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## Perioperative frozen section examination in parotid gland tumors

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### ABSTRACT

**CONTEXT:** The minimal recommended surgical approach to parotid tumors is partial parotidectomy with resection of the superficial lobe of the gland. Histologic diagnosis prior to surgery is not possible, as incisional biopsies are contraindicated due to the possibility of facial nerve injury or incomplete tumor resection. Thus, the biopsies tend to be perioperative.

**OBJECTIVE:** To compare the results of frozen section examination with the definitive pathological diagnosis.

**DESIGN:** Accuracy study by retrospective analysis.

**Setting:** Head and Neck Surgery Service of Heliópolis Hospital, São Paulo, Brazil.

**SAMPLE:** 153 cases of parotid gland tumors treated between 1977 and 1994.

**DIAGNOSTIC TEST:** Frozen section and pathological diagnosis.

**MAIN MEASUREMENTS:** Sensibility and specificity of the frozen section examination.

**RESULTS:** Frozen section study diagnosed 19 (12.4%) malignant and 127 (83.7%) benign tumors. Sensitivity of the frozen sections for malignancy was 61.5% (95% CI 54 to 69%) and specificity was 98% (95% CI 94 to 100%), and this result is comparable to the literature.

**CONCLUSIONS:** We consider that frozen section examination for salivary gland tumors 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 the surgeon's experience.

**KEY WORDS:** Frozen section. Head and Neck tumors. Parotid gland tumors. Salivary gland tumors

### INTRODUCTION

Perioperative frozen sections have been used by pathologists for more than a hundred years but this method only became widely applied with the development of the cryostat in 1950. Initially, it was found useful in breast tumor surgery but its use has been widened to the diagnosis of other lesions in other organs.

This diagnostic alternative is especially useful when data cannot be obtained on the histological patterns of diseases in organs that are only accessible by surgery, and when the type of treatment is based on pathologic findings. Diseases that arise as nodules in salivary glands or the thyroid are examples that can illustrate this situation.

As early as 1958, Pitts et al<sup>1</sup> highlighted the pathologist's difficulties in reaching the right diagnosis for salivary gland tumors and this difficulty was also mentioned by other authors like Nakasawa et al<sup>2</sup> in 1968 and Didzans & VanNostrand<sup>3</sup> in 1984.

The minimal recommended surgical approach to parotid tumors is partial parotidectomy with resection of the superficial lobe of the gland. Histologic diagnosis prior to surgery is not possible, as incisional biopsies are contraindicated due to the possibility of facial

nerve injury or incomplete tumor resection. Thus, the biopsies tend to be perioperative.<sup>4,5,6</sup>

Unlike salivary gland tumors of the oral cavity, in which a simple inspection of the lesion by an experienced examiner can strongly suggest the benign or malignant nature of the disease,<sup>7</sup> in early parotid tumors clinical evidence of malignancy usually cannot be found, and imaging methods and fine needle aspiration biopsy (FNAB)<sup>8,9</sup> have limitations in making this differentiation.<sup>8,9</sup> In this way, the decision on the extent of surgery must in many cases be made in the operating theater based on frozen section examination and on the surgical findings.

With the objective of evaluating the importance of frozen sections in surgical decisions, we retrospectively analyzed cases treated by parotidectomy in our service, comparing the frozen section diagnosis to clinical and surgical findings and operating decisions.

## METHODS

A retrospective analysis was made of 153 cases of parotid gland tumors treated at the Head and Neck Service of Heliópolis Hospital, São Paulo, Brazil, between 1977 and 1994. The ages ranged from 8 to 84 years and there were 70 men and 83 women. The results of frozen section examination were compared with the definitive pathologic diagnosis. Sensitivity and specificity of frozen section examination for malignancy were calculated as follows: Sensitivity =  $nm/(nm + nib)$  and Specificity =  $nb/(nb + nin)$ , where  $nm$  = number of cases identified correctly as malignant;  $nib$  = histologically malignant cases with inconclusive or benign result at frozen section;  $nb$  = number of cases identified correctly as benign; and  $nin$  = histologically benign cases with inconclusive or malignant result at frozen section.

## RESULTS

Frozen section examination identified 128 benign cases (83.7%), 19 (12.4%) malignant and in 6 (3.9%) was inconclusive. The definitive pathologic diagnosis showed 26 (17%)

malignant cases and 127 (83%) benign cases. Comparing the perioperative result with definitive diagnosis, 10% (16/153) were true positive, 81% (124/153) true negative, 2% (3/153) false positive, 7% (10/153) false negative, 17% (95% CI 11 to 23) prevalence, 84% (95% CI 78 to 90) positive predictive value, 93% (95% CI 88 to 97) negative predictive value, 26.05 positive likelihood ratio and 0.39 negative likelihood ratio. Thus, the sensitivity for malignancy was 61.5% (95% CI 54 to 69) and the specificity was 98% (95% CI 95 to 100) (Table 1).

In the seven cases of benign disease in which the frozen section results were inconclusive or 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). Among the ten cases of malignant disease in which the frozen section results were inconclusive or false negative, there was preoperative facial palsy in five of them, a previous pathological study or positive FNAB for malignancy in three cases, and tumor invasion of the facial nerve in five cases, thereby not allowing conservative dissection (Table 2).

## DISCUSSION

Saltzstein & Nahum<sup>11</sup> in 1973 emphasized that the only indication for frozen section examination was the need for decisions on immediate actions. This should therefore not be routinely used without knowing its real benefit. Agreeing with Winship & Rosvoll,<sup>12</sup> they believed that a close discussion between pathologist and surgeon is fundamental in obtaining highly reliable final results. Cross et al<sup>13</sup> stated that the role of frozen sections in diagnosis and treatment of salivary gland lesions was still not well established. Hillel & Fee<sup>14</sup> and Rigual et al<sup>15</sup> stressed that the surgeon's capability of assessing frozen section results is very important in avoiding iatrogenic problems. Granick et al<sup>16</sup> suggested that the best guide for decisions was the surgical findings.

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 3).<sup>1-3,8,13-20</sup>

In our series there was a sensitivity of 61.5% and specificity of 98% for malignancy diagnosis. The pathological diagnosis of the salivary gland tumor is difficult even for experienced pathologists. When the pathologist is not sure about the diagnosis he may be inclined to give an inconclusive or benign diagnosis because he is afraid of the consequences of a misdiagnosis for the patient. On the other hand, a wrong diagnosis of benign tumor usually leads to complementary procedures that can minimize the consequences of error. Thus, the rates of specificity for malignancy increase because the diagnosis of a malignant tumor is only established when the pathologist is sure about it. Hoffmann et al<sup>21</sup> 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<sup>22</sup> 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.

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. Among the 10 false negative or inconclusive cases, in 9 of them there were clinical findings that suggested malignancy or a positive FNAB for malignant cells or intraoperative malignant characteristics. Thus, the surgical procedure was suitable for the cases. Megerian & Maniglia<sup>23</sup> in 1994 suggested that FNAB might be complementary to frozen sections. This has been studied in our service for salivary gland tumors and merits future publication.

In this series the sensitivity for malignancy was 61.5% and the specificity was 98%. These results must be interpreted carefully by the surgeon in association with the clinical history and surgical findings. In this way, the possibility for errors will be decreased, especially if the surgeon discusses each case with the pathologist in the operating theater, so as to broaden the data on the case and improve the sensitivity of the diagnosis.

**Table 1 - Definitive and perioperative (frozen section) diagnosis**

Benign (histologically)	Frozen section	Malignant (histologically)	Frozen section
Pleomorphic adenoma	81(b=78, m=03)	Adenocarcinoma	6(b=01, m=04, i=01)
Warthin's tumor	17(b=16, i=01)	Squamous cell carcinoma	6(b=01, m=04, i=01)
Inflammatory reaction	8(b=08)	Mucoepidermoid carcinoma	4(b=01, m=03)
Lymphoreticular hyperplasia	6(b=05, i=01)	Adenoid cystic carcinoma	3(b=02, m=01)
Salivary gland cyst	5(b=05)	Undifferentiated carcinoma	3(b=02, m=01)
Monomorphic adenoma	3(b=03)	Lymphoma	1(m=01)
Acinic cell adenoma	2(b=02)	Malignant mixed tumor	1(m=01)
Lipoma	1(b=01)	Melanoma	1(m=01)
Basaloid adenoma	1(b=01)	Acinic cell carcinoma	1(b=01)
Gland hypertrophy	1(b=01)	Mixoid tissue	1(b=01)
Reactional lymphoid hyperplasia	1(b=01)		
<b>TOTAL</b>	<b>127</b>	<b>TOTAL</b>	<b>27</b>
<b>b=122 (94.5%); m=03 (2.3%); i=02 (3.2%)</b>		<b>b=09 (30.8%); m=17 (61.5%); i=02 (7.6%)</b>	

b- benign; m- malignant; i- inconclusive

## CONCLUSION

Frozen sections for parotid tumors are on their own insufficient for making radical decisions.

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**Table 3 - Results of frozen section examination for malignant tumors of salivary glands**

Author	N	Sensitivity (%)	Specificity (%)
Rigual et al <sup>15</sup>	23	90	96
Cross et al <sup>13</sup>	10	90	98
*Granick et al <sup>16</sup>	52	82	97
*Didzans & VanNostrand <sup>3</sup>	20	85	98
Pitts et al <sup>1</sup>	7	85	-
Nakazawa et al <sup>2</sup>	19	84.2	-
Wheelis & Yarrington <sup>17</sup>	52	88	98
Chann et al <sup>18</sup>	13	70	100
** Heller et al <sup>8</sup>	45	69	96
* Miller et al <sup>19</sup>	25	60	94
* Hillel & Fee <sup>14</sup>	14	43	95
Cohen et al <sup>20</sup>	3	0	92
Carvalho et al (present study)	26	61.5	98

\* - only parotid tumors; \*\* - including extraglandular tumors

**Table 2 - False negative or inconclusive cases of malignant neoplasms from frozen section examination**

Case	Clinical History	FSF	Surgery	Histological Diagnosis
1	Facial palsy and FNAB positive for malignancy	Inconclusive	Resection of the lesion with positive margins	Squamous cell carcinoma
2	Previous pathological diagnosis of squamous cell carcinoma	Benign	Partial parotidectomy with preservation of the facial nerve	Squamous cell carcinoma
3	Facial palsy plus previous pathologic diagnosis of squamous cell carcinoma	Inconclusive	Total parotidectomy	Adenocarcinoma
4	Facial palsy	Pleomorphic adenoma	Total parotidectomy with reconstruction of the facial nerve	Adenocarcinoma
6	Patient with no malignant signals	Benign	Partial parotidectomy and facial nerve reconstruction	Undifferentiated carcinoma
7	Fixed tumor with skin invasion	Benign	Total parotidectomy with positive margins	Undifferentiated carcinoma
8	Facial palsy	Benign	Total parotidectomy with sacrifice of facial nerve branches	Adenoid cystic carcinoma
9	Previous surgery and radiotherapy without pathologic diagnosis; recurrent facial tumor	Benign	Total parotidectomy with sacrifice of facial nerve	Adenoid cystic carcinoma
10	Parotid tumor with previous biopsy of acinic cell carcinoma	Benign	Total parotidectomy with sacrifice of facial nerve. Nerve and skin macroscopic invasion	Acinic cell carcinoma

FSF = Frozen Section Findings

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## RESUMO

**CONTEXTO:** O procedimento cirúrgico mínimo geralmente aceitável para a abordagem de tumores de parótida é a parotidectomia parcial com retirada do lobo superficial da glândula. Há uma impossibilidade de se ter o diagnóstico prévio histológico da lesão antes do procedimento cirúrgico, pois biópsias incisionais são contra-indicadas pela possibilidade de secção inadvertida de ramos do nervo facial e ressecção incompleta da lesão. Assim, a biópsia é comumente intracirúrgica.

**OBJETIVO:** Comparar os resultados do exame anatomopatológico intra-operatório por congelação com os resultados do diagnóstico definitivo através do exame de parafina. **TIPO DE ESTUDO:** Estudo exato pela análise retrospectiva. **LOCAL:** Serviço de cirurgia de Cabeça e Pescoço do Complexo Hospitalar Heliópolis, São Paulo, Brasil. **TESTE DIAGNÓSTICO:** Exame anatomopatológico intra-operatório por congelação e exame por parafina. **VARIÁVEIS ESTUDADAS:** Sensibilidade e especificidade do exame por congelação. **RESULTADOS:** Ao exame por congelação, em 19 casos (12,4%) o diagnóstico foi de neoplasia maligna e em 128 (83,7%) o diagnóstico foi de tumor benigno. A sensibilidade para malignidade foi de 61,5% e a especificidade foi de 98%. Esses resultados são equivalentes aos referidos na literatura. Os resultados falso-positivos ou negativos não interferiram na conduta adotada pois, para a decisão do tratamento, foi considerado o conjunto de dados clínicos, achado cirúrgico e anátomo patológico. **CONCLUSÕES:** O exame por congelação para os tumores da glândula salivar, empregado isoladamente não é suficiente para decidir a melhor conduta, e sua interpretação deve ser feita correlacionando os achados clínicos e intra-operatórios, associados à experiência do cirurgião.

**PALAVRAS-CHAVE:** Exame por congelação. Neoplasia de glândula salivar. Carcinoma de parótida.