Frozen Section as a Diagnostic Test for Major Salivary Gland Tumors

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Abstract- Major salivary gland tumors are uncommon and the exact nature of these tumors is not obvious. This study was carried out to compare the histological results of intraoperative frozen sections against those of permanent reports for major salivary glands masses. One hundred thirty-nine patients with major salivary gland masses who were candidates for surgery underwent an intraoperative frozen section biopsy. A permanent histological examination was then performed for definite diagnosis and its result was compared with that of the frozen section. Sensitivity, specificity, accuracy and the positive and negative predictive values were analyzed. The frozen section had 98.4% sensitivity, 87% specificity, 97.1% accuracy, 98.4% positive predictive value and 87% negative predictive value in differentiating between non-neoplastic and neoplastic lesions. In addition, the frozen section's identification of a mass as either benign or malignant showed 98% sensitivity, 100% specificity, 99.2% accuracy, 100% positive predictive value and 99% negative predictive value. Based on the current study's findings, it can be suggested that the frozen section is considerably accurate in the diagnosis of malignant versus benign lesions of major salivary glands, regardless of the exact histopathological type of the malignant tumors.

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Introduction

Salivary gland tumors are uncommon lesions and account for 2 to 6.5% of all neoplasms of the head and neck region (1).

Major salivary glands include the parotid, sublingual, and submandibular gland. Eighty percent of salivary gland tumors occur in the parotid gland and, among them, 80% are benign (2). Clinical assessment, along with fine needle aspiration (FNA), has a success rate of 65% in detecting malignancy (3,4).

These glands not only have lesions from their own glandular cells, but can also host lesions originating from other sources, such as the lymph nodes.

Difficulty in diagnosing the exact nature of salivary lesions is due to their histological complexity. Salivary lesions, especially carcinoma, have many histological subtypes arising from a variety of their stem cells.

Frozen section (FS) offers the best guarantee of optimum histological results due to having assessed tissue before the end of surgery. However, it should be noted that the results may differ from the permanent histological results.

The main aim of performing FS during surgery is to differentiate the malignant lesions from the benign and to perform a more aggressive surgery at one time. The limited number of accurate pre-operative methods for determining the nature of salivary gland lesions highlights the necessity and the critical role of FS in intra operative decision-making.

FS has the following four goals: firstly, to decrease overtreatment, secondly, to decrease the initial under treatment of malignant lesions and the need for second surgery, thirdly, to increase the chances of saving the facial nerve and, fourthly, to assess margins regardless of tumor involvement (5,6). The value of intraoperative FS varies in existing literature from 40 to 100% (7-9).

This study was carried out with the aim of assessing the diagnostic accuracy, sensitivity and specificity of the frozen section procedure in major salivary gland surgery.

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Patients and Methods

During the years 2008 to 2010, all patients (139 patients, 82 male and 57 female) enrolled in this study had been suffering from major salivary gland masses. They had been referred to the AmirAlam Otolaryngology tertiary referral Hospital and been considered for surgery based on clinical findings. The mean age was 39.9 ± 18.07, ranging from 18 months to 82 years old. All patients underwent a surgical procedure, during which an intraoperative FS was performed on all masses.

Some patients had undergone an FNA procedure before enrolling in the study. However, these results were reported by different pathologists and so were not considered in the study.

The histological diagnoses of all lesions were reviewed by an expert pathologist with 20 years of experience and these were classified according to the 2005 World Health Organization Classification System (10).

The permanent histological results were first reported by the staff pathologist and then by the above mentioned pathologist participating in the study. Both pathologists were blinded to the FS results. The study compared the FS against the permanent results, after which sensitivity, specificity, accuracy, and the positive and negative predictive values were calculated.

It should be mentioned that the fees for the frozen section procedure were provided by a university research grant and the patients were not charged for this.

Results

Neoplastic versus non neoplastic lesions

Among the 139 FS procedures, 15 were non-neoplastic and 124 neoplastic, of which 76 were benign and 48 malignant. Of the 124 neoplastic lesions, 122 were correctly diagnosed by FS indicating 98.4% sensitivity. Of the 15 non-neoplastic FS results, 13 were true negative and two were false positive, rendering 87% specificity and 97.1% accuracy (Table 1).

98% of lesions diagnosed by FS as neoplastic were truly neoplastic based on the histological evaluation on permanent sections.

Malignant versus non-malignant lesions

As FS correctly diagnosed malignancy in 33 out of 34 malignant lesions, the sensitivity of FS for identifying malignant versus benign lesions was 97% in this series while the specificity and accuracy were 100% and 99% respectively.

All lesions categorized as malignant by FS were confirmed as malignant in permanent histopathological examinations, thus resulting in a 100% positive predictive value (Table 2).

The accuracy of FS in identifying neoplastic lesions was 99%, in contrast to 96% for non neoplastic lesions. This could indicate that the accuracy of FS for identifying malignant lesions, regardless of the exact histopathological diagnosis, was higher than that when differentiating neoplasm from non-neoplasm.

The accuracy of FS for reporting the exact tumor typing was 90% in benign lesions as opposed to 59% in malignant lesions. In other words, FS more accurately recognizes the tumor type among benign lesions than malignant.

The accuracy of FS in the diagnosis of lymphoma was 83.3%. Only one out of six cases of lymphoma was incorrectly diagnosed and this was low grade lymphoma. In this case, a total parotidectomy was performed due to clinical uncertainty. This emphasizes the benefits of FS in preventing unnecessary surgery (Table 3).

Table 1. Neoplastic vs. non-neoplastic lesions.

		Permanent histological diagnosis		Total
		Neoplastic	Non-neoplastic	
Frozen	Neoplastic	122	2	124
Section diagnosis	Non-neoplastic	2	13	15
Total		124	15	139

Table 2. Malignant vs. non-malignant lesions.

		Permanent histological diagnosis		Total
		Malignant	Non-malignant	
Frozen	Malignant	47	0	47
Section diagnosis	Non-malignant	1	91	92
Total		48	91	139

Table 3. Most important histologic tumor type and FS findings and prevalence of final histological diagnosis.

Histological category		Histological diagnosis	No of cases	Percentage	FS diagnosis	
					Correct	*False*
Neoplastic	*Benign*	Pleomorphic adenoma	50	35.97	50	0
		Warthin tumors	8	5.75	7	1
		Basal cell adenoma	3	2.15	3	0
	Malignant	Lymphoma	6	4.31	5	1
		MEC (mucoepidermoid carcinoma)	9	6.47	7	2
		Squamous cell carcinoma	8	5.75	8	0
		Adenoid cystic carcinoma	3	2.15	3	0
Non-neoplastic		Reactive lymph node	3	2.15	2	1
		TB	2	1.43	1	1
		Granolomatosis cystitis	2	1.43	1	1

Discussion

Our results show that reactive lymphadenitis was the most common non-neoplastic lesion. Pleomorphic adenoma not only was the most common type of tumor among the benign lesions but it was also the most common lesion overall (35.97%).

The Malignancy rate was 34% in our study compared to the reported wide range of 21-46% (1). Mucoepidermoid carcinoma was the most frequent tumor while squamous cell carcinoma and lymphoma were second and third respectively. Consistently with Zbären *et al.* (2), FS has a relatively high accuracy in detecting lymphoma.

Frozen section in tumor typing

In this study, 70 of the 76 (92%) benign tumors were diagnosed accurately, while this figure was only 70% for malignant tumors (34 of 48). The accuracy of tumor typing reported by Iwai *et al.* was 97.2% for benign cases and 75.0% for malignant tumors (7). These results were similar to those of Iwai *et al.* for malignant lesions, although slightly lower by 5%. Based on a previous work by Zbären *et al.* it was assumed that FS could type benign lesions more exactly than malignant lesions (12). It has also been pointed out that differentiating a neoplasm from an inflammatory lesion (13) and a benign from a malignant tumor is possible by FS (13,14). As an example, the most common parotid neoplasm, pleomorphic adenoma, can correctly be diagnosed by FS (13) although the histological appearance of pleomorphic adenoma encompasses a wide range (11). Nevertheless, it should be kept in mind that the results of FS should be carefully evaluated and matched with clinical findings and the pathologist's report (14).

This study indicated that there may be no false negative results for benign versus malignant tumors. However, 1.7% (2 of 124) false negative results were reported for non-neoplastic versus neoplastic tumors. The false negative results found in literature are between 4% and 24% (12,15).

Distinguishing malignant from benign lesions by FS has 94.7% accuracy, 100% sensitivity, and 87.5% specificity according to Wong *et al.* report (5), whereas Carvalho *et al.* reported 61.5% sensitivity and 98% specificity (9). Other percentages have also been obtained in other studies for the sensitivity, specificity, and accuracy of FS by *Seethala et al* (6). The different results among studies may be explained by the familiarity of individual pathologists with FS. In tertiary referral centers where FS is a routine procedure, a higher rate of accuracy, sensitivity, and specificity is expected. This particular study enlisted an expert pathologist with 20 years of experience.

Based on these findings, FS of the parotid gland is highly reliable in differentiating between benign and malignant lesions and non-neoplastic from neoplastic lesions. In conclusion, the current study suggests that frozen section has a considerable accuracy in the diagnosis of malignant versus benign tumors regardless of the exact histopathological type of malignant tumor. Clinical and radiological findings are of great value in defining the location and extension of tumor and should be used in decision making. Although the evaluation of tumor margins is possible with the aid of FS, its accuracy of defining the histopathologic diagnosis is still in doubt.

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