Journal of Rashid Latif Medical College 1 (2022) 25-31

Journal of Rashid Latif Medical College

journal homepage: www.jrlmc.org

Original Article

Diagnostic Accuracy of Frozen Section in Salivary Gland Neoplasms

Fakeha Rehman[1], Hafiz Muhammad Bilal Saleh[1], Shehzad Shafqat Qureshi[1]
1Department of Pathology, Services Institute of Medical Sciences

KEY WORDS:

Frozen section, salivary glands, neoplasms, cryosectioning

ABSTRACT

Introduction: Research over the years has systematically revealed that morphological, histological, and molecular data from human cancers available to pathologists has revolutionized quantitative systems science. By measuring morphological parameters such as tumor stage and grade, it is now possible to integrate relatively large data sets thus reconceptualization of knowledge available, provides better prediction of the behavior of tumors and their interaction with the host. Histological diagnosis prior to surgery is not possible, as incisional biopsies are contraindicated due to the possibility of facial nerve injury and incomplete resection of the tumor. **Objective:** To compare the results of the frozen section examination with definitive histological diagnosis. Identifying malignancy intraoperatively can have a significant impact on the management of the salivary gland tumors. **Materials and Methods:** The study was done in Histopathology department of SIMS/Services hospital, Lahore. 40 cases of salivary gland neoplasms previously diagnosed on FNAC. **Results:** Comparing the perioperative result with definitive diagnosis, 10% (6/40) were true positive, 77.5% (31/40) true negative, 7.5% (3/40) false positive, 0% (0/40) false negative, prevalence, 66.6% positive predictive value and 100% negative predictive value. Thus, the sensitivity of frozen section for malignancy was 100% and the specificity was 91%. **Conclusion:** We consider that frozen section examination for salivary gland neoplasms is not sufficient on its own for deciding on the best management. Their interpretation must be correlated with clinical and intraoperative findings, in association with surgeon's experience.

Introduction

The histopathology of salivary gland tumours is extremely varied and complex. Amongst the epithelial neoplasms alone, at least 9 different adenomas and 17 different carcinomas are recognized. Furthermore, a host of nonepithelial tumours, lymphomas, secondary tumours and tumour-like lesions may also arise in the salivary glands, contributing to the diagnostic difficulty.[1-4] Distinguishing neoplastic from non-neoplastic lesions and benign from malignant tumours of the major salivary glands is extremely important in their management. In particular, since salivary gland tumours are almost always treated surgically, identifying malignancy either preoperatively or intraoperatively is crucial, for this can have a significant impact on the type, extent and radicality of surgery.[5-7] While the history and clinical examination remain important in this respect, and while there are classic symptoms and signs which may suggest malignancy, most malignant salivary neoplasms have unremarkable features, and are not readily distinguishable from their benign counterparts on clinical criteria alone.[8]

Preoperative imaging in the form of computed tomographic (CT) or magnetic resonance imaging (MRI) scanning is frequently employed to characterise a lesion prior to surgery. However, while certain radiologic features favor or suggest the diagnosis of malignancy, imaging findings on their own are frequently not sufficiently specific or reliable to make a diagnosis.[9-14] Fine needle aspiration cytology (FNAC) has been

Correspondence address: Department of Pathology, Services Institute of Medical Sciences. sohnia@gmail.com

widely used for many years as a method for assessing salivary gland lesions preoperatively. The reported sensitivity and specificity of FNAC is high for benign salivary neoplasms, but is less good for malignant tumours. In particular, the specific accuracy for distinguishing between the various types of malignant tumours is poor. This is not surprising, as some salivary gland malignancies cannot be identified by cytological features alone.[14-18] Several salivary carcinomas contain admixtures of similar cell types, and oftentimes it is the relative proportion of different cells, or the architectural arrangement of those cells, that defines the tumour. Furthermore, some carcinomas can only be distinguished from their benign adenoma counterparts by the presence of capsular or peritumoural invasion. This, unfortunately, is not assessable on FNAC.[18-22]

This study was aimed to determine the diagnostic accuracy of the frozen section diagnosis of the salivary gland neoplasms with the final histopathological diagnosis taking histopathology as gold standard. With the objective of evaluating the importance of frozen sections in surgical decisions, we analyzed cases treated by excision of salivary gland tumors in our service, comparing the frozen section diagnosis to final histological diagnosis.

Materials and Methods

A prospective analysis was made of 40 cases of salivary gland tumors operated at all the surgical departments of the Services Hospital, Lahore, between December 2010 and June 2011. Patients with lymphoma, melanoma, and sarcoma (*n* = 11 patients), and metastatic carcinoma (*n* = 36 patients), as well as patients with obviously untreatable disease (*n*= 6 patients), were excluded from the analysis. Furthermore, nine patients with false-positive FNAC findings (malignant cytology and benign histology) also were excluded from the study. None of these patients had a history of a parotid gland tumorsor further neoplasms of the head and neck region. carcinomas were staged according to the InternationalUnion Against Cancer TNM classification system. Twenty-five tumors were classified as T1, 33 tumorswere classified as T2, 17 tumors were classified as T3,and 26 tumors were classified as T4. The histologic diagnoses of all tumors were reviewedby an experienced staff pathologist and wereclassified according to the World Health Organizationclassification system. Tumors were grouped further into high-grade and low-grade malignancies. According to most authors, adenocarcinoma not otherwise specified, squamous cell carcinoma, undifferentiatedcarcinoma, and salivary duct carcinoma are consideredhigh-grade carcinomas. With regard to thesolid histologic pattern of adenoid cystic carcinoma,many authors have pointed out the less favorableprognosis associated with those tumors, which oftendemonstrate a fulminating progression in many patients. This aggressive clinical behavior correlateswell with the histologic characteristics of the solidpattern, such as numerous mitotic figures, cellular andnuclear pleomorphism, and tumor cell necrosis.Therefore, the solid type of adenoid cystic carcinomawas included in the high-grade group.

The appropriate tissues were snap frozen in liquid nitrogen, embedded in OCT (polyethylene glycol-based embedding medium) and sectioned on a Tissue-Tek cryostat at -24°C. The sections were examined microscopically and diagnoses made by staff pathologists. The diagnostic interpretations were recorded in the frozen section request form and in the patients' chart as well as verballycommunicated to the surgeon by an intercom system.

Data Analysis

All the collected information was entered into SPSS version 10.0. Age was presented as mean ± SD. Gender was presented as frequency and percentage. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy of frozen section was calculated taking histopathology as gold standard.(Figure 1, Table 1 and Table 2).

Results

Out of 40 cases included in this study, 26 were females and 14 were males. The age range of the patients was from 16 to 78 years with a mean of 47 years. Frozen section examination identified 31benign cases (83.7%) and 9 (12.4%) malignant. No inconclusive diagnosis was given. The definitive pathologic diagnosis showed 34 benign cases and 6 malignant cases. All the tumor types observed in this study are summarized in figure 5.

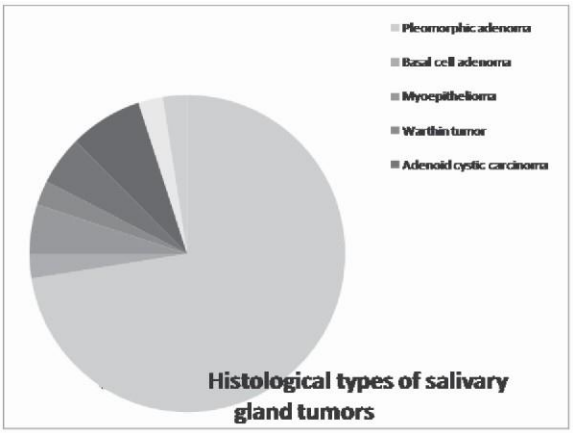

Figure 1: shows histological types of tissue tumors.

Comparing the perioperative result with definitive diagnosis, 10% (6/40) were true positive, 77.5% (31/40) true negative, 7.5% (3/40) false positive, 0% (0/40) false negative, prevalence, 66.6% positive predictive value and 100% negative predictive value. Thus, the

sensitivity of frozen section for malignancy was 100% and the specificity was 91%.

In the three cases of benign disease in which the frozen section results were false positive, no extended surgical procedure or facial nerve sacrifice was performed, as the surgeon's clinical impression prevailed (clinical history plus macroscopic perioperative findings).

Table 1: AccurateTumor typing: Histologic and True-Positive Frozen Section Diagnoses(*n* = 37)

Histological diagnosis	Frozen section diagnosis
Accurate tumor typing(n=37)	
31 pleomorphic adenomas	31 pleomorphic adenomas
2 mucoepidermoid carsacinomas	2 mucoepidermoid carsacinomas
1 adenoid cystic carcinoma	1 adenoid cystic carcinoma
1 myoepithelioma	1 myoepithelioma
1 basal cell adenoma	1 basal cell adenoma
1 carcinoma ex pleomorphic adenoma	1 carcinoma ex pleomorphic adenoma
1 oxyphilic adenoma	1 oxyphilic adenoma

Table 2: shows misdiagnosed specimen

Histological diagnosis	
Inaccurate tumor typing (n=3)	
1 pleomorphic adenoma	1 mucoepidermoid carcinoma
1 pleomorphic adenoma	1 adenoid cystic carcinoma
1 pleomorphic adenoma with mucinous areas	1 mucoepidermoid carcinoma

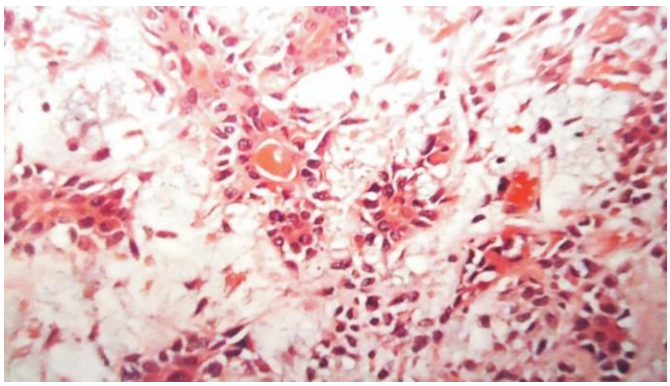

Figure 2: Myoepithelial cells in pleomorphic adenoma

Three cases of pleomorphic adenoma were misdiagnosed as malignant on frozen section.(table2) One was pleomorphic adenoma with squamous metaplasia(figure 6) in which the section taken revealed only scattered squamous cells but no keratin pearls were observed. The second case was pleomorphic adenoma with adenoid cystic like areas (figure 4)misinterpreted as adenoid cystic carcinoma. While the third case was of pleomorphic adenoma with focal mucinous change misinterpreted as low grade mucoepidermoid carcinoma.(figure 5)

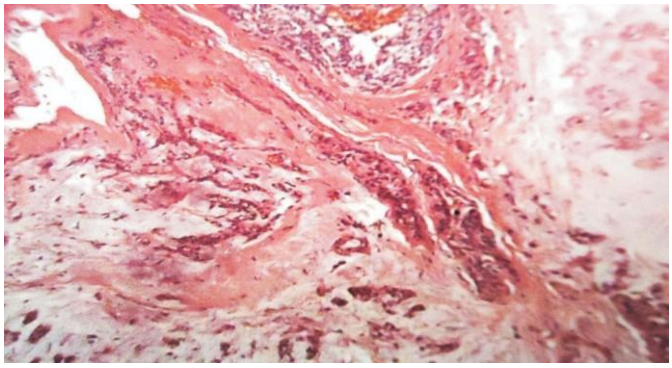

Figure 3: Myxoid matrix in pleomorphic adenoma

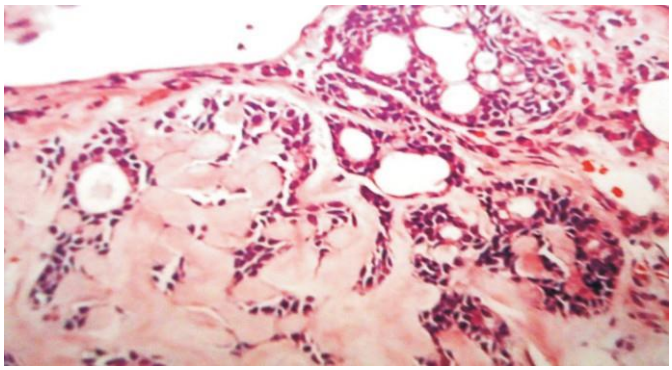

Figure 4: Adenoid cystic like areas in pleomorphic adenoma

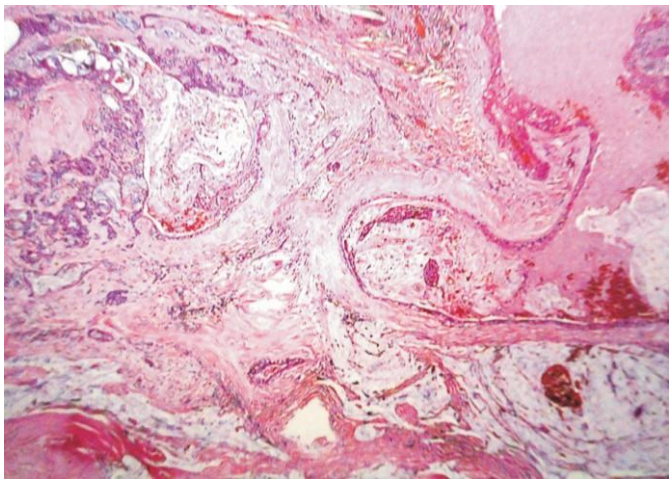

Figure 5: Mucinous areas in pleomorphic adenomamimicking mucoepidermoid carcinoma

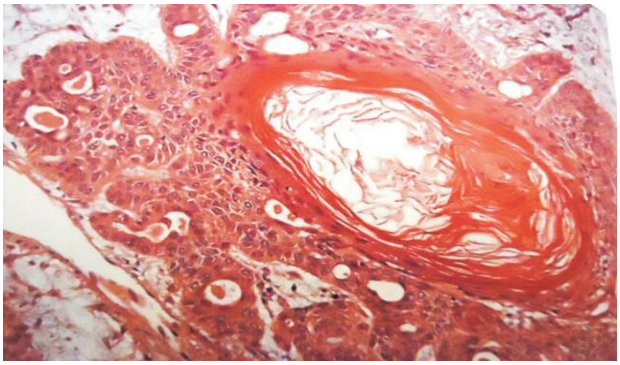

Figure 6: Squamous metaplasia in pleomorphic adenoma

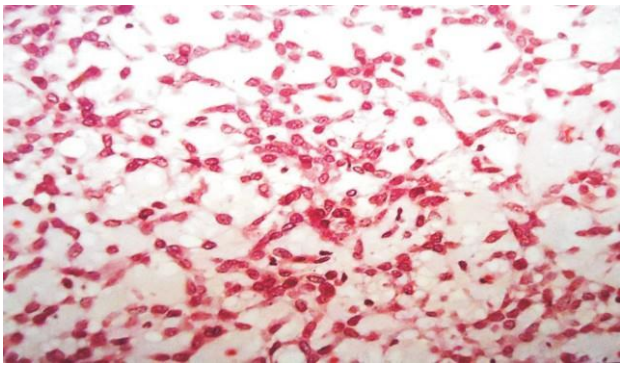

Figure 7: Myoepithelioma

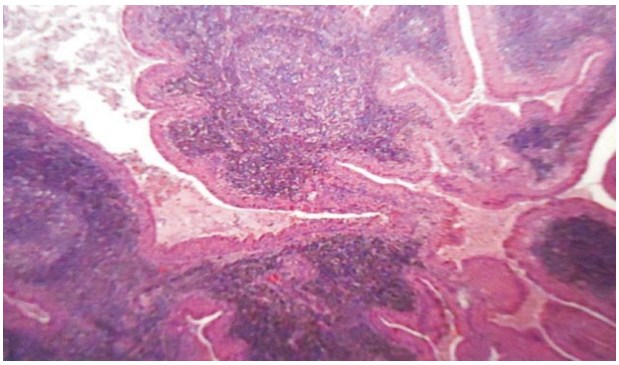

Figure 8: Warthin's tumor

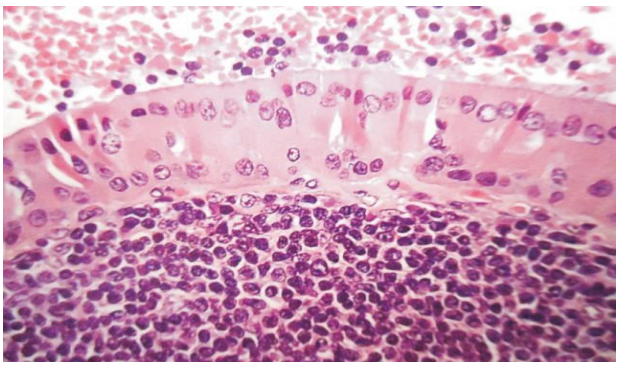

Figure 9: Warthin tumor

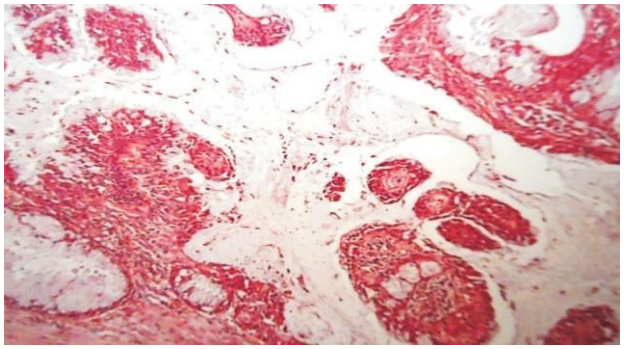

Figure 10: Mucoepidermoid carcinoma

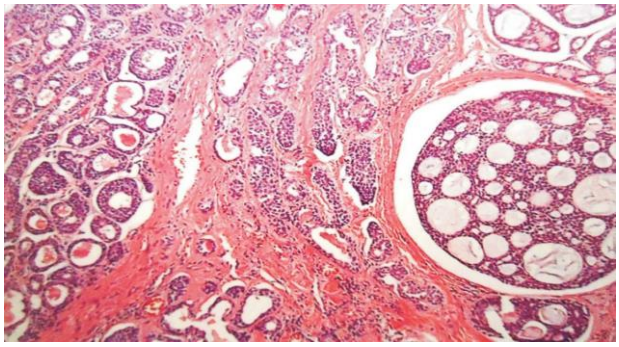

Figure 11: Adenoid cystic carcinoma

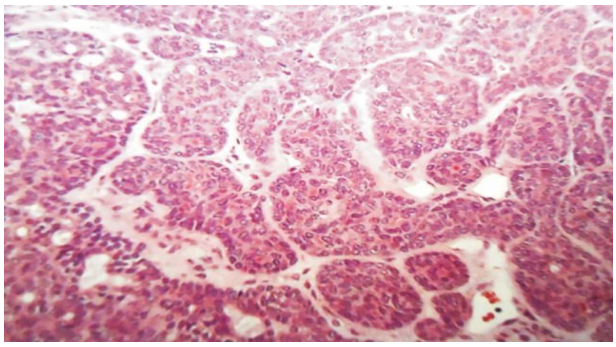

Figure 12: basal cell adenoma

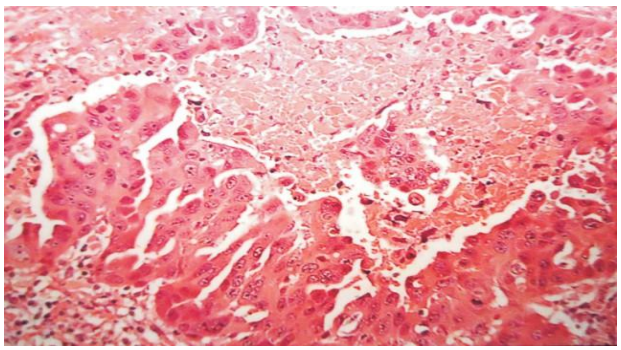

Figure 13: carcinoma ex pleomorphic adenoma

Discussion

In salivary gland lesions, an effective therapeutic approach requires the knowledge of whether a tumor is benign or malignant.

Previous literature provides evidence highlighting comparison between frozen section and FNAC. It is understandable that FNAC is useful in avoiding surgery (inflammatory lesions). For planning the extent of surgery of malignant salivary neoplasms, the histological subtype and/or grade should be determined; therefore a histological diagnosis by frozen section is required[23]. Moreover, reliance on FNA findings at the expense of clinical, radiologic and intraoperative findings is unwarranted. Regardless of whether FNA C is used routinely or selectively in patients with parotid masses, the findings should contribute to, and not replace the overall diagnostic impression.[24-27]

Previously it has been proved that frozen section is better than FNAC regarding the diagnosis of malignancy, tumor grading and tumor typing[28].

The results with frozen sections are very variable and case series are frequently too small or heterogeneous, not separating parotid tumors from other salivary gland tumors. When only malignant tumors are analyzed, the surgeon should decide the extent of the procedures, and the sampling problems are more evident. Results from other authors using frozen sections in malignant salivary gland tumors are similar to ours (tables 1 and 2).[1-3,8,13-20]

In our series there was a sensitivity of 61.5% and specificity of 98% for malignancy diagnosis. Diagnostic accuracy for frozen section is reported to be 92.3%. More specifically, exclusion of the deferred diagnosis further enhanced the accuracy to 96%.[29-32]

However, it is well recognized that frozen section analysis for malignant salivary gland tumours is more difficult and less accurate than for benign tumors, and analysis of benign and malignant tumors separately, revealed a notable difference.The accuracy of frozen section for identifying lesions as malignant was excellent (97%), but the accuracy for identifying lesions as benign was significantly lower (62.5%). In particular, the inaccuracy appears to lie with false positive diagnosis.[33-35]

In our series, no deferred was made. This is again similar to what is reported in very few articles in the literature. While every effort is made to keep the deferral rate low, it is sometimes not possible to obtain a definite diagnosis on frozen section. In such situations, we recognize that a deferred diagnosis is preferable to either a false positive or false negative diagnosis.

Hoffmann et al[7] reported doing frozen-section histopathological analysis to determine whether the tumor was malignant and, if it was a high-grade tumor, to identify whether the neoplasm was a lymphoma, and for analyzing suspicious lymph nodes. Eisele et al[36] considered that, if a definite diagnosis of malignancy could not be made by frozen section assessment, further surgery should be deferred until a final histopathological diagnosis was obtained.[37-39]

In our cases no major procedure was performed in false positive cases because in the surgeon's opinion the resection was adequate and there was no facial nerve invasion. It has previously been suggested that FNAB might be complementary to frozen sections. In this series the sensitivity for malignancy was 98%. and the specificity was 61.5%.

Studies concerning the accuracy rate of intraoperative frozen section diagnosis in headand neck surgery average 96 to 97%. In two recent reports, experience with intraoperativefrozen section diagnosis in head and neck surgeryfound a consistent discrepancy rate of 2%.

But there is evidence that substantiates the fact that final needle aspiration is a reliable method. Proof of the concept was provided after analysi of 173 benign tumors, 159 (91.9%) were diagnosed correctly and 110 of 144 (> 60%) were typed. Of 36 malignant tumors, malignancy was recognized in 22 cases (61.1%). There were nine false-negatives[40].

Frozen section thus is still, however, more accurate than FNAC and may add information that alters management and improves the outcome. But they should be interpreted cautiously, but clinical assessment and FNAC should be correlated also.

Conclusion

Frozen section should be performed for all the salivary gland tumors at the time of surgery for an unexpected frozen section result can and does influence the surgical management of the patient. Therefore, FS for salivary gland tumors on their own are insufficient for making radical decisions.

References

1. Rapoport A, Andrade Sobrinho J, Carvalho MB, Magrin J, Fava AS. Cancer of the parotid gland.IntSurg 1981;66:243-6.
2. Rapoport A, Carvalho MB, Fava AS. Diagnóstico e tratamento das neoplasias das glândulassalivaresmenores: estudo de 55 casos. Rev Col Bras Cir 1988;15:289-93
3. Carvalho MB, Rapoport A, Andrade Sobrinho J, et al. Estudoclínico e terapêutico do câncer de parótida. Rev Paul Med 1977;90:97
4. Rapoport A, Carvalho MB, Fava AS, Magrin J, Andrade Sobrinho J. Tumoresmistos da glândulaparótida: estudo de 100 casos. Rev Col

Bras Cir 1979;6:103-6.

5. Upton DC, McNamar JP, Connor NP, et al. Parotidectomy: ten-year review of 237 cases at a single institution. *Otolaryngol Head Neck Surg.* 2007;136:788-792.
6. Wheelis RF, Yarington CT. Tumors of the salivary glands. *Arch Otolaryngol.*1984;110:76–77
7. Hoffman H, Funk G, Endres D. Evaluation and surgical treatment of tumors of the salivary glands. In: Thawley SE, Panje WR, Batsakis JG, LIndberg RD, editors. Comprehensive management of head and neck tumors. Philadelphia: WB Saunders; 1999:1147-81.
8. Eisele DW, Kleinberg LR, O'Malley BB. Management of malignant salivary gland tumors. In: Harrison LB, Sessions RB, Hong WK, editors. Head and neck cancer: a multidisciplinary approach. Philadelphia: Lippincott-Raven; 1999:721-48
9. Freidman M, Rice DH,and Spiro RH. Difficult decisions in parotid surgery. Otolaryngol Clin North Am 1986; 19 (4): 637-645.
10. Jarayam N, Ashim D, Rajwanshi A, Radhika S and Banerjee CK.The value of fine needle aspiration cytology in the cyto diagnosis of salivary gland lesions.Diagn Cytopathol 1989; 5 (4): 349-354.
11. Mondal A, Das MM and Mukherjee PK. Fine needle aspiration cytology in the diagnosis of salivary gland tumors. Indian Med Assoc 1989; 87 (5): 108-110
12. Schmidt RL, Hall BJ, Wilson AR, et al. A systematic review and meta-analysis of the diagnostic accuracy of fine needle aspiration cytology for parotid gland lesions. *Am J Clin Pathol.* 2011;136:45-59.
13. Atula T, Gre´nman R, Laippala P, Klemi PJ. Fine-needle aspiration biopsy in the diagnosis of parotid gland lesions.*DiagnCytopathol.* 1996;15:185–190.
14. Layfield LJ, Tan P, Glasgow BJ.Fine-needle aspiration of salivary gland lesions.*Arch Pathol Lab Med.* 1987;111:346– 353
15. Conley J. controversies regarding therapy of tumors of the salivary gland. In: Thawley SE, Panje WR, eds. Comprehensive management of head and neck tumors. Philadelphia, Pa: WB Saunders; 1987: 1151
16. Klijanienko J, Vielh P. Fine-needle sampling of salivary gland lesions. IV. Review of 50 cases of mucoepidermoid carcinoma with histologic correlation. *DiagnCytopathol.* 1997;17:92–98.
17. Hillel AD, Fee WE. Evaluation of frozen section in parotid gland surgery. Arch Otolaryngol 1983; 109: 230-2.
18. Rigual NR, Milley P, Loré JM, Kaufman S. Accuracy of frozen section diagnosis in salivary gland neoplasms. Head Neck Surg 1986; 8: 442-6.
19. Lincolin LJ, Gopez E, Hirschowitz S. cost efficiency analysis for fine needle aspiration in the workup of parotid and submandibular gland nodules. Diagn Cytopathol 2006; 34 (11): 734-738
20. O'Donnell ME, Salem A and Badger SA. Fine needle aspiration at a regional head and neck clinic: a clinically beneficial and cost-effective service. Cytopathol 2008; 34 (9):194-198
21. Hughes JH, Volk EE and Wilber DC. Pitfalls in salivary gland fine needle aspiration cytology: lessons f rom the college of American pathologistsinterlaboratory comparison program in nongynecological cytology. Arch Path Lab Med 2005; 129 (1): 26-31
22. Cajulis RS, Gokaslan ST, Yu GH, Frias-Hidvegi D. Fine needle aspiration biopsy of the salivary glands. *ActaCytol.* 1997; 41: 1412–1420.
23. Salgeralli S, Alasio L, Tradati N, Bartoli C, Chiesa F, Pilotti S. Fine-needle aspiration of parotid masses. *Cancer.*1993; 72:2306–2311.
24. Dindzans LJ, VanNostrand AWP. The accuracy of frozen section diagnosis of parotid lesions.*J Otolaryngol.*1984;13: 382–386.
25. Hillel AD, Fee WE. Evaluation of frozen section in parotid gland surgery. *Arch Otolaryngol.*1983;109:230–232.
26. Miller RH, Calcaterra TC, Pagila DE. Accuracy of frozen section diagnosis of parotid lesions.*Ann Otolaryngol.* 1979; 88:573–576.
27. Winship T, Rosvoll RV. Frozen sections: an evaluation of 180 cases. Surgery 1959; 45:462-6.
28. Zabern P, Megerian CA, Maniglia AJ. Parotidectomy: a ten year experience with fine needle aspiration and frozen section biopsy correlation. *Ear Nose Throat J.* 1994;73:377–380.
29. Rigual NR, Milley P, Lore JM, Kaufman S. Accuracy of frozen section diagnosis in salivary gland neoplasms. *HeadNeck.* 1986;8:442–446.
30. Cohen MB, Ljung B-ME, Boles R. Salivary gland tumors. *Arch Otolaryngol Head Neck Surg.* 1986;112:867–869.
31. Granick MS, Erickson ER, Hanna DC. Accuracy of frozen section diagnosis in salivary gland lesions.*Head Neck Surg.* 1985;7:465–467.
32. Weinberger MS, Rosenberg WW, Meurer WT, Robbins KT. Fine-needle aspiration of parotid gland lesions. *Head Neck.* 1992;14:483–487.
33. Lurie M, Misselevitch I, Fradis M. Diagnostic value of fine needle aspiration from parotid gland lesions. *Isr Med AssocJ.* 2002;4:681–683.
34. Klijanienko J, El-Naggar AK, Vielh P. Fine-needle sampling findings in 26 carcinoma ex pleomorphic adenomas: diagnostic pitfalls and clinical

considerations. *DiagnCytopathol.* 1999;21:163–166.

35. Mukunyadzi P. Review of fine-needle aspiration cytology of salivary gland neoplasms, with emphasis on differential diagnosis. *Am J ClinPathol.*2002;118:100–115.
36. Eistele RJ, Ikemura K, Ohya R. The accuracy and usefulness of frozen section diagnosis.*Head Neck.* 1990;12:298–302.
37. Zapanta PE, Truelson JM. Salivary glands, fine needle aspiration. 2009.http://emedicine.medscape.com/article/8822 91-overview
38. Dhanalakshmi ML and Rao LK. Fine needle aspiration cytology and histopathology of salivary gland lesions: acorrelative study in a rural teaching hospital. J Chinese cLin Med 2009; 4(2): 537-541
39. Winship M, Smith Frable MA, Frable WJ. Fine-needleaspirationbiopsy of salivary glands.*Laryngoscope.*1991;101:245–249.
40. Zurrida S, Alasio L, Tradati N, Bartoli C, Chiesa F, Pilotti S. Fine-needle aspiration of parotid masses. *Cancer.*1993; 72:2306–2311.