# Diagnostic Yield of ThinPrep Preparation in the Assessment of Fine-Needle Aspiration Biopsy of Salivary Gland Neoplasms

Jennifer Hipp, M.D., Ph. D., Beatrice Lee, M.D., Matthew E. Spector, M.D., and Xin Jing, M.D.*

**Background:** *Fine-needle aspiration (FNA) has been widely recognized as an important modality in assessment of salivary gland neoplasms, and specimens are often processed as conventional smears. We conducted the current study to evaluate the diagnostic utility of ThinPrep preparation as an alternative method for assessment of salivary gland neoplasms.*

**Methods:** *A computer SNOMED search from the pathology database at our institution between July 1999 and June 2012 was conducted to identify FNA cytology specimens of salivary gland lesions for which follow-up surgical specimens revealed neoplasms. The FNA specimens were divided into two cohorts: one cohort consisted solely of the specimens in which all needle passes were collected into CytoLyt solution and only ThinPrep slides were prepared; and the other cohort included the specimens prepared with conventional smears. Diagnostic performance of the two cohorts was compared.*

**Results:** *Nondiagnostic rate of ThinPrep preparation was significantly higher than that of conventional smears (40% vs.18%;* P *<0.001). Among the diagnostic specimens, although more indeterminate diagnoses were generated in ThinPrep preparation compared to conventional smears (40% vs. 26%;* P *= 0.024), absolute cytohistologic concordant rate for the positive cases (type of neoplasms specified) is similar between the two preparations (80% vs. 86%;* P *= 0.354). Furthermore, there is no significant difference in rate of accurate diagnosis (correct typing of benign versus malignant neoplasm) between the two preparations (70% vs. 81%;* P *= 0.057).*

**Conclusions:** *ThinPrep may be considered as another practical method of specimen preparation in the assessment of salivary gland neoplasms, particularly when FNA is performed without immediate assistance from cytology.* Diagn. Cytopathol. 2015;43:98–104. 

*Key Words:* fine needle aspiration; ThinPrep preparation; salivary gland neoplasms

Fine-needle aspiration (FNA) is a useful triage tool in the assessment of salivary gland lesions; it aims to distinguish neoplastic from non-neoplastic lesions. Furthermore, it may make a distinction between benign and malignant neoplasms as well as between low-grade and high-grade neoplasms. FNA cytology specimens are commonly processed as multiple conventional smears which are stained with Giemsa, Diff-Quik and/or Papanicolaou stains. Using conventional smear preparation, diagnostic sensitivity ranges from 63% to 93% and specificity ranges from 90% to 100% while achieving 86% to 97% diagnostic accuracy.[1–7]

ThinPrep (Cytyc Corporation [now Hologic®], Marlborough, MA) was introduced into our cytology practice as an alternative method for processing salivary gland FNA specimens more than 10 years ago. Generally, ThinPrep preparation has a number of advantages over conventional smear preparation, such as easier submission of the specimen, that is directly rinsed in the CytoLyt® collecting medium (Cytyc Corporation [now Hologic], Marlborough, MA), fewer numbers of slides examined, well-preserved nuclear details, and a cleaner background. On the other hand, for each specimen only one ThinPrep slide is routinely prepared, and it represents a random sample obtained from multiple needle passes. ThinPrep preparation produces cytological artifacts including apparent discohesion with smaller cellular clusters, fragmented cellular sheets, more single cells, and cellular shrinkage.[8] These artifacts could possibly cause cytological misinterpretation.

Department of Pathology, The University of Michigan, Ann Arbor, Michigan

*Correspondence to: Xin Jing, M.D., Department of Pathology, University of Michigan, 1500 E. Medical Center Drive, 2G332 UH, Ann Arbor, MI 48109-0054, USA. E-mail: xinjing@med.umich.edu

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**Table I.** Specific Type of Neoplasms Diagnosed by ThinPrep Preparation and the Corresponding Histology Diagnosis

| *Cytology diagnosis* | *N* | *Histology-proven, N (%)* | *Other histology diagnoses (n)* |
|---|---|---|---|
| Benign | | | |
| Pleomorphic adenoma | 27 | 25 (93) | Adenoid cystic carcinoma (1), neuroendocrine tumor (1) |
| Warthin's tumor | 17 | 14 (82) | Pleomorphic adenoma (1), acinic cell carcinoma (1), mucoepidermoid carcinoma (1) |
| Subtotal for benign | 44 | 39 (89) | — |
| Malignant | | | |
| Acinic cell carcinoma | 7 | 6 (86) | Warthin's tumor (1) |
| Adenoid cystic carcinoma | 1 | 1 (100) | — |
| Mucoepidermoid carcinoma | 11 | 4 (36) | Pleomorphic adenoma (1), canalicular adenoma (1), salivary duct carcinoma (3), squamous cell carcinoma (2) |
| Myoepithelial carcinoma | 1 | 1 (100) | — |
| Subtotal for malignant | 20 | 12 (60) | — |
| Total (%) | 64 | 51 (80) | — |

In the current study, we evaluated the diagnostic yield of ThinPrep preparation as an alternative specimen processing method in the assessment of FNA biopsy of salivary gland neoplasms as compared to conventional smear preparation.

## Methods

A computer SNOMED search from the pathology database at our institution between July 1999 and June 2012 was conducted to identify FNA cytology specimens of salivary gland lesions which were followed by surgical management and histologic diagnoses of salivary gland neoplasms were then established. The FNA specimens were divided into two cohorts: one cohort consisted solely of the specimens in which all needle passes were collected into the CytoLyt solution and only Papanicolaou-stained ThinPrep slides were then prepared (1 slide/specimen); and the other cohort included the specimens prepared with conventional smears which were stained with both Diff-Quik and Papanicolaou stains.

All FNA procedures were performed with or without ultrasound guidance by otolaryngologists, radiologists, or cytopathologists. The size of needles ranged from 21 to 26 gauge, and the salivary gland masses ranged from 0.5 cm to 15 cm. A total of two to seven passes were performed for each FNA procedure, at the discretion of the performing physician.

The original cytologic diagnosis was recorded for each of the FNA specimens. Since the study only included cases with histology-confirmed salivary gland neoplasms, FNA cytologic diagnoses were divided into non-diagnostic, positive and indeterminate categories. The diagnosis was designated as "non-diagnostic" when original cytology report indicated the specimen being unsatisfactory, or only containing cyst contents or normal salivary gland elements. The diagnosis was considered "positive" when the type of neoplasm was specified whereas the "indeterminate" category referred to cases in which a descriptive interpretation was rendered with or without differential diagnoses. The corresponding histologic diagnosis was also documented for each diagnostic case, and cyto-histologic correlation was then performed. Absolute cyto-histologic concordance was achieved when the cytologic diagnosis of a specific neoplasm was confirmed by the follow-up histology. A cytologic diagnosis was considered accurate if the neoplasm was correctly designated as either benign or malignant.

The nondiagnostic rate, rate of indeterminate diagnosis, absolute cyto-histologic concordant rate, and rate of accurate diagnosis were calculated for both ThinPrep and conventional preparations. The parameters were then compared between the two cohorts by using $\chi^2$ test with the help of the SigmaStat.3.5 program (Systat Software, Inc.). The level of difference was considered statistically significant when $P$ value $\leq 0.05$.

To document the cytomorphological features of ThinPrep preparation, the available ThinPrep slides and the corresponding histology slides were retrospectively reviewed.

## Results

The study included a total of 178 ThinPrep and 191 conventional specimens. Of the 178 ThinPrep specimens, 72 (40%) were non-diagnostic while 35 out of 191 (18%) conventional specimens were nondiagnostic. The difference in non-diagnostic rate is significantly different ($\chi^2 = 20.84$, d$f = 1$; $P < 0.001$).

Among the 106 diagnostic ThinPrep specimens, 64 had a "positive" cytologic diagnosis with the type of neoplasm specified, including 44 benign and 20 malignant

**Table II.** ThinPrep Specimens with Indeterminate Interpretations and the Follow-Up Histology Diagnoses

| Case | Cytologic differential diagnoses | Histology diagnosis |
|---|---|---|
| 1 | Pleomorphic adenoma vs. PLGA | Pleomorphic adenoma |
| 2 | Pleomorphic adenoma vs. mucoepidermoid carcinoma | Pleomorphic adenoma |
| 3 | Pleomorphic adenoma vs. mucoepidermoid carcinoma | Pleomorphic adenoma |
| 4 | Pleomorphic adenoma vs. mucoepidermoid carcinoma | Pleomorphic adenoma |
| 5[a] | Pleomorphic adenoma vs. myoepithelioma | Pleomorphic adenoma |
| 6 | Pleomorphic adenoma vs. PLGA | Adenoid cystic carcinoma |
| 7[b] | Pleomorphic adenoma vs. trabecular adenoma | Adenoid cystic carcinoma |
| 8 | Pleomorphic adenoma vs. adenoid cystic carcinoma | Adenoid cystic carcinoma |
| 9[b] | Pleomorphic adenoma vs. myoepithelioma | Adenoid cystic carcinoma |
| 10[a] | Warthin's tumor vs. oncocytic metaplasia | Warthin's tumor |
| 11[a] | Warthin's tumor vs. sialadenitis | Warthin's tumor |
| 12[a] | Warthin's tumor vs. sialadenitis | Warthin's tumor |
| 13 | Warthin's tumor vs. mucoepidermoid carcinoma | Warthin's tumor |
| 14 | Warthin's tumor vs. mucoepidermoid carcinoma | Warthin's tumor |
| 15[a] | Warthin's tumor vs. oncocytoma | Warthin's tumor |
| 16 | Warthin's tumor vs. mucoepidermoid carcinoma | Squamous cell carcinoma |
| 17 | Warthin's tumor vs. mucoepidermoid carcinoma | Squamous cell carcinoma |
| 18 | Warthin's tumor vs. adenocarcinoma | Salivary duct carcinoma |
| 19 | Warthin's tumor vs. malignant neoplasm | PDC |
| 20 | Warthin's tumor vs. lymphoma | Follicular lymphoma |
| 21[b] | Warthin's tumor vs. lymph node | MALT lymphoma |
| 22[c] | Warthin's tumor vs. oncocytoma | Oncocytic cyst |
| 23[c] | Warthin's tumor vs. oncocytoma | Bronchial cleft cyst |
| 24[c] | Warthin's tumor vs. reactive | Negative for neoplasm |
| 25[c] | Warthin's tumor vs. reactive | Negative for neoplasm |
| 26[c] | Acinic cell carcinoma vs. adenocarcinoma | Pleomorphic adenoma |
| 27[a] | Adenoid cystic carcinoma vs. basal cell carcinoma | Adenoid cystic carcinoma |
| 28[a] | Adenoid cystic carcinoma vs. basal cell carcinoma | Adenoid cystic carcinoma |
| 29[c] | adenoid cystic carcinoma vs. PLGADC | Myoepithelioma |
| 30[a] | Low grade neoplasm | Pleomorphic adenoma |
| 31[a] | Low grade neoplasm | Warthin's tumor |
| 32 | Low grade neoplasm | Adenoid cystic carcinoma |
| 33 | Low grade neoplasm | PLGA |
| 34[c] | Carcinoma ex PA vs. mucoepidermoid carcinoma | Pleomorphic adenoma |
| 35[a] | Mucoepidermoid carcinoma vs. skin tumor | Mucoepidermoid carcinoma |
| 36[a] | Mucoepidermoid carcinoma vs. squamous cell carcinoma | Mucoepidermoid carcinoma |
| 37[a] | Mucoepidermoid carcinoma vs. squamous cell carcinoma | Squamous cell carcinoma |
| 38[a] | Mucoepidermoid carcinoma vs. squamous cell carcinoma | Squamous cell carcinoma |
| 39[a] | Mucoepidermoid carcinoma vs. squamous cell carcinoma | Squamous cell carcinoma |
| 40[a] | Mucoepidermoid carcinoma vs. squamous cell carcinoma | Salivary duct carcinoma |
| 41[a] | Mucoepidermoid carcinoma vs. squamous cell carcinoma | PDC |
| 42[a] | Mucoepidermoid carcinoma vs. adenocarcinoma | Carcinoma ex PA |

[a]Cases with accurate cytologic diagnosis (correct typing of benign vs. malignant neoplasm).
[b]Cases with cytologic under-interpretation.
[c]Cases with cytologic over-interpretation.
PLGA: polymorphous low grade adenocarcinoma; carcinoma ex PA: carcinoma ex pleomorphic adenoma; PDC: poorly differentiated carcinoma.

neoplasms (Table I). The corresponding histology confirmed absolute cyto-histologic concordance in 39 of 44 (89%) benign and 12 of 20 (60%) malignant cases, respectively. The combined rate of cyto-histologic concordance reached 80% (51/64). Although ThinPrep detected neoplasms in the remaining 13 specimens, the type of the neoplasms was not correctly identified. In this regard, acinic cell carcinoma was misinterpreted as Warthin's tumor and vice versa; mucoepidermoid carcinoma was misinterpreted as pleomorphic adenoma and vice versa; Warthin's tumor was misdiagnosed as pleomorphic adenoma or low grade mucoepidermoid carcinoma; pleomorphic adenoma was misdiagnosed as adenoid cystic carcinoma or neuroendocrine tumor; mucoepidermoid carcinoma was misdiagnosed as salivary duct carcinoma, squamous cell carcinoma, and canalicular adenoma.

The remaining 42 (40%) diagnostic ThinPrep specimens were classified as "indeterminate." Follow-up histology confirmed the presence of one neoplasm/malignancy included in the differential diagnosis in 57% (24 of 42) of the cases. Cytologic under-interpretation occurred in three (7%) cases whereas over-interpretation occurred in seven (17%) cases. With regard to the latter, four cases showed potential of false positive interpretation of neoplasm as differential diagnoses included Warthin's tumor, and the follow-up histology revealed no neoplasm (Table II).

Accurate cytologic diagnosis (correct typing of benign versus malignant neoplasm) was rendered in 57

**Table III.** Specific Type of Neoplasms Diagnosed by Conventional Smears and the Corresponding Histology Diagnosis

| *Cytology diagnosis* | *N* | *Histology-proven, N (%)* | *Other histology diagnoses(n)* |
|---|---|---|---|
| Benign | | | |
| Pleomorphic adenoma | 75 | 67 (89) | Non-neoplastic (2), Warthin's tumor (2), basal cell adenoma (1), myoepithelioma (1), mucoepidermoid carcinoma (1), chondrosarcoma (1) |
| Warthin's tumor | 12 | 10 (83) | Pleomorphic adenoma (1), non-neoplastic (1) |
| Basal cell adenoma | 1 | 0 | Epithelial myoepithelial carcinoma (1) |
| Myoepithelioma | 1 | 0 | Pleomorphic adenoma (1) |
| Subtotal for benign | 89 | 77(86) | — |
| Malignant | | | |
| PLGA | | 1 (100) | — |
| Acinic cell carcinoma | 5 | 3 (60) | Warthin's tumor (1), pleomorphic adenoma (1) |
| Adenoid cystic carcinoma | 4 | 4 (100) | — |
| Carcinoma ex PA | 1 | 0 | Pleomorphic adenoma (1) |
| Mucoepidermoid carcinoma 14 | 14 | 13 (93) | Squamous cell carcinoma (1) |
| Salivary ductal carcinoma | 1 | 1 (100) | — |
| Squamous cell carcinoma | 1 | 1 (100) | — |
| Subtotal for malignant | 27 | 23 (85) | — |
| Total (%) | 116 | 100 (86) | — |

PLGA: polymorphous low grade adenocarcinoma; carcinoma ex PA: carcinoma ex pleomorphic adenoma.

of 64 "positive" cases and 17 of 42 "indeterminate" cases. Overall, an accurate cytologic diagnosis was rendered in 70% (74 of 106) of all diagnostic ThinPrep specimens.

Among the 156 diagnostic conventional specimens, 116 had a "positive" cytologic diagnosis with the specific type of neoplasm, including 89 benign and 27 malignant neoplasms (Table III). The corresponding histology confirmed absolute cyto-histologic concordance in 77 of 89 (86%) benign and 23 of 27 (85%) malignant cases, respectively. The combined rate of cyto-histologic concordance reached 86% (100 of 116).

The remaining 40 (26%) diagnostic conventional specimens were classified as "indeterminate." As can be seen in Table IV, follow-up histology confirmed the presence of one neoplasm/malignancy included in the differential diagnosis in 55% (22 of 40) of the cases. Cytologic under-interpretation occurred in one (2%) case whereas cytologic over-interpretation occurred in two (5%) cases.

Accurate cytologic diagnosis was rendered in 106 of 116 "positive" cases and 20 of 40 "indeterminate" cases. Overall rate of accurate diagnosis reached 81% (126 of 156).

Table V summarizes the result of statistical analysis of the diagnostic performance of ThinPrep preparation in comparison to conventional smear preparation.

Both cytology and the corresponding histology slides were available for retrospective review in 71 cases with ThinPrep preparation. The cytomorphologic features demonstrated by ThinPrep preparation are summarized in Table VI.

## Discussions

FNA is a simple and well-tolerated diagnostic method which provides a tissue diagnosis compared to imaging studies such as MRI. FNA has an impact on management and treatment of salivary gland neoplasms in terms of preoperative patient counseling, better surgical planning, and better selection of surgery candidates.[4]

The advantages and disadvantages of utilizing ThinPrep technique for assessment of non-gynecological specimens have been previously described.[8] We found only two published studies in the English literature which compared diagnostic accuracy of ThinPrep preparation with that of conventional smear preparation for salivary gland FNA.[9,10] These two former studies included 58 and 40 cases, respectively. Both studies used a split-sample technique in which conventional smears were prepared first and then a ThinPrep slide was prepared from fixative solution containing residual needle rinses**.** We report the first study in which diagnostic performance was evaluated for non-split-sample ThinPrep preparation. Accordingly, all needle passes were dedicated to the Cytolyt solution from that one ThinPrep slide was prepared for each specimen. Our data demonstrates that in comparison to conventional smear preparation, ThinPrep preparation may provide compatible cyto-histologic concordant rate for the positive cases (type of neoplasms specified) and overall rate of accurate diagnosis (correct typing of benign versus malignant neoplasm).

Similar to the previously reported,[10] ThinPrep preparation in the current study had a higher non-diagnostic rate than that of conventional smear preparation. The higher non-diagnostic rate seemed to be related to sampling issues rather than misinterpretation as the original report indicated the non-diagnostic ThinPrep preparations being pauci-cellular, containing cyst contents or normal salivary gland elements. It is noteworthy to mention that the conventional smears in the current study were prepared by the cytology team and a rapid on-site evaluation (ROSE)

**Table IV.** Conventional Smear Preparation with Indeterminate Interpretations and the Follow-Up Histology Diagnoses

| *Case* | *Cytologic differential diagnoses* | *Histology diagnosis* |
|---|---|---|
| 1[a] | Pleomorphic adenoma vs. Warthin's tumor | Acinic cell carcinoma |
| 2 | Pleomorphic adenoma vs. adenoid cystic carcinoma | Adenoid cystic carcinoma |
| 3[b] | Pleomorphic adenoma vs. myoepithelioma | Pleomorphic adenoma |
| 4 | Pleomorphic adenoma vs. PLGA | High grade carcinoma |
| 5[b] | Pleomorphic adenoma vs. myoepithelioma | Pleomorphic adenoma |
| 6[b] | Basal cell adenoma | Pleomorphic adenoma |
| 7[b] | Warthin's tumor vs. lymph node | Warthin's tumor |
| 8[b] | Warthin's tumor vs. lymph node | Warthin's tumor |
| 9 | Warthin's tumor vs. mucoepidermoid carcinoma | Warthin's tumor |
| 10 | Warthin's tumor vs. mucoepidermoid carcinoma | Warthin's tumor |
| 11 | Warthin's tumor vs. mucoepidermoid carcinoma | Mucoepidermoid carcinoma |
| 12[b] | Adenoid cystic carcinoma vs. myoepithelial carcinoma | Myoepithelial carcinoma |
| 13[b] | Adenoid cystic carcinoma vs. myoepithelial carcinoma | Myoepithelial carcinoma |
| 14 | Myoepithelioma vs. myoepithelial carcinoma | Squamous cell carcinoma |
| 15 | Basaloid neoplasm | Squamous cell carcinoma |
| 16 | Basaloid neoplasm | Basal cell carcinoma |
| 17 | Basaloid neoplasm | Adenoid cystic carcinoma |
| 18 | Basaloid neoplasm | Adenoid cystic carcinoma |
| 19 | Basaloid neoplasm | Adenoid cystic carcinoma |
| 20[c] | Low grade neoplasm vs. mucocele | Mucocele |
| 21 | Low grade neoplasm | Warthin's tumor |
| 22 | Low grade neoplasm | Pleomorphic adenoma |
| 23 | Low grade neoplasm | Basal cell adenoma |
| 24 | Low grade neoplasm | Mucoepidermoid carcinoma |
| 25 | Low grade neoplasm | Mucoepidermoid carcinoma |
| 26 | Low grade neoplasm | Mucoepidermoid carcinoma |
| 27[b] | Low grade carcinoma | PLGA |
| 28[b] | High grade carcinoma | Squamous cell carcinoma |
| 29[c] | Mucoepidermoid carcinoma vs. cyst | Benign cyst |
| 30[b] | Mucoepidermoid carcinoma vs. squamous cell carcinoma | Squamous cell carcinoma |
| 31[b] | Mucoepidermoid carcinoma vs. squamous cell carcinoma | Squamous cell carcinoma |
| 32[b] | Mucoepidermoid carcinoma vs. squamous cell carcinoma | Squamous cell carcinoma |
| 33[b] | Mucoepidermoid carcinoma vs. squamous cell carcinoma | Squamous cell carcinoma |
| 34[b] | Mucoepidermoid carcinoma vs. salivary duct carcinoma | Salivary ductal carcinoma |
| 35[b] | Mucoepidermoid carcinoma vs. salivary duct carcinoma | Squamous cell carcinoma |
| 36[b] | Mucoepidermoid carcinoma vs. salivary duct carcinoma | High grade carcinoma |
| 37[b] | High grade neoplasm | Salivary duct carcinoma |
| 38[b] | PDC | PDC |
| 39[b] | PDC | Epithelial myoepithelial ca |
| 40[b] | ADC | Salivary duct carcinoma |

[a]Cases with cytologic under-interpretation.
[b]Cases with accurate cytologic diagnosis (correct typing of benign vs. malignant neoplasm).
[c]Cases with cytologic over-interpretation.
PLGA: polymorphous low grade adenocarcinoma; carcinoma ex PA: Carcinoma ex pleomorphic adenoma; PDC: poorly differentiated carcinoma.

was provided at the time of the FNA procedures. However, assessment of benefit of ROSE for FNA diagnosis of salivary gland neoplasms is beyond the scope of this study.

One of the aforementioned studies using split-sample technique considered a diagnosis accurate if it was correctly designated as either benign or malignant. The authors reported that the rate of accurate diagnosis could reached up to 60% in cellular specimens using ThinPrep preparation, and ThinPrep correctly identified 63% (25 of 40) of the pleomorphic adenomas.[10] Of the 64 cases in our study with a specific diagnosis of either benign or malignant, an accurate diagnosis was established in 80% (51 of 64) of the cases, and ThinPrep correctly classified 93% (25 of 27) of the pleomorphic adenomas. The difference in precision between the current and former studies may be attributed to bias of the split-sample technique of the latter.

While evaluating the diagnostic yield of FNA cytology for salivary gland lesions, the vast majority of the previous studies, with one exception,[10] incorporated cases with an "indeterminate" diagnosis into the "positive" category. Given the bias due to handling indeterminate results in this manner, Schmidt et al have recommended subclassification of cytology results into categories of positive, negative, indeterminate, and inadequate; as well as separation of neoplasm from malignancy while reporting diagnostic accuracy.[11] The current study used a similar approach by separating the cases with indeterminate cytologic interpretations from the cases with specific diagnoses. For the 64 cases with specific "positive" diagnoses, cyto-histologic concordance reached 80%, which is comparable to that of

conventional smear preparation in the current study (86%) and the cyto-histologic concordant rate previously reported by the others (79%).[1] One previous study using conventional smear preparation correctly typed 92% of pleomorphic adenomas, 75% of Warthin's tumors, and 33% of malignant neoplasms, suggesting that conventional smear preparation appears to be more reliable for correctly typing benign than malignant salivary gland neoplasms.[4] We observed the similar finding for ThinPrep preparation; however, the current study showed that conventional smear preparation correctly typed similar percentage of pleomorphic adenoma (89%), Warthin's tumors (83%) and malignant neoplasms (85%). Estimating an accuracy rate for the subpopulations of cases with specific diagnoses, either benign or malignant is important. In this regard, prior to performing a FNA procedure, otolaryngologists often have a clinical impression that comes from a CT, MRI or ultrasound image as well as the overall history of the patient. Pleomorphic adenomas appear well-circumscribed, with low intensity on T1-weighted images and high intensity on T2-weighted images, whereas Warthin's tumor is homogenous and enhancing on CT scan because of high mitochondrial counts. The latter also occurs exclusively in the parotid gland and is more common in smokers. Cancers are more invasive on imaging and patient can present with pain or facial nerve paralysis. FNA may provide a more specific pre-operative tissue diagnosis that plays an important role in preoperative patient counseling, better surgical planning, and better selection of surgery candidates.

**Table V.** Diagnostic Performance of ThinPrep Preparation in Comparison to Conventional Smear Preparation

| *Parameters* | *ThinPrep (%)* | *Conventional (%)* | *P value ($\chi^2$; df = 1)* |
|---|---|---|---|
| Positive | | | |
| Absolute cyto-histologic concordance | 80 | 86 | 0.354 (0.860) |
| Benign | 89 | 86 | 0.945 (0.005) |
| Malignant | 60 | 85 | 0.105 (2.623) |
| Indeterminate | | | |
| Rate of indeterminate diagnosis | 40 | 26 | 0.024 (5.106) |
| Histology-confirmed differential diagnosis | 57 | 55 | 0.978 (0.001) |
| Overall rate of accurate diagnosis | 70 | 81 | 0.057 (3.611) |

The challenges in distinguishing different types of salivary gland neoplasms have been encountered with conventional smear preparation. In this regard, diagnostic dilemmas on FNA assessment of salivary gland neoplasms existed not only in differentiating benign neoplasms (i.e. cellular pleomorphic adenoma, monomorphic adenoma, Warthin's tumor) from malignant neoplasms (i.e. polymorphous low-grade adenocarcinoma and acinic cell carcinoma) but also in distinguishing between non-neoplastic lesions (i.e. chronic sialadenitis with squamous metaplasia, lymphoepithelial cyst) and neoplasms (i.e. Warthin's tumor, oncocytoma, and low grade mucoepidermoid carcinoma).[7] With regard to the diagnostic specimens, ThinPrep preparation provided more indeterminate diagnoses than conventional smear preparation. The finding may be related to attenuation of cytomorphologic features in ThinPrep compared to conventional smear preparation.

It has been documented that background material such as the stroma of pleomorphic adenoma may be attenuated and less conspicuous in ThinPrep preparation.[9,10] However, for reviewers with hands-on, practical experience, it is not difficult to appreciate the fibrillary stroma in a majority of the cases. We also found some features which may be useful to differentiate cellular pleomorphic adenoma (with scant or absent stroma) from adenoid cystic

**Table VI.** Cytomorphologic Features Demonstrated by ThinPrep Preparation

| *Histologic diagnosis* | *Cytomorphologic features* |
|---|---|
| Pleomorphic adenoma ($n$ = 25) | 75% of the specimens are moderate to hypercellular with well-preserved epithelial cells and myoepithelial cells; 50% have coexisting fibrillary stroma, and 25% show scant or no stroma. The remaining 25% of the specimens are hypocellular with accompanying fibrillary stroma. |
| Warthin's tumor ($n$ = 18) | 50% of the specimens are moderate to hypercellular with well-preserved oncocytes, lymphocytes, and amorphous debris in the background. The remaining 50% of the specimens are hypocellular containing oncocytes and lymphocytes or oncocytes and amorphous debris. The oncocytes are arranged as single cells or sheets and have granular cytoplasm, round nuclei and distinct nucleoli. Shrunken nuclei with mild nuclear membrane irregularity may be seen. |
| Adenoid cystic carcinoma ($n$ = 6) | All specimens are moderate to hypercellular with or without stroma. Some spheres of stroma are present. The cells appear monotonous and basaloid and are arranged in a ball-like configuration with a smooth contour. |
| Acinic cell carcinoma ($n$ = 4) | All specimens are moderate to hypercellular with single cells or sheets of cells. The cells have vacuolated to granular cytoplasm, round nuclei, and distinct nucleoli. Naked nuclei, lymphocytes, and amorphous debris appear in 40% of the specimens. |
| High-grade carcinoma ($n$ = 13) | All specimens are moderate to hypercellular with malignant-looking cells. 50% of the specimens show necrotic debris in the background. |
| Myoepithelioma arising in pleomorphic adenoma ($n$ = 1) | Cellular specimen with a mixture of epithelial cells, myoepithelial cells, and fibrillary stroma. Myoepithelial cells are not a prominent component. |
| Low-grade lymphoma ($n$ = 1) | Cellular specimen with a numerous monotonous population of lymphocytes. |
| Neuroendocrine tumor ($n$ = 1) | Cellular specimen with a monotonous population of plasmacytoid cells. |
| Benign ($n$ = 2) | Cellular specimen with many normal acini and rare oncocytes. |

carcinoma; epithelial cells in pleomorphic adenoma appear as sheets or loose groups compared to the tight ball-like arrangement with smooth outlines in adenoid cystic carcinoma. Regarding Warthin's tumor, it is a diagnostic challenge to distinguish Warthin tumor from acinic cell carcinoma when the latter demonstrates naked nuclei, lymphocytes, and amorphous debris. However, it is not uncommon to appreciate oncocytes with shrunken or crenated nuclei in Warthin's tumor whereas cells of acinic cell carcinoma often have round nuclei and distinct nucleoli. In two of the four cases that were initially concerning for Warthin's tumor, the ThinPrep slides contained a notable amount of benign salivary acini in addition to a scant amount of oncocytes. One should be cautious to avoid over-interpretation of the presence of oncocytes in such scenarios. It is noteworthy to mention that it is extremely difficult to make a distinction among high grade malignant neoplasms, including high-grade mucoepidermoid carcinoma, salivary duct carcinoma, squamous cell carcinoma, and carcinoma ex pleomorphic adenoma. Although moderate- to well-differentiated neuroendocrine tumors rarely occur in salivary glands,[12] single or loose groups of plasmacytoid-looking tumor cells of these neoplasms on the ThinPrep slide could be possibly mistaken as myoepithelial cells in pleomorphic adenoma.

In conclusion, the current study is the first to focus on the diagnostic utility of non-split-sample ThinPrep preparation for FNA assessment of salivary gland neoplasms. Our data demonstrates that ThinPrep may be considered as another practical method of specimen preparation in the assessment of salivary gland neoplasms, particularly when FNA procedure is performed without immediate assistance from cytology.

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