In recent decades, fine needle aspiration cytology (FNAC) has been established as an efficient diagnostic tool for superficial masses, including salivary gland lesions. FNAC is technically simple, safe, fast, and cost-effective. However, FNAC traditionally demonstrates relatively low sensitivity in comparison with its high specificity for diagnosing salivary gland tumors. According to a previous meta-analysis by Schmidt et al., the average sensitivity and specificity determined in 6,169 cases were 80% and 97%, respectively. Recent studies report that the sensitivity and specificity of FNAC range between 64%–90% and 86%–100%, respectively.

The low sensitivity of FNAC can be attributed to several factors, but is primarily due to the difficulty of diagnosing low-grade carcinomas by cellular morphology alone.

Core needle biopsy (CNB) is a relatively new technique for diagnosing salivary gland lesions. Since intact tissue cores can be retrieved using ultrasound-guided CNB, improved specimen adequacy is expected. The sensitivity and specificity of salivary gland CNB are reportedly 92%–94% and 99%–100%, respectively. Preoperative evaluation of salivary gland lesions should provide the clinicians with a treatment plan including the type and extent of surgical intervention needed. For this purpose, differentiating benign from malignant tumors is crucial, and moreover, information on the grade and specific type of the tumor will further aid in the choice of therapeutic procedures.

With the aim of establishing the most accurate diagnostic tool as new techniques emerge, we compared the diagnostic accuracy and accurate tumor subtyping rates of CNB and FNAC performed for the preoperative evaluation of patients with salivary gland lesions, especially when malignancy is suspected.

Materials and Methods

Between July 2008 and June 2013, 708 tumors in the major salivary glands were surgically resected from 705 patients at Asan Medical Center in Seoul, Korea. Of these 708 cases, 562 cases...
RESULTS

Characteristics of the examined cases

The locations of the 562 surgical cases included parotid gland (n = 472), submandibular gland (n = 88), and sublingual gland (n = 2). Histologic diagnoses included 103 malignant and 459 benign tumors. Malignant tumors included 21 mucoepidermoid carcinomas, 17 salivary duct carcinomas, 17 carcinoma ex pleomorphic adenomas, 12 adenoid cystic carcinomas, 10 acinic cell carcinomas, 7 basal cell adenocarcinomas, 5 adenocarcinomas not otherwise specified, 3 epithelial-myoepithelial carcinomas, 3 squamous cell carcinomas, 2 oncocytic carcinomas, 1 cystadenocarcinoma, 3 malignant lymphomas, 1 rhabdomyosarcoma, and 1 undifferentiated pleomorphic sarcoma. Benign tumors included 305 pleomorphic adenomas, 96 Warthin tumors, 37 basal cell adenomas, 7 myoepitheliomas, 3 oncocytomas, 1 lymphadenoma, 5 neurogenic tumors (4 schwannomas and 1 neurofibroma), 3 vascular tumors (2 hemangiomas and 1 lymphangioma), and 2 lipomas.

When the general characteristics of the CNB and FNAC groups were compared to exclude selection bias, the proportion of malignancy, location, laterality, and multiplicity were not significantly different between the two groups (Table 1). One significant difference was the tumor size. The average size of tumors in the FNAC group was bigger than that in the CNB group (p = .006), which can be explained by the fact that generally patients with larger palpable tumors are sent to the Pathology Department for FNAC.

Specimen adequacy

Regarding the specimen adequacy of the 228 CNB specimens and 371 FNAC samples, the unsatisfactory rate tended to be lower following CNB (2.6%) than FNAC (6.2%) (Table 2). A total of 33 cases underwent CNB after FNAC. Adenoid cystic carcinoma, salivary duct carcinoma, and oncocytoma showed high rates for multiple diagnostic procedures (3/12, 3/17, and 1/3, respectively).

Accuracy

The sensitivity of detecting malignant tumors using the CNB method was significantly higher (88.2%) than that with FNAC (58.2%) (p = .006) (Table 3). The specificity, PPV, and NPV of CNB were slightly higher than those of FNAC, without significant differences.

False-negative and -positive cases

A total of 29 false-negative cases and 5 false-positive cases are listed in Table 4. False-negative results by CNB were restricted to cases of basal cell adenocarcinoma, carcinoma ex pleomorphic adenoma, and epithelial-myoepithelial carcinoma, while false-negative results by FNAC were found in a wide range of tumors.

Table 1. General characteristics of salivary gland tumors according to CNB and FNAC

| Characteristic                  | CNB (n = 228) | FNAC (n = 371) | p-value |
|--------------------------------|---------------|----------------|---------|
| Malignant:benign tumor         | 54:174        | 62:309         | .479    |
| Size (mean ± SD, cm)           | 2.57 ± 1.22   | 2.85 ± 1.21    | .006    |
| Site                           |               |                |         |
| Parotid                        | 171 (75.0)    | 329 (88.7)     | .150    |
| SMG                            | 56 (24.8)     | 40 (10.8)      |         |
| SLG                            | 1 (0.4)       | 2 (0.5)        |         |
| Laterality                     |               |                | .687    |
| Left                           | 126 (55.2)    | 193 (52.0)     |         |
| Right                          | 100 (43.9)    | 175 (47.2)     |         |
| Bilateral                      | 2 (0.9)       | 3 (0.8)        |         |
| Multiplicity                   | 14 (6.1)      | 13 (3.5)       | .560    |

Values are presented as number (%) unless otherwise indicated.

CNB, core needle biopsy; FNAC, fine needle aspiration cytology; SD, standard deviation; SMG, submandibular gland; SLG, sublingual gland.
including adenoid cystic carcinoma, acinic cell carcinoma, adenocarcinoma not otherwise specified, mucoepidermoid carcinoma, oncocytic carcinoma, and malignant lymphoma (Fig. 1). No high-grade carcinomas (e.g., salivary duct carcinoma) were diagnosed as false-negatives by either method. False-positive results from neither method exhibited specific patterns; they might be the result of misinterpretation of pathologic findings, with or without artifacts.

### Accurate tumor subtyping

The accurate tumor subtyping rates of the salivary gland tumors were significantly higher with CNB (88.3%) than with FNAC (70.7%) (p < .001) (Table 5). Immunohistochemical studies for tumor subtyping were performed in 11 CNB samples: CD117 in adenoid cystic carcinoma; smooth muscle actin, calponin, and p63 in pleomorphic adenoma; and S100 protein in oncocytic carcinoma.

### Table 2. Unsatisfactory rates and repeated diagnostic procedure rates of salivary gland tumors according to histologic diagnoses

| Histologic diagnoses   | Unsatisfactory rates | Rates for multiple procedures |
|------------------------|----------------------|------------------------------|
|                        | CNB                  | FNAC                         |
| Malignancy             | 0/9 (1.6)            | 1/6 (3.2)                    |
| ACC                    | 1/4                  | 0/7 (1.10)                   |
| AcCC                   | 0/2                  | 1/3 (0.5)                    |
| ANOS                   | 0/2                  | 1/5 (0.7)                    |
| BADC                   | 0/5                  | 1/13 (1.17)                  |
| CPA                    | -                    | 1/2 (0.1)                    |
| CystADC                | -                    | 0/1                          |
| EMC                    | 0/2                  | 0/2                          |
| MEC                    | 1/15                 | 1/7 (1.21)                   |
| OC                     | -                    | 0/2                          |
| SCC                    | 1/3                  | 0/1                          |
| SDC                    | 0/10                 | 1/10 (3.17)                  |
| ML                     | 0/1                  | 0/2                          |
| RMS                    | 0/1                  | -                            |
| UPS                    | 0/1                  | 0/1                          |
| Subtotal               | 3/54 (6.5)           | 7/62 (11.3)                  |
| Benign                 | PA                   | 1/117 (10.199)               |
|                       | WT                   | 2/33 (3.70)                  |
|                       | BA                   | 0/16 (0.24)                  |
|                       | LA                   | 0/1                          |
|                       | ME                   | 0/2 (0.6)                    |
|                       | Oncocytoma           | 0/2 (1.2)                    |
|                       | NT                   | 0/3 (1.3)                    |
|                       | VT                   | 0/3                          |
|                       | Lipoma               | 1/2                          |
| Subtotal               | 3/174 (1.7)          | 16/309 (5.2)                 |
| Total                 | 6/228 (2.6)          | 23/371 (6.2)                 |

Values in parentheses are presented as percentage.

CNB, core needle biopsy; FNAC, fine needle aspiration cytology; ACC, adenoid cystic carcinoma; AcCC, acinic cell carcinoma; ANOS, adenocarcinoma, not otherwise specified; BADC, basal cell adenocarcinoma; CPA, carcinoma ex pleomorphic adenoma; CystADC, cystadenocarcinoma; EMC, epithelial-myoepithelial carcinoma; MEC, mucoepidermoid carcinoma; OC, oncocytic carcinoma; ML, malignant lymphoma; RMS, rhabdomyosarcoma; UPS, undifferentiated pleomorphic sarcoma; PA, pleomorphic adenoma; WT, Warthin tumor; BA, basal cell adenoma; LA, lymphadenoma; ME, myoepitheloma; NT, neurogenic tumor; VT, vascular tumor.

### Table 3. Accuracy of preoperative CNB and FNAC for diagnosing salivary gland tumors

| Characteristic            | CNB | FNAC | p-value |
|---------------------------|-----|------|---------|
| No. of cases              | 228 | 371  | -       |
| No. of unsatisfactory     | 222 (97.4) | 348 (93.8) | - |
| No. of adequate malignant | 51  | 55   | .078    |
| No. of preop. Dx as benign| 45  | 32   | .253    |
| No. of adequate benign    | 171 | 293  | .212    |
| No. of preop. Dx as benign| 170 | 289  | .009    |
| Sensitivity (%)           | 88.20 | 58.20 | .006 |
| Specificity (%)           | 99.40 | 98.60 | .742 |
| Positive predictive value | 97.80 | 88.90 | .253 |
| Negative predictive value | 96.60 | 92.60 | .121 |

CNB, core needle biopsy; FNAC, fine needle aspiration cytology; preop., preoperative; Dx, diagnosis.

### Table 4. False-negative and -positive results determined by preoperative CNB and FNAC

| Histologic diagnoses | CNB   | FNAC |
|----------------------|-------|------|
| Malignancy           |       |      |
| ACC                  | -     | PA (n = 1), benign cyst (n = 1), mucocele (n = 1) |
| AcCC                 | -     | Oncocytoma (n = 1) |
| ANOS                 | -     | WT (n = 1) |
| BADC                 | BA (n = 2) | BA (n = 2), benign cyst (n = 1) |
| CPA                  | PA (n = 2) | PA (n = 7) |
| EMC                  | BA (n = 1), PA (n = 1) | PA (n = 1), benign lesion (n = 1) |
| MEC                  | -     | PA (n = 2), benign cyst (n = 1), mucocele (n = 1) |
| OC                   | -     | Oncocytoma vs WT (n = 1) |
| ML                   | -     | Benign lymphoid lesion (n = 1) |
| Benign (false-positive results) |       | CPA (n = 1), LG malignancy (n = 1) |
| PA                   | MEC (n = 1) | ACC (n = 2) |

CNB, core needle biopsy; FNAC, fine needle aspiration cytology; ACC, adenoid cystic carcinoma; PA, pleomorphic adenoma; AcCC, acinic cell carcinoma; ANOS, adenocarcinoma, not otherwise specified; WT, Warthin tumor; BADC, basal cell adenocarcinoma; BA, basal cell adenoma; CPA, carcinoma ex pleomorphic adenoma; EMC, epithelial-myoepithelial carcinoma; MEC, mucoepidermoid carcinoma; OC, oncocytic carcinoma; ML, malignant lymphoma; ME, myoepitheloma; LG, low grade.
neurogenic tumor. Tumor typing rates of benign tumors by CNB and FNAC were 91.8% and 80.5%, respectively (p = .003). For malignant tumors, accurate tumor subtyping was achieved in 39 of 51 CNB cases (76.5%), but in only 10 of 55 FNAC cases (18.2%) (p = .002). For a few special entities, both methods faced diagnostic difficulties. Since the diagnosis of basal cell adeno-
In 1999, Buckland et al. introduced US-CNB using an 18-gauge needle, instead of fine needle aspiration using a 23-gauge needle, to evaluate salivary gland lesions. They reported satisfactory results based on their experiences of diagnosing and treating parotid gland masses in up to 220 patients. The technique was soon adopted by other groups as well; small series of CNB results for salivary gland tumors have been reported from several countries, including the UK, Taiwan, Japan, and Germany.

Our current study of 228 CNB and 371 FNAC procedures demonstrates the superiority of CNB over FNAC for diagnosing salivary gland tumors in terms of adequacy (97.4% vs 93.8%), sensitivity (88.2% vs 58.2%), specificity (99.4% vs 98.6%), PPV (97.8% vs 88.9%), NPV (96.6% vs 92.6%), and accurate tumor subtyping (88.3% vs 70.7%). Among these measures, differences in the sensitivity and tumor typing rate were statistically significant. These results are based on the histological confirmation of surgically treated cases. Although this type of design tends to lead to verification bias, we did not include follow-up cases because our aims were to compare the accuracy of the two tests for specific diagnoses. As a result, the sensitivities of both methods may have been overestimated due to verification bias. Even if the bias affected both methods, the sensitivity of CNB appears to be markedly improved, which can be attributed to the ability to recognize tumor structures by histological examination in CNB and not just cellular morphology alone as in FNAC.

The diversity and rarity of salivary gland carcinomas tend to provide diagnostic challenges for pathologists. Diagnosis of malignancy can be difficult when the cells in question pose no significant cytologic atypia. In addition, pathologists’ experience and knowledge can affect the accuracy of FNAC. In our current study, no high-grade carcinomas, including salivary duct carcinoma and squamous cell carcinoma, were diagnosed as false-negatives using FNAC; however, low-grade carcinomas, including adenoid cystic carcinoma, acinic cell carcinoma, mucoepidermoid carcinoma, and adenocarcinoma not otherwise specified, were occasionally misinterpreted as benign lesions. The PPV and NPV, which are not affected by verification bias, were also higher in CNB than in FNAC, though the differences were not statistically significant. These results are based on the histological confirmation of surgically treated cases. Although this type of design tends to lead to verification bias, we did not include follow-up cases because our aims were to compare the accuracy of the two tests for specific diagnoses. As a result, the sensitivities of both methods may have been overestimated due to verification bias. Even if the bias affected both methods, the sensitivity of CNB appears to be markedly improved, which can be attributed to the ability to recognize tumor structures by histological examination in CNB and not just cellular morphology alone as in FNAC.

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The difficulties of diagnosing basal cell adenocarcinoma, oncocytic carcinoma, and carcinoma ex pleomorphic adenoma apply to not only FNAC, but also to CNB when invasive and/or malignant foci are not sampled. For example, we misinterpreted two epithelial-myoepithelial carcinomas as pleomorphic adenoma in one and basal cell adenoma in the other, and one pleomorphic adenoma as mucoepidermoid carcinoma in CNB. Salivary gland carcinomas and oncocytic carcinoma requires extracapsular invasion by definition, none of these cases could be diagnosed using either CNB or FNAC. Similarly, the diagnosis of carcinoma ex pleomorphic adenoma was not possible without concomitant carcinoma and pleomorphic adenoma components, even by CNB. The diagnosis of epithelial-myoepithelial carcinoma was difficult by either method, most likely due to its resemblance to pleomorphic adenoma, its low-grade nature, and a low index of suspicion (Fig. 2).

**DISCUSSION**

In 1999, Buckland et al. introduced US-CNB using an 18-gauge needle, instead of fine needle aspiration using a 23-gauge needle.
Accuracy of Core Biopsy for Salivary Gland

Fig. 2. Difficult samples for both core needle biopsy and fine needle aspiration. (A) Surgical specimen of basal cell adenocarcinoma shows extracapsular invasion which cannot be confirmed in core needle biopsy (B) or fine needle aspiration cytology (C). (D) Epithelial-myoepithelial structures of epithelial-myoepithelial carcinoma can be mistaken for those of pleomorphic adenoma in both core needle biopsy (E) and fine needle aspiration cytology (F), because of the lack of obvious cellular atypia.

Vary gland tumors are diverse and also analogous with specific architectural patterns such as epithelial-myoepithelial structures which are present in various benign and malignant tumors. Interpreting a limited number of cores can be difficult, even for experienced pathologists. Nonetheless, accurate tumor subtyping rates were generally higher for CNB than for FNAC (88.3% vs 70.7%). In particular, malignant tumors were more often accurately classified using CNB than FNAC (76.5% vs 18.2%) in
comparison to the benign tumors (91.8% vs 80.5%). Both high-
and low-grade carcinomas could be more specifically diagnosed
by CNB than by FNAC.

Some clinicians prefer FNAC because it has technical advan-
tages such as simplicity of the procedure, safety, cost-effectiv-
ness, and the lack of need for ultrasound assistance. However,
the CNB procedure is generally well tolerated under local anes-
thesia, and the actual complication rate of CNB appears to be
far less than expected. The major complications of salivary gland
biopsy include facial nerve injury and tumor seeding along the
biopsy track. However, experienced radiologists can avoid facial
nerve injury by tracing the main intraparotid vessels or the pa-
rotid duct, which can be easily identified on ultrasound.14–18 Tu-
mor seeding was once considered a significant complication when
performing large needle biopsy on cancers, and the needle di-
ameter and number of passes are assumed to be related to this
risk.19 However, such evidence is lacking in the case of salivary
gland tumors. Two cases of tumor seeding following needle bi-
opsy of the salivary gland using 14–16-gauge needles have been
previously reported, but a few reports of tumor seeding follow-
ing FNAC have also been reported more recently.20–22 However,
low the risk, some authors have suggested surgical removal of
the biopsy track at the time of surgery.23–25

No studies on the use of 18-gauge CNB to assess the salivary
glands, including our present series, have reported these major
complications. The minor complications that have been report-
ed following salivary gland CNB include subclinical hemato-
ma,21,12,14–16,18,20 temporary facial weakness after local anes-
thesia,11 and the formation of salivary fistulas.17 Fistula developed
after post-biopsy acute parotitis and did not present with tumor
seeding.17 Increased awareness of this rare complication would
help provide better patient care and follow-up.

In conclusion, CNB is an accurate and safe method for diag-
nosing salivary gland lesions, and provides significant superiori-
ty in accurate tumor subtyping in comparison to FNAC. We
recommend CNB as the primary diagnostic tool for preopera-
tively evaluating salivary gland masses, especially when mali-
gnancy is suspected.

Conflicts of Interest

No potential conflict of interest relevant to this article was
reported.

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