

# Accuracy of intraoperative consultation in lesions of the salivary glands: analysis of 748 cases

## *Acurácia da consulta intraoperatória em lesões das glândulas salivares: análise de 748 casos*

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### ABSTRACT

**Introduction:** Lesions of the salivary glands are uncommon, representing 2% to 6.5% of all neoplasms of head and neck, and because of the difference in treatment between them, an accurate diagnosis is essential. The cytological study by fine-needle aspiration (FNA) biopsy is a highly accurate method used to diagnose lesions of the salivary glands. Intraoperative consultation (IOC), in its turn, is a test that provides diagnosis during surgery, aiming to differentiate malignant from benign lesions and to enable the most appropriate surgical approach. **Objective:** To evaluate the accuracy of IOC in salivary gland lesions. **Material and methods:** A survey was conducted in the database of Instituto Nacional de Câncer (Inca) into IOC for diagnosis of salivary gland lesions from January 2001 to December 2012, and found 748 cases. Diagnosis made at IOC (IOCD) was compared with the gold standard histopathological diagnosis and classified into: 1) consenting; 2) discordant; and 3) indeterminate. From these data, sensitivity, specificity and accuracy were calculated. **Results:** Among the 748 IOCs, results were concordant in 656 cases (88%), discordant in 56 (7%), and indeterminate in 36 (5%). Sensitivity was 78%, specificity 99% and accuracy 92%. **Conclusion:** Our results indicate that IOC in salivary gland lesions is highly accurate and can contribute to the surgical approach.

**Key words:** intraoperative consultation; salivary glands; accuracy; neoplasia; pathology.

### INTRODUCTION

Neoplasms of the salivary glands are uncommon and account for 2% to 6.5% of all neoplasms originated in head and neck; 80% of them arise in the parotid gland and 80% are benign<sup>(1, 2)</sup>. Histology of salivary gland neoplasms is extremely varied and complex, with several known types of adenomas, carcinomas, lymphomas, metastatic neoplasms, besides non-neoplastic lesions, what contributes to diagnostic difficulty<sup>(1, 2)</sup>. Due to the differences in treatment between non-neoplastic and neoplastic lesions, and between benign and malignant neoplasms, an accurate diagnosis is fundamental<sup>(3, 4)</sup>. The cytological study by fine-needle aspiration (FNA) is a highly accurate method used for the diagnosis of salivary gland lesions, but its sensitivity is high for benign lesions, and not as high for the malignant ones, especially in what refers to their classification<sup>(5-7)</sup>.

The intraoperative consultation (IOC) is an exam that reaches diagnosis during the surgery, aiming to differentiate

benign from malignant lesions and to enable the most suitable surgical conduct<sup>(8, 9)</sup>. The limited number of highly accurate preoperative methods to determine the nature of salivary gland lesions emphasizes the role of IOC in surgical decisions, and according to the consulted literature, the accuracy of IOC ranges from 40% to 100%<sup>(2, 5, 6, 8, 10-12)</sup>. IOC is aimed at: a) avoiding a more aggressive treatment; b) sparing a second surgical procedure; c) assessing surgical margins<sup>(8, 9)</sup>.

The objective of this study is to assess accuracy, sensitivity and specificity of IOC in salivary gland lesions at Instituto Nacional de Câncer (Inca).

### MATERIAL AND METHODS

This is a retrospective descriptive study of IOC in salivary gland lesions held at Inca from January 2001 to December 2012. After approval by Inca Ethics Committee (CAE: 14748113200005274), a

survey was carried out in the computerized system of the Division of Pathology (Dipat) on the IOC performed in salivary gland lesions; 748 cases were found.

They were defined as:

1. IOC diagnosis (IOCD): diagnosis made during IOC;
2. histopathological diagnosis (HPD): final histopathological diagnosis;
3. gold standard: standard exam used for comparison with the exam to be tested, aimed at assessing its exactness; in this study, HPD was the used gold standard;
4. positive concordant cases: positive HPD and IOCD (true positive [TP]);
5. negative concordant cases: negative HPD and IOCD (true negative [TN]);
6. positive discordant cases: positive HPD and negative IOCD (false negative [FN]);
7. negative discordant cases: negative HPD and positive IOCD (false positive [FP]);
8. indeterminate cases (IC): cases in which IOCD was not conclusive;
9. sensitivity: capacity of the exam to offer correct positive (TP) diagnoses;
10. specificity: capacity of the exam to offer correct negative (TN) diagnoses;
11. positive predictive value (PPV): probability of the positive cases to be actually positive;
12. negative predictive value (NPV): probability of the negative cases to be actually negative;
13. accuracy: ability of an exam to obtain results equal to those obtained by the gold standard.

The World Health Organization (WHO) histological classification is used in routine diagnoses of salivary gland tumors by Dipat/Inca<sup>(11)</sup>. The statistical analyses were described through absolute frequency and percentages for the qualitative and average variables (standard deviations), and through medians for the quantitative variables. Data were organized by means of univariate, bivariate, and contingency tables. For the proportional comparison between sexes, the ratio male: female was used. Sensitivity, specificity, PPV, NPV, and accuracy were used comparing the diagnostic methods, that is, IOCD with HPD (gold standard). The statistical decisions were taken at the significance level  $\alpha = 0.05$  (5%). In order to calculate sensitivity, specificity, PPV, NPV, and accuracy, a double-entry table was used for the results of IOCD and HPD tests, considering: A) positive concordant cases (TP); D) negative concordant cases (TN); B) positive discordant cases (FP);

C) negative discordant cases (FN); AC) total of HPD positive cases; BD) total of HPD negative cases; AB) total of IOC positive cases; CD) total of IOC negative cases; ABCD) total of cases. Based on these pieces of information, sensitivity  $[= A \div (A + C) \times 100]$ ; specificity  $[= D \div (B + D) \times 100]$ ; PPV  $[= A \div (A + B) \times 100]$ , NPV  $[= D \div (C + D) \times 100]$  and accuracy  $[= (A + D) \div (A + B + C + D) \times 100]$  of the IOCD were calculated.

A literature search was conducted in PubMed, Cochrane Database, Medline and SciELO. The key words used were: intraoperative consultation, accuracy intraoperative consultation, sensitivity intraoperative consultation and specificity intraoperative consultation, and salivary gland tumors.

## RESULTS

The 748 IOC were carried out in 659 patients: 356 females and 303 males. The mean age was 57.6 years; the minimum age was 6; and the maximum age, 89. Four hundred eighteen lesions were located in the parotid gland (63%), 133 in minor salivary glands (20%), and 108 in the submandibular gland (16%).

In the 748 performed IOC, diagnoses were concordant in 656 (88%) cases, discordant in 56 (7%), and indeterminate in 36 (5%). Among the 656 concordant cases, 487 were TN; and 169, TP. Among the 56 discordant cases, seven were FP, and 49 were FN. Among the seven FP cases, five had HPD of pleomorphic adenoma; and two, of adenoma (**Table 1**).

Among the 49 FN cases, HPD found 18 cases of adenoid cystic carcinoma, ten of mucoepidermoid carcinoma, eight of acinar cell carcinoma, four of adenocarcinoma not otherwise specified (NOS), three of myoepithelial carcinoma, two of basal cell carcinoma, two of carcinoma ex pleomorphic adenoma, one of Polymorphous low-grade adenocarcinoma, and one of non-Hodgkin lymphoma (**Table 2**). Among the 36 cases of indeterminate IOCD, ten had HPD of benign lesion; and 26, of malignant lesion (**Table 3**).

**TABLE 1** – IOC in of salivary gland lesions at Inca, from January 2001 to December 2012. FP cases ( $n = 7$ )

| HPD                 | <i>n</i> | IOCD                      | <i>n</i> |
|---------------------|----------|---------------------------|----------|
| Pleomorphic adenoma | 5        | Adenocarcinoma            | 2        |
|                     |          | Mucoepidermoid carcinoma  | 1        |
|                     |          | Acinar cell carcinoma     | 1        |
|                     |          | Metastatic adenocarcinoma | 1        |
| Adenoma             | 1        | Mucoepidermoid carcinoma  | 1        |
|                     |          | Adenoid cystic carcinoma  | 1        |

IOC: intraoperative consultation; Inca: Instituto Nacional de Câncer; FP: false positive; HPD: histopathologic diagnosis; IOCD: diagnosis made at intraoperative consultation.

**TABLE 2 – IOC in salivary gland lesions at Inca, from January 2001 to December 2012. FN cases (n = 49)**

| HPD                                   | n  | IOCD                  | n  |
|---------------------------------------|----|-----------------------|----|
| Adenoid cystic carcinoma              | 18 | Absence of malignancy | 12 |
|                                       |    | Pleomorphic adenoma   | 6  |
| Mucoepidermoid carcinoma              | 10 | Absence of malignancy | 5  |
|                                       |    | Pleomorphic adenoma   | 3  |
|                                       |    | Warthin tumor         | 2  |
|                                       |    | Absence of malignancy | 4  |
| Acinar cell carcinoma                 | 8  | Adenoma               | 2  |
|                                       |    | Pleomorphic adenoma   | 1  |
|                                       |    | Oncocytoma            | 1  |
| Adenocarcinoma NOS                    | 4  | Pleomorphic adenoma   | 3  |
|                                       |    | Oncocytic adenoma     | 1  |
| Myoepithelial carcinoma               | 3  | Pleomorphic adenoma   | 3  |
| Basal cell carcinoma                  | 2  | Adenoma               | 1  |
|                                       |    | Pleomorphic adenoma   | 1  |
| Carcinoma ex pleomorphic adenoma      | 2  | Pleomorphic adenoma   | 2  |
| Polymorphous low-grade adenocarcinoma | 1  | Adenoma               | 1  |
| Non-Hodgkin lymphoma                  | 1  | Absence of malignancy | 1  |

IOC: intraoperative consultation; Inca: Instituto Nacional de Câncer; FN: false negative; HPD: histopathologic diagnosis; IOCD: diagnosis made at intraoperative consultation; NOS: not otherwise specified.

**TABLE 3 – IOC in salivary gland lesions at Inca, from January 2001 to December 2012. Indeterminate cases (n = 36)**

| HPD                                   | n         |
|---------------------------------------|-----------|
| <b>Benign lesions</b>                 | <b>10</b> |
| Pleomorphic adenoma                   | 4         |
| Absence of neoplasia                  | 4         |
| Basal cell adenoma                    | 2         |
| <b>Malignant lesions</b>              | <b>26</b> |
| Adenocarcinoma NOS                    | 6         |
| Mucoepidermoid carcinoma              | 5         |
| Acinar cell carcinoma                 | 4         |
| Polymorphous low-grade adenocarcinoma | 3         |
| Epithelial-myoepithelial carcinoma    | 3         |
| Adenoid cystic carcinoma              | 2         |
| Salivary duct carcinoma               | 1         |
| Carcinoma ex pleomorphic adenoma      | 1         |
| Lymphoma                              | 1         |

IOC: intraoperative consultation; Inca: Instituto Nacional de Câncer; HPD: histopathologic diagnosis; NOS: not otherwise specified.

Based on the number of TP, TN, FP and FN, sensitivity was 78%; specificity, 99%; PPV, 96%; NPV, 91%; and accuracy, 92% (Table 4).

Among the 748 IOC performed in salivary gland lesions, HPDs were benign in 504 (67%) and malignant in 244 (33%). HPDs are listed in Table 5.

**TABLE 4 – Distribution of benign and malignant diagnoses made at IOC and by histopathological examination**

| IOC      | HPD         |             |                     |
|----------|-------------|-------------|---------------------|
|          | Positive    | Negative    | Total               |
|          | Positive    | A = 169     | B = 7               |
| Negative | C = 49      | D = 487     | C + D = 536         |
| Total    | A + C = 218 | B + D = 494 | A + B + C + D = 712 |

IOC: intraoperative consultation; HPD: histopathologic diagnosis; IOCD: diagnosis made at intraoperative consultation.

**TABLE 5 – IOC in salivary gland lesions at Inca, from January 2001 to February 2012. Lesions were separated into benign and malignant, and according to histological classification (n = 748)**

| HPD                                   | Total (%)       |
|---------------------------------------|-----------------|
| <b>Benign lesions</b>                 | <b>504 (67)</b> |
| Pleomorphic adenoma                   | 285 (38)        |
| Absence of neoplasia                  | 120 (16)        |
| Warthin tumor                         | 80 (11)         |
| Basal cell adenoma                    | 14 (2.7)        |
| Canalicular adenoma                   | 2 (0.26)        |
| Myoepithelioma                        | 2 (0.26)        |
| Cystadenoma                           | 1 (0.13)        |
| <b>Malignant lesions</b>              | <b>244 (33)</b> |
| Adenoid cystic carcinoma              | 101 (13.5)      |
| Mucoepidermoid carcinoma              | 58 (7.7)        |
| Adenocarcinoma NOS                    | 22 (3)          |
| Acinar cell carcinoma                 | 19 (2.5)        |
| Polymorphous low-grade adenocarcinoma | 14 (1.8)        |
| Epithelial-myoepithelial carcinoma    | 6 (0.8)         |
| Myoepithelial carcinoma               | 5 (0.6)         |
| Carcinoma ex pleomorphic adenoma      | 5 (0.6)         |
| Salivary duct carcinoma               | 4 (0.5)         |
| Malignant hematopoietic neoplasm      | 4 (0.5)         |
| Basal cell carcinoma                  | 3 (0.4)         |
| Metastatic carcinoma                  | 1 (0.1)         |
| Mixed carcinoma                       | 1 (0.1)         |
| Oncocytic carcinoma                   | 1 (0.1)         |

IOC: intraoperative consultation; Inca: Instituto Nacional de Câncer; HPD: histopathologic diagnosis; NOS: not otherwise specified.

## DISCUSSION

Surgical resection is the main treatment in most salivary gland lesions, and the extension of the procedure differs according to HPD. Surgeries are extensive in malignant neoplasms, and conservative in benign lesions<sup>(1, 13, 14)</sup>. It is essential for the pathologist to know the type of treatment that will be administered based on IOCD, being of utmost importance that differentiation be made between benign and malignant neoplasms, since FN and FP IOCD may lead to inadequate surgical treatments<sup>(1, 3, 8, 13, 14)</sup>.

There is a lot of debate over the value of IOC, principally due to the high accuracy of the cytological diagnosis by material obtained through FNA. However, many authors realize its worth<sup>(1, 3, 6, 14, 17)</sup>.

In this work, among the 56 discordant diagnoses, seven were FP. FP diagnoses may lead to more aggressive and unnecessary surgeries. FP rates in the consulted literature ranged from 0% to 12%<sup>(1, 3, 4, 6, 14, 17)</sup>. In our study, FP diagnoses represented 1% of all cases (five had HPD of pleomorphic adenoma, and two of basal cell adenoma). The pleomorphic adenoma is characterized by the proliferation of epithelial and myoepithelial cells in variable amounts, and it may be difficult to differentiate the most cellular tumors from mucoepidermoid carcinoma, adenoid cystic carcinoma, and carcinoma ex pleomorphic adenoma<sup>(1, 6, 9, 15)</sup>.

Among our 56 discordant diagnoses, 49 were FN. This diagnosis may cause harm to patients and lead to an inadequate treatment, with the need of a second surgical intervention or complementary radiotherapy. FN rates in the studied literature ranged from 0% to 3.4%<sup>(1, 2, 11, 14-16)</sup>, while the rate found in the present study was 6%, therefore much higher than those reported. Among the 49 FN cases, 19 had IOCD of pleomorphic adenoma (39%) and six of monomorphic adenoma (12.2%). This result highlights the difficulty of interpreting very cellular epithelial lesions at IOC.

IOCD is classified as indeterminate when a diagnostic conclusion is not possible. In the studied literature, variation was from 0% to 63%, while in the present work, the rate was 5%<sup>(1, 2, 11, 14-16)</sup>. Among our cases of indeterminate IOCD, 26 (72%) had HPD of malignant neoplasia;

and 10 (28%), of benign neoplasia. The analysis of indeterminate IOCD cases is important for diagnosis improvement.

In the consulted studies, IOC sensitivity ranged from 62% to 100%; specificity, from 90% to 100%; and accuracy, from 88% to 100%. Our results were 78% for sensitivity, 99% for specificity, and 92% for accuracy, being compatible with the literature<sup>(1, 2, 14, 15, 18)</sup>.

In our study, among the 748 performed IOCs, HPD was negative in 67% and positive in 33% of the cases, similar data to some works in the literature<sup>(1, 2, 12, 18)</sup>. Among our cases, the most common HDP was that of pleomorphic adenoma, corresponding to 37.93%, a similar frequency to those obtained in other publications<sup>(2, 6)</sup>. Pleomorphic adenoma is the most common of the salivary gland tumors, followed by Warthin tumor<sup>(1, 13)</sup>. The importance of adenoma, as well as other benign lesions, being diagnosed during IOC is that the surgical conduct is limited to superficial lobectomy, when in the parotid; or to complete excision, when it involves major or minor salivary glands<sup>(1, 3, 13, 16)</sup>.

## CONCLUSION

Our results indicate that IOC in lesions of the salivary glands has high accuracy, and it may also contribute to the surgical conduct.

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## RESUMO

**Introdução:** As lesões das glândulas salivares são incomuns, representando de 2% a 6,5% de todas as neoplasias da região da cabeça e do pescoço. Devido à diferença de tratamento entre elas, é fundamental um diagnóstico preciso. O estudo citológico por meio de punção aspirativa por agulha fina (PAAF) é um método com alta acurácia utilizado para o diagnóstico das lesões das glândulas salivares; já a consulta intraoperatória (CIO) é um exame que oferece o diagnóstico no decorrer da cirurgia, tendo como objetivo diferenciar as lesões malignas das benignas e possibilitar a conduta cirúrgica mais adequada. **Objetivo:** Avaliar a acurácia da CIO nas lesões das glândulas salivares realizadas em uma instituição. **Material e métodos:** Realizou-se uma pesquisa sobre as CIOs realizadas para diagnóstico nas lesões das glândulas salivares no Instituto Nacional de Câncer (Inca) no período de janeiro de 2001 a dezembro de 2012, sendo encontrados 748 casos. Os diagnósticos de CIO foram comparados com o diagnóstico histopatológico (DHP), considerado padrão-ouro, e classificados em: 1) concordantes, 2) discordantes e 3) indeterminados. A partir desses dados, foram calculadas sensibilidade, especificidade e acurácia. **Resultados:** Das 748 CIOs realizadas, os resultados foram concordantes em 656 casos (88%), discordantes em 56 (7%) e indeterminados em 36 (5%). A sensibilidade foi de 78%; a especificidade, de 99%; e a acurácia, de 92%. **Conclusão:** Nossos resultados indicam que a CIO em lesões das glândulas salivares tem alta acurácia, podendo contribuir para a conduta cirúrgica.

**Unitermos:** consulta intraoperatória; glândulas salivares; acurácia; neoplasia; patologia.

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