

# Updates in Salivary Gland Fine Needle Aspiration Biopsy

## The Use of the Milan System and Ancillary Testing



Edward B. Stelow, MD

### KEYWORDS

• Fine needle aspiration biopsy • Salivary gland • Milan System • Ancillary Testing

### Key points

- Salivary gland fine needle aspiration biopsies remain common specimens seen by most cytology services.
- The diagnostic diversity and overlap between many of the lesions seen with these biopsies impart many challenges for the cytopathologist, rendering most specific diagnoses impossible with cytology alone.
- Here, the use of the Milan System for the classification of salivary gland fine needle aspiration biopsy is discussed, together with the potential use of ancillary testing in arriving at definitive diagnoses.

### ABSTRACT

**S**alivary gland fine needle aspiration biopsies remain common specimens seen by most cytology services. The diagnostic diversity and overlap between many of the lesions seen with these biopsies impart many challenges for the cytopathologist, rendering most specific diagnoses impossible with cytology alone. Here, the use of the Milan System for the classification of salivary gland fine needle aspiration biopsy FNAB is discussed, together with the potential use of ancillary testing in arriving at definitive diagnoses.

### OVERVIEW

The usefulness of fine needle aspiration biopsy (FNAB) varies from site to site. With the thyroid, it

is typically used as a screening test to determine whether a patient has surgery for a nodule and what type of surgery he or she will undergo.<sup>1</sup> Pancreatic FNAB is typically used to definitively diagnose mass lesions and, in most cases, diagnosis is required before the initiation of nonsurgical therapy.<sup>2</sup> With lung FNAB, the use is similar; however, the need for extensive ancillary testing to triage toward targeted or immunomodulating therapies typically requires the obtainment of more abundant materials than are required for diagnosis alone.<sup>3</sup>

Fine needle aspiration of salivary gland mass lesions for the triage and treatment of patients has been performed for more than 50 years.<sup>4</sup> At this site, FNAB is used most similarly to FNAB of the thyroid, as a method to direct whether and to what extent surgical therapy is necessary.<sup>5</sup> There are some differences, however.

Department of Pathology, UVA Hospital, University of Virginia, MC 800214, Jefferson Park Avenue, Charlottesville, VA 22908, USA

E-mail address: edstelow@yahoo.com

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Unlike with the thyroid, where most nodules are nonneoplastic and do not require surgery, most salivary gland mass lesions represent neoplasia and require surgery.<sup>1,6-8</sup> Neoplastic thyroid histology, although fret with interobserver variability and morphologic overlap, is relatively straightforward. The World Health Organization classification system for neoplasia of the salivary gland is much more complicated and many of the lesions show marked histologic overlap and/or require the assessment of parameters that can only be seen on histologic sections (eg, vascular invasion) to determine whether the neoplasm is malignant.<sup>9</sup> The World Health Organization currently lists more than 30 benign and malignant epithelial tumors. This is further complicated by the fact that lymph nodes are frequently intimately associated with the parotid gland and that those lymph nodes represent common sites of metastases for cancers of the facial skin or sinonasal tract.<sup>10</sup>

Because of the numerous entities, the frequent histologic overlap between those entities, and the necessity for histology to fully classify some lesions, FNAB of the salivary gland often results in imprecise diagnoses, although there are again notable exceptions (eg, most reactive lymph nodes and pleomorphic adenomas can be diagnosed definitively).<sup>6,7</sup> As such, FNABs of salivary gland masses are often signed out with descriptive diagnoses of recurring categories.

THE MILAN SYSTEM FOR THE CLASSIFICATION OF SALIVARY GLAND FINE NEEDLE ASPIRATION BIOPSY DIAGNOSES

RISK

Because descriptive diagnoses or categories can vary greatly between institutions, there has recently been a movement to systematize salivary gland FNAB sign-out.<sup>7,11-14</sup> The consensus system is now referred to as The Milan System. It uses a 6-tiered classification system akin to that used at other sites (eg, the thyroid gland; Table 1). The system itself uses and attempts to codify the most common interpretations seen with salivary gland FNAB.

The categorical system is supposed to allow for risk stratification and treatment, although, similar to the Bethesda System for the classification of Pancreatic Cytologic samples, specific diagnoses or subcategories within the system may be the best predictor of malignancy. For example, an interpretation of suspicious for a high-grade malignancy may function differently than an interpretation of suspicious for low-grade malignancy, and

Table 1  
Milan system for the classification of salivary gland fine needle aspiration biopsy

I	Nondiagnostic
II	Nonneoplastic
III	Atypical
IV	Neoplasm
IVa	Benign neoplasm
IVb	Neoplasm of unknown malignant potential
V	Suspicious for malignancy
VI	Malignant neoplasm

different surgical treatment may be required for the 2 interpretations.

The data regarding outcomes for the Milan tiered approach are limited at this time.<sup>7,15-17</sup> The risk that a nondiagnostic interpretation will be associated with benign or malignant neoplasia may be up to 44% and 25%, respectively, reports 1 study based on a retrospective study of the literature.<sup>7</sup> This finding likely reflects the overall risks for salivary gland mass lesions that present for biopsy. Included here, too, are aspirates that show only cyst contents, a known proportion of which represent neoplasia, especially low-grade mucoepidermoid carcinoma.

The same retrospective study estimates that aspirates interpreted as nonneoplastic have risks for benign and malignant neoplasia of 13% and 10%, respectively.<sup>7</sup> It is unclear what causes these errors. Interpretative error seems unlikely aside from with low-grade lymphocytic malignancies.<sup>18</sup> Sampling likely plays a role, and it may be that some changes seen with salivary gland histology adjacent to neoplasia may lead to the false judgment that they represent the mass lesion itself. This would be akin to a diagnosis of chronic pancreatitis for an aspirate of a pancreatic mass, where the chronic pancreatitis has developed secondary to an unsampled adenocarcinoma.<sup>19</sup> It may also be that some samples showing only normal salivary gland have been included here.

Two recent studies have looked at the more subjective interpretations of atypical and suspicious by accumulating data retrospectively from multiple institutions.<sup>16,17</sup> In 1 study, the authors found that approximately 4% of salivary gland FNABs were interpreted as atypical, and that the risks for benign and malignant neoplasia were 7% and 19%, respectively.<sup>16</sup> It should be noted, however, that only 31% of cases had follow-up. The authors of the other article found that 2.2% of salivary gland FNABs were interpreted as

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