Accuracy of preoperative fine needle aspiration in diagnosis of malignant parotid tumors

Hani Z. Marzouki, MSc, FRCSC, *Mohammed A. Altabsh,* MD, *Mohammed O. Albakrei,* MD, *Talal A. Al-Khatib,* MHPE, FRCSC, *Mazin A. Merdad,* MPH, FRCSC, *Nada J. Farsi,* MSc, PhD.

ABSTRACT

الأهداف: تحديد دقة التشخيص من الابرة الدقيقة الشافطة للكشف عن الأورام النكفية الخبيثة.

الطريقة: أجرينا دراسة استعادية لجميع المرضى الذين شخصت إصابتهم بأورام الغدة النكفية حميدة أو خبيثة في مستشفى الملك عبد العزيز الجامعي، بين يناير 2004م ومايو 2015م. وشملت مجموع 43 مريضا في التحليل النهائي. وقد تم الحصول على النتائج المرضية في الأنسجة و بيانات فحوصات FNA من السجلات الطبية. وقدرت الحساسية والنوعية والقيمة التنبؤية السلبية، والقيمة التنبؤية الإيجابية من FNA للكشف عن الآفات الخبيثة مقارنة مع المعيار الذهبي، التشريح المرضي.

النتائج: تم تشخيص 5 حالات إيجابية لمرض السرطان باستخدام التشريح المرضي ولم تشخص عن طريق FNA، تم تشخيص 3 آفات خبيثة باستخدام كل من FNA والتشريح، وحددت 32 حالة حميدة على أساس التشريح وتحليلFNA. وكان مجموع انتشار الأورام النكفية الخبيثة 15.8%. وكانت حساسية FNA للكشف عن الورم الخبيث 50%، وكانت خصوصية الأداة 100%. مع القيمة التنبؤية الإيجابية 100% والقيمة التنبؤية السلبية 91.4%.

الخاتمة: الإبرة الشافطة الدقيقة هي أداة اختبار محددة للغاية، ولكنها متوسطة الحساسية. نحن نؤيد استخدام هذا الأسلوب كأداة أولية لتشخيص اورام الغدة النكفية الخبيثة، كما هو إجراء آمن وسريع، وغير مؤلم، مقارنة بالتشريح المرضي.

Objectives: To determine the diagnostic accuracy of fine needle aspiration (FNA) for detecting malignant parotid tumors.

Methods: We conducted a retrospective study of all patients diagnosed with benign or malignant parotid gland tumors in King Abdulaziz University Hospital, Jeddah, Saudi Arabia, between January 2004 and May 2015. The records of 65 subjects were obtained. Histopathological findings and data from FNA examinations were obtained from medical records. Twenty-three subjects were excluded due to missing FNA, histopathology results or both. The sensitivity, specificity, negative predictive value, and positive predictive value of FNA for detecting malignant lesions were estimated and compared with the gold standard, histopathology.

Results: The specimens of 5 cases were insufficient for diagnosis; therefore, 38 cases were diagnosed by FNA and had histopathological reports. Three cases were diagnosed positive for cancer using histopathology and missed by FNA, 3 were diagnosed as malignant lesions using both FNA and histopathology, and 32 cases were determined benign based on histopathology and FNA analysis. The total prevalence of parotid malignancies was 15.8%. The sensitivity of FNA for detecting malignancy was 50%, and the specificity was 100%; with a positive predictive value of 100% and negative predictive value of 91.4%.

Conclusion: Fine needle aspiration is a highly specific, but only moderately sensitive test. We support the use of this method as an initial tool for diagnosing parotid gland malignancies, as it is a safe, rapid, and painless procedure, compared to histopathology.

Saudi Med J 2017; Vol. 38 (10): 1000-1006
doi: 10.15537/smj.2017.10.20988

From the Department of Otolaryngology-Head and Neck Surgery (Marzouki, Altabsh, Albakrei, Al-Khatib, Merdad), and the Department of Dental Public Health (Farsi), Faculty of Dentistry, Jeddah, King Abdulaziz University, Kingdom of Saudi Arabia.

Received 8th May 2017. Accepted 14th July 2017.

Address correspondence and reprint request to: Dr. Hani Z. Marzouki, Assistant Professor & Consultant, Head & Neck Oncology, Microvascular Reconstruction, Department of Otolaryngology-Head and Neck Surgery, Jeddah, King Abdulaziz University, Kingdom of Saudi Arabia.
E-mail: hanimarzouki@gmail.com
ORCID ID: orcid.org/0000-0002-0707-1851

The parotid glands are the largest major salivary glands, and play an important role as exocrine glands, which aid in the process of mastication and swallowing.[1,2] Salivary gland cancers account for approximately 3% to 6% of all head and neck tumors, with an overall world-wide incidence of approximately 0.4 - 13.5 cases per 100,000 diagnosed each year; of these, 80% are located in the parotid glands.[3,4] Many non-neoplastic, benign neoplasms, and malignant neoplastic diseases originate in the parotid gland.[5,6] Of these, mucoepidermoid carcinomas are the most common.[1] Parotid gland cancer is a rare malignancy, and can be an aggressive form of salivary gland cancer if not detected at an early stage.[1,2,5,7] However, most parotid gland cancers can be treated effectively, if detected in the early stages.[1] In general, parotid cancers can originate as primary cancers, or as metastases from adjacent structures.[2,8] Diagnostically, it can be difficult to differentiate between primary and secondary lesions.[1,2,8] Previous studies have shown that older age, male gender, a tumor size ≥4 cm, extraparenchymal extensions, cervical nodal metastasis, and distant metastasis, are all associated with a decreased survival rate.[8] A preoperative understanding of the nature of parotid tumors, such as their invasive capacity, is of significant importance, as this can determine the optimum surgical approach and treatment plan. Unfortunately, differentiation between benign and malignant parotid tumors cannot be carried out using simple physical examination or radiographic analysis.[9-11] In our institution, the standard methods for the preoperative assessment of parotid lesions include CT scans and fine needle aspiration (FNA). Fine-needle aspiration is the main initial diagnostic tool for head and neck masses.[12] It is widely used preoperatively, because it is a safe, cost effective, rapid, and painless procedure, compared to histopathology methods, which are the gold standard for analyzing parotid tumors.[5,9] When FNA is performed by experienced operators and interpreted in the context of clinical information, it can be a highly effective test for diagnosing the nature of the tumor.[12] However, the accuracy of FNA is operator dependent, and varies between clinics. Furthermore, some studies have suggested that the use of FNA could lead to possible neoplastic cells seeding.[13,14] The aim of our study was to determine the diagnostic accuracy of FNA for detecting malignant parotid tumors preoperatively, in King Abdulaziz University (KAU) Hospital, Jeddah, Saudi Arabia, in which FNA accuracy had not been previously assessed.

Disclosure. Authors have no conflict of interests, and the work was not supported or funded by any drug company.

Methods. We performed a retrospective study of all patients diagnosed with benign or malignant parotid gland tumors in KAU Hospital in Jeddah, between January 2004 and May 2015. This study was approved by the King Abdulaziz University research ethics board and the need for consent was waived (Application no. 237-15).

Data collected were (i) patient demographic factors, including age and gender; (ii) lesion characteristics, including depth and loci of the tumor (superficial lobe/deep lobe/both lobes), and lesion size; (iii) patients' previous history of cancer; and (iv) FNA method used (ultrasound-guided, direct, indirect). The characteristics of patients and lesions were compared as frequencies and percentages for categorical variables, and means and standard deviation for continuous variables. Patient age and tumor size data were collected as continuous variables. Tumor size was categorized into 2 categories, using the 50th percentile (4 cm) as a cut-off point. All other variables were treated as categorical variables.

Histopathology and FNA data collection and statistical analyses. Information concerning histopathological and FNA diagnoses were collected from medical charts and the hospital database. Pathologists within a central laboratory in KAU Hospital performed all diagnostic analyses. The proportions of each disease category diagnosed by histopathology and FNA were calculated. We categorized FNA and histopathology results into 3 categories: benign, malignant, or insufficient for diagnosis. For each case, the results from FNA examinations were compared with histopathology results. Subjects diagnosed with a malignancy by both histological examination and FNA analysis were considered true positives (TP), and those who had no malignancy on both FNA and histopathology were classified as true negatives (TN). Subjects were categorized as false positives (FP), when malignancy was diagnosed by FNA, but not histopathology. When malignancy was detected using histopathology but FNA failed to identify it, subjects were categorized as false negatives (FN). The sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) for detecting malignant lesions by FNA were estimated based on the histopathology results.

For these calculations, the following formula were used:[15] Sensitivity = TP/TP + FN; Specificity = TN/TN + FP; PPPV = TP/TP + FP; NPV = TN/TN + FN; Total accuracy =TP + TN/total number of cases

Statistical analyses were analyzed using Stata version 12.1 software (StataCorp LP, College Station, Texas, USA).

Results. *Subject and lesion characteristics.* Initially, 65 parotidectomy cases were identified. We excluded 3 subjects with missing histopathology results, 19 subjects with missing FNA findings or for whom FNA was not performed, and one subject with missing histopathology and FNA results.

A total of 43 patients were included in the final analysis. The included patient and lesion characteristics are presented in **Table 1**. The mean age of the participants was 41.2 ± 18.2 years, with equal proportions of males and females. Eighty-one percent of the participants had no previous history of cancer. Forty-nine percent of the tumors were larger than 4 mm in size, intraoperatively; the remaining lesions were smaller. The superficial lobe was affected in 65% of cases, followed by 14% for deep lobes and 21% for both lobes. Fine needle aspiration diagnoses were obtained using the direct FNA method in 49% of the cases, whereas 39.5% were performed using ultrasound guidance. The FNA method used for the remaining cases was unknown.

Tumor classification using fine needle aspiration. Of the 43 cases included in the final analysis, the FNA results of 5 were inconclusive. Of the 38 conclusive aspirations, 3 were malignant and 35 were benign (**Table 2**). Pleomorphic adenoma or mixed tumors were the most common benign lesions (n=30; 86%), and the remainder was one of each of the following lesions, monomorphic adenoma, Warthin's tumor, benign lymphoepithelial cell, benign acinar cell, and scanty lymphoid cell lesions. The 3 malignant lesions diagnosed by FNA were mucoepidermoid carcinoma, acinic cell carcinoma, and squamous cell carcinoma SCC.

Tumor classification using histopathology. Acinic cell carcinoma was the most common malignant condition diagnosed by histopathology (43% of cases). Consistent

Table 1 - Demographics and lesion characteristics (N=43).

Variable	n (%)
Age, mean (SD)	41.2 (18.2)
Gender	
Male	21 (48.9)
Female	22 (51.2)
Previous history of cancer	
No	34 (81.0)
Yes	5 (11.9)
Size of lesion	
≤3 cm	13 (41.9)
>3 cm	18 (58.1)
Intraoperative size of tumor	
≤4 cm	22 (51.2)
>4 cm	21 (48.8)
Depth of lesion	
Superficial lobe	28 (65.1)
Deep lobe	6 (14)
Both lobes	9 (20.9)
Fine needle aspiration method	
Ultrasound guided	17 (39.5)
Direct	21 (48.8)
Unknown	5 (11.6)

Table 2 - Diagnosis of parotid lesions using fine needle aspiration and histopathological analysis.

Diagnosis of parotid lesions	n	(%)
Histopathological diagnosis		
Malignant lesions		
Mucoepidermoid carcinoma high grade	1	(14.3)
Mucoepidermoid carcinoma low grade	1	(14.3)
Acinic cell carcinoma	3	(42.9)
SCC	1	(14.3)
Epithelial /myoepithelial carcinoma	1	(14.3)
Benign lesions		
Pleomorphic adenoma or mixed tumor	23	(63.9)
Warthin tumor (papillary cystadenoma or lymphomatosum or adenolymphoma)	7	(19.4)
Chronic granulomatous lymphadenitis	1	(2.8)
Benign lymphepithelial cell	2	(5.6)
Basal cell adenoma	1	(2.8)
Castleman's disease	1	(2.8)
Non-necrotizing granulomatos sialanditis	1	(2.8)
Fine needle aspiration diagnosis		
Malignant lesions		
Mucoepidermoid carcinoma low grade	1	(33.3)
Acinic cell carcinoma	1	(33.3)
Squamous cell carcinoma	1	(33.3)
Benign lesions		
Pleomorphic adenoma or mixed tumor	30	(85.7)
Monomorphic adenoma	1	(2.9)
Warthin tumor (papillary cystadenoma or lymphomatosum or adenolymphoma)	1	(2.9)
Scanty lymphoid cell	1	(2.9)
Benign lymphepithelial cell	1	(2.9)
Benign acinar cell	1	(2.9)

Table 3 - Comparison of fine needle aspiration (FNA) and histopathology diagnoses of parotid lesions.

Diagnoses	Number	Status
FNA diagnoses		
Pleomorphic adenoma or mixed tumor*	30	
Monomorphic adenoma*	1	
Warthin tumor (papillary cystadenoma or lymphomatosum or adenolymphoma)*	1	
Scanty lymphoid cell*	1	
Benign lymphepithelial cell*	1	
Benign acinar cell*	1	
Mucoepidermoid carcinoma low grade‡	1	
Acinic cell carcinoma‡	1	
Squamous cell carcinoma‡	1	
Insufficient for diagnosis	5	
Pathologic diagnosis		
Pleomorphic adenoma or mixed tumor*	19	TN
Warthin tumor (papillary cystadenoma or lymphomatosum or adenolymphoma)*	5	TN
Basal cell adenoma*	1	TN
Castleman's disease*	1	TN
Acinic cell carcinoma‡	2	FN
Epithelial /Myoepithelial carcinoma‡	1	FN
Non-necrotizing granulomatos sialanditis‡	1	TN
Pleomorphic adenoma or mixed tumor*	1	TN
Warthin tumor (papillary cystadenoma or lymphomatosum or adenolymphoma)	1	TN
Chronic granulomatous lymphadenitis	1	TN
Benign lymphepithelial cell	1	TN
Pleomorphic adenoma or mixed tumor	1	TN
Mucoepidermoid carcinoma low grade‡	1	TP
Acinic cell carcinoma‡	1	TP
Squamous cell carcinoma‡	1	TP
Warthin tumor (papillary cystadenoma or lymphomatosum or adenolymphoma)*	1	---
Pleomorphic adenoma or mixed tumor*	2	---
Benign lymphepithelial cell*	1	---
Mucoepidermoid carcinoma high grade‡	1	---

*benign, ‡malignant, TN - true negative, TP - true positive

with the FNA examination results, pleomorphic adenomas or mixed tumor types were the most common benign conditions (64%) (**Table 2**).

Accuracy of FNA diagnoses. To determine the FNA diagnostic efficacy, the FNA diagnosis for each case was compared with the histopathological diagnosis, as illustrated in **Table 3**. Cases with insufficient FNA results were excluded from further analyses. In most cases, there was an agreement between the FNA and histopathological diagnoses; however, exact disease classification required further diagnostic tests for some subjects. There were 3 false negatives, of which 2 subjects were diagnosed with acinic cell carcinomas, and one case had malignant epithelial/myoepithelial carcinoma, based on histopathological examination; however, these cases were diagnosed as benign pleomorphic adenomas or mixed tumors using FNA (**Table 3**). There were no false positive results.

The prevalence of parotid masses in the study sample; and the diagnostic efficacy of FNA for determining parotid malignancy, including specificity, sensitivity, PPV, NPV, and diagnostic accuracy, are presented in **Table 4**.

Discussion. The main purpose of performing FNA prior to parotid surgery is to differentiate benign from malignant disease. As an initial diagnostic tool, FNA methods allow clinicians to determine whether surgery is necessary, and to determine the extent of surgery required. This approach has resulted in a significant reduction in the number of surgical procedures used to treat salivary gland swellings by approximately 30%; however, surgical biopsy and subsequent histopathology analysis is still considered the gold standard for assessing tumor metastatic potential.[10] Previous studies have claimed that in most cases, FNA is unsuitable or unnecessary, due to its low sensitivity, high rate of false negatives, and because the anatomical location of the lesion is more important for determining the appropriate surgical approach.[16] Importantly, surgical biopsies can lead to significant complications for the patient, such as fistula formation, tumor implantation, and facial nerve damage; and are also prone to sampling errors, namely, the failure to obtain an effective representation of cells from the tumor.[10,16] Hence, an advantage of FNA is that it allows surgeons to discuss treatment options with patients prior to performing more invasive procedures, and in some cases prevent unnecessary surgeries.

Similar studies have reported the accuracy of FNA ranging from 69% to 98%, and specificities ranging from 88% to 100%. In comparison, our results suggest a lower sensitivity ranging from 52% to 98%; the inconsistency between our findings and previous reports could be due to our limited sample size. Furthermore, most studies analyzed general salivary gland tumors, whereas we selectively analyzed parotid gland tumors. A detailed comparison between the diagnostic capabilities of FNA for salivary gland tumor reported in other studies, and the present findings, is presented in **Table 5**.

These previous studies have highlighted high rates of false negatives and low sensitivity as major limitations to the application of FNA for assessing salivary gland malignancy.[16-18] These contradictory findings could

Table 4 - Sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of fine needle aspiration (FNA).

Values	Histopathology		Total	Percentage	95% confidence interval
	Cancer	Non-cancer			
Fine needle aspiration					
Positive	3 (TP)	0 (FP)	3		
Negative	3 (FN)	32 (TN)	35		
Total	6	32	38		
Disease prevalence				15.8	(6.0 - 31.25)
Sensitivity				50.0	(11.8 - 88.2)
Specificity				100	(89.1 - 100)
Positive predictive value				100	(29.2 - 100)
Negative predictive value				91.4	(76.9 - 98.2)
Diagnostic accuracy				92.1	(78.6 - 98.3)

TN - true negative, TP - true positive, FP - false positive

Table 5 - Comparison of the diagnostic efficacy of FNA for assessment of parotid masses reported in the present study and in the previous studies.

Studies	Year	Total FNA	Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (%)	NPV (%)
Jayaram et al[24]	1994	247	91.0	88.0	98.0	81.2	98.4
Orell et al[25]	1995	325	85.5	99.5	-	-	-
Cristallini et al[26]	1997	153	97.6	98.43	97.98	-	96.9
Shintani et al[27]	1997	43	88.9	94.1	93.0	-	-
Cajulis et al[28]	1998	151	91.0	96.0	-	-	-
Boccato et al[29]	1998	841	98.0	98.0	97.0	-	-
Stewart et al[30]	2000	341	92.0	100	98.0	-	-
Zbaren et al[22]	2001	228	64.0	95.0	86.0		
Lurie et al[31]	2002	52	66.0	100	69.2	-	-
Hartimath et al[5]	2011	41	90.9	96.6	95.1	90.0	96.7
Ali et al[11]	2011	129	84.0	98.0	94.0	93.0	95.0
Nguansangiam et al[10]	2012	290	81.3	99.1	97.0	92.9	97.5
Mallon et al[16]	2013	201	52.0	98.0	92.0	78.0	93.0
Present study	2017	42	50.0	100	92.1	100	91.4

have resulted from our small sample size, in which larger studies would be more likely to encounter false positives; therefore, reducing the PPV and specificity.[19] In the present study, 3 of 6 malignant lesions detected using histopathology were missed by FNA, which could be attributed to problems with the sampling technique. This resulted in a sensitivity of only 50%. Additionally, 5 FNA specimens were insufficient for diagnosis, due to large amounts of blood or scanty tissue sampling. However, the specificity of FNA in this study was 100%, which suggests that FNA has a very low likelihood of falsely diagnosing non-malignant parotid growths as cancerous. Previously reported PPVs for FNA of salivary gland lesions ranged from 78-100%, and NPVs ranged from 85-98%.[9,16,20-22] The PPV of FNA calculated for the present study was 100%, and the NPV was 91.4%. Our PPV was likely higher compared to previous reports, due to the absence of false positives, which could be attributed to the small sample size and low prevalence of malignancy in parotid tumors. Additionally, variables such as the pathologist's level of experience, FNA technique, promptness of sample evaluation, and sampling errors, might influence the accuracy of FNA for diagnosing malignancy in parotid masses. For this reason, many institutions recommended the use of ultrasonography assisted FNA, in order to reduce the likelihood of sample errors.[23,24] The limited sample size in our study, and absence of information

in medical records regarding some of these factors, prevented us from performing multivariate analyses, to assess the broader determinants of FNA accuracy for parotid cancer diagnosis.

The retrospective nature of this study was another limitation. Inadequate data in some medical records was evident during data extraction. We therefore recommend further measures be taken in KAU Hospital, to ensure that sufficient and accurate medical records are obtained in the future. Access to a more comprehensive database will enhance superior patient care, and enable conducting future studies to understand parotid malignancies, and improve the accuracy of diagnosing parotid gland cancers.

In conclusion, based on our findings, FNA is a highly specific, but only moderately sensitive test. We support its application as an initial tool for diagnosing parotid gland malignancies; it is a relatively safe, rapid and non-invasive approach, compared to the surgical biopsies. However, future studies are required, to assess factors related to accuracy of FNA diagnosis, which can vary significantly. A more comprehensive evaluation of this technique, and a comparison of the different methods, such as ultrasound-guided FNA, will help to inform clinicians and surgeons on the best approach to diagnosing and treating parotid tumors.

References

1. Ho K, Lin H, Ann DK, Chu PG, Yen Y. An overview of the rare parotid gland cancer. ***Head Neck Oncol*** 2011; 3: 40.
2. Makki FM, Mendez AI, Taylor SM, Trites J, Bullock M, Flowerdew G, et al. Prognostic factors for metastatic cutaneous squamous cell carcinoma of the parotid. ***J Otolaryngol Head Neck Surg*** 2013; 42: 14.
3. Tian Z, Li L, Wang L, Hu Y, Li J. Salivary gland neoplasms in oral and maxillofacial regions: a 23-year retrospective study of 6982 cases in an eastern Chinese population. ***Int J Oral Maxillofac Surg*** 2010; 39: 235-242.
4. Stenner M, Klussmann JP. Current update on established and novel biomarkers in salivary gland carcinoma pathology and the molecular pathways involved. ***Eur Arch Otorhinolaryngol*** 2009; 266: 333-341.
5. Hartimath B, Kudva A, Singh Rathore A. Role of fine-needle aspiration cytology in swellings of the parotid region. ***Indian J Surg*** 2011; 73: 19-23.
6. Akhavan-Moghadam J, Afaaghi M, Maleki AR, Saburi A. Fine needle aspiration: an atraumatic method to diagnose head and neck masses. ***Trauma Mon*** 2013; 18: 117-121.
7. Deschler DG, Eisele DW. Surgery for primary malignant parotid neoplasms. ***Adv Otorhinolaryngol*** 2016; 78: 83-94.
8. Chen MM, Roman SA, Sosa JA, Judson BL. Prognostic factors for squamous cell cancer of the parotid gland: an analysis of 2104 patients. ***Head Neck*** 2015; 37: 1-7.
9. Piccioni LO, Fabiano B, Gemma M, Sarandia D, Bussi M. Fine-needle aspiration cytology in the diagnosis of parotid lesions. ***Acta Otorhinolaryngol Ital*** 2011; 31: 1-4.
10. Nguansangiam S, Jesdapatarakul S, Dhanarak N, Sosrisakorn K. Accuracy of fine needle aspiration cytology of salivary gland lesions: routine diagnostic experience in Bangkok, Thailand. ***Asian Pac J Cancer Prev*** 2012; 13: 1583-1588.
11. Ali NS, Akhtar S, Junaid M, Awan S, Aftab K. Diagnostic accuracy of fine needle aspiration cytology in parotid lesions. ***ISRN Surg*** 2011; 2011: 721525.
12. Singh Nanda KD, Mehta A, Nanda J. Fine-needle aspiration cytology: a reliable tool in the diagnosis of salivary gland lesions. ***J Oral Pathol Med*** 2012; 41: 106-112.
13. Engzell U, Esposti PL, Rubio C, Sigurdson A, Zajicek J. Investigation on tumour spread in connection with aspiration biopsy. ***Acta Radiol Ther Phys Biol*** 1971; 10: 385-398.
14. Mighell AJ, High AS. Histological identification of carcinoma in 21 gauge needle tracks after fine needle aspiration biopsy of head and neck carcinoma. ***J Clin Pathol*** 1998; 51: 241-243.
15. Lalkhen AG, McCluskey A. Clinical tests: sensitivity and specificity. ***Continuing Education in Anaesthesia, Critical Care & Pain*** 2008; 8: 221-223.
16. Mallon DH, Kostalas M, MacPherson FJ, Parmar A, Drysdale A, Chisholm E, et al. The diagnostic value of fine needle aspiration in parotid lumps. ***Ann R Coll Surg Engl*** 2013; 95: 258-262.
17. Tandon S, Shanhab R, Benton JL, Ghosh SK, Sheard J, Jones TM. Fine-needle aspiration cytology in a regional head and neck cancer center: comparison with a systematic review and meta-analysis. ***Head Neck*** 2008; 30: 1246-1252.
18. Hughes JH, Volk EE, Wilbur DC. Pitfalls in salivary gland fine-needle aspiration cytology: lessons from the College of American Pathologists Interlaboratory Comparison Program in Nongynecologic Cytology. ***Arch Pathol Lab Med*** 2005; 129: 26-31.
19. Zbären P, Nuyens M, Loosli H, Stauffer E. Diagnostic accuracy of fine-needle aspiration cytology and frozen section in primary parotid carcinoma. ***Cancer*** 2004; 100: 1876-1883.
20. Javadi M, Asghari A, Hassannia F. Value of fine-needle aspiration cytology in the evaluation of parotid tumors. Indian ***J Otolaryngol Head Neck Surg*** 2012; 64: 257-260.
21. Zurrida S, Alasio L, Tradati N, Bartoli C, Chiesa F, Pilotti S. Fine-needle aspiration of parotid masses. ***Cancer*** 1993; 72: 2306-2311.
22. Zbären P, Schär C, Hotz MA, Loosli H. Value of fine-needle aspiration cytology of parotid gland masses. ***Laryngoscope*** 2001; 111: 1989-1992.
23. Christensen RK, Bjorndal K, Godballe C, Krogdahl A. Value of fine-needle aspiration biopsy of salivary gland lesions. ***Head Neck*** 2010; 32: 104-108.
24. Jayaram G, Verman AK, Sood N, Khurana N. Fine needle aspiration cytology of salivary gland lesions. ***J Oral Pathol Med*** 1994; 23: 256-261.
25. Orell SR. Diagnostic difficulties in the interpretation of fine needle aspirates of salivary gland lesions: the problem revisited. ***Cytopathology*** 1995; 6: 285-300.

26. Cristallini EG, Ascani S, Farabi R, liberati F, Maccio T, Peciarolo A, et al. Fine needle aspiration biopsy of salivary gland, 1985-1995. ***Acta Cytol*** 1997; 41: 1421-1425.
27. Shintani S, Matsuura H, Hasegawa Y. Fine needle aspiration of salivary gland tumors. ***Int J Oral Maxillofac Surg*** 1997; 26: 284-286.
28. Cajulis RS, Gokaslan ST, Yu GH, Frias-Hidvegi D. Fine needle aspiration biopsy of the salivary glands. A five-year experience with emphasis on diagnostic pitfalls. ***Acta Cytol*** 1997; 41: 1412-1420.
29. Boccato P, Altavilla G, Blandamura S. Fine needle aspiration biopsy of salivary gland lesions. A reappraisal of pitfalls and problems. ***Acta Cytol*** 1998; 42: 888-898.
30. Stewart CJ, MacKenzie K, McGarry GW, Mowat A. Fine-needle aspiration cytology of salivary gland: a review of 341 cases. ***Diagn Cytopathol*** 2000; 22: 139-146.
31. Lurie M, Misselevitch I, Fradis M. Diagnostic value of fine-needle aspiration from parotid gland lesions. ***Isr Med Assoc J*** 2002; 4: 681-683.

Withdrawal policy

By submission, the author grants the journal right of first publication. Therefore, the journal discourages unethical withdrawal of manuscripts from the publication process after peer review. The corresponding author should send a formal request signed by all co-authors stating the reason for withdrawing the manuscript. Withdrawal of a manuscript is only considered valid when the editor accepts, or approves the reason to withdraw the manuscript from publication. Subsequently, the author must receive a confirmation from the editorial office. Only at that stage, are the authors free to submit the manuscript elsewhere.

No response from the authors to all journal communication after review and acceptance is also considered unethical withdrawal. Withdrawn manuscripts noted to have already been submitted or published in another journal will be subjected to sanctions in accordance with the journal policy. The journal will take disciplinary measures for unacceptable withdrawal of manuscripts. An embargo of 5 years will be enforced for the author and their co-authors, and their institute will be notified of this action.