles embedded within the gland.

The extra-temporal facial nerve roughly divides the parotid gland into superficial and deep lobes. In the substance of the gland, the main trunk divides into two branches which further subdivide into the five motor nerves to the facial muscles; namely temporal, zygomatic, buccal, marginal mandibular and cervical nerves. Sensory nerve supply to the gland is from the greater auricular and auriculotemporal nerve. The auriculotemporal nerve also carries post-ganglionic secretomotor fibres from the otic ganglion to the parotid gland.

The basic unit of the salivary gland consists of an acinus, a secretory duct and a collecting duct. Each acinus is composed of a circular grouping of cells surrounding a potential space which in turn leads to an intercalated duct. Beyond this, a striated duct joins with its counterparts from adjacent secretory units so that a succession of excretory ducts of increasing size are eventually formed. These eventually merge to form the main duct of the gland.

The cells comprising the acini in salivary glands are backed by a basement membrane, outside of which other cells may be secretory or myoepithelial. In the parotid gland, the cells making up the acini secrete mainly serous fluid, while in the submandibular and sublingual glands the cells are mainly mucus secreting. Secretion in the parotid gland is much less viscous than that of the other major salivary glands.

Salivary gland tumours constitute 3% of all head and neck tumours. They are a heterogeneous group of tumours and new histological subtypes are progressively introduced into their classification. Approximately 85% of these tumours arise from the parotid gland, majority of which are pleomorphic adenomas (1). Mucoepidermoid is the most common malignant primary tumour of the parotid gland. In the setting where HIV is prevalent, lympoepithelial cyst should be considered especially when there is bilateral parotid enlargement or the lesion is cystic with no suggestive evidence of malignancy such as facial nerve dysfunction.

The diagnostic approach to a parotid gland mass includes history-taking, physical examination of the entire head and neck area, as well as all relevant investigations (3). Imaging techniques may assist in providing further information regarding the size, precise anatomical site and other characteristics of the mass but cannot confirm histological diagnosis.

Fine needle aspiration cytology (FNAC) is relied upon for preoperative diagnosis of parotid tumours. If FNAC is diagnostic of primary malignancy of the parotid gland, the minimum recommended curative surgical procedure would be total parotidectomy. Additional steps are added based on the grade of the tumour and/or clinical or evidence of metastasis after imaging investigation(s). The value of fine needle aspiration cytology (FNAC) in the diagnosis of parotid gland masses is controversial partly due to its variable specificity (33-100%) and low sensitivity (67-100%) for differentiating between benign and malignant lesions (2). It is not uncommon for a patient to be subjected to a radical procedure for malignancy only for histology to show benign disease, and vice versa.

CHAPTER 2: LITERATURE REVIEW

Fine needle aspiration cytology (FNAC) is an accepted method for preoperative evaluation of head and neck tumours. FNAC in the parotid gland is a safe, reliable, rapid and cost-effective procedure as the parotid gland is easily accessible for ease of procedure. Furthermore, FNAC in tumours of the parotid gland can be performed in an outpatient setting. In the parotid gland, it is a valuable tool in differentiating between benign and malignant masses.

It is also useful for distinguishing between neoplastic and non-neoplastic lesions (3, 4). Preoperative diagnosis obtained with FNAC can guide decisions in terms of necessity and appropriateness of surgery, extent of resection and inclusion of a neck dissection therefore enhancing preoperative counselling (5). The sensitivity and specificity of parotid gland FNAC in distinguishing benign and malignant disease is 67-100% and 33-100%; whilst differentiating between neoplastic from non-neoplastic disease is reported to be between 79-100% and 71-100%, respectively (4). A number of factors contribute to the variability in the diagnostic accuracy of parotid gland FNAC (6, 7). Some of these factors include the following:

a) The experience of the pathologist may be affected by geographical location owing to difference in referral patterns and the prevalence of benign and malignant disease within a specific area.

b) The technique of obtaining the specimen may be poor leading to insufficient material for cytological analysis.

c) Complexity of salivary gland tissue architecture and morphology of the cells.

d) Overlapping morphological features between some of the benign and malignant parotid gland tumours.

Confirmation of malignancy in any tumour is based on demonstration of invasion of the basement membrane as seen on histopathology specimens. This parameter cannot be examined on FNAC specimens. Additionally, atypical cells, which are frequently reported following FNAC; may be found in both benign and malignant tumours (8, 9) which further compounds the accuracy of FNAC.

The number and diversity of salivary gland neoplasms is vast and the World Health Organisation (WHO) has classified them into various categories and subtypes.

Parotid lesions which are frequently misdiagnosed on preoperative FNAC include acinic cell carcinoma, basal cell adenoma, Warthin's tumour, lymphoid lesions, and chronic sialadenitis.

Acinic cell carcinoma is prone to a false negative diagnosis on cytopathology due to the absence of certain morphologic features. With acinic cell carcinoma, there is absence of necrosis, pleomorphism and high mitotic activity usually associated with malignancy (11). Basal cell and pleomorphic adenomas are usually confused with adenoid cystic carcinoma due to similar stromal and cellular characteristics (8, 12).

Lymphoid lesions usually yield both a false-negative and false-positive diagnoses. Other methods used to analyse FNAC specimens such as immunohistochemistry may assist in providing diagnostic accuracy with these lesions (8). Chronic sialadenitis may frequently be associated with certain types of malignancy and thus some malignant cases may be classified as reactive sialadenitis (9). Warthin's tumour of the parotid gland is a benign neoplasm that generally presents with metaplastic changes in the

epithelium which can be associated with atypia. This could lead to misdiagnosis of carcinoma (12).

There is wide heterogeneity of study populations and variation in reported accuracy of fine needle aspiration cytology in the parotid gland. It was therefore essential to explore the relationship between FNAC and histopathology findings in order to ascertain the usefulness of preoperative FNAC for patients presenting with mass lesions of the parotid gland. Based on experience in their clinical setting the investigators have noted an apparent doubtful reliability of FNAC in the diagnosis of malignant tumours of the parotid gland as compared to benign neoplasms.

CHAPTER 3: MATERIALS AND METHODS

3.1 Study design, period and setting

A record review of patients that had a preoperative FNAC and parotidectomy for parotid gland mass at CHBAH ENT Department. A record of all parotidectomies, clinical notes and laboratory results was obtained for the study period. (January 2013 to December 2017).

3.2 Aims and objectives

Aim

To determine the diagnostic value of preoperative FNAC in patients presenting with parotid gland masses at CHBAH.

Objectives

The study objectives included determination of demography and clinical findings in patients presenting with parotid gland masses, to determine the incidence of the various histologic types of parotid gland neoplasms and to compare preoperative FNAC with histology following parotidectomy for parotid gland masses at CHBAH.

3.3 Data collection and analysis

Collected data was collated and transferred to an excel spreadsheet. Categorical data such as gender, diagnosis and type of surgical procedure were summarised using counts and percentage. The average or median was used to aggregate continuous data such as age. Sensitivity, specificity, accuracy, positive predictive value and negative predictive was calculated. The chi-square test was used for comparison of categorical data. Statistical significance was set at a p-value below 0.05.

3.4 Inclusion and Exclusion criteria

Inclusion criteria:

All adult patients over the age of eighteen years with unilateral and bilateral parotid masses that had a parotid gland FNAC and subsequent parotidectomy during the study period.

Exclusion criteria:

Patients without preoperative FNAC and non-traceable postoperative histology results, redo parotidectomies and patients under the age of 18 years.

3.5 Ethics

Ethics approval for the study was obtained from the Human Research Ethics Committee (Certificate clearance number: M180333).

Permission was sought from the hospital CEO and the head of the National Health Laboratory Services.

CHAPTER 4: RESULTS

A total of 77 records of patients who had parotidectomy were accessed.14 patients were excluded as 5/14 (35.7%) were below the age of 18 years, 2/14 (14.3%) had re-do parotidectomies, in 4/14 (28.6%) patients' histology results could not be found possibly due to wrong patient details recorded on the laboratory form. 3/14 (21.4%) patients had no traceable FNAC results.

4.1 Demographics

The final sample was made up of 63 patients that had a preoperative FNAC and parotidectomy for parotid gland mass. 52% (33/63) of the patients were males and their mean age was 43.33 ± 12.867 years (range: 23-74 years) and 29% were above the age of 50 years (Figure1).

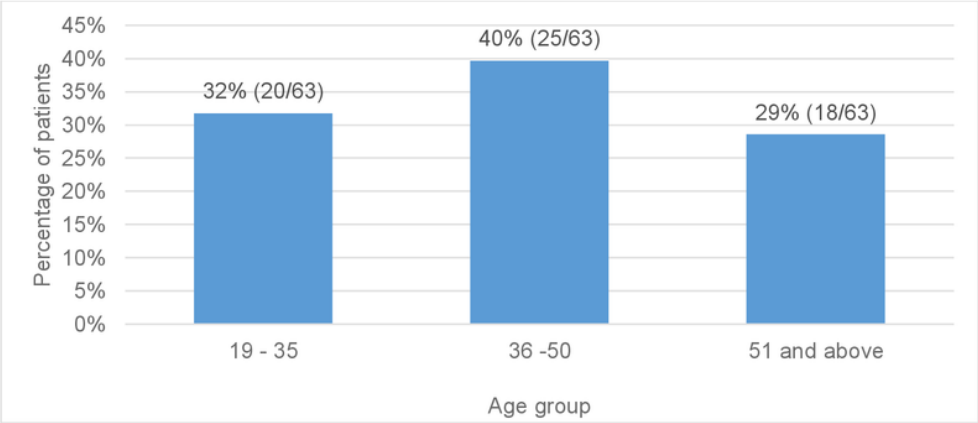


Figure 1: Age distribution of patients following FNAC (N = 63).

4.2 Clinical presentation

All patients presented with a mass which was painful in 12.7% (8/63) and 1.6% (1/63) had facial nerve paralysis. 76.2% (48/63) had a solid architecture on imaging (Table 1).

Table 1: Clinical presentation and imaging findings in patients with parotid masses (N=63)

Parameter	Finding	Frequency
Mass	Yes	63 (100%)
Nature of mass	Complex	6 (9.5%)
	Cystic	9 (14.3%)
	Solid	48 (76.2%)
Pain	Present	8 (12.7%)
	Absent	55 (87.3%)
Facial nerve palsy	Yes	1 (1.6%)
	No	62 (98.4%)
Other	Previous stab injury to parotid gland	1 (1.6%)
	Recurrent sialadenitis and previous gunshot to parotid area	1 (1.6%)
	Skin ulceration	1 (1.6%)
	No	60 (95.2%)

4.3 FNAC results

In 87% of the patients the masses were neoplastic, 3% were inflammatory while the other 10% were inconclusive (Figure 2). 79% of FNAC results yielded benign neoplasms (Figure 3)

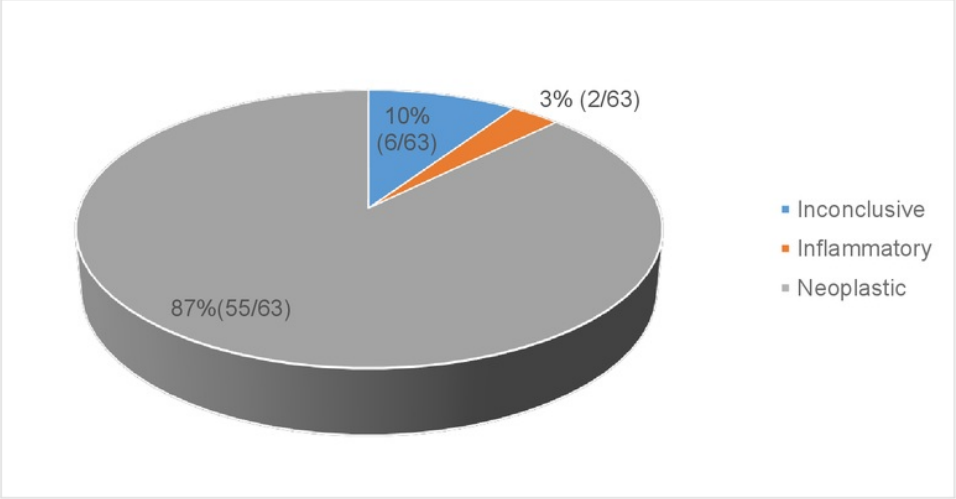


Figure 2: FNAC Neoplastic/Non-neoplastic (N=63)

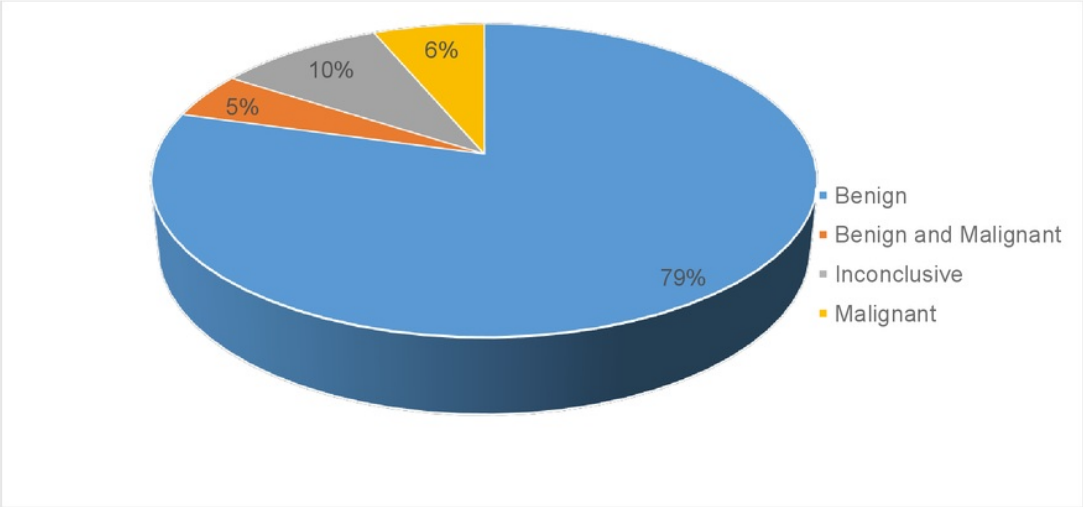


Figure 2: FNAC Benign and Malignant

Diagnosis of isolated pleomorphic adenoma was captured in 42.9% (27/63) of the cases. Adenoid cystic adenoma was the most common malignant diagnosis, followed by mucoepidermoid carcinoma was found in 1.6% (1/63) of the tumours (Table 2).

Table 2: Breakdown of diagnostic findings following FNAC (N= 63)

Benign and Inflammatory	**Frequency**	**Malignant**	**Frequency**
Pleomorphic adenoma	27 (42.9%)	Adenoid cystic Ca	2 (3.2%)
Lymphoepithelial cyst	16 (25.4%)	Mucoepidermoid Ca	1 (1.6%)
Inconclusive	6 (9.5%)	Poorly differentiated carcinoma	1 (1.6%)
Differential Diagnosis (PA and others)	4 (6.3%)		
Others	6 (9.5%)		
Total	**59 (93.7%)**		**4 (6.3%)**

4.4 Histology results

Histology results revealed that 86% 54/63) of the patients had neoplastic pathology, 8% (5/63) were inflammatory while the other 6% (4/63) had combined neoplastic and inflammatory pathology within the same parotid gland. Benign neoplasm was reported in 71% (45/63) of histology results (Figure 4).

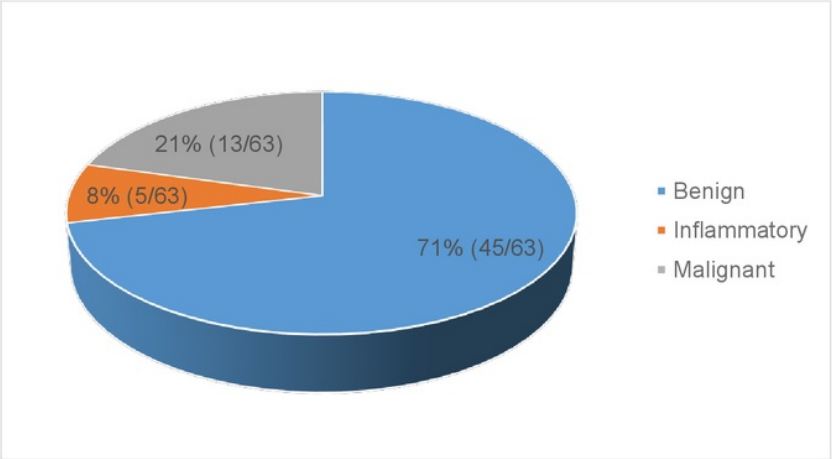


Figure 4: Breakdown of histology results according to pathological findings

42.3% (26/63) of histology results showed pleomorphic adenoma whereas mucoepidermoid carcinoma was confirmed in 4.8% (3/63). Pleomorphic adenoma was the commonest benign tumour at 51% (26/51) followed by lymphoepithelial cyst at 15.5% (8/51). Mucoepidermoid Ca was the commonest malignancy at 25% (3/12) (Table 3).

Table 3: Histology results following parotidectomy. (N=63)

Malignant tumours	Number (%)	Benign and inflammatory	Number
Mucoepidermoid Carcinoma	3 (25%)	Pleomorphic adenoma	26 (51%)
Adenoid cystic Carcinoma	2 (16.7%)	Lymphoepithelial Cyst	8 (16.3%)
Adenocarcinoma	2 (16.7)	Multiple pathology	5 (10.2%)
Carcinoma ex-pleomorphic adenoma	2 (16.7%)	Granulomatous inflammation (Including TB)	2 (4%)
Acinic Cell Carcinoma	1 (8.3%)	Others	10 (16.3%)
Non-Hodgkin's lymphoma	1 (8.3%)		
Oncocytoma	1 (8.3%)		
Total	**n= 12**		**n= 51**

The benign and malignant results for histology are shown below.

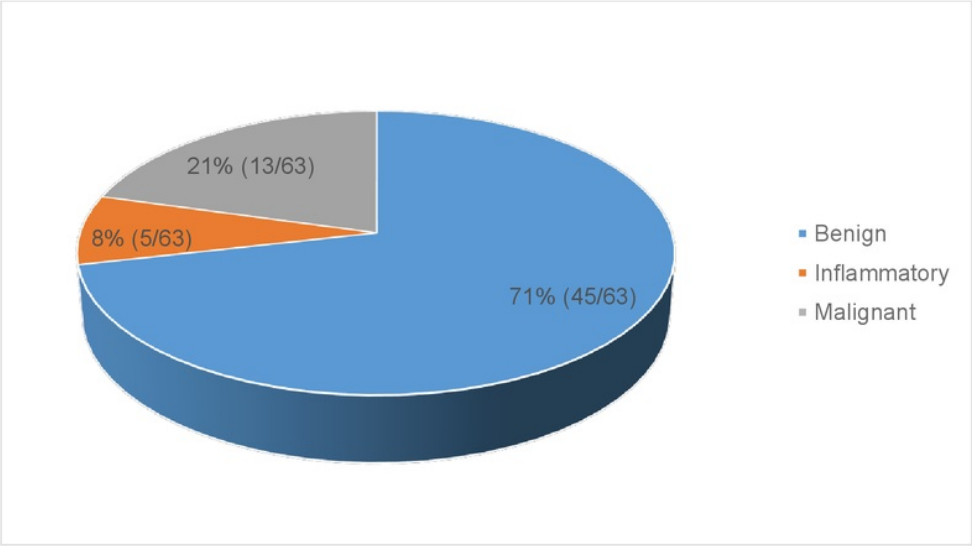


Figure 5: Benign, malignant and inflammatory distribution

The neoplastic/non-neoplastic results for histology are as shown below;

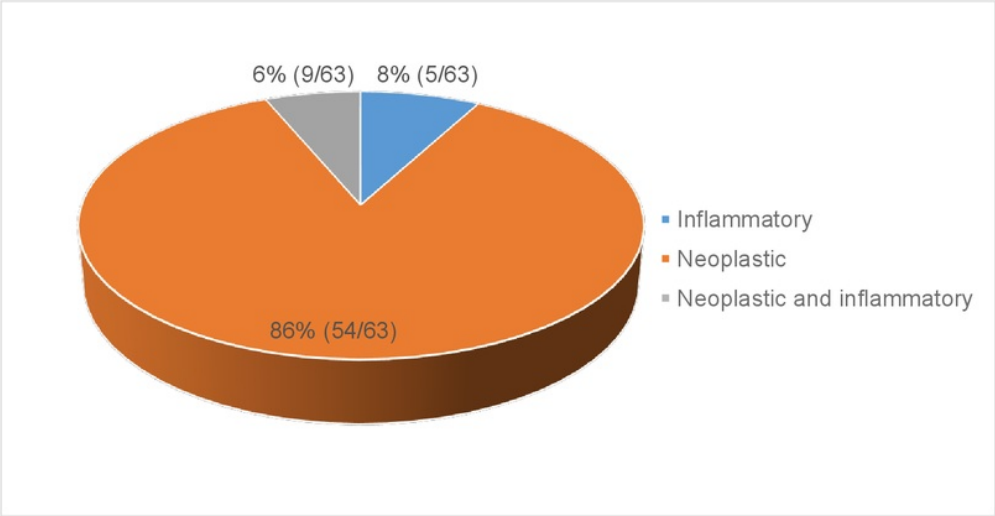


Figure 6: Histology Neoplastic/Non-neoplastic

4.5 Comparison between FNAC and Histology results

45/63 (71.4%) patients were identified as having benign tumours on FNAC. 41/63 (65%) were confirmed to have benign tumours on postoperative histology. Only 4/13 (30.8%) cases classified as malignant on FNAC were confirmed to true on histology (Table 5). The sensitivity and specificity of FNAC in the detection of malignancy was found to be 33.3% and 97.6% respectively. The negative predictive value was 83% and positive predictive value at 80%. The accuracy of the FNAC test was 83% (Table 6)

Table 4: Comparison of FNAC and histology results (N= 63)

Histology	FNAC			Overall	P-value
	Benign	Inflammatory	Malignant		
Benign	41 (91.1%)	3 (60%)	6 (46.2%)	50 (79.4%)	.000
Borderline*	1 (2.2%)	0 (0%)	2 (15.4%)	3 (4.8%)	
Inconclusive	3 (6.7%)	2 (40%)	1 (7.7%)	6 (9.5%)	
Malignant	0 (0%)	0 (0%)	4 (30.8%)	4 (6.3%)	
Total	n=45	n=5	n=13	N=63	

*Borderline = differential diagnosis of benign and malignant disease

Table 5: Sensitivity, specificity, negative predictive value, positive predictive and accuracy

Type	Sensitivity	Specificity	NPV	PPV	Accuracy
Malignant	33%	97.6%	83%	80%	83%
Benign	83%	100%	33%	100%	90%

4.6 Relationship between age group and histology results

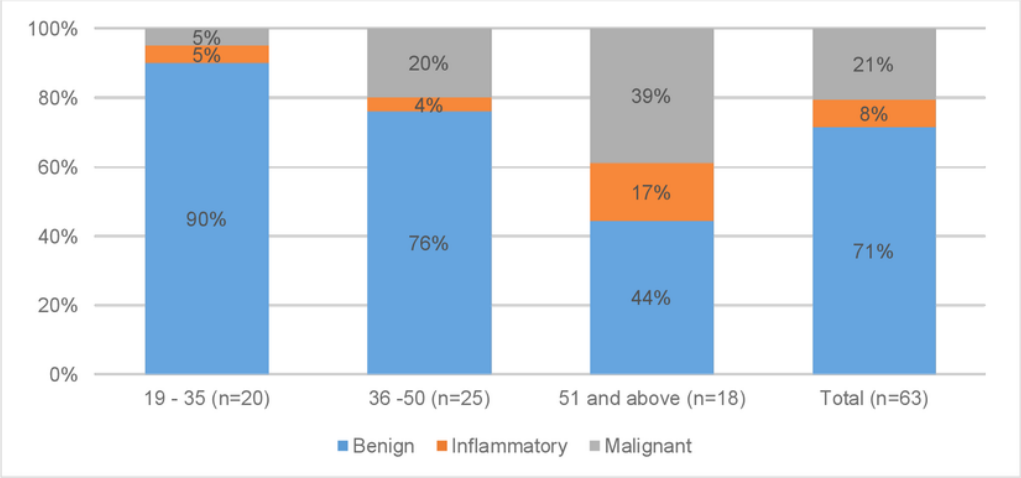


Figure 7: Distribution of pathological findings in age groups (N=63)

There was a significant relationship between age and histology results since the p-value was less than 0.05 (p-value = 0.032). It can also be noted from the table and the bar chart that the proportion of malignant increases with increasing age. The proportion is 5% among the 19 – 35 years age group, 20% within the 36 – 50 and 38.9% within the 51 years and above age group (Table 7).

Table 6: Histology- Benign, Malignant and inflammatory disease (N=63)

Parameter	19 - 35 (n=20)	36 -50 (n=25)	51 and above (n=18)	Total (N=63)	P-value
Benign	90.0%	76.0%	44.4%	71.4%	0.032
Inflammatory	5.0%	4.0%	16.7%	7.9%	
Malignant	5.0%	20.0%	38.9%	20.6%	

Table 7: Histology - Neoplastic and inflammatory (N=63)

Parameter	19 - 35 (n=20)	36 -50 (n=25)	51 and above (n=18)	Total (N=63)	P-value
Inflammatory	5.0%	4.0%	16.7%	7.9%	.388
Neoplastic	85.0%	88.0%	83.3%	85.7%	
Neoplastic and inflammatory	10.0%	8.0%	0.0%	6.3%	

There was however no significant relationship between neoplastic and in disease and age group of the patient since the p-value of 0.388 was greater than 0.05.

4.7 RELATIONSHIP BETWEEN CLINICAL SIGNS AND HISTOLOGY

It can be noted that none of the patients that were benign presented with any pain while 60% that had inflammatory and 38.5% of the patients that were malignant felt pain. The p-value for the association between histology and pain is significant as indicated by a p-value of 0.000 < 0.05. There was however no significant relationship between underlying pathology and occurrence of facial nerve palsy (p-value = 0.142 > 0.05) since the p-value was greater than 0.05. Relationship between histology and pain as well as histology and facial nerve palsy was assessed and the results are shown below.

Table 8: Histology results association with clinical presentation (N=63)

Clinical Presentation	Present/ Absent	Histology Benign/Malignant			Total N %	P-value
		Benign	Inflammatory	Malignant		
		n=45	n=5	n=13	N=63	
Pain	Present	0.0%	60.0%	38.5%	12.7%	.000
	Absent	100.0%	40.0%	61.5%	87.3%	
Facial Nerve Palsy	Yes	0.0%	0.0%	7.7%	1.6%	.142
	No	100.0%	100.0%	92.3%	98.4%	

4.8 Relationship between type of parotidectomy and FNAC results

Table 9: Relationship between type of parotidectomy and FNAC (N= 63)

Type of parotidectomy	Benign	Benign + Malignant	Malignant	Inconclusive	p-value
Type of parotidectomy	58.0%	66.7%	25.0%	50.0%	P = 0.532
Right superficial parotidectomy	38.0%	33.3%	50.0%	50.0%	
Right total parotidectomy	4.0%	0.0%	25.0%	0.0%	

CHAPTER 5: DISCUSSION

The aim of the study was to ascertain the usefulness of fine-needle aspiration cytology

(FNAC) in clinical decision-making for parotid gland masses at CHBAH. This was done by comparing the preoperative FNAC results with the post-operative histology results.

5.1 Summary of results

The results showed that, of the 45/63 (71%) patients that had FNAC results that showed benign tumour, 41/63 (91.1%) of them had a corresponding histology result showing benign tumour.

In terms of malignant tumours; of the 13 patients that had malignant histology results, only 4 cases (30.8%) of them had been correctly identified as malignant on FNAC. This means that the sensitivity and specificity of FNAC in identifying malignant parotid gland tumours in this study was 33.3% and 97.6% respectively.

The positive and negative predictive value of FNAC was calculated to be 80% and 83%.

These results are in keeping with the current figures in the literature (1).

This also proves the initial hypothesis of the study which stated that, FNAC is more accurate in the diagnosis of benign tumours than that of malignant tumours.

5.2 Demographics

The study only consisted of adult patients. The average age of presentation was 43.33 years. The age groups were further subdivided into 3 groups; 19-35. 36-50 and >51. It was noted that there was a significant relationship between age and final histology results. The incidence of malignant disease increased with age and this is in keeping with current literature on the incidence of salivary gland malignancies in relation to age.

5.3 Clinical presentation

All patients studied presented with a parotid mass.

Facial nerve palsy

Only one patient, whose histology result was a malignant tumour, presented with facial nerve palsy. No statistical value could be attached to this.

Pain

Patients that reported pain as a symptom had final histology results showed malignancy or inflammatory disease. This is in keeping with current studies on clinical presentation and furthermore, it forms part of important preoperative planning and decision-making where the FNAC is inconclusive or incongruent with clinical signs.

Cystic lesions

9.5% (n=6) of the patients presented with cystic lesions. 5 of them were confirmed to have lymphoepithelial cyst and 1 patient had an epidermal inclusion cyst. Cystic lesions of the parotid gland can be divided into three categories; non-neoplastic cysts, benign tumours with macrocystic change and malignant tumours with macrocystic change. Layfield et al found that the cytologic features of benign lymphoepithelial cysts

were well described in literature and consist of cellular smears with a mixed population of lymphocytes (19).

In our study, the FNAC results was able to correctly classify the 5 cases of lymphoepithelial cysts preoperatively and therefore guide management accordingly.

5.4 Incidence of benign and malignant tumours on histology

The most common benign tumour of histology was pleomorphic adenoma 41.3% (n=26), followed by lymphoepithelial cyst 15.9% (n=10). This may be as a result of the high prevalence of HIV in the study population resulting in the high incidence of benign lymphoepithelial cyst which is known to be associated with retroviral disease. The average prevalence of HIV-associated salivary gland disease in Africa is estimated at 19% (12).

The most common malignant tumour found was mucoepidermoid carcinoma and this is in keeping with current literature for parotid gland malignancies.

7.9% (n=5) of patients had multiple pathology on histology, of note is that all of these patients had lymphoid disease in association with either benign lymphoepithelial cyst or chronic sialadenitis. Obstruction in the salivary gland dusts caused by lymphoid hyperplasia forms the basis of pathogenesis of such disease process resulting in the multiple gland pathology isolated.

5.5 Comparison of benign and malignant tumours and inflammatory disease on FNAC and histology

On FNAC, 79% of patients were classified as having benign tumours compared to 71% on histology. 10% of results were inconclusive on FNAC, 6% malignant as compared to 21% on histology. From this comparison, it can be noted that malignant tumours were rare as compared to benign tumours. 5% had a differential diagnosis of benign and malignant disease on FNAC and 8% showed inflammatory results.

Of the 10% (n=6) of patients that were inconclusive of FNAC, 4 had benign tumours (pleomorphic adenoma, basal adenoma, Warthin's tumour and lipoma), one had a malignant hematolymphoid tumour (Non-Hodgkin Lymphoma) and one had chronic sialadenitis on histology. On review of the literature, it was noted that pleomorphic adenoma, basal cell adenoma, warthin's tumour and lymphoid lesions are some of the most commonly misdiagnosed on FNAC.

Pleomorphic adenoma

This neoplasm is biphasic. The epithelial component may represent variety of histologic patterns which may be ductal, squamous or exhibit some cytologic atypia. Lack of stromal component in the aspirated specimen may sometimes lead to a false positive diagnosis of mucoepidermoid carcinoma (19).

Basal adenoma

Basal cell adenoma has hyperchromatic nuclei but has been described as "benign-appearing and without pleomorphism. It may results in false positive diagnosis of mucoepidermoid carcinoma and cylindromatous type may be confused with adenoid cystic adenoma

Warthin's tumour

This neoplasm cytologically mimics many other lesions of the salivary glands such as mucoepidermoid carcinoma, acinic cell carcinoma, and squamous cell carcinoma, oncocytoma and lymphoepithelial cyst. This is as a result of the characteristic squamous metaplasia which is commonly confused with squamous cell carcinoma (8, 20).

Lipoma

Lipomatous lesions are relatively uncommon in the salivary glands. The highest reported incidence of lipomas in the parotid gland is 4.4% with the highest incidence in males (21). In our study, only 1.59% (n=1) was confirmed to have a lipomatous lesion which is in keeping with the reported rarity of this lesion in the parotid gland.

Non-Hodgkin's Lymphoma

Lymphomas located in the salivary glands are rare and for about 2-5% of all salivary glands tumours (22). In places of high prevalence rates of HIV, such as our study setting, the incidence of lymphomas in the head and neck region has been rising. As discussed in earlier chapters, lymphoid lesions present a diagnostic challenge on FNAC leading to either a false negative or false positive result. In the one case found in our study, a parotidectomy was performed following an inconclusive FNAC result where a surgical procedure was not indicated.

Non-neoplastic conditions

3.1% (n=2) of the cases in the study were found to have granulomatous inflammation on postoperative histology. One of them had a positive Ziehl-Nielsen stain (Tuberculosis). Tuberculosis of the parotid gland is a rare occurrence and has a very similar clinical presentation to parotid neoplasms. In immunodeficiency states, such

as HIV, this lesion needs to be considered in the differential diagnosis of parotid gland mass.

In our study, the FNAC results showed lymphoepithelial cyst on one patient and was inconclusive on the other. These two cases confirm the diagnostic difficulties of FNAC in inflammatory lesions. The unreliable FNAC, combined with the fact that these lesions can present similarly to neoplasms, can often lead to decisions resulting in unnecessary surgical management as it occurred in these two cases.

5.6 Relationship between FNAC result and surgical procedure

There was no statistical significance between the type of surgical procedure performed and FNAC result. This may be due to other presenting features, clinical signs and other tools such as imaging being used in surgical decision-making.

5.7 Limitations

The study relied mainly on records over a period of five years and the challenge encountered was that some details were incorrectly entered, making it very difficult to trace both FNAC and histology results of each patient. This meant that with every incomplete or incorrect record, that patient could not be included in the study. Parotid gland masses are also managed by other departments such as General Surgery at CHBAH, these records were not reviewed. This further skews the sample as it is not a true representation of all patients presenting with parotid gland masses to this institution.

Only patients from one academic hospital CHBAH were studied which introduces some bias into the study.

CONCLUSION

Fine-needle aspiration cytology in parotid gland masses is more reliable in the diagnosis of benign tumours with less reliability in the case of malignant tumours. Inflammatory diseases and lymphoid lesion of the parotid gland pose a diagnostic challenge clinically and on FNAC and misdiagnosis may lead to unwarranted surgical management. Therefore, evaluation of the patient with a parotid mass should include all the available tools including FNAC to guide management accordingly.

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APPENDIX A

Data Collection Sheet

Comparison between Preoperative Fine-needle Aspiration Cytology and Histology results of parotid gland masses at Chris Hani Baragwanath Academic Hospital.

i) Patient Study Number:

ii) Gender:

iii) Age:

iv) Year of diagnosis:

v) Presenting complaint:

Mass	Pain	Facial nerve palsy	Ulceration	Other

vi) Nature of enlargement : Solid/Cystic/Complex

vii) Size

viii) Presence/absence of Cervical lymphadenopathy

ix) FNAC diagnosis:

x) Type of Surgical procedure:

xi) Histology: Benign/Malignant/Grading of malignancy

xii) Specific Histology

xiii) Laterality : Right/Left/Bilateral

xiv) Imaging findings

APPENDIX B

Chris Hani Baragwanath Academic Hospital

P.O Bertsham

Soweto

2013

05 March 2018

Enquiries: ENT Department

Tel: 011 9338118

To The Hospital CEO

Re: DR F.B Mdletshe Research Project in ENT Department

This letter serves to certify that the above doctor was employed as a Registrar in the Ear, Nose and Throat, Head and Neck Surgery from 01/01/2014 to 31/12/2017. She completed her 4th year of training successfully on 31/12/2017 and obtained the specialist qualification (Fellowship in the College of Otorhinolaryngology).

She plans to carry out research for her Master of Medicine degree on the topic of "Comparison between Preoperative Fine-needle Aspiration Cytology and Post-operative Histology results of parotid masses at Chris Hani Baragwanath Academic Hospital".

Permission has been granted for the study to proceed in the ENT Department.

Thank you

Yours sincerely

.....

Dr MRI Ahmed

Head of Department of ENT, Head and Neck Surgery

APPENDIX C

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

MEDICAL ADVISORY COMMITTEE

CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

PERMISSION TO CONDUCT RESEARCH

Date: 18th April 2018

TITLE OF PROJECT:

Comparison between Preoperative Fine Needle Aspiration Cytology and Post-operative Histology results of Parotid Gland masses at Chris Hani Baragwanath Academic Hospital

UNIVERSITY: Witwatersrand

Principal Investigator: Dr F B Mdletshe

Department: ENT

Supervisor : Dr Bombil

Permission Head Department (where research conducted): Yes

The Medical Advisory Committee recommends that the said research be conducted at Chris Hani Baragwanath Academic Hospital. The CEO / management of Chris Hani Baragwanath Academic Hospital is accordingly informed and the study is subject to:-

- **Permission having been granted by the Committee for Research on Human Subjects of the University of the Witwatersrand.**
- The Hospital will not incur extra costs as a result of the research being conducted on its patients within the hospital
- The MAC will be informed of any serious adverse events as soon as they occur
- Permission is granted for the duration of the Ethics Committee Approval.

.....
Recommended
(On behalf of the MAC)
Date: 18/04/2018

.....
Approved/Not Approved
Hospital Management
Date: 23/04/18

APPENDIX D

NATIONAL HEALTH LABORATORY SERVICE
UNIVERSITY OF THE WITWATERSRAND – JOHANNESBURG

SCHOOL OF PATHOLOGY
Division of Anatomical Pathology

NATIONAL HEALTH LABORATORY SERVICE

P.O. Box 1038, Johannesburg 2000
Tel : +27-11-489-8477
+27-11- 489-8479
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Division of Anatomical Pathology
Faculty of Health Sciences
York Road
Parktown e-mail : martin.hale@nhls.ac.za

Professor MJ Hale MBChB (Rhodesia) FCPath (SA). LRCP, LRCS, LRCP&S (Edinburgh & Glasgow)
Professor & Head: Division of Anatomical Pathology,

Human Research Ethics Committee (Medical)
University of the Witwatersrand
Johannesburg
20000

September 6, 2018

Re: Consent for access to NHLS database

This letter serves to confirm that the Department of Anatomical Pathology at the University of the Witwatersrand and NHLS is happy to assist Dr FB Mdletshe with her project entitled "The usefulness of preoperative fine needle aspiration Cytology in the management of parotid gland masses at Chris Hani Baragwanath Academic Hospital".

Notwithstanding the requirement that research projects should comprise the researchers work only, it is recognized that publication of such work is encouraged. In the event that the information used comprises the diagnosis only then joint authorship from a member of staff in the Department of Anatomical Pathology would not be expected. However should additional information be extracted from the report for purposes of further interpretation such as morphological details and immunohistochemical profiles, it would be expected that this would be done in conjunction with a member of staff in the Department of Anatomical Pathology and that joint authorship would follow in resulting publications. Dr Mdletshe will be in contact with the Department of Anatomical Pathology in respect of this.

Assuring you of the Department of Anatomical Pathology's co-operation in this and future research projects.

With best wishes.

Yours sincerely,

Professor MJ Hale
Head: Department of Anatomical Pathology

APPENDIX E

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Dr Fanelesibonge Brightness Mdletshe

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M180333

NAME: (Principal Investigator)	Dr Fanelesibonge Brightness Mdletshe
DEPARTMENT:	Neurosciences (ENT) Chris Hani Baragwanath Academic Hospital
PROJECT TITLE:	Comparison between Preoperative Fine-needle Aspiration Cytology and Post-operative Histology Results of Parotid Gland Masses at Chris Hani Baragwanath Academic Hospital
DATE CONSIDERED:	06/04/2018
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Prof T. Luvhengo
APPROVED BY:	Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	27/09/2018

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the Third Floor, Faculty of Health Sciences, Phillip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193, University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in **March** and will therefore be due in the month of **March** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

Date 04/03/19

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG | FACULTY OF HEALTH SCIENCES

CERTIFICATE OF SUBMISSION FOR EXAMINATION OF MASTERS RESEARCH REPORT / DISSERTATION OR PHD THESIS SIGNED BY HIGHER DEGREES CANDIDATES

Full name	**Fanelesibonge Brightness Mdletshe**
Student number	**1138887**

Title of submitted Research Project: :

The Usefulness of Fine-needle aspiration cytology in the management of parotid gland masses at Chris Hani Baragwanath Academic Hospital

NB: If this title is different to your previously approved title, no further action can be taken by the Faculty Office until a change of title has been approved.

Contact no	**0827297970**	E-mail	**fanelsm@gmail.com**

1. If you are likely to move in the next 6-12 months, please give the anticipated date of move: _____
2. I hereby submit my **Masters (research report) / Masters (dissertation) / PhD thesis for examination** (Select whichever is applicable)
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   c) Done research using animals **Yes / (No)**
      If yes: I have included a copy of the animal ethics committee clearance certificate as an appendix in this document **Yes/No**
   d) Done research using human subjects, human tissue or patient records **(Yes) / No**
      If yes: I have included a copy of the human ethics clearance certificate as an appendix to the research document **(Yes)/No**

7. I understand that I may not graduate unless my University fees have been paid in full.
8. My Supervisor(s) names, departments, telephone numbers and email addresses are as follows:

Name	**Professor Thifheli Luvhengo**		
Department	**General Surgery**		
Telephone	**0114883373**	**E-mail**	**luvhengo@wits.ac.za**
Name	**Dr Dipuo Masege**		
Department	**ENT**		
Telephone	**0119338110**	**E-mail**	**dipuo.masege@wits.ac.za**
Name			
Department			

1

Telephone		E-mail	

List all publications, which you have published in peer-reviewed journals from your postgraduate research report/dissertation/thesis during the course of your studies in the Faculty of Health Sciences (Include authors, year, title of paper, name of journal, volume number and page numbers). This information is mandatory.

Signature of candidate: _____ Date: 04/03/19

1138887:Dr._Mdletshe_Research_Report_Final.pdf

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