

Original Article

Diagnostic performance of fine-needle aspiration in salivary gland tumours

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ABSTRACT

INTRODUCTION. The aim of this study was to evaluate the diagnostic performance of fine-needle aspiration (FNA) cytology and further evaluate the risk of malignancy (ROM) in patients with salivary gland neoplasms in a five-year period in Region Zealand, Denmark.

METHODS. Retrospectively, we identified all patients with an FNA from a salivary gland neoplasm who underwent surgery from 1 January 2020 through 31 December 2024. Descriptive statistics were performed, and sensitivity, specificity, positive and negative predictive values and ROM were estimated.

RESULTS. We identified 435 patients who had a preoperative FNA and underwent surgical excision within the study period. The cohort had a small female preponderance, a mean age of 59.2 years and involvement of the parotid gland in 84.6% of cases. An assessment of the diagnostic efficacy of the FNA between benign and malignant cases reported a sensitivity of 50.0%, a specificity of 97.9%, a positive predictive value of 78.4%, a negative predictive value of 92.7% and an accuracy of 92.0%. The risk of malignancy was low in benign FNAs (0-0.6%) and high in FNAs with malignancy or suspicion hereof (75.0-100%).

CONCLUSIONS. With an accuracy of 91.5% in distinguishing benign from malignant neoplasms, FNA plays a crucial role in both diagnosis and patient counselling. The inherent uncertainty must be considered when recommending and planning surgical interventions or follow-up, especially in unresolved cases.

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In Denmark, the annual incidence of benign salivary gland neoplasms is reported to be approximately 380 [1], whereas the mean annual incidence of salivary gland cancers was 84 cases from 2018 to 2022 [2]. This corresponds to approximately 5% of cancers in the head and neck region [3]. Since its development at the Memorial Sloan-Kettering Cancer Center in the 1930s, fine-needle aspiration (FNA) cytology has been the predominant diagnostic method internationally in evaluating tumours in the salivary glands [4]. Accurate cytological diagnosis of salivary gland neoplasms can, however, be difficult. This diagnostic uncertainty is clinically consequential because cytological findings often inform both whether surgery is indicated and, if so, the extent of the procedure. The histopathology of salivary gland tumours is varied and complex, with a diverse morphology resulting in a great number of tumour types recognised by the World Health Organization [5]. Thus, it is acknowledged that FNA from a salivary gland tumour is a diagnostic method that demands a high level of expertise to be of diagnostic and clinical value [4-8].

In 2018, the Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) was introduced [9]. The MSRSGC is a standardised classification system for reporting the results of FNAs of salivary gland neoplasms, aimed at streamlining the communication between pathologists and clinicians. Although many pathology departments around the world have adopted the MSRSGC, it is not used as a national standard in Denmark, where well-established diagnostic categories remain in routine use. These categories are applied as overall cytological categories in the present study.

The aim of this study is to evaluate the diagnostic performance of salivary gland FNA cytology in differentiating benign from malignant lesions and to estimate the corresponding risk of malignancy (ROM) for each cytological category. We conducted a five-year retrospective study of all salivary gland FNAs with surgical excision performed at the Department of Otorhinolaryngology, Head and Neck Surgery, Zealand University Hospital, Køge, Denmark, which serves a catchment population of approximately 850,000 inhabitants.

Methods

This was a five-year retrospective study including all patients undergoing surgical excision of salivary gland tumours with a preoperative FNA at the Department of Otorhinolaryngology, Head and Neck Surgery at Zealand University Hospital, Køge, Denmark.

Using the Systematised Nomenclature of Medicine (SNOMED) codes in the Danish Pathology Data, we identified 904 patients with an FNA from a salivary gland during the period from 1 January 2020 to 31 December 2024. Among these, 435 patients subsequently underwent surgery within the study period and were included in the analysis. The patients were identified by their unique personal identification number (the CPR number).

Information on the following variables was collected retrospectively and entered anonymised into a REDCap database: gender, age, affected salivary gland, FNA date and cytological diagnosis, repeat FNAs (date and cytological diagnosis) and surgical histopathological diagnosis. An FNA was defined as the result of a single procedural session, including one or more needle passes and aspirations.

Histological diagnosis was considered the gold standard; pathologists stating the histological diagnosis were not blinded to the cytological diagnosis or clinical assessments, and the diagnoses were not re-evaluated.

Diagnostic performance was quantified by sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and overall accuracy for malignant changes. Cases were classified as: true positive (malignant cytology and histology), false negative (benign cytology and malignant histology), false positive (malignant cytology and benign histology) and true negative (benign cytology and histology). We a priori classified 'tumour cells', 'atypical cells' and 'non-diagnostic' as non-malignant cytology and, accordingly, as part of the negative index in calculations to avoid upward bias in sensitivity and to reflect real-world clinical decision-making.

ROM was defined as the proportion of cases with malignant histology within each final cytological category. ROM was reported both including and excluding lymphomas.

Data were analysed in R Statistical Software. Descriptive statistics were produced. Diagnostic performance metrics and ROM were calculated as defined above.

Trial registration: not relevant.

Results

We identified 435 patients who had a preoperative FNA and underwent surgical excision within the study period. Most tumours were in the parotid gland, with pleomorphic adenoma (PA) being the predominant histological diagnosis (44.8%). The mean age was 59.2 years, with a small preponderance of females (53.8%). The descriptive data are presented in **Table 1**.

TABLE 1 Descriptive characteristics of the cohort ($N_{\text{tot}} = 435$).

	Parotid gland ($N_p = 368$ (84.6%))	Submandibular gland ($N_s = 57$ (13.1%))	The sublingual gland & minor salivary gland ($N_{sm} = 10$ (2.3%))	Total
<i>Sex, n (% of total)</i>				
Male				201 (46.2)
Female				234 (53.8)
<i>Age, mean $\pm$ SD, yrs</i>				
				59.2 $\pm$ 15.8
<i>Histology diagnosis, n (% of group)</i>				
Warthin tumour	95 (25.8)	0	0	95
Pleomorphic adenoma	165 (44.8)	24 (42.1)	3 (30.0)	192
Other benign neoplasm	36 (9.8)	0	1 (10.0)	37
Malignant ^a	49 (13.3)	7 (12.3)	2 (20.0)	58
Other ^b	23 (6.3)	26 (45.6)	4 (40.0)	53

a) Also includes lymphomas; in the 3 groups, there were 6, 1, and 0 lymphomas, respectively.

b) Histological cases not fitting in the other categories; it mainly includes inflammatory conditions and other non-neoplastic changes.

In the 435 patients, a total of 663 FNAs were performed. Due to non-diagnostic initial results, a second and a third FNA were performed in 39.1% and 13.3% of cases, respectively (**Table 2**). Despite repeated FNAs, 5.5% of cases had persistently non-diagnostic cytology.

TABLE 2 Preoperative fine-needle aspirations.

Overall cytological category	SNOMED code	FNA sessions performed, n (%)			Unique patients ^a , n (%)
		1st FNA	2nd FNA	3rd FNA	
Benign tumour	Warthin tumour	54 (12.4)	21 (12.4)	4 (6.9)	70 (16.1)
	Warthin tumour, obs pro	12 (2.8)	6 (3.5)	2 (3.4)	13 (3.0)
	Pleomorphic adenoma	134 (30.8)	25 (14.7)	6 (10.3)	152 (34.9)
	Pleomorphic adenoma, obs pro	6 (1.4)	2 (1.2)	2 (3.4)	8 (1.8)
	Other benign tumour	4 (0.9)	1 (0.6)	-	4 (0.9)
	Other benign tumour, obs pro	1 (0.2)	-	-	-
Atypia	Atypical cells	8 (1.8)	2 (1.2)	1 (1.7)	10 (2.3)
Tumour, uncertain if malignant or benign	Tumour cells	46 (10.6)	24 (14.1)	7 (12.1)	68 (15.6)
	Tumour cells, obs pro	8 (1.8)	6 (3.5)	-	9 (2.1)
Suspicious for malignancy	Suspicious for malignancy	10 (2.3)	6 (3.5)	8 (13.8)	20 (4.6)
Malignancy	Malignancy	16 (3.7)	6 (3.5)	1 (1.7)	18 (4.1)
Non-neoplastic	Other	43 (9.9)	22 (12.9)	10 (17.2)	34 (7.8)
	Other, obs pro	7 (1.6)	3 (1.8)	1 (1.7)	5 (1.1)
Non-diagnostic	Non-diagnostic and other non-diagnostic	86 (19.8)	46 (27.0)	16 (27.6)	24 (5.5)
Total		435 (100)	170 (39.1)	58 (13.3)	-

FNA = fine-needle aspiration; SNOMED = Systematized Nomenclature of Medicine.

a) The number of unique patients shows how many patients ended up with the SNOMED code.

With 29 true positive cases, 369 true negatives, 29 false negatives and eight false positive cases, we observed a sensitivity of 50.0%, a specificity of 97.9%, a PPV of 78.4%, an NPV of 92.7% and an overall diagnostic accuracy of 91.5% in differentiating benign from malignant tumours (Table 3).

TABLE 3 Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for prediction of malignancy, with literature comparison.

	Present study (N = 435)	Lee et al. [10] (N = 421)	Chrabańska et al. [7] (N = 101)	Fakhry et al. [11] (N = 249)	Singh et al. [12] (N = 56)	Tochtermann et al. [13] (N = 753)	Postema et al. [14] (-)	Lui et al. [15] (N = 5,647)
Sensitivity, %	50.0	76.5	75	80	76.9	94.6	88	78.0
Specificity, %	97.9	99.1	100	89.5	97.1	99.3	99	98.0
PPV, %	78.4	92.9	100	-	-	97.9	95	-
NPV, %	92.7	96.6	96	-	-	98.2	97	-

ROM estimates across cytological categories are presented in Table 4. For some cytological categories, the ROM estimates are derived from a relatively small number of cases; accordingly, these proportions should be interpreted with caution due to limited statistical precision. Furthermore, the estimates include only patients with surgery within the study period. FNAs in the categories “Warthin tumour”, “pleomorphic adenoma” and “other benign” demonstrated low ROMs, whereas the categories “suspicious of malignancy” or “malignancy” had the highest ROMs. The ROM for FNAs with the diagnosis “tumour cells” was 19.1%, and that of “atypical cells” was 70.0%. When excluding lymphomas, the ROM for “atypical cells” decreased to 10.0%. For persistently non-diagnostic cases, the ROM was 12.0%.

TABLE 4 Risk of malignancy (ROM) for each cytological category.

Diagnosis	ROM, %
Warthin tumour	0.0
Warthin tumour, obs pro	0.0
Pleomorphic adenoma	0.6
Pleomorphic adenoma, obs pro	12.5
Other benign tumour	0.0
Atypical cells	10.0 (70.0) ^a
Tumour cells	19.1
Tumour cells, obs pro	11.1
Suspicious for malignancy	65.0 (75.0) ^a
Malignancy excluding lymphomas	88.9
Other	6.9 (10.3) ^a
Other, obs pro	0.0
Non-diagnostic and other non-diagnostic	12.0

a) The ROM in the parenthesis includes lymphomas.

Among 58 malignant cases, two had benign cytology, and 21 were categorised as “tumour cells” or “atypical cells”, including seven lymphomas. Three non-diagnostic FNAs had malignant histology at surgery.

Discussion

Tumours in the salivary glands need evaluation and thorough examination, where FNA is the first-line diagnostic procedure. FNA-based diagnoses are interpreted alongside the clinical presentation, imaging findings and comorbidities to guide indications for surgery, consistent with national guidelines [16]. FNA is a simple and minimally invasive procedure allowing preoperative evaluation of salivary gland lesions in an outpatient setting.

In accordance with previous literature, we report that the majority of tumours in our sample occurred in the parotid gland and were benign, with a relatively low incidence of malignancy, at 13.3% [7, 12, 13, 17, 18].

Our primary aim was to evaluate the diagnostic performance of FNAs in distinguishing benign from malignant lesions in the salivary glands before surgery. Diagnostic performance varies with multiple factors: FNA technique, needle gauges, number of passes and utilisation of ultrasound [15]. The sensitivity and specificity of salivary gland FNA cytology further depend on the operator’s skills, the quality of the specimen, the pathologist’s experience and the presence or absence of cystic components [6]. In our clinical setting, FNAs are performed by both junior residents and consultants, each with individual preferences regarding technique, including the use

of ultrasound and number of passes. Furthermore, it should be considered which supplementary diagnostic tests are available. In Denmark, most diagnoses are based solely on smear morphology.

Our benign diagnostic concordance compares favourably to the literature. Collela et al. reported that a benign cytological diagnosis was concordant with histological diagnosis in 95.6% of all cases [4]. Chraba&ska et al. reported a sensitivity of benign neoplasms of 86% [7], and Tochtermann et al. found correct cytological classification of PA and Warthin tumours in 74.5% and 80.9% of cases, respectively [13]. We observed high concordance for Warthin tumour and PA (92.9% and 96.3%, respectively) and an NPV of 92.7%, indicating strong performance within international ranges.

Several studies reported variability in the reported sensitivity and specificity across studies [7, 10-15]. However, these estimates are closely related to differences in the diagnostic setup. We observed high specificity (97.9%) with an overall accuracy of 91.5% for binary discrimination, but with a limited sensitivity (50.0%). Wang et al. calculated sensitivity and specificity based on various definitions of positive and negative outcomes using the MSRSGC categories and thereby showed that these measures rely highly on how the indices are defined [19]. In our study, “suspicious of malignancy” and “malignancy” were considered the positive index, whereas the cytological diagnoses “tumour cells”, “atypical cells” and “non-diagnostic” were considered a part of the negative index. These correspond to the Milan categories IVB, III and I, respectively. The inclusion of these cytological diagnoses in the negative index resulted in 24 malignant cases being classified as false negatives, which substantially reduced diagnostic performance. In addition, we observed that most re-FNAs were done on the basis of non-diagnostic samples. Some re-FNAs showed the same result as a previous one and were most likely control tests. This is the case for both malignant and benign cases. Heterogeneity in these analytical choices likely contributes to inter-study differences in sensitivity, PPV and NPV. The definition of positive or negative indexes varies among the studies, and information on whether the categories “tumour cells” and “atypical cells” are defined as positive or negative is often lacking, leading to a variation in results [7, 10-15]. Although in this study, most lymphomas were included in the “atypical cells” category, we retained this classification to mirror how such borderline findings are managed in routine practice.

Therefore, we consider ROM a valuable complementary metric for cross-study comparison and for clinical decision-making within specific cytological categories. Our estimates are based only on patients with both cytology and surgery, resulting in ROMs of 0.0-0.6% in the benign cytological categories and ROMs of 75.0-100% in the malignant category or in cases of suspicion thereof. In concordance with our findings, the Milan System reported the ROM of “benign neoplasm” (Category IVA) to be under < 3%, whereas “suspicious for malignancy” (Category V) and “malignant” (Category VI) were reported to be 83% and > 98%, respectively [20].

In Danish practice, the categories “tumour cells”, “atypical cells” and “non-diagnostic” are used when cytology cannot be definitely classified as benign or malignant. The clinical guidelines recommend surgery following an FNA diagnosis of “tumour cells”, an approach supported by our estimated ROM of 19.1%. By contrast, the ROM of 70% for “atypical cells” fell to 10% after lymphomas were excluded, suggesting that this category frequently reflects lymphoid atypia in our setting. Most re-FNAs were performed due to non-diagnostic FNAs. Among these cases, the ROM was 12% for those that subsequently proceeded to surgery.

In this study, preoperative FNA predicted benign versus malignant diagnosis in more than 90% of cases when considered as a binary outcome. Reducing false negatives should remain a priority to ensure appropriate treatment selection. Although false positives may risk overtreatment, only eight such cases occurred in the five-year study period.

This study holds some limitations. The retrospective design and modest cohort size limit interference. Among 904 patients with salivary gland FNA, only 49% underwent surgery within the study period, and we lack outcome

data for the remainder (e.g. surgery outside the study period, surveillance, or clinical discharge). Stratification across several cytological categories yields small numbers for some ROM estimates, reducing statistical precision. This must be taken into consideration in a clinical setting. Our findings do not allow us to establish a ROM cut-off that independently mandates surgery. Finally, pathologists were not blinded to cytology or clinical data, although any resultant bias is likely limited in this context.

Conclusions

FNA is the first-line choice when evaluating salivary gland neoplasms, being an effective and cost-beneficial method with high safety. In this regional, five-year cohort, FNA achieved an overall accuracy of 91.5% in distinguishing benign from malignant lesions, supporting its central role in preoperative assessment and patient counselling.

The inherent diagnostic uncertainty must be considered when recommending and planning either surgical interventions or follow-up, especially in indeterminate cases. The ROM associated with each cytological category provides valuable clinical guidance. However, several ROM estimates in this study were based on a small number of cases and should therefore be interpreted with caution. Larger, multicentre studies would strengthen the evidence base and improve the precision of ROM estimates. Category-specific ROM should be considered adjunctive evidence and interpreted alongside clinical presentation, imaging and multidisciplinary judgement when formulating management plans.

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REFERENCES

1. Ovesen T, von Buchwald C. Lægebog i øre-næse-hals-sygdomme og hoved-hals-kirurgi. 3. ed. Munksgaard, 2020
2. NORDCAN. Danmark. Spytkirtel. <https://gco.iarc.fr/media/nordcan/factsheets/94/dk/countries/208/spytkirtel-30-danmark-208.pdf> (Jul 2026)
3. DAHANCA. Årsrapport 2024. DAHANCA, 2024. www.dahanca.dk/CA_Adm_Web_Page?WebPageMenu=3&CA_Web_TabNummer=0 (Jul 2026)
4. Colella G, Cannacale R, Flamminio F, Foschini MP. Fine-Needle Aspiration Cytology of Salivary Gland Lesions: A Systematic Review. J Oral Maxillofac Surg. 2010;68(9):2146-2153. <https://doi.org/10.1016/j.joms.2009.09.064>
5. World Health Organization. Head and Neck Tumours. WHO Classification of Tumours. 5th ed. Vol. 9. IARC publications, 2022.
6. Taniuchi M, Terada T, Kawata R. Fine-Needle Aspiration Cytology for Parotid Tumors. Life (Basel). 2022;12:1897.

<https://doi.org/10.3390/life12111897>

7. Chraba&ska M, Kiczmer P, Drozdowska B. Salivary gland lesions: diagnostic reliability and challanges of fine needle aspiration cytology. *Int J Clin Exp Pathol*. 2021;14(1):54-62
8. Mckenzie J, Lockyer J, Singh T, Nguyen E. Salivary gland tumors: an epidemiological review of non-neoplastic and neoplastic pathology. *Br J Oral Maxillofac Surg*. 2023;61:12-18. <https://doi.org/10.1016/j.bjoms.2022.11.281>
9. Faquin WC, Rossi ED, Baloch Z, et al., eds. *The Milan System for Reporting Salivary Gland Cytopathology*. Springer, 2018. <https://doi.org/10.1007/978-3-319-71285-7>
10. Lee JLL, Tan HM, Chua DYS, et al. The Milan System for Reporting Salivary Gland Cytology: A Retrospective Analysis of 1384 Cases in a Tertiary Southeast Asian Institution. *Cancer Cytopathol*. 2020;128:348-358. <https://doi.org/10.1002/cncy.22245>
11. Fakhry N, Antonini F, Michel J, et al. Fine-needle aspiration cytology in the management of parotid masses: Evaluation of 249 patients. *Eur Ann Otorhinolaryngol Head Neck Dis*. 2012;129:131-135. <https://doi.org/10.1016/j.anorl.2011.10.008>
12. Singh A, Haritwal A, Murali BM. Correlation between cytology and histopathology of the salivary gland. *Australas Med J*. 2011;4(2):66-71. <https://doi.org/10.4066/AMJ.2011.518>
13. Tochtermann G, Nowack M, Hagen C, et al. The Milan system for reporting salivary gland cytopathology - A single-center study of 2156 cases. *Cancer Med*. 2023;12:12198-12207. <https://doi.org/10.1002/cam4.5914>
14. Postema RJ, van Velthuysen MLF, van den Brekel MWM, et al. Accuracy of Fine-Needle Aspiration Cytology of Salivary Gland Lesions in the Netherlands Cancer Institute. *Head Neck*. 2004;26:418-424. <https://doi.org/10.1002/hed.10393>
15. Lui CC, Jethwa AR, Khariwala SS, et al. Sensitivity, Specificity and Posttest Probability of Parotid Fine-Needle Aspiration: A Systematic Review and Meta-analysis. *Otolaryngol Head Neck Surg*. 2016;154:9-23. <https://doi.org/10.1177/0194599815607841>
16. DAHANCA. Diagnostic work-up and Treatment of Salivary Gland Cancer. DAHANCA, 2025. www.dmcg.dk/siteassets/kliniske-retningslinjer/opdelt-paa-dmcg/hoved-halscancer/dahanca_diagnostic-work-up-and-treatment-of-salivary-gland-cancer_v.2.0_admgodk_160626_.pdf (Jul 2026)
17. Aegisdottir AL, Tryggvason G, Jonsdottir AM, Johansson JG. Salivary gland tumors in Iceland 1986-2015: a nationwide epidemiological analysis over a 30-year period. *APMIS*. 2020;129:55-60. <https://doi.org/10.1111/apm.13090>
18. Naz R, Hashmi AA, Khurshid A, et al. Diagnostic role of fine needle aspiration cytology (FNAC) in the evaluation of salivary gland swelling: an institutional experience. *BMC Res Notes*. 2015;8:101. <https://doi.org/10.1186/s13104-015-1048-5>
19. Wang Z, Zhao H, Guo H, An C. Application of the Milan System for Reporting Salivary Gland Cytopathology: A Systematic review and meta-analysis. *Cancer Cytopathol*. 2022;130:849-859. <https://doi.org/10.1002/cncy.22604>
20. Rossi ED, Baloch ZW, Barkan G, Foschini MP. Second edition of the Milan System for Reporting Salivary Gland Cytopathology: Refining the role of salivary gland FNA. *J Am Soc Cytopathol*. 2023;13(1):67-77. <https://doi.org/10.1016/j.jasc.2023.08.004>