Rapid on-site evaluation with dynamic telecytopathology for ultrasound-guided fine-needle aspiration of head and neck nonthyroid lesions

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Abstract

**Background:** Rapid on-site evaluation (ROSE) at the time of ultrasound-guided fine-needle aspiration (USGFNA) of head and neck lesion is essential for obtaining adequate samples and providing the preliminary diagnosis. We summarize our experience with ROSE of USGFNA on head and neck nonthyroid lesions using telecytopathology.

**Materials and Methods:** Real-time images of Diff-Quik stained cytology smears were obtained at ultrasound suite with an Olympus DP-70 digital camera attached to an Olympus CX41 microscope, and transmitted via ethernet by a cytotechnologist to a cytopathologist in cytopathology laboratory who rendered a preliminary diagnosis. Live communication was conducted with Vocera voice communication system. The ultrasound suite was located on different floor from the cytopathology laboratory. Accuracy of ROSE via telecytopathology was compared with an equal number of cases that received ROSE, prior to introduction of telecytopathology, via conventional microscopy.

**Results:** Rapid on-site evaluation was performed on a total of 116 USGFNA of head and neck nonthyroid lesions. The telecytopathology system and conventional microscopy was used to evaluate equal number of cases (58 each). Preliminary diagnoses of benign, atypical/suspicious for malignancy, and positive for malignancy were 72.4%, 17.2% and 10.3% for telecytopathology, and 69.0%, 10.3% and 20.7% for conventional microscopy. None of the cases were deemed unsatisfactory. The overall concordance between the preliminary and final diagnoses was 94.8% for telecytopathology and 98.3% for conventional microscopy and was not statistically significant (P = 0.309). The causes of discordant preliminary and final diagnoses were mainly attributed to availability of cell block and Papanicolaou-stained slides for review or flow cytometry results for lymphoma cases at the time of final sign out.

**Conclusions:** Telecytopathology is comparable with conventional microscopy in ROSE of USGFNA of head and neck nonthyroid lesions.

**Key words:** Fine-needle aspiration, head and neck, telecytopathology, ultrasound-guided

INTRODUCTION

Fine-needle aspiration (FNA) cytology has emerged as a procedure of choice for all head and neck lesions. In addition to being cost effective, it is associated with low morbidity and high diagnostic accuracy.[1-3] Performance
of head and neck aspiration under ultrasound-guidance coupled with rapid on-site evaluation (ROSE) assessment by cytopathologist, in relation to the clinical context thereby deciding on adequacy and need for additional biopsies, further improves the diagnostic accuracy and cost effectiveness.\(^{[1]}\) On-site assessment of samples also contributes to enhanced diagnostic yield of samples for ancillary studies such as immunohistochemical analysis, bacterial cell cultures, flow cytometry and gene rearrangement studies for unsuspected cases of lymphoma.\(^{[4]}\)

Ultrasound-guided fine-needle aspiration (USGFNA) procedures are time-consuming and adversely affect time management for cytopathologists.\(^{[1,5]}\) Distances of ultrasound suites from the pathology laboratory can make timely assessment by an on-site cytopathologist difficult. Even though collaboration of a radiologist or clinician performing the procedure and the ROSE cytopathologist is essential for optimizing the yield and efficiency of USGFNA of head and neck lesions, the staffing, time, and cost constraints have precluded the availability of ROSE in every institution.

Dynamic telepathology systems focus on transmission of live video images that are viewed electronically in real-time at a remote site, in contrast to static telepathology systems that are based on capturing of images in a digital format and then transmitting them to distant observers.\(^{[6-8]}\) Advancements in telepathology technology have made it feasible to use dynamic telepathology for cytologic specimens. However, most studies using dynamic telecytopathology have been retrospective.\(^{[9-11]}\) Only a few studies have focused on the application of dynamic telecytopathology for initial real-time on-site diagnosis in aspiration cytology and these have been restricted mainly to the pancreas, thyroid, lung, axillary lymph nodes, and mediastinum.\(^{[12-20]}\) There continues to be a need for other organ-based and body site-specific studies on the use of telecytopathology for immediate assessment of FNA to evaluate its pitfalls and limitations.

In this study, we present our experience with the use of dynamic telecytopathology for preliminary on-site evaluation and diagnosis of USGFNA of nonthyroid head and neck lesions and compare it with conventional microscopic ROSE by a cytopathologist. We excluded thyroid lesions because in prior studies it has been shown that immediate assessment of thyroid USGFNA via telecytopathology assures adequacy of the cytology sample and may reduce number of passes per nodule.\(^{[13,18]}\)

**MATERIALS AND METHODS**

The study involved USGFNA of head and neck nonthyroid lesions performed by a radiologist (AS) at a remote US suite located on the 3rd floor of the west wing of the hospital and evaluation of slides by the cytopathologist located in a cytopathology laboratory on the sixth floor of the south wing (a block away from the ultrasound suite, 5 min of travel time one way) of the hospital. The on-site cytotecnologist prepared cytology smears that included Diff-Quik (Mercedes Medical, Sarasota, FL, USA) – stained slides and alcohol-fixed smears that were later stained with the Papanicolaou method in the laboratory. Each USGFNA pass involved visualization of the lesion with high-frequency ultrasound imaging and obtaining cytological samples from the lesion. The total number of Diff-Quik – stained slides prepared on-site ranged from two to four slides per pass. Additional material was collected for cell block or ancillary studies as needed. On average, three passes (range, 2–5) were performed per procedure for both groups. Each pass was evaluated separately irrespective of use of the telecytopathology system or conventional on-site method for immediate assessment. Additional passes were performed only if the prior pass did not yield adequate material for preliminary diagnosis. In contrast to the conventional on-site method, which required the cytopathologist to be physically present at the ultrasound suite to evaluate the slides prepared on-site, telecytopathology assessment could be performed from the cytopathologist’s office or any computer accessible through the hospital’s ethernet network. The time spent for review of each pass during telecytopathology or conventional microscopic preliminary interpretation was recorded. This study received institutional review board exemption.

**Case Selection**

Telecytopathology was introduced in our remote ultrasound suite in January 2014. We evaluated all consecutive cases of USGFNA of head and neck nonthyroid lesions that underwent telecytopathology on-site assessment from January 2014 to October 2014. We also reviewed the same number of consecutive cases of USGFNA of head and neck nonthyroid lesions that had conventional microscopic on-site evaluation prior to introduction of telecytopathology at our ultrasound suite.

The telecytopathology system consisted of an Olympus (Olympus America, Center Valley, PA, USA) CX41 microscope and a digital camera with NetCam software (Olympus) [Figure 1]. A 2.11-megapixel cooled digital color camera (Olympus DP70) was used for image acquisition with the microscope (Olympus CX41) and a Dell (Round Rock, TX, USA) desktop computer with a direct ethernet connection. NetCam software used a Transmission Control Protocol/Internet protocol to transmit live video images over the internet via an assigned static IP address [Figures 2 and 3]. The computer and the image server required log-in, and the IP address was known to the faculty or the operators of the microscope. The original size of the acquired image...
was 1600 × 1200 pixels, with the NetCam-transmitted image having a resolution of 1600 × 1200 pixels.

We did not perform any validation protocol for the present study. However, prior to introduction of telecytopathology at our hospital in November 2009, an internal validation testing was completed which was fairly similar to a recent validation study by McCarthy et al.[21] Briefly, slides from 15 previously signed FNA cases with unequivocal benign and malignant diagnosis from various body sites were used. Trained cytotechnologists controlled the microscopes at remote site and pathologist reviewed real-time images of slides from each case at their workstation. The concordance rate between telecytopathology evaluation and prior FNA diagnosis ranged from 95% to 100% amongst different cytopathologists and was considered sufficient for clinical use.

Different cytotechnologists with 12–20 years of experience and well conversant with the telecytopathology system operated the microscope at the remote site. Two cytopathologists with experience in aspiration cytology of USG-FNA of head and neck lesions could not control the microscope or camera and interacted with the cytotechnologists via the Vocera (San Jose, CA, USA) voice communication system, which enabled hands-free, voice-controlled wireless voice communication using the wearable Vocera B3000 Badge.

Vocera is a personal communication tool that uses voice over Internet protocol. The system consists of the Vocera System Software and wearable Vocera Communication Badge. The system software houses the centralized system intelligence that allows for digital recognition of voice and communication between individual badge wearers, group of badge wearers or landline communication. The party or person to be contacted may be contacted by name, title or by telephone number. Our cytotechnologist worked with slide staining protocol and telecytopathology system in a room adjacent to ultrasound suite, and this obviated the overhearing of preliminary discussions between the pathologists and cytotechnologists in the procedure room.

The preliminary diagnosis was communicated to the radiologist. The live video images were transmitted continuously without any lag time as the cytotechnologist moved the slide on the stage, and the pathologist could view on the desktop screen what the cytotechnologist was seeing at the microscope. The Olympus microscope had objectives from ×4 to ×40. Low-power objectives of ×10 and ×4 were used to assess overall cellularity of the smears and to identify areas that may require review under a higher-power ×40 objective for better cytologic details. Diagnostic cytology categories that were used for preliminary on-site evaluation and final cytologic diagnosis were as follows:

- **Benign:** Cytologic features characteristic of benign conditions, e.g., reactive lymph nodes, granulomatous...
lymphadenitis, benign salivary gland neoplasms, branchial cleft cysts and inflammatory processes

- Suspicious or atypical: Cases with cytologic features suspicious for malignancy or cases with atypical cytologic features where malignant neoplasm could not be excluded
- Malignant: Cases with obvious cytologic features of malignancy. We did not have any unsatisfactory cases in both groups. The initial and final cytologic interpretations for the majority of the telecytopathology cases were performed by two cytopathologists. Although the conventional cases were diagnosed by two other faculty cytopathologists, the initial and final interpretations on these cases were also rendered by the same cytopathologist in accordance with the practice at our institution.

Statistical Analysis
Accuracy was defined by agreement between the preliminary and final interpretations in the two groups. Suspicious or atypical category cases were considered concordant if the final diagnostic category was the same or malignant. All case slides on discrepant cases that did not meet the criterion for concordance as stated above were reviewed to assess the cause of discrepancy. The association between the three preliminary diagnostic categories (benign, suspicious/atypical, and malignant) and the two diagnostic methods (telecytopathology and conventional) was analyzed using Pearson’s Chi-squared statistic. An exact P value was obtained via Monte Carlo simulation. The proportions of concordance between preliminary and final diagnoses for telecytopathology and conventional methods were compared using relative risk, and a corresponding 95% confidence interval (CI) was constructed based on large sample theories. All computations were performed using SAS/STAT PROC FREQ software (version 9.3) of the SAS system for Windows (SAS Institute, Cary, NC, USA).

RESULTS
There were 58 consecutive USGFNA of nonthyroid head and neck lesions that were evaluated by telecytopathology from January to October 2014 and 58 consecutive cases with conventional on-site evaluation from July to December 2013. The time spent for review of each pass ranged from 1 to 3 min in both telecytopathology and conventional microscopic preliminary interpretation.

Table 1 compares the preliminary diagnosis rendered via telecytopathology and conventional on-site microscopy. There was no statistically significant difference (exact $P = 0.217$) in proportion of cases (telecytopathology versus conventional microscopy) in the benign, atypical/ suspicious, malignant, and unsatisfactory categories.

Table 2 shows the follow-up final cytologic diagnosis on all USGFNAS with preliminary diagnosis rendered via telecytopathology. All six cases with initial telecytopathology diagnosis of malignant corresponded with a final cytologic diagnosis of malignant. Forty of 42 cases with an initial benign diagnosis corresponded with benign diagnosis on final cytology and the remaining 2 were reclassified as malignant. Of the 10 cases with an initial telecytology diagnosis of atypical or suspicious, final cytologic diagnosis included malignant and benign. Remaining one case with final cytologic diagnosis of basaloid neoplasm continued to be categorized as atypical/suspicious since malignant neoplasm could not be ruled out. In summary, the final cytologic diagnosis in the telecytopathology group was 70.7% benign, 1.7% atypical/ suspicious and 27.5% malignant.

Table 3 shows the follow-up final cytologic diagnosis on all USGFNAS with preliminary diagnosis rendered via conventional on-site microscopy. All cases with an initial conventional on-site diagnosis of malignant (12 cases) corresponded with a final cytologic diagnosis of malignant. Of the 6 cases with an initial cytologic diagnosis of atypical/suspicious all were reclassified as malignant on final cytology. Of the 40 benign cases with an initial cytologic diagnosis of benign, in 39 cases there was correspondence with a benign diagnosis on final cytology, and 1 case was reclassified as malignant. In summary, the final cytologic diagnosis in this group was 67% benign and 33% malignant.

Table 1: Preliminary diagnostic categories used for on-site evaluation by telecytopathology and the conventional method

| Category                | Frequency (%) | Telecytopathology | Conventional | Total |
|-------------------------|---------------|-------------------|--------------|-------|
| Negative/benign         | 42 (72.4)     | 40 (69)           | 82           |
| Atypical/suspicious     | 10 (17.2)     | 6 (10.3)          | 16           |
| Positive for malignancy | 6 (10.3)      | 12 (20.7)         | 18           |
| Total                   |               | 58                | 58           | 116   |

Table 2: Preliminary telepathology on-site and final cytologic diagnosis

| Category               | Benign | Atypical/ suspicious | Malignant | Total |
|------------------------|--------|----------------------|-----------|-------|
| Negative/benign        | 40     | 2                    | 2         | 42    |
| Atypical/suspicious    | 1      | 1                    | 8         | 10    |
| Positive for malignancy| 6      | 6                    | 6         | 6     |
| Total                  | 41     | 1                    | 16        | 58    |
The accuracy rate of preliminary telecytopathology and conventional on-site microscopy diagnosis was 94.8% (54/58) and 98.3% (57/58), respectively [Table 4]. The relative risk is 0.96 with a 95% CI of (0.90, 1.03), which is within the commonly selected equivalence bound (0.8, 1.25). Thus, we are confident from a statistical point of view that the concordance rates are comparable between the two evaluation methods.

Analyses of causes of discrepancy in the preliminary and final interpretations in telecytopathology cases and on-site conventional microscopy cases are given under the review column in Tables 5 and 6, respectively. The causes of discrepancy in two cases of Hodgkin’s lymphoma were attributable to the difficulty in the distinction of Reed–Sternberg (RS) cells in the background of polymorphous lymphocytes from immunoblasts. Availability of cell block material allowed for immunostaining of CD 30 and CD 45 positive and CD 15 negative RS cells confirming the diagnosis of Hodgkin’s disease. One case that was perceived to be atypical on initial telecytopathology evaluation was categorized as benign on final cytologic diagnosis and comprised of benign salivary gland elements and chronic inflammation. The ductal epithelium exhibited reactive changes that were interpreted as atypical at the time of initial evaluation. A case of small lymphocytic lymphoma was interpreted as benign on initial cytologic evaluation using conventional microscopy because small lymphocytic population that was identified on the smear was thought to be benign. However, flow cytometry evaluation of the aspirate confirmed it to be a case of small lymphocytic lymphoma.

**DISCUSSION**

Increasing numbers of studies in the recent cytology literature have demonstrated the usefulness of dynamic and static telecytopathology systems to review cytology smears remotely over an Internet connection.[10‑20,23‑25] Dynamic systems appear to be more accurate compared with static systems.[6‑8] In the current study, we performed ROSE of USGFNA of head and neck nonthyroid lesions, exclusively, via a dynamic live and remotely operated telecytopathology system and compared it with on-site evaluation by a pathologist using conventional microscopy. To the best of our knowledge, this is the first case series assessing the role of dynamic telecytopathology for rapid preliminary diagnosis and evaluation of USGFNA of head and neck nonthyroid lesions. We demonstrated comparable and high diagnostic accuracy in both groups.

### Table 3: Preliminary conventional on-site and final cytologic diagnosis

| Category       | Benign | Atypical/suspicious | Malignant | Total |
|----------------|--------|---------------------|-----------|-------|
| Negative/benign| 39     | 1                   | 40        |       |
| Atypical/suspicious | 6     | 6                   |           |       |
| Positive for malignancy | 12   | 12                  |           |       |
| Total           | 39     | 19                  | 58        |       |

### Table 4: Summary of concordance pairs for telepathology and conventional group

| Concordance | Telepathology (%) | Conventional microscopy (%) |
|-------------|-------------------|-----------------------------|
| No          | 3 (5.2)           | 1 (1.7)                     |
| Yes         | 55 (94.8)         | 57 (98.3)                   |

These calculations were generated from the data in Tables 2 and 3. Cases were considered concordant if the final diagnostic category was the same as the preliminary one or if the final diagnostic category was malignant when the preliminary diagnostic category was atypical/suspicious. The relative risk regarding the concordance rates between the method groups is 0.96 with a 95% CI of (0.9, 1.03). CI: Confidence interval

### Table 5: Discrepancy between preliminary telepathology and final diagnosis

| Preliminary | Final diagnosis | Explanation |
|-------------|----------------|-------------|
| Benign      | Malignant      | RS cells were perceived as immunoblasts in the background of polymorphous lymphocytes. |
| (Hodgkin lymphoma) | Cell block material captured numerous RS cells and immunostains aided in the diagnosis |
| Benign      | Malignant      | Polymorphous lymphocytes obscured the few RS cells present on Diff-Quik stained slides. |
| (Hodgkin lymphoma) | Cell block material captured numerous RS cells and immunostains aided in the diagnosis |
| Atypical    | Benign salivary gland elements and chronic inflammation | Reactive ductal epithelium exhibited nuclear enlargement that was perceived as atypical. Papanicolaou stain and cell block material were able to better delineate the reactive features and chronic inflammation |

### Table 6: Discrepancy between conventional on-site and final diagnosis

| Preliminary | Final diagnosis | Explanation |
|-------------|----------------|-------------|
| Benign      | Malignant      | Lymphoid elements seen on Diff-Quik stain were thought to be reactive. Flow cytometry study confirmed diagnosis of lymphoma |
| (small lymphocytic lymphoma) | | |
Discrepancies between on-site preliminary diagnosis and final diagnosis were identified using both telecytopathology and conventional microscopy assessment methods and were not statistically significant. These difficulties can be categorized as interpretative difficulties and lack of availability of additional material on Papanicolaou-stained slides and cell block material. Similar discrepancies were noted in a prior study on aspirates from various body sites.[12,14,15] Interpretative difficulties and the importance of the collection of additional material for ancillary studies for diagnosis of head and neck aspirates using conventional microscopy have been well described.[20] The importance of additional Papanicolaou-stained slides for review of cytologic features and collection of material for ancillary studies (e.g., flow cytometry or cell block material for immunostains that facilitated final diagnosis in all discrepant cases) cannot be overemphasized.

The success of telecytopathology depends on the experience of the on-site operator (e.g., an experienced cytotechnologist or senior resident with an interest in cytopathology or a cytopathology fellow) who can effectively operate the slides on the on-site microscope, transmit real-time images, and project significant findings while being in audio contact with the attending cytopathologist.[8] Also, the pathologist must be well familiarized with the use of telecytopathology for interpretation of real-time images. In our study, both the pathologist and the on-site operator were familiarized with the use of the telecytopathology system. The pathologist did not perceive any difficulty in interpretation of the real-time online images due to their high quality and resolution. Our study shows that an experienced surrogate (cytotechnologist, senior resident, or cytology fellow) can manage field selection for telecytopathology by being in audio contact with the cytopathologist who will render the final report.

In our study, we did not have any unsatisfactory cases, and this may be attributable to the expertise of single interventional radiologist with 15 years of experience who performs this procedure at our institution. The protocol of evaluating each pass for adequate material and continuing to perform up to 5 passes if the pass was deemed inadequate helped eliminate unsatisfactory cases.

The difference in the average time spent for review of each pass in both telecytopathology and conventional microscopic preliminary interpretation was not statistically significant. However, in contrast to conventional microscopic initial evaluation, where the pathologist is required to be physically present in the ultrasound suite, telecytopathology preliminary interpretation allowed the cytopathologist to use dead time between passes (which ranged from 5 to 20 min) to perform other routine office work, including sign out of routine cases. Telecytopathology also offered the opportunity to discuss the difficult cases with colleagues who can view the real-time images from any computer within the hospital network system.

In summary, we demonstrate that on-site telecytopathology preliminary evaluation for USGFNA of head and neck nonthyroid lesions appears to be highly accurate and comparable with conventional microscopic preliminary interpretation. Interpretative difficulties and lack of Papanicolaou-stained slides and cell block material at the time of on-site evaluation represent common limitations of both conventional microscopy and telecytopathology preliminary evaluation of USGFNA of head and neck nonthyroid lesions and may contribute to diagnostic difficulties in a few cases. Our study supports use of telecytopathology for ROSE of USGFNA of head and neck nonthyroid lesions. The low cost of the telecytopathology equipment (approximately $6,000, excluding the microscope) makes it a suitable alternative in situations where distance and time constraints may preclude cytopathologists from rendering preliminary on-site evaluations at distant and multiple locations.

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